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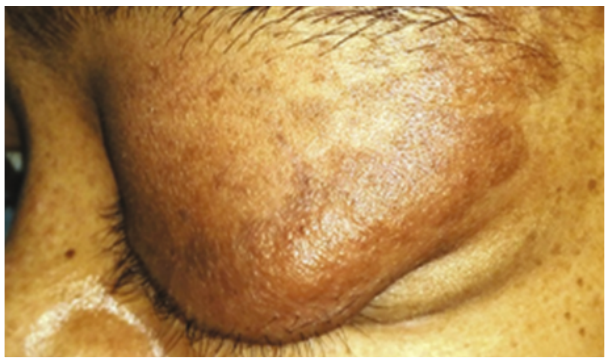

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Contents

Contents (contd.)

The Art and Science of Telling a Story

Before I start on this theme, let me update you on the developments related to Indian Pediatrics Case Reports. Our website (*www.ipcares.Org*) and online manuscript submission and processing system (*https://review.jow.medknow* com/ipcares) have become functional. Unfortunately, the latter tends to exhibit technical glitches on occasion. We sincerely hope these are teething problems that will eventually fade away. However, dear readers, if you face any problems, please contact us at *ipcares2020@gmail.com*, and we will try to resolve them.

My inaugural editorial was titled "Every Story Worth Telling Should be Told."[1] I continue in the same vein with a step-by-step approach describing how to tell your story in such a way that it is not only accurate, but it will catch the interest of the editor/reviewer, so that the likelihood of acceptance is higher. The first step is simple; ask yourself honestly, "Is your story really worth telling?" Is the case in question, a rare entity that has never or hardly been described before; was there something unusual about the presentation or manifestations that can expand the clinical phenotype; did you face challenges while establishing the diagnosis or use diagnostic tests in an innovative way; and did you learn something new from whatever standard intervention that was used (beneficial or adverse events) or see some unexpected or unusual outcome. Can you bring out some clinically relevant perspective from the case that can add to current knowledge? Choose whichever aspect you want to focus on, but remember, these decisions cannot be based on your personal experience. You need to do an extensive literature search to find evidence to support whichever dimension is selected. Once you are sure that the scientific content is valid and true, move to the next step. If not, look for another case.

The second step is finding the "right journal." An editor will select your case report for peer review, only if it is alignment with the aims and scopes of the journal, and of interest to its readers. To have a general idea, see what kinds of cases have been published earlier. Once, you have honed onto the journal, check the "Instructions for authors." If you want to win a game, it stands to reason that you must know its rules. Every journal has its own set of guidelines that need to be complied with. Go through them, and see how they have been applied by other authors, in published articles. Check the permissible number of words, figures/tables, and references and the subheadings that are used to organize the content, and format your manuscript accordingly. Determine beforehand how many authors will qualify for authorship, and whether the journal guidelines permit that many. Ascertaining this serves to avoid unnecessary heartburn and conflict among colleagues, at a later stage. Make sure you have the requisite paperwork (consent forms, copyright transfer forms, etc.) ready.

The third step is presenting your case in an accurate, transparent, and honest manner. Remember to record the details of the basic components of history and examination that is critical for any clinical case presentation. Those are the basic building blocks that can be pruned later on. The narrative should be arranged in a logical sequence and presented in the proper timeline. Refer to the CARE guidelines and checklist[2] and structure the content accordingly, ensuring the journal's format is also retained. Lay more emphasis on the predecided aspect that you want to highlight and shorten or remove other elements of the case that may not be that relevant. Be sure to provide details of the clinical reasoning that was applied for every critical decision in diagnosis and management so that the reader can understand the thought process that was involved.

The fourth step is ensuring that your style of writing is good, or at least not substandard. The content should be presented in paragraphs, preferably one paragraph dealing with a single context. Use proper grammar (punctuation, tense, etc.) and correct spelling. If you are not proficient in English, do not worry. There are software that are available for checking grammar and spelling, and you can request a friend or colleague who is competent in scientific writing to edit your work before submission. Do not be excessively verbose or use "flowery" language. This is not an English literature essay, but a scientific piece of work. Remove irrelevant material and avoid repetitions. For an editor, there is nothing more distressing than having to reject an article that has good scientific content, simply on the grounds that the presentation of content remains poor, despite giving feedback in the reviewer's and editorial comments.

Finally, before submission, it is always a good idea to get a critical appraisal by experienced senior colleagues who have their own corpus of published work, and heed their comments positively. Make sure that all the authors approve the draft and fulfill the responsibilities and criteria of authorship. Do not gift authorship, and do not deny authorship to those who deserve/qualify. Last but not the least, if your article is rejected by the first journal, do not despair. Learn from the experience, and do not give up. After a suitable period of "cooling off," look at your article under the lens of the reviewer and modify it accordingly. Then go back to the second step and find another journal for submitting the article. The most common reason for a worthy article not getting published is a lack of perseverance on the part of the author.

I hope you find this article helpful. If even 10% of our readers who are in the initial phases of their publishing curve, end up submitting a case report to a medical journal after reading this, I will consider my job well done. I look forward to receiving a flood of well-written case reports of novel scientific content. May the games begin!

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There are no conflicts of interest.

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Case Report

Treatment of Highly Fatal Extensive Childhood Mucormycosis with Complications: A Success Story

Aakash Chandran Chidambaram, Jaikumar Govindaswamy Ramamoorthy, Reena Gulati, Bhawana A Badhe[1]

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Abstract

Background: Mucormycosis is a highly fatal infection that affects immunocompromised individuals. Treatment is difficult and mortality is high when associated with complications. It is rare as a presenting feature of diabetes mellitus (DM) in children. **Clinical Description:** We describe a child who presented with extensive rhino-orbital invasive mucormycosis and subsequently diagnosed as Type 1 DM. She further developed cavernous sinus thrombosis and internal carotid artery thrombosis known to be associated with very high risk of mortality. **Management:** Aggressive medical management with posaconazole and liposomal amphotericin B for 12 weeks and early debridement of orbito-cerebral lesions led to complete resolution. **Conclusion:** Saving children with complicated extensive invasive mucormycosis is possible with aggressive prolonged antifungal therapy and early debridement of lesions.

Keywords: Cavernous sinus thrombosis, diabetes mellitus, fatal infection, internal carotid artery thrombosis, rhino-cerebral-orbital mucormycosis

Mucormycosis is recognized to be the second most frequent invasive fungal disease, after aspergillosis.[1] Patients with poorly controlled diabetes mellitus (DM), immunosuppressed patients, and persons who have sustained severe trauma to soft tissue are at increased risk of infection. Despite technological advances and advent of newer antifungal drugs, survival has been approximately 60% over the past two decades.[2] Patients with diabetes tend to develop rhino-cerebral-orbital disease, those with hematological malignancies develop sino-pulmonary disease, and patients sustaining trauma manifest necrotizing skin and soft tissue infections.[2-4]

Clinical Description

An 8-year-old girl was brought to the emergency with complaints of swelling over the right cheek for 5 days and drooping of right eyelid along with diplopia for 2 days. She had polyuria and easy fatigability for the previous 2 weeks. Intravenous antibiotics were administered elsewhere for 2 days and referred due to rapidly worsening cheek swelling. There was no history of fever, dysuria, vomiting, abdominal pain, blurring of vision, or seizures. The diffuse painless swelling of 3 cm × 3 cm over the right maxilla had no tenderness or erythema. Ophthalmic examination revealed a vision of 6/60, ptosis, complete external ophthalmoplegia, and chemosis. Right pupil reacted sluggishly though fundus appeared normal. The left eye was normal. An ulcer was present over the right hard palate opposite the first molar tooth with a defect that extended into the maxillary sinus. Examination of other systems was normal.

Management and Outcome

Initial blood investigations revealed a very high blood glucose (346 mg/dL). Classical osmotic symptoms with high blood sugar levels confirmed a diagnosis of DM. Hemoglobin A1C (HbA1C) was highly elevated (19.5%), suggesting a long duration of the disease unknown to parents. In the absence of ketoacidosis, subcutaneous insulin therapy was initiated. The constellation of the above examination

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findings with a background of DM roused the suspicion of mucormycosis, and she was immediately started on liposomal amphotericin-B (lampB) (4 mg/kg/day) and posaconazole (5 mg/kg/day). Computed tomography of brain showed extensive rhino-orbital disease. Microscopy of the slough from oral ulcer showed broad aseptate hyphae suggestive of mucor. Hence, urgent functional endoscopic sinus surgery with debridement was performed, opening up the paranasal sinuses. Postsurgery magnetic resonance imaging (MRI) brain revealed extension of lesion with 2 cm × 2 cm abscess in the right temporal region with thrombosis of cavernous sinus and internal carotid artery [Figure 1a]. The lesion appeared to engulf the orbital apex with subtle enhancement of right optic nerve sheath, imposing a danger of perineural spread. A frontotemporal craniotomy with evacuation of abscess was performed.

Her blood glucose was strictly controlled with subcutaneous insulin throughout hospital stay. Biopsy of the debrided tissue confirmed invasive mucormycosis [Figure 2a and b], and antifungals were given for 6 weeks. She developed hypokalemia during the course of lampB therapy which was managed medically. A repeat MRI brain after 6 weeks showed a residual lesion [Figure 1b], and hence, treatment was continued for 6 more weeks. After 12 weeks of lampB and intermittent posaconazole (availability problems), there was a significant clinical improvement with the resolution of radiological lesions. Antifungals were stopped and the child was discharged on subcutaneous insulin and enoxaparin after 3 months of hospital stay. She is currently well at 6-month follow-up, with 6/6 vision in both eyes, complete resolution of cheek swelling, ptosis, and ophthalmoplegia with no cranial nerve deficits. An obturator was placed to close the palatal defect with recovery of good functional speech at present. Enoxaparin was discontinued after 8 months since there was no progression or worsening of the flow void in internal carotid artery and resolution of the thrombotic lesions. Her HbA1C had dropped to 7.1% at follow-up.

Discussion

Our patient had undiagnosed DM type-I at the time of presentation, a known risk factor for mucormycosis. Aggressive, relentless tissue invasion, and infarction secondary to angioinvasion are the hallmarks of mucormycosis.

Rhino-orbital-cerebral mucormycosis (ROCM) is the most common form of mucormycosis in diabetic patients. She was diagnosed as ROCM on a strong clinical suspicion with the presence of facial swelling, pain, change in visual acuity, and ocular movements. The mode of spread from the paranasal sinuses to the orbit occurs through the nasolacrimal duct or through the natural dehiscence in the papyraceous blade. Uncontrolled blood glucose and diabetic ketoacidosis are major risk factors for the development of ROCM. Roden *et al*. found that 66% of patients with mucormycosis in DM had infection of the paranasal sinuses and 43% had cerebral extension.[3] The European registry of mucormycosis and the French RetroZygo cohort identified that rhinocerebral disease was strongly associated with DM.[4] Pediatric data from India reported 9%–36% of mucormycosis cases among children with diabetes.[5,6] A prospective multicentric study on mucormycosis reported that 23% of the patients with mucormycosis had a previously undiagnosed DM, presenting for the first time with mucormycosis (ROCM) as was the case with our patient.[5]

Cavernous sinus thrombosis (CST) associated with RCOM is less common. Studies show that CST was reported in 11% of RCOM patients in diabetic adults.[5,6] However, reports of CST or internal carotid artery thrombosis following RCOM in pediatric patients are very few.[7-9] The mortality rate of 30%–70% in patients with mucormycosis increases further with this complication.[10] Hence, a high index of suspicion and early aggressive treatment including surgery are paramount for survival. Delayed diagnosis, inadequate surgical debridement, and spread beyond sinonasal cavity contribute to poor prognosis. Amphotericin B and isavuconazole are the mainstays of treatment in mucormycosis. Availability and cost are major limiting factors for adequate treatment in resource-limited countries such as India. Our patient responded well to a total 6 weeks of posaconazole and 12 weeks of lampB therapy with complete radiological clearance from the infected regions and is currently well after 2 years of follow-up.

The positive outcome of our patient reaffirms that high index of suspicion for invasive fungal infections in the setting of DM or immunocompromised patients, aggressive

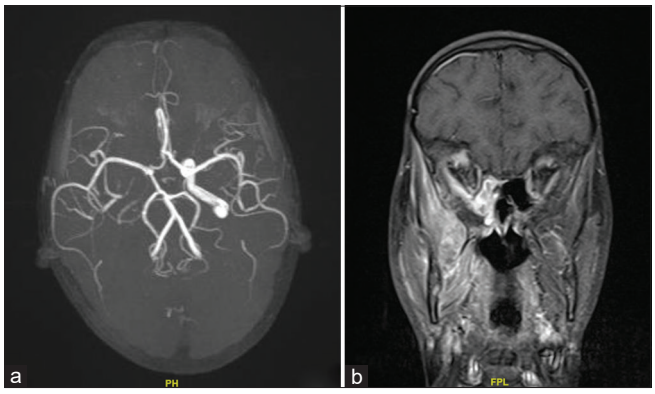

Figure 1: (a) Magnetic resonance imaging showing internal carotid artery thrombosis. (b) Magnetic resonance imaging showing cavernous sinus thrombosis and abscess in the temporal region

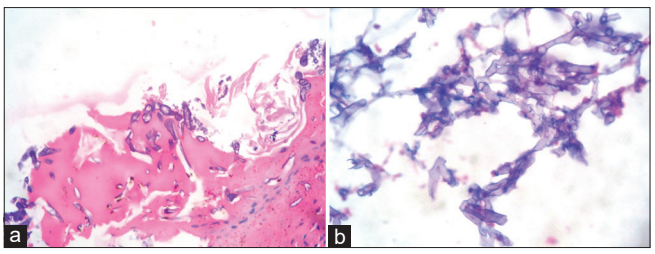

Figure 2: (a) Section shows broad aseptate fungal organisms with right-angled branching suggestive of mucormycosis. (×40 magnification). (b) Gomori methenamine silver stain highlighting the fungal organisms

debridement with early initiation, and appropriate duration of antifungal therapy can save lives. Although rare, invasive mucormycosis can be the only presenting feature of DM, missing which can lead to devastating consequences for the patients.

Lessons learnt

- Children with mucormycosis may have underlying undiagnosed diabetes mellitus
- Aggressive debridement and early antifungal therapy and strict blood sugar control are the mainstreams of treatment of mucormycosis
- The duration of antifungal therapy might have to be extended until radiological clearance of the lesion has been achieved.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Kikuchi-Fujimoto Disease: A Clinical Enigma

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Abstract

Background: Kikuchi Fujimoto disease (KFD) is a rare, benign self-limited disease characterized by prolonged regional lymphadenopathy associated with or without systemic signs or symptoms. It is a rare diagnosis in children. Due to the lack of pathognomonic clinical symptoms/signs, KFD poses a significant challenge to the clinician. Its diagnosis is confirmed by lymph node biopsy. **Clinical Description:** A 12.5-year boy presented with chronic cervical lymphadenopathy of 6-week duration, associated with mild-moderate fever, pain, and weight loss. He had raised erythrocyte sedimentation rate, leukopenia, lymphopenia, and thrombocytopenia. Mantoux test was positive. He was managed as a case of tuberculous lymphadenopathy till the lymph node biopsy confirmed the diagnosis of KFD. **Management:** The child recovered without medications. There has been no recurrence or relapse in 1.5 years of follow-up. **Conclusion:** This case report highlights the importance of considering the diagnosis of KFD in children presenting with persistent or chronic lymphadenopathy.

Keywords: Histiocytic necrotizing lymphadenitis, Kikuchi-Fujimoto disease, lymphadenopathy

Kikuchi-Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is a rare, idiopathic self-limiting disorder characterized by prolonged regional lymphadenopathy associated with/without systemic signs and symptoms. It was first described in 1972 by Kikuchi.[1,2] Reported mostly in adult females below 40 years of age; it is a rare diagnosis in children and most studies in them are retrospective.[3,4] Its cause is unknown; assumed to be an unidentified agent, probably a virus that triggers a self-limiting autoimmune process in a genetically predisposed person.[5]

There are no specific symptoms/signs, and this poses a challenge for clinical diagnosis and on many occasions; children are misdiagnosed or undergo extensive investigations. The diagnosis is established by histopathology of lymph node biopsy.

We report a case that highlights the importance of considering KFD in a pediatric patient presenting with chronic cervical lymphadenitis.

Clinical Description

A 12.5-year-old boy presented with gradually increasing lymph node swelling on the right side of the neck associated with pain for 6 weeks. He had mild-moderate fever without chills/rigors and weight loss of 1.5 kg. There was no anorexia, lethargy, cough, rash, bleeding manifestations, joint pain, ear discharge, vomiting and loose stools. He had received antibiotics without any clinical response.

He weighed 52.4 kg with a height of 159 cm and body mass index of 20.78 kg/m^2 (between 23 and 27 adult equivalent, Revised Indian Academy of Pediatrics Growth Charts). Vital parameters were normal. Neck examination revealed 2–3 right-sided cervical lymph nodes in the posterior triangle, largest measuring 3 cm × 3 cm, matted, firm with normal overlying skin. There was no hepatosplenomegaly and systemic examination was normal.

Management and Outcome

Investigations [Table 1] during this period of illness revealed mild anemia, a drop in total leukocyte count and lymphocyte count (lymphopenia). He also had thrombocytopenia in

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Table 1: Investigations of Kikuchi - Fujimoto disease in a 12.5-year-old boy

Week of illness	2-3nd weeks	6-7th weeks
Investigations		
Hemoglobin, g (%)	10.5	11.5
TLC/uL	5100	1670
Lymphocyte count (%)	42	31
Neutrophil count (%)	48	63
Platelet count/uL	0.93×10^6	2.05×10^6
ESR mm at end of 1 h	50	60
Serum AST U/L	73	
Anti-HIV antibodies 1 and 2	Negative	
Sputum for AFB	Negative	
ZN stain for AFB (aspirate and biopsy material)	Negative	
NAA test (xpert MTB/RIF assay) for MTB (aspirate and biopsy material)	Negative	
CRP (normal <5 mg/dl)	17	
Complement C3 level (normal 80-156 mg/dl)	224	
Complement C4 (normal 12-43), mg/dl	59.4	
ANA	Negative	
Flurometric bactec MGIT liquid culture for mycobacteria tuberculosis at 3 and 6 weeks	No growth	

TLC: Total leucocyte count, ESR: Erythrocyte sedimentation rate, AST: Aspartate aminotransferase, HIV: Human immunodeficiency virus, AFB: Acid-fast bacilli, ZN: Ziehl Neelsen, NAA: Nucleic acid amplification, CRP: C-reactive protein, ANA: Anti-nuclear antibody, MGIT: Mycobacteria growth indicator tube, MTB: Mycobacteria tuberculosis, RIF: Resistance to rifampin

the initial week of illness. Peripheral smear demonstrated anisocytosis and hypochromasia, erythrocyte sedimentation rate (ESR), and serum aspartate aminotransferase (AST) were raised. Mantoux test was positive; 15 mm × 15 mm but chest X-ray was normal.

Ultrasonography (USG) neck demonstrated variable-sized hypoechoic, noncalcific bilateral coalescent lymph nodes with areas of necrosis/breakdown. Mesenteric, suprapancreatic, retropancreatic, peripancreatic, and mesenteric lymph nodes were visualized on the USG abdomen. Lymph node aspiration cytology revealed reactive lymphoid cells, neutrophils with necrosis, and karyorrhectic debris.

Lymph node biopsy of the cervical lymph node was done. Histopathology of the excised lymph node [Figure 1] demonstrated effaced architecture with large areas of necrosis, abundant nuclear debris surrounded by abundant histiocytes and lymphocytes, and mixed inflammatory cells surrounding soft tissue. Granuloma, epithelioid cells, giant cell, and atypical cells were absent. The above findings were suggestive of KFD.

Ziehl–Neelsen stain for acid-fast bacilli and the Nucleic acid amplification (NAA) test i.e, Xpert MTB/RIF assay for mycobacterium tuberculosis (MTB) were negative on aspirate and biopsy material.

This child was empirically started on antitubercular medications based on the clinical history of fever, chronic lymphadenopathy, weight loss, and positive Mantoux test. He became afebrile within 48 h of biopsy and remained afebrile thereafter; hence, antitubercular medications were discontinued after the diagnosis of KFD was confirmed on histopathology.

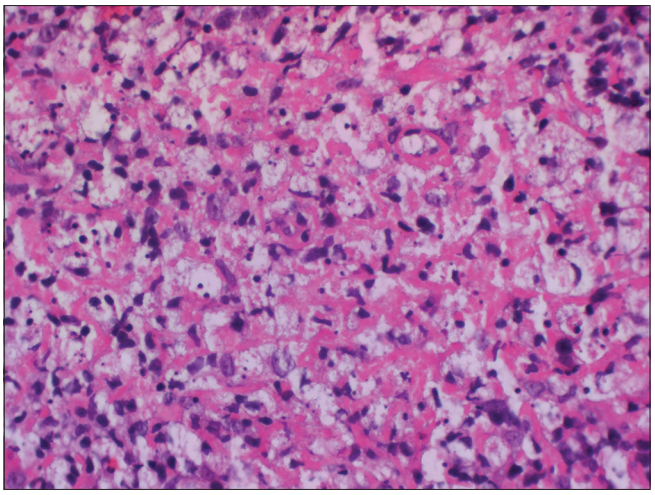

Figure 1: Lymph node showing areas of necrosis and abundant nuclear debris surrounded by lymphocytes and numerous histiocytes (×400)

Further investigations revealed raised C-reactive protein (CRP) and complement C3 and C4 levels. Anti-nuclear antibody (ANA) was negative.Culture for MTB using Flurometric Bactec Mycobacteria growth indicator tube (MGIT) liquid culture, did not reveal any growth at 3rd and 6th week.

He remained symptom free with no recurrence or appearance of new symptoms on follow-up for 18 months.

Discussion

Our patient presented with chronic cervical lymphadenopathy associated with fever and was suspected to have tuberculosis initially. The diagnosis of KFD was subsequently established on histopathology of the excised lymph node. Cases having similar presentation have been reported previously, where diagnosis of KFD was established later on reviewing the biopsy report.[3,6]

KFD, a rare condition in children, is assumed to be due to multifactorial etiology, i.e., hyperresponse of the immune system, induced by viral infections such as Epstein–Barr virus, Human Herpes virus 6 and 8, HIV, parvovirus, influenza virus, Human T-cell leukemia virus Type 1, *Cytomegalovirus*, Parainfluenza virus, and other organisms. It is predominantly a disease of people of Asian descent and Human Leucocyte Antigen class II genes namely HLA DPA*01 & HLA DPB1*0202, present frequently in them have been identified as related to the KFD.[5,7]

Boys are affected twice compared to girls and have a mean age above 10 years. The presentation is mainly unilateral cervical lymphadenopathy which is firm, tender, matted, and varies in size between 0.5 and 4 cm. Axillary, abdominal, and

inguinal lymph nodes may be involved. Associated symptoms such as fever, weight loss, fatigue, night sweats, nausea, vomiting, diarrhea, headache, arthralgia, myalgia, skin rash, and hepatosplenomegaly are observed.[3,4]

KFD in both adults and children is associated with anemia, leukopenia, monocytosis, presence of atypical lymphocytes, elevated ESR, CRP, AST, alanine transaminase, and lactate dehydrogenase. Autoimmune antibody studies, including lupus erythematosus (LE) cell test and rheumatoid factor and ANA studies, are generally negative; these findings may help the clinician distinguish Kikuchi disease from systemic LE (SLE).[3,4] The computed tomography scan findings of the neck include unilateral, homogeneous enlargement of multiple lymph nodes affecting levels II–V with perinodal infiltration, and nodal necrosis.[8]

The diagnosis of KFD is confirmed by excisional lymph node biopsy. Histopathological characteristics are specific and consist of areas of paracortical necrosis, abundant karyorrhectic nuclear remains, polymorphous cell population and fibrin deposits, apoptosis with destroyed cells, intense phagocytic activity, and neutrophils and plasmatic cells absence.[9]

The differential diagnosis of KFD includes infectious lymphadenitis of different etiologies, autoimmune lymphadenopathy (primarily SLE lymphadenopathy), and non-Hodgkin lymphoma. Histopathological features that distinguish KFD from lymphoma include incomplete architectural effacement with patent sinuses, the presence of numerous reactive histiocyte, relatively low mitotic rate, and the absence of Reed Stenberg cells. Special stains, immunohistochemistry, microbiological studies, and correlation with serologic and molecular studies can be helpful to confirm the diagnosis.[10]

Patients usually recover spontaneously without any sequelae. Fever usually decreases after the lymph node removal; the possible explanation being the removal of the focus which originates the inflammatory process. Thus, excisional biopsy has diagnostic as well as therapeutic benefits. In our patient, resolution of fever after biopsy was observed.

Few children require drugs such as nonsteroidal anti-inflammatory drugs, oral corticosteroids, hydroxychloroquine, or intravenous immunoglobulins depending on the severity.[4]

Recurrence has been reported in 7.5%–12.2% of children.[3,4] Patients with recurrent episodes are more likely to have fever, fatigue, extranodal involvement, and remain symptomatic for a long duration. Sometimes, KFD may evolve into an autoimmune syndrome, mostly SLE which makes it necessary to follow-up with these children.[10]

Cervical lymphadenopathy is a common problem in the pediatric population. It is an important task in managing these cases; to identify and differentiate the benign conditions from the serious ones requiring specific treatment. KFD can be misdiagnosed as tubercular lymphadenitis in the regions where tuberculosis is prevalent[6] as was observed in our case. Early biopsy in the presence of persistent lymphadenopathy may be of great help to avoid unnecessary investigations in such situations.

Diagnosis of KFD is a challenge to the clinician. It should be considered in the differential diagnosis of chronic persistent lymphadenopathy in children.

Lessons learnt

- KFD should be considered in the differential diagnosis of chronic cervical lymphadenopathy in children
- The diagnosis is confirmed by excisional lymph node biopsy of the involved lymph node.
- Recurrence though rare is a possibility and long-term follow-up is necessary.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

High Axial Myopia in Neurofibromatosis Type 1

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Abstract

Background: Clinicians must be aware of phenotypic variability in neurofibromatosis type 1 (NF 1) presentations. There is perhaps a limited understanding on progression of NF 1 in prepubertal years and the subsequent threat to vision. Progressively increasing myopia may go unnoticed under a severely ptotic eyelid that gathers attention, due to a disfiguring mass in patients with NF 1. High myopia may result in recalcitrant amblyopia if not tackled early with multidisciplinary management. **Clinical Description:** A 12 year old girl had a history of progressively increasing left upper eyelid ptosis due to an upper eyelid mass, first noticed at the age of 1 year and eventually resulted in severe ptosis by the age of 5 years. However, this went unnoticed until she was diagnosed with NF 1 at the age of 12 years. Best corrected visual acuity was 6/6 (Plano) in the right eye (OD) and counting finger 2 m with − 15.0 diopter spheres in the left eye (OS). Peripheral fundus examination was normal in both eyes. Levo elevation and abduction were limited OS. Hypotropia, pulsatile proptosis, and depression of the globe were clinically attributable to enlargement of orbital tissues and lid problems. Contrast enhanced computed tomography scan revealed plexiform NF with extraconal extensions. Axial length was 21.94 mm OD and 28.92 mm OS. B scan ultrasound revealed a posterior staphyloma OS. **Management:** The patient underwent a debulking surgery of the eyelid mass which on histopathological examination confirmed plexiform NF. Surgery resulted in a cosmetic reduction in ptosis; however, any intervention was relatively too late to rehabilitate the left eye. **Conclusions:** Eye care certainly has its regional differences. High axial myopia may result in low VA and recalcitrant amblyopia that may go unrecognized and comes with management challenges to the attending ophthalmologist and allied specialties dealing with these cases of NF 1.

Keywords: Anisometropic amblyopia, high axial myopia, neurofibromatosis type 1, optic pathway glioma

Neurofibromatosis type 1 (NF 1, also known as von Recklinghausen disease) is one of the most common genetic disorders. Several ophthalmic associations exist which include the characteristic Lisch nodules, retinal or choroidal hamartomas, retinal ischemia, optic pathway gliomas, or congenital glaucoma.[1,2] Anterior scleral staphyloma has also been documented in the literature.[3] Reduction in visual acuity (VA) is commonly attributed to an underlying optic pathway glioma. However, that may not always be true. The point worth describing this case is to alert clinicians and primary eye care professionals of one such presentation of NF 1 that results in a reduction in VA accompanied with management challenges as was observed in a 12-year-old girl.

Clinical Description

The child was apparently well till the age of 1 year when she was detected with unilateral ptosis in the left eye (OS) due to an upper lid mass. At this stage, the ptosis was reportedly mild for which the parents never sought an ophthalmic consultation and no documentation was made of ptosis severity and VA assessment. By the age of 5 years, there was severe ptosis attributed to the eyelid mass involving the entire left upper eyelid. The parents were too apprehensive to allow a corrective surgery for ptosis as explained by a local physician at village although the nature of this mass remained unknown as no formal specialist opinion was sought. No comment was made on the VA at this stage. The child never realized that the vision

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in her left eye was significantly reduced as she was mostly dependent on her apparently normal right eye with good visual acuity for carrying out her daily activities binocularly and this continued for last seven years dating from her current presentation at 12 years of age. In her current presentation at 12 years, she was diagnosed with NF 1(Figure. 1a, b) based on the presence of clinical signs which included a plexiform neurofibroma of the left upper eyelid, multiple Lisch nodules on the iris along-with café-au-lait macules over her neck, back, trunk, bilateral legs and arms [Table 1].[1-3]

Management and Outcome

In this presentation to an ophthalmologist, unaided acuity was 6/6 in the right eye and counting finger at 1 m OS. Best-corrected VA was 6/6 (Plano) in the right eye (OD) and counting finger 2 m with − 15.0 diopter spheres OS. Until all this time, there was no awareness of refractive error/amblyopia, and no management of either of these was undertaken. Right eye was essentially normal [Figure 1a and c-e]. The difference in marginal reflex distance 1 between two eyes was more than 4 mm with a poor levator function (less than 4 mm), pointing to severe ptosis OS causing complete occlusion. Levo-elevation and abduction were limited OS. Hypotropia, pulsatile proptosis, and depression of the globe were observed and were clinically attributable to enlargement of orbital tissues and lid problems. Both eye media were clear. Indirect ophthalmoscopy revealed that the right eye fundus was within normal limits, and the left optic disc was large with a cup to optic disc ratio of 0.4:1, parapapillary atrophy, and a normal periphery. Atrophy with a normal periphery on indirect ophthalmoscopy. Contrast-enhanced computed tomography scan confirmed the presence of PN having extraconal extensions, causing globe hypotropia, dysplasia of the left sphenoid wing, and loss of volume of the temporal lobe [Figure 1c and d]. Left vitreous cavity appeared enlarged and so was the left globe axial length [Figure 1c and f]. Further, axial length measurement on A-scan showed a markedly increased value for the left eye (21.94 mm OD; 28.92 mm OS). B-scan ultrasound revealed a posterior staphyloma [Figure 1f]. She underwent a debulking surgery of the upper eyelid neurofibroma, which on histopathological examination confirmed plexiform NF. To add, both eyes always maintained normal intraocular pressures throughout (OD 15 mmHg, OS 16 mmHg).

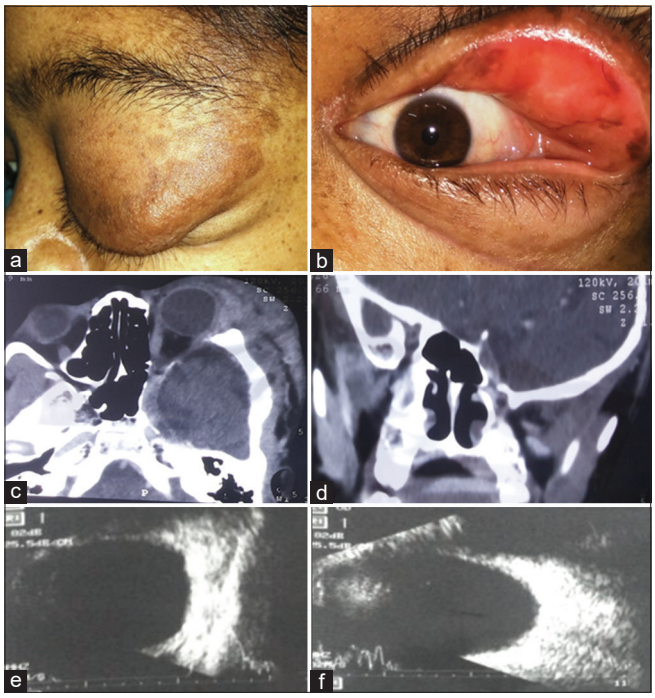

Figure 1: Patient presented with left upper eyelid plexiform neurofibroma (a). Globe hypotropia was seen with eyelid thickening (b). Contrast-enchanted computed tomographic scan revealed the presence of plexiform neurofibroma having extraconal extensions causing proptosis (c), dysplasia of the left sphenoid wing (c and d), and loss of volume of the temporal lobe (d). Right eye was normal on B-scan (e). Left eye had increased axial length (c and f)

Discussion

Manifestations of NF 1 can be extremely unpredictable. Newly diagnosed cases require close observation with ophthalmological examination and imaging. A comprehensive examination should be performed by the eye health professional at least every 6 months throughout the period of visual development up to the age of 8 years as this is the critical period during which amblyopia may develop.[4] The frequency of examinations is increased if orbital–periorbital PN (OPPN) is rapidly growing. At every visit, the eye care professional should assess VA, intraocular pressure, and ocular motility and perform cycloplegic refraction to monitor for the development of amblyopia, glaucoma, strabismus, optic nerve disease, ptosis, proptosis, or a cavernous sinus involvement. Anisometropic amblyopia may result due to ptosis or increased axial length and has been observed in up to 43% of children with OPPN.[1,4] Stimulus deprivation amblyopia resulting from significant ptosis has been reported in roughly one-third to one-half of patients. However, the current body of literature for unilateral myopia in NF is limited and so is the association of high myopia in NF 1.[2,5,6] This has been suggested in a study conducted by Lévy *et al*. that the release of growth mediators by the neurofibroma affects the globe locally via autocrine and paracrine signaling defects possibly due to a significant upregulation of genes and causes eyeball enlargement.[6] Nearly thirty genes that were studied were found to be upregulated which encoded transcription factors, growth factors, secrete proteins, cytokines, and their receptors.[6] Hoyt, Billson and other co-authors have supported the role of local growth factors in progressive globe enlargement that can be observed in NF1 independently of intraocular hypertension/glaucoma. Whether to attribute the pathogenesis of the development of staphyloma to the absence of the sphenoid wing or orbital roof remains uncertain as of now.[3] Optic pathway glioma in children with NF 1 is not associated with increased prevalence of anisometropia. Both stimulus deprivation and anisometropia were contributors to the development of

Table 1: Diagnostic criteria for neurofibromatosis type 1

Clinical feature	Progression of clinical sign with age
Diagnostic criteria for NF 1 includes the presence of at least 2 of the following criteria	
6 or more café-au-lait spots of 5 mm in prepubertal and 15 mm in adulthood	Present at birth in many individuals and increase in size and number over the first 5-7 years of life. They are less frequent in the older age groups
Axillary freckling	May not appear until 5-7 years of age. Freckles in the axillary or inguinal region are usually seen in all subjects aged 11-20 years, more so (95%) in those aged 11 years or older
Two or more NF or one plexiform NF	May appear in childhood but more commonly develop in teenagers or adults. Progression of severity of cutaneous manifestations is more between 20 and 39 years of age. Number of NF increase from 4% in the age group under 6 years to 100% in that over 41 years
Lisch's hamartomas	Unusual before 2 years. Onset is usually in the teenage. Increase considerably with age. They are present in 90% of adults
Optic pathway glioma	Found in 15% of patients. Usually between 15 months and 7 years of age, results in decreased color vision/visual acuity or pallor of the optic disc in later stages
Bone dysplasia	Skeletal abnormalities which include (bony dysplasia, bony erosion, demineralization, nonossifying fibromas [occur mainly in late childhood or early teenage years], and scoliosis [severe rapidly progressive kyphoscoliosis between 3 and 5 years of age]) more in children aged 16 years or younger. Pseudoarthrosis is seen at birth or within first few months of life
One affected first-degree relative	Half of all cases are familial

NF: Neurofibromas

amblyopia in this case.[7,8] Clinical studies do suggest that the incidence of myopia is significantly higher in children with unilateral congenital ptosis, but this is a rare finding in humans unlike the animal experiments.[7] The severe ptosis that was fully established by the age of 5 years in this child possibly may have worked like an artificial lid stitch limiting eye opening. It might have deprived the developing globe of a clear retinal image, hence hindering the normal physiological process of emmetropization culminating in asymmetric enlargement of the axial length. This mechanism of axial myopia has been studied in animal experiments on tree shrews and rhesus monkeys.[7,9] Ptosis may usually induce some corneal astigmatism in the affected eye which however was absent in this child, and therefore, the sole contribution of this acquired ptosis in inducing myopia to the extent of −15.00 D seemed unlikely yet not totally impossible. Amblyopia normally coexists with strabismus and refractive errors, which include astigmatism, anisometropia, and ametropia that can manifest as amblyopia, irrespective of the presence of ptosis. Surgical management in cases with progressively increasing OPPN is still debatable and is dependent on the judgment of the clinician. Unfortunately, no confident evidence-based recommendations with a long follow-up exist.[10] Complete removal of OPPN surgically in early childhood is feasible in only a small subset of affected patients as the tumor is diffuse and involves the surrounding region or the organ in a widespread manner. OPPN growth following surgery in younger patients is well known. Although a debulking surgery at an early stage to reduce the degree of ptosis may be an attempt to prevent stimulus deprivation, the above-mentioned facts compromise the functional outcomes of surgery in NF and the prognosis remains poor. Surgery did reduce the mechanical ptosis in the patient, but it at this stage was relatively late to rehabilitate the left eye and reverse deep amblyopia that had already set in as a result of high axial myopia. Wearing corrective spectacles remained a challenge with the postsurgery tumor size and so was the amblyopia therapy.

This case highlights the fact that small OPPN restricted to the eyelid presenting as mild ptosis may go unnoticed and so is the presence of associated high axial myopia that might also go undetected if timely refraction is not performed. The knowledge of occurrence of this entity must be known to all physicians, nurses, and other healthcare providers, especially the primary healthcare worker screening for visual and structural eye problems in a nonspecialist setting. Prompt reference to an eye healthcare professional at an early stage is necessary. Management decisions depend on case to case basis over a life time of follow-up and should include the input from a multidisciplinary team of general practitioner, neuro-oncology, optometry/ophthalmology/neuro-ophthalmology, craniofacial and plastic surgery, and genetics. The fact that directing all focus toward a disfiguring mass and hunting for diagnosing optic pathway glioma as a possible etiology for amblyopia with a significant battery of tests should not be the rule. A basic investigation like refraction to predict evolving amblyopia early may direct holistic management of these children.

Lessons learnt

- The cause for reduction in visual acuity in patients with neurofibromatosis type 1 (NF 1) is not always an optic pathway glioma but may possibly be due to high myopia
- Late presentation of the patient to the attending ophthalmologist comes with a challenge for their appropriate rehabilitation
- There is perhaps a limited understanding on progression of NF 1 in prepubertal years and the subsequent threat to vision.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's father has given consent for images and other clinical information to be reported in the journal. The patient's father understands that the names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Exposure to Pornography in a Young Boy: Diagnosis and Management

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Abstract

Background: Child sexual abuse is highly prevalent in India, both among boys and girls; however, few studies have studied sexual abuse of male children. The present case report highlights the challenges of diagnosis and management of a young boy who presented with marked hyperactivity and sexual acting out behaviors subsequent to his repeated exposure to pornography. **Clinical Description:** H, a 5-year-old boy, presented with a 2 month history of hyperactivity, poor concentration, inappropriate touching, and self-stimulation. H also displayed sexual knowledge beyond that of what would be expected of his age and developmental level. The Child Sexual Behavior Inventory was administered that showed an unusually high score on the (sexual abuse specific items, sexual behaviors that are atypical for child's age and gender). **Management and Outcome:** The use of therapeutic interventions such as building a therapeutic relationship, environmental change, family counseling, and nondirective play therapy helped in remitting most of the child's behavioral difficulties. **Conclusions:** Parents need to be active participants in the digital lives of their children and exercise controls on what they view online. Since pediatricians are often the first points of contact for a child with aberrant behaviors, they need to be aware of the law on the protection of children against sexual offenses and the range of types of sexual offenses against children.

Keywords: Adverse childhood experiences, child sexual abuse, pornography, problem sexualized behaviors

A large majority of Indian children face chronic and multiple adverse childhood experiences including neglect, child maltreatment, loss of a parent, and sexual abuse.[1] The term "developmental trauma" is used as a way of conceptualizing the distress experienced by children exposed to early and chronic trauma, although it is not a diagnostic category in the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5. A recent review of 19 meta-analyses (559 studies, 28 outcomes, 4 million participants) reported that child sexual abuse (CSA) was associated with several long-term physical, psychiatric, and psychosocial health outcomes including conversion symptoms, anxiety, depression, substance abuse, and posttraumatic stress disorder.[2]

In India, the prevalence of CSA is extremely high, with many cases going unreported. A national-level study, conducted by the Ministry of women and child development, covering 13 Indian states and 12,447 participants (5–18 years) reported that nearly half had been exposed to some forms of sexual abuse. Out of the 21% who were exposed to extreme forms of sexual abuse, 57% were boys.[3] Sexual abuse includes both contact and noncontact abuse. Noncontact activities include involving children in looking at online sexual images and activities, using children in the production of sexual content, and encouraging children to behave in sexually aberrant ways. The protection of children against sexual offenses (POCSO) Act 2012 along with the Juvenile Justice Act 2015 serves as a legislative shield for the POCSO.[4] Although prevalence rates of CSA are high in India, there is limited published literature on effective management strategies. Hence, clinicians working with children have limited awareness and experience regarding the management of these challenging cases in a child-friendly and culturally sensitive way. In this case report, we discuss a

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case of a young boy who presented with marked hyperactivity and sexual acting out to highlight the challenges in making the diagnosis and management of problem sexualized behaviors (PSBs).

Clinical Description

H, a 5-year-old boy, from an extended rural family was brought by his mother to the pediatric department of a tertiary care center, with a 2-month history of hyperactivity, poor concentration, inappropriate touching of his private parts, and self-stimulation. The history revealed that H was an easy to manage child but of late had become extremely hyperactive and displayed unremorseful disruptive behavior at school. On few occasions, H was observed to have touched his classmates inappropriately. The child also displayed sexual knowledge beyond what would be expected of his age and developmental level. He would use sexually graphic words, like "oral sex" and "intercourse." These behaviors were a source of significant parental mortification and despite verbal warnings, reprimands, and physical punishment, the PSBs persisted. As a result of his atypical sexual behavior, the child was suspended from the school and advised to seek treatment. The parents sought several consultations with pediatricians and psychiatrists; however, the PSBs did not subside.

A comprehensive psychosocial evaluation by the social pediatrics and child psychology team was undertaken including in-depth interviews of parents and evaluation of the child using standardized measures. The parental interview revealed a history of marital conflict and spousal abuse. On evaluation, H was a cooperative child and participated in all tasks with enthusiasm. The child was given the task of drawing a person and house-tree-person (HTP) test. The use of drawings is an ideal tool for evaluation of young verbally immature children as they can reveal critical information regarding development and emotional issues. H told the treating team that his cousin had showed him "pictures of nude men and women" on his smartphone. In view of the child's sexual acting out, the Child Sexual Behavior Inventory (CSBI) was administered. The CSBI indicates the overall level of sexual behavior in children (2–12 years). It provides scores on 9 sub-domain scores including self-stimulation, sexual interest, sexual intrusiveness, sexual knowledge, voyeuristic behavior, boundary problems, exhibitionism, gender role behavior, and sexual anxiety. The CSBI yields several scores including a total score which indicates the overall level of PSBs the child exhibits, (developmentally related sexual behavior, sexual behaviors that are developmentally normal), and sexual abuse specific items (SASI, sexual behaviors that are atypical for child's age and gender).[5] The child's narrative of sexual abuse was further corroborated by the unusually high score on SASI (score >6 standard deviation above the mean) and his drawings which showed several signs of sexual abuse on the draw-a-person test (missing pupils, emphasized hair, phallic symbol, and sharp elongated lines) and HTP test (missing person, circuitous pathways leading nowhere) [Figure 1].[6] Since the child also displayed easy distractibility and hyperactivity, the Vanderbilt attention-deficit hyperactivity disorder (ADHD) diagnostic rating scale forms (parent and teacher) to the parents and class teacher, respectively, were also administered to assess for symptoms of ADHD. The teacher's responses suggested concerns in attention and academics, while the mothers' responses suggested concerns in hyperactivity, oppositional, and defiant behaviors. However, the number of symptoms endorsed fell short of the ADHD criteria. The final diagnosis was adjustment disorder to developmental trauma. The case was initially reported to the child welfare committee who further referred it to the District Child Protection Unit for management as per the POCSO and Juvenile Justice Act.

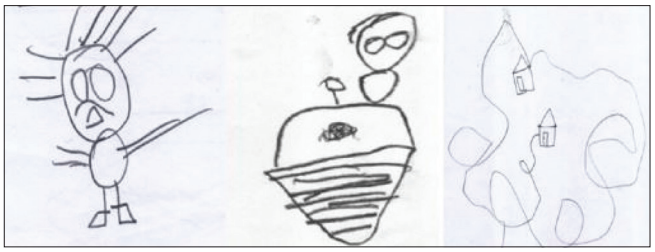

Figure 1: Drawings of the child (draw-a-person and house-tree-person)

Management and outcome

A comprehensive management plan was drawn out. To ensure that the boy had no contact with the alleged perpetrator, an environmental change was suggested, and the family moved in with the maternal grandparents. Parents were counseled regarding the need for fostering stable and respectful relationships within the family and work together as a team to support the child. Several sessions of nondirective play therapy along with the mother were conducted. The initial symbolic play themes reflected aggressive actions possibly re-enactment of sexual scenes that had been witnessed. However, over time H worked out his hostile impulses and his play became more constructive. The symbolic theme of "rescue from monsters" emerged consistently in the child's play. Follow-up, 18 months after the initiation of therapy, revealed that except for some occasional hyperactivity and inattention, the aberrant sexual behaviors had resolved completely [Figure 2].

Discussion

This case report highlights the establishment of diagnosis and management of a child who developed PSBs after exposure to online pornographic viewing. In recent years, easy accessibility and availability of mobile devices have substantially expanded child and adolescent access to pornography, regardless of age, gender, and geographical location. This may occur either intentionally or unintentionally. Several socioeconomic, demographic, and family factors are linked to increased exposure to pornography, including male sex, lower socioeconomic status, traumatic negative life experiences, lower level of caregiver supervision, and poor

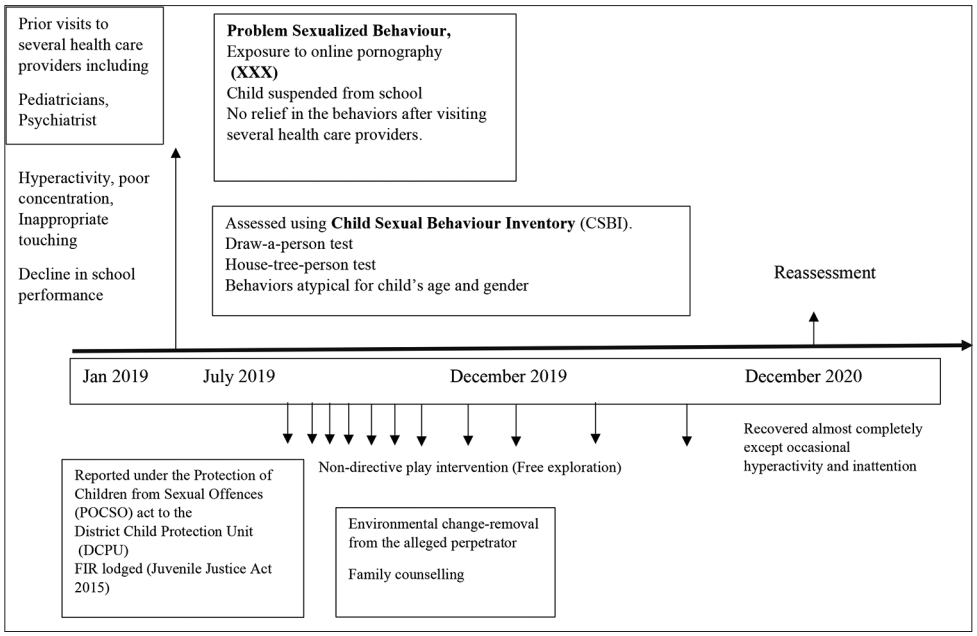

Figure 2: Schematically presents the timeline of the case presentation and management

emotional bonding with caregivers.[7] Exposure to sexually explicit content viewing in young children increases the risk for early initiation of PSBs, sexual offending, unsafe sexual health practices, unhealthy attitudes supportive of sexual violence against women, and stronger beliefs in gender stereotypes.[8] The national child abuse study revealed that nearly one-fourth of children surveyed (5–12 years) had been exposed to pornographic material.[3] Given the magnitude of this problem, pediatricians need to be sensitized and have a high index of suspicion when they encounter young children with symptoms of inappropriate sexual behaviors, knowledge of sexual topics, regressive behaviors such as thumb sucking or bedwetting, nightmares, overly compliant behavior, and excessive fearfulness.

Research on treatment modalities has found trauma-focused behavioral therapy and nondirective play therapy as useful therapeutic tools for victims of sexual abuse.[9,10] Abused children can therapeutically correct their traumas in fantasy and through their actions in play, creative artwork, and stories. For example, the use of water in play symbolically indicates cleansing of thoughts and actions, and the use of "weapons" to chase away "bad guys" in imaginative play may indicate increasing feelings of empowerment. The themes of play change from negative to positive as the child gains mastery over his trauma.[9] It is important to co-opt parents as co-therapists as they can aid in treatment with filial sessions at home. Moreover, since most intrafamilial sexual abuse occurs in the context of a dysfunctional family, clinicians need to counsel parents regarding the importance of fostering stable relationships within the family.

Recent research has focused on primary prevention programs such as parent education, the involvement of school teachers, and community health workers to prevent sexual abuse.[7] Since many children and adolescents are digitally connected for prolonged periods, especially post the pandemic, the range of online risks such as inadvertent exposure to sexually explicit images and materials, sexting, sharing of explicit images, cyberbullying, and exploitative relationships are bound to increase. Parents need to be active participants in the digital lives of their children and exercise controls on what they view on the internet. Critical viewing of digital content can help viewers to reflect on the messages contained in visual content including pornography. Since pediatricians are often the first point of contact for children with behavioral and emotional problems, they are uniquely placed to provide anticipatory counseling to parents and children alike.

Lessons learnt

- Child health professionals need to be aware of the new online threats emerging in recent times of increased use of smartphones and other electronic devices among children and adolescents
- Aberrant sexual behaviors, increased fearfulness, regressive behaviors, and excessive clinginess in young children may be some indicators of CSA
- CSA requires early diagnosis and multidisciplinary management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Case Report

Giant Juvenile Fibroadenoma in a Young Female-A Diagnostic Dilemma

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Abstract

Background: Fibroadenoma is the most common breast lesion among pediatric female population. A giant fibroadenoma is rare, characterized by a rapidly growing tumor, with a mass >5 cm diameter in greatest dimension and/or weighing more than 500 gm. Phyllodes tumor range from benign to malignant. Both have similar presentation. **Clinical Description:** An 11-year-old girl presented with rapidly progressive, painless increase in the size of the left breast over 2 months. Local examination revealed a firm nontender mass involving the upper inner and outer quadrants of the left breast along with the retro-areolar region. The mass was mobile and measured approximately 11 cm × 10 cm. The overlying skin was normal, although with dilated veins and free from underlying mass. The clinical phenotype was suggestive a phyllodes tumor in view of rapid progression and large size. However, the ultrasonogram and fine-needle aspiration cytology favored a fibroadenoma. **Management:** It was decided to perform a "Nipple-areolar complex sparing lumpectomy" with deferment of reconstructive surgery. Adequate lump excision was achieved while maintaining proper cosmesis. The histopathological findings of the excision biopsy confirmed the final diagnosis of fibroadenoma. **Conclusion:** A large breast mass in a pediatric/adolescent girl poses a diagnostic dilemma to the treating surgeon. Proper evaluation is needed to differentiate between several benign breast masses from malignant ones. The definitive diagnosis is made histologically. Total excision of the lump with conservation of nipple and areola is indicated to make a definitive diagnosis and to relieve the compression of the normal breast tissue.

Keywords: Breast, giant juvenile fibroadenoma, phyllodes tumor

Breast development is a part of the normal physical changes in an adolescent female. Any asymmetry of size, abnormality, or mass in the breast is an issue of concern for affected individuals and their families.[1] Most breast masses in the pediatric age group are benign in nature. Fibroadenoma is the most common benign tumor found in the breast. It usually affects individuals younger than 30 years and is common in African Americans. It is referred to as a juvenile fibroadenoma if it manifests between 10 and 18 years of age. A giant fibroadenoma is a rare variant (constituting 0.5% of all fibroadenomas) that is characterized by a rapidly growing tumor, with a mass >5 cm diameter in the greatest dimension and/or weighing more than 500 gm.[2] It is important to differentiate giant juvenile fibroadenoma from other breast mass lesions with same clinical presentation, namely phyllodes tumor and virginal hypertrophy as the management options differ. Fibroadenoma being a benign condition can be observed in some cases or treated by surgical excision while phyllodes tumor can be either benign or malignant and treatment requires excision with negative margins.[3] On the other hand, virginal breast hypertrophy is a rare benign disease, characterized by rapid and excessive growth of one or both breasts during the peripubertal period. Symptomatic treatment is applied as a first step and the reconstruction process may be delayed until the postpubertal period.

We present this case report because of the rarity of the condition, the challenges it poses to the treating surgeon in terms of establishing diagnosis and performing surgical excision with or without breast reconstruction.

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Clinical Description

An 11-year-old prepubertal girl presented with a month history of asymmetrical enlargement of the left breast. The sudden increase in size of the left breast in comparison to the other was initially mistaken as normal breast growth. Localized pain, discomfort, redness, or nipple discharge was absent. There was no history of preceding trauma, fever, anorexia, or weight loss. There was no significant family history of similar complaints in any female members of the family. The girl had never been exposed to radiation or taken any estrogen supplementation other hormones or drugs in the past.

General physical examination revealed stable vital parameters, age-appropriate body mass index, and sexual maturity rating (Tanner Stage III) in the unaffected breast. There was no pallor, icterus, or significant cervical, axillary or inguinal lymphadenopathy. On local examination, a firm nontender mass was felt involving the upper inner and outer quadrants of the left breast along with the retro-areolar region. The mass was mobile and measured approximately 11 cm × 10 cm [Figure 1]. The overlying skin was normal and free from underlying mass, although dilated veins were present over the swelling. There was no nipple discharge. The right breast was normal. There were no significant findings on the systemic examination.

On the basis of the seemingly benign clinical presentation, two close differential diagnoses were kept, phyllodes tumor (in view of the short history, rapid progression, and large size) and giant fibroadenoma (in view of the age). Confirmatory investigations (localized imaging and histopathological examination) were planned to differentiate between the two.

Management and Outcome

Routine hematological investigations did not reveal any evidence of acute or chronic inflammation. Biochemical tests were normal. Ultrasonography of the left breast showed a large homogeneous lesion involving almost the entire breast, indicative of a fibroadenoma. Fine-needle aspiration cytology (FNAC) smears were moderately cellular, consisting of benign ductal epithelial cells arranged in large cohesive sheets, tissue fragments, cohesive clusters and focal cribriform pattern. Interspersed myoepithelial cells and occasional stromal fragments were seen, also suggestive of a fibroadenoma.

The patient and her parents were counselled regarding the need of lumpectomy and possible disfigurement of the breast postoperatively. It was also explained that the risk of a malignant phyllodes tumor would only be confirmed after postoperative tissue biopsy. A plastic surgery consult was taken for considering postsurgical breast reconstruction. Delayed breast reconstruction was advised in view of better outcomes after the completion of pubertal breast growth. Often, normal breast development takes care of the discrepancy in size that occurs directly postoperatively, and reconstruction is not required at all. Thus, conservative surgical excision was planned by "Nipple-areolar complex sparing lumpectomy," in order that the compression of the normal breast tissue by the abnormal tissue would be relieved. Intraoperatively, the mass was delivered intact, i.e., the lump was excised leaving the nipple-areolar complex *in situ*. The lumpectomy specimen appeared grossly homogeneous, was grayish white in color, and 10 cm × 10 cm × 5 cm in size, with a skin flap of 8 cm × 3.5 cm with grossly unremarkable skin surface [Figure 2a and b]. The histopathological examination revealed circumscribed well-encapsulated tumor comprising of biphasic epithelial and stromal proliferation [Figure 3]. The epithelial component shows glands with pericanalicular patterns and mild epithelial hyperplasia with preserved myoepithelial layer. No significant cytological atypia noted in epithelial component. The stromal component showed mild cellularity and mild anisonucleosis. The final diagnosis was that of ajuvenile giant fibroadenoma. The postoperative course was uneventful, with drain removal on the 3rd postoperative day and discharge by the 4th day. When the patient was followed up after a week, the wound and nipple areolar complex were healthy. There was no discharge from the wound or necrosis of the skin flap or nipple areolar complex.

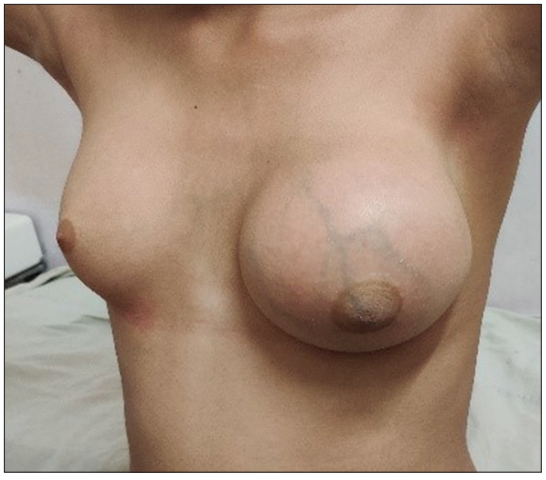

Figure 1: Large mass occupying upper part of left breast

Discussion

Giant juvenile fibroadenomas are rubbery, mobile, and nontender masses that are composed of epithelium and/or

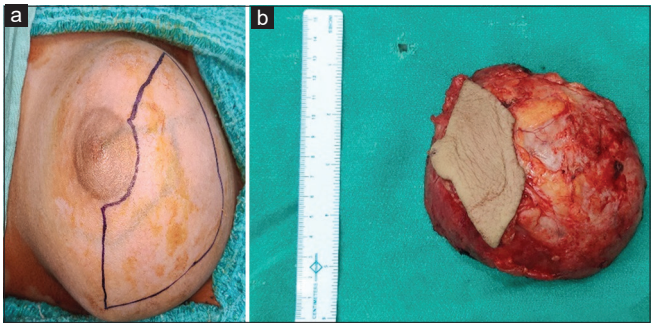

Figure 2: (a) preoperative photograph with marking of incision site (b) excised well encapsulated mass with excised skin

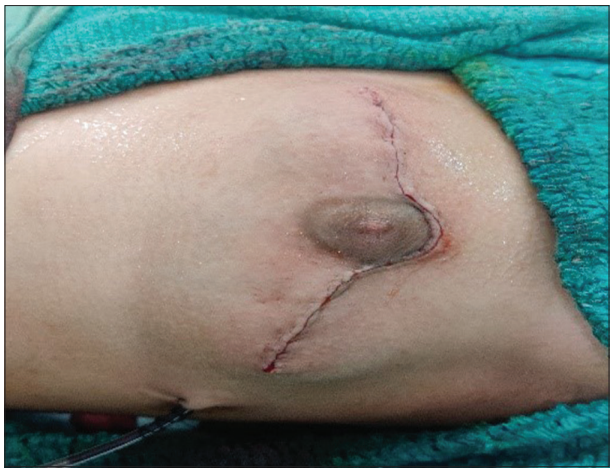

Figure 3: Photograph taken after closure of incision

stroma of the terminal lobule of the breast. The most common site is the upper outer quadrant of the breast. They are multiple in 10%–15% cases and exhibit bilateral involvement in 10%. Although etiology is still unknown, hormonal factors have been implicated. Some major factors postulated are excessive estrogen stimulation, increased estrogen receptor sensitivity, and/or decreased estrogen antagonist sensitivity.[3]

It is difficult to differentiate a giant juvenile fibroadenoma from other that share the same presentation, i.e., phyllodes tumors and virginal hypertrophy. A giant fibroadenoma disfigures the breast and may affect the growth of normal breast tissue due to a direct pressure effect but carries no malignant potential. In contrast, the nature of a phyllodes tumor ranges from being benign to being locally malignant. Virginal hypertrophy occurs due to estrogenic stimulation, resulting in unequal growth of the breast buds and leading to asymmetrical enlargement. Other clinical features that need to be factored in while arriving at a clinical diagnosis are age, duration, and size: Phyllodes occur in older individuals, display rapid growth and are large (3 cm and larger)[4] and bossellated whereas fibroadenomas are seen in younger patients, demonstrate slower progression and are usually small, except for giant fibroadenomas.

Tissue biopsy is critical in establishing the diagnosis in large lesions. Histologically, phyllodes tumors differ from giant fibroadenomas by the presence of leaf-like structures and stromal cell atypia.[5] Virginal hypertrophy is characterized by abundant connective tissue with duct proliferation and lack of lobule formation. Isolated FNAC cannot differentiate between a phyllodes tumor and giant fibroadenoma[6] and require core needle biopsy for greater accuracy. However, due to the psychological and emotional effects of core needle biopsy in young patients, excisional biopsy is preferred as a diagnostic cum therapeutic method.[7,8]

The goal of treatment is complete excision of the tumor, preservation of the areola and nipple, and achievement of symmetrical breasts.[7,8] Reconstructive methods are usually needed after resection of large breast lesions to attain bilateral symmetry.

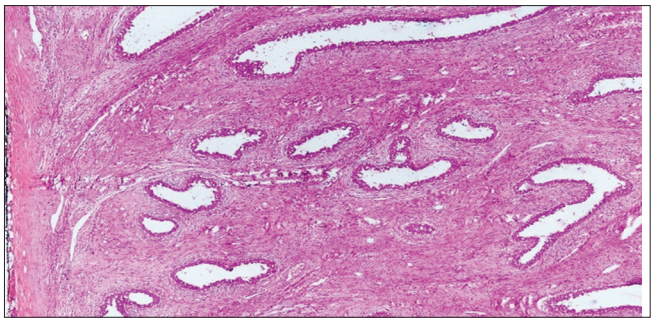

Figure 4: Circumscribed encapsulated nodule composed of admixture of epithelial and stromal elements in near equal proportions. (H&E x 40)

However, according to a systematic review, reconstructive surgery is not commonly done in giant fibroadenomas.[7,8] In our case, conservative surgery was performed as the preoperative diagnosis was still unclear clinical suspicion being a phyllodes tumor, while FNAC favoring a fibroadenoma.

There are three basic principles for breast reconstruction: Preserving all the normal breast parenchyma; adjusting the skin envelope; and positioning the nipple-areola complex so that it is symmetrical with the opposite breast.[9] The extremely large size of tumor led us to anticipate the possibility of requiring reconstructive surgery, but we managed adequate closure with sparing of nipple areolar complex in our patient, despite the size [Figure 4]. The decision of a nipple-areolar sparing lumpectomy was taken preoperatively so that adequate cosmesis could be achieved, if reconstruction was needed. Thus, we managed to follow all the three principles and achieved adequate lump excision while maintaining proper cosmesis. The long-time prognosis is good as the lesion is benign.

Lessons learnt

- Breast masses in pediatric and adolescent girls are usually benign
- The final diagnosis is established by histopathological findings
- Conservative breast surgery is preferred for breast masses in the pediatric and adolescent age groups.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Weill–Marchesani Syndrome: A Rare Cause of Ectopia Lentis and Short Stature

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Abstract

Background: Weill–Marchesani syndrome (WMS) is a rare heritable connective disorder characterized by short stature, brachydactyly, stiff joints and distinctive ocular manifestations of microspherophakia, myopia, ectopia lentis, and glaucoma. It is caused by either biallelic pathogenic variants in *ADAMTS10, ADAMTS17,* and *LTBP2* or heterozygous pathogenic variants in *FBN1* genes. **Clinical Description:** We describe a case of 6-year-old girl who had short stature, high myopia, and bilateral ectopia lentis. The visual acuity was 6/18 (−25.00/−3.00 × 35) in both the eyes with an intraocular pressure (IOP) 15 mmHg and 17 mmHg in right and left eye, respectively. The clinical exome sequencing identified a heterozygous pathogenic c.2413T>C in *FBN1* gene confirming the diagnosis of WMS. **Management:** The proband was prescribed a trial of contact lenses and she is under regular follow-up. The patient is being regularly monitored for any signs of lens displacement, raised IOP. She has been planned for lens extraction, to prevent glaucoma, in case of any progression of symptoms or rise in IOP. **Conclusion:** WMS should be suspected in any child with short stature and high myopia. The rarity of this disorder often results in diagnostic delay and dreaded complications of secondary glaucoma and blindness.

Keywords: Brachydactyly, ectopia lentis, short stature

Weill–Marchesani syndrome (WMS) is rare genetic disorder with a reported prevalence of 1/100,000 population.[1] It was named after George Weill and Oswald Marchesani who first described this entity in 1932 and 1939, respectively.[2] WMS has now been classified under acromelic dysplasias for the last few years.[3] WMS can be inherited in an autosomal recessive (AR) or autosomal dominant (AD) manner due to pathogenic variations in *ADAMTS10, ADAMTS17, LTBP2,* or *FBN1* gene, respectively.[1,4,5] In a large series of 128 patients, AD, AR, and sporadic causes accounted for 47%, 39%, and 16% cases, respectively.[6] As a number of hereditary and genetic conditions can result in ectopia lentis, identification of exact etiology is necessary to predict the prognosis and plan future management and surveillance. We describe a case of WMS in a girl with high myopia with progressive visual diminution and short stature.

Clinical Description

A 6-year 5-month-old girl, first born to 3rd-degree consanguineous parents, was referred to the genetic clinic for the evaluation of short stature and visual problems. She was born preterm at 32 weeks, small for gestational age (birth weight: 1.3 kg) with an APGAR score of 8/9 at 1 and 5 min. She had respiratory distress syndrome requiring respiratory support in the form of continuous positive airway pressure for the first 3 days. The baby remained admitted in neonatal intensive care unit for the first 15 days of life for prematurity, low birth weight, and feeding issues. There was no history of neonatal jaundice, seizures, and apnea of prematurity. Her eye evaluation and BERA screening were normal on follow-up. However, subsequently, over the next few months, parents noticed delay in achieving gross motor and language milestones. She started neck holding at 7 months, sitting at

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15 months, standing at 2 years, and walking at 2.5 years. Similarly, speech was also delayed. She started speaking one-word at 18 months and two-word sentences at 3 years. At the time of presentation, with an age of 6 years 5 months, she could climb up and downstairs, run, and jump, going to a school but with poor scholastic performance (borderline intelligence quotient of 74), could talk in sentences, recite rhymes, and recognized alphabets, numbers, colors.

At 3.5 years of age, when she started going to school, parents also noticed that she was not growing well and looked small compared to other children of her age. Furthermore, she used to hold books close to her eyes while reading for which she was prescribed high-powered glasses at 4 years of age. For the past 3 months before presenting to us, she had painless decline in vision for which she was evaluated and detected to have bilateral ectopia lentis. There was no history of ectopia lentis or early vision loss and short stature in any of the family members.

Examination at 6 years 5 months demonstrated a proportionate short stature with a height of 101 cm (−3.2 z), arm span of 104 cm, upper segment:lower segment ratio: 1:1, and a mid-parenteral height of 168 ± 8 cm. She weighed 14.2 kg (−2.76 z) and had a head circumference of 48 cm (<−2 SD) with brachycephaly. She was noted to have a synophrys, hypertrichosis over the face with low anterior and posterior hairline, downslanted palpebral fissures, and use of high-powered refractive glasses. There was mild brachydactyly [Figure 1]. Examination of her joints was normal with no stiffness though the skin had a thick texture. Rest of systemic examination was unremarkable. Two-dimensional echocardiography performed for the evaluation of valvular and vascular pathology was normal. This was performed to look for any congenital cardiac defect as may be present in any syndromic diagnosis and especially for aortic root dilatation to rule out possibility of Marfan syndrome and other collagenopathy.

On ophthalmological evaluation, she had bilateral high myopia with best-corrected visual acuity in right eye: 6/18 (−25.00/−3.00 × 35) and left eye: 6/18 (−25.00/−3.00 × 35). Intraocular pressure (IOP) using an Icare tonometer in right eye was 15 mmHg and left eye was 17 mmHg. Anterior segment evaluation showed bilateral deep anterior chamber, iridodonesis, and mild nasal subluxation of a spherical and clear lens in both eyes. Fundus evaluation showed normal-sized discs with cup-to-disc of 0.6, normal foveal reflex, tessellated retina with peripheral areas of lattice degeneration. These findings were suggestive of high myopia, bilateral mild lens subluxation (ectopia lentis), and early changes of retinal degeneration. In view of short stature and high myopia with bilateral ectopia lentis, she was suspected to have WMS and was evaluated for the same.

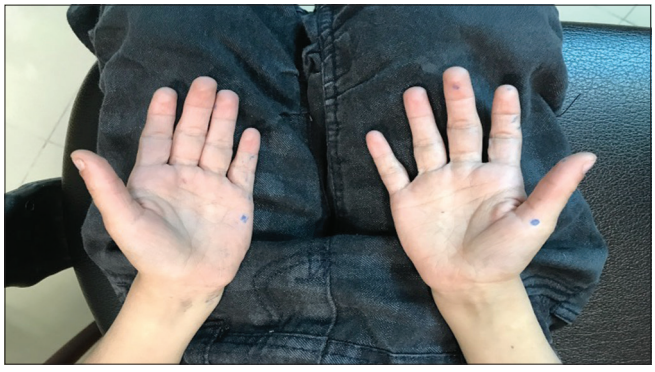

Figure 1: Showing brachydactyly

Management and outcome

Clinical exome sequencing study identified a heterozygous variant in exon 20 of FBN1 gene (c.2413T > C; p.C805R; NM_000138.4) confirming the diagnosis of AD, WMS 2. This variant has been previously reported in a patient with congenital ectopia lentis.[7] It is classified as likely pathogenic by revised ACMG criteria (PM1+PM2+PM5+PP2+PP3). The proband has been prescribed a trial of contact lenses. The child is under follow-up to watch for further signs of lens displacement, to monitor IOP and do lens removal to prevent glaucoma, in case of any progression of symptoms. WMS is a multisystem disorder where, apart from short stature (100%), intellectual disability (11%–17%), and brachydactyly which were present in index case; cardiac anomalies are an important feature. The spectrum of cardiac anomalies includes patent ductus arteriosus, mitral valve prolapse, pulmonary, and aortic stenosis. These were ruled out by normal echocardiography.

Discussion

Bilateral ectopia lentis has been associated with genetic conditions such as Marfan syndrome, WMS, homocystinuria, Ehler-Danlos syndrome (EDS), hyperlysinemia, and sulfite oxidase deficiency.[8] Marfan syndrome and homocystinuria are usually associated with a thin tall stature and arachnodactyly, whereas EDS usually has joint laxity as a characteristic feature. Hyperlysinemia and sulfite oxidase deficiency present with intellectual disability and seizures as main manifestations. The presence of cardinal features of short stature, brachydactyly, high myopia, and bilateral ectopia lentis narrowed the diagnosis to WMS in the index case which was later confirmed by genetic testing.

WMS is a disorder with distinctive skeletal and ocular manifestations. Ocular complications such as high myopia, ectopia lentis, glaucoma, and optic neuropathy due to chronic elevation of IOP are the cause of main morbidity associated with this disorder.[2] Weakened zonular fibers and microspherophakia predispose to lens displacement, more commonly in nasal and downward direction as in index case. Glaucoma occurs secondary to displacement of lens into the anterior chamber of the eye and resultant pupillary block and angle closure.[1,5] Furthermore, these patients develop central corneal thickness with age which can further increase the IOP.[2] Retinal degenerative changes as in our case can be seen secondary to high myopia.[2,5]

Most of the patients with WMS have high myopia for many years and present late with complications because of

unawareness about this condition among the physicians. The rate of legal blindness, defined as a visual acuity of 20/200 or less in the better eye with best correction, is approximately 30%.[9] Glaucoma is seen in nearly all the patients by the fourth decade[9] which underscores the importance of early diagnosis and genetic testing in these patients.

There are no universally accepted treatment guidelines for the treatment of ectopia lentis and glaucoma in WMS. Regular surveillance is recommended and can be individualized for each patient depending on his clinical features. Removal of abnormally small lens is usually required to control the IOP. In cases of advanced glaucoma, combined lens extraction and trabeculectomy may be required.[9] The index case has been prescribed contact lenses. She is under regular follow-up for increase in IOP and signs of lens displacement. We plan a surgical intervention in case of any further progression of symptoms. Important thing to note in these patients is that miotic and mydriatics should be avoided as they can precipitate glaucoma due to induction of pupillary block.[5]

Short stature is a consistent finding seen in nearly all the affected individuals with a reported average height of 130–157 cm in females with WMS.[1] The other important musculoskeletal features which aid in the early diagnosis are brachydactyly with short metacarpals which was seen in index case.

Intellectual disability has been reported in 11%–17% cases with WMS and is always mild in nature.[1] The index child had borderline intelligence with poor scholastic performance.

Although many cases of WMS have been reported from India, but without confirmed molecular diagnosis. This case also highlights the variable clinical expressivity of *FBN1*-related disorders. In a previously reported patient with this pathogenic variation in *FBN1* gene, the clinical phenotype was of congenital ectopia lentis in contrast to complete clinical phenotype of WMS as seen in our case.[7] Furthermore, in our case, as there was consanguinity, we suspected AR WMS but genetic analysis showed an inheritance of AD variety of WMS. Clinical distinction between AR and AD forms of this disease has not been possible till now.[6] In familial cases, AD WMS shows complete penetrance with variable expression.[1] The need of further genetic studies has been counseled and emphasized to the parents.

WMS is a multisystemic disease affecting predominantly eyes, bone and joints, height, and skin. The combination of short stature and myopia should prompt for an early evaluation. Early suspicion and surgical intervention scan avoid complications of glaucoma and blindness. Molecular genetic testing is important for proper patient management and counseling as well as screening of other family members to avoid recurrence.

Lessons learnt

- Proportionate short stature with high myopia at an early age must always be evaluated to rule underlying genetic etiology like WMS which requires more vigilant monitoring and follow-up
- Early diagnosis and genetic studies help in planning ocular surveillance and prevent fearful complication of glaucoma and blindness
- This case reiterates the point that the presence of consanguinity does not automatically transcribe into an AR disorders and that an AD disorders should also be considered, depending upon the phenotype of the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

False Negative Critical Congenital Heart Disease Screening Result Arising from a Complex Cardiac Disease with Duct Dependent Systemic Circulation

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Abstract

Background: Critical congenital heart disease (CCHD) encompasses congenital structural heart defects that cause significant morbidity and mortality in the first few weeks of life unless treated and/or require surgery or catheter intervention within the 1st year of life. Since these deteriorate acutely due to their cardiac condition, they may be misdiagnosed as septicemia or perinatal asphyxia, especially in resource-poor settings. The American Academy of Pediatrics recommends universal screening with pulse oximetry after 24 h of life by a simple screening protocol. Although specificity is high, CCHD may be missed. We present a case who screened negative became symptomatic on day 10 of life and was finally diagnosed with a CCHD. **Clinical Description:** A full-term baby with uneventful postnatal course and negative CCHD screening was discharged on day 2 of life. He returned on day 10 with cardiogenic shock. Echocardiography confirmed interrupted aortic arch with large ventricular septal defect (VSD), moderate-sized atrial septal defect (ASD), and a small, restrictive patent ductus arteriosus (PDA). The initial false-negative result was attributed to the presence of large VSD that leads to equalization of preductal and postductal oxygen saturations. **Management:** The baby was stabilized with prostaglandin infusion and ventilatory support. He underwent staged repair with end-to-end anastomosis of interrupted segment and PDA ligation in the first sitting. The postoperative course was uneventful, and the patient was discharged home at day 25 of life. He is planned for VSD and ASD repair in follow-up. **Conclusion:** Complex heart diseases may behave unusually due to complicated inter-related hemodynamics arising from the various lesions. Primary health-care personnel should recognize the limitations of CCHD screening protocol and learn to counsel parents accordingly.

Keywords: Critical congenital heart disease screening, duct-dependent systemic circulation, pulse oximetry

Congenital heart disease (CHD) is the most common defect identified at birth, with a reported incidence of 7–8/1000 live births.[1,2] Critical CHD (CCHD) encompasses congenital structural heart defects that cause significant morbidity and mortality in the first few weeks of life unless treated and/or require surgery or catheter intervention within the 1st year of life.[3] The incidence of CCHD is reportedly 2–3/1000 live births[1] and causes 30%–50% mortality due to birth defects. Clinically, these present as hypoxemia in the early neonatal period. Causes of CCHD are usually patent ductus arteriosus (PDA) dependent structural anomalies which present with cardiovascular collapse, acidosis, and death within the first few days of life, parallel to the closure of the PDA. Mortality is preventable if timely identification is made, and reconstructive surgery is undertaken.

The American Academy of Pediatrics has recommended universal screening of newborns by pulse oximetry to rule

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out CCHD at 24 h of life or as late as possible if the discharge is before 24 h.[4] Oxygen saturation in the right upper limb and lower limb is measured simultaneously. A baby passes the screen (negative screen) if the oxygen saturation measurement is ≥95% in the right hand or foot with an absolute difference ≤3% between the right hand and foot. The screen is considered failed (positive screen) if any oxygen saturation measurement is <90%. If the oxygen saturation is between 90% and 95%, or if absolute difference is >3%, the measurement is repeated after an hour. The baby fails if the same findings are present on three serial measurements, each separated by 1 h. This protocol is simple, cost-effective and can be performed by any trained health-care worker.[5] It is possible for a child who has passed the screen to still have a CCHD and also for a baby who has failed the screen to not have a CCHD. We report a case of a baby in whom a CCHD was missed, despite performing a pulse oximetry test, and explain the underlying pathophysiological reasons for this.

Clinical Description

A full-term male infant was born to a second-degree consanguineous, booked, and immunized primigravida mother with birth weight of 3.5 kg by a spontaneous vaginal delivery. Apgar score was normal. The antenatal period had been uneventful. At birth, the vital parameters were normal. The physical examination was unremarkable, with no cyanosis, or external congenital anomalies. The baby was shifted to the mother and breastfeeding initiated. The CCHD screening protocol was performed at 24 h of life. The baby passed as the oxygen saturation levels were >95% in both the right upper and lower limbs. Urine and meconium were passed normally. The baby was discharged at 48 h of life after undergoing a routine physical evaluation.

On day 10 of life, the baby presented to emergency with a history of poor feeding, lethargy, and abnormal breathing for 12 h. Before that, the baby had been well and on exclusive breastfeeds. There was no history of fever, vomiting, or diarrhea. The baby was in shock with respiratory distress (respiratory rate = 70–75 breaths/min) but normothermic and euglycemic. The arterial blood gas analysis revealed severe metabolic acidosis (pH 6.9) with HCO_3 – 12 mmol/L, Base excess - "-23 mmol/L", and lactate – 18 mmol/L. Shock was managed as per protocol until perfusion stabilized with epinephrine infusion. Mechanical ventilation was started. After stabilization, clinical examination revealed absent lower limb pulses and differential blood pressure (BP) in all four limbs with a clinical gradient of 40 mmHg between the upper and lower limbs (right upper limb – 110/77 mmHg, left upper limb – 98/60 mm Hg, left lower limb – 70/65 mmHg, and right lower limb – 72/64 mmHg). The apex beat was in the left 5th intercostal space, 0.5 cm lateral to the midclavicular line. The rest of the cardiovascular and respiratory examination was normal. There was no hepatomegaly. The chest radiograph showed cardiomegaly with pulmonary plethora. Electrocardiogram was unremarkable apart from sinus tachycardia (180/min). Complete blood counts were within normal limits. Biomarkers of acute infection (C-reactive protein and procalcitonin) were negative. Liver function and kidney function tests were normal.

The clinical phenotype of cardiogenic shock with differential BP in the manifesting in the 2nd week of life was suggestive of a CCHD with involvement of the duct-dependent systemic circulation. Echocardiography clinched the final diagnosis; an interrupted aortic arch (IAA) with a tiny PDA that was supplying the descending aorta, transverse arch hypoplasia, large ventricular septal defect (VSD), moderate atrial septal defect (ASD), dilated right ventricle, and biventricular dysfunction [Figure 1a].

Management and outcome

Prostaglandin infusion (0.05 mcg/kg/min) was started immediately that resulted in improvement in lower limb perfusion and BP. A continuous PDA murmur now became audible in the left 2nd intercostal space. Repeat echocardiography after 12 h showed increase in the size of the PDA and improved biventricular systolic function [Figure 1b]. Computerized tomography angiography confirmed echo findings and displayed crisscross origin of the pulmonary arteries. The brachiocephalic artery, left common carotid artery, and left subclavian artery emerged in the proximal part of the aortic arch before interruption [Figure 2a and b]. Over the next few days, the baby was weaned off ventilatory and inotropic support. On the 20th day of life, he underwent an end-to-end anastomosis of the IAA along with PDA ligation [Figure 3a and b]. The postoperative course was uneventful, and the baby was discharged within a week. The echocardiogram showed a good-sized reconstructed arch with

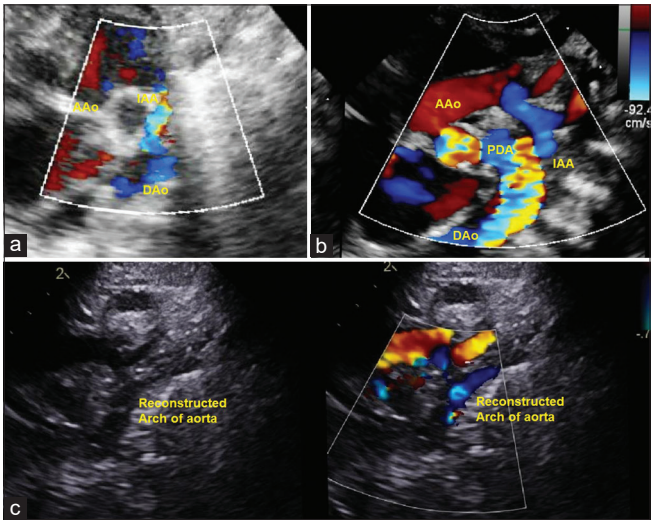

Figure 1: (a) Two-dimensional echocardiography with color Doppler showed interrupted aortic arch with segment after interruption supplied by flow from a tiny patent ductus arteriosus; (b) 12 h after starting prostaglandin echocardiography showed large patent ductus arteriosus continuing as descending aorta; (c) reconstructed aortic arch after surgical correction. (AAo: Ascending aorta, DAo: Descending aorta, IAA: Interrupted aortic arch, PDA: Patent ductus arteriosus)

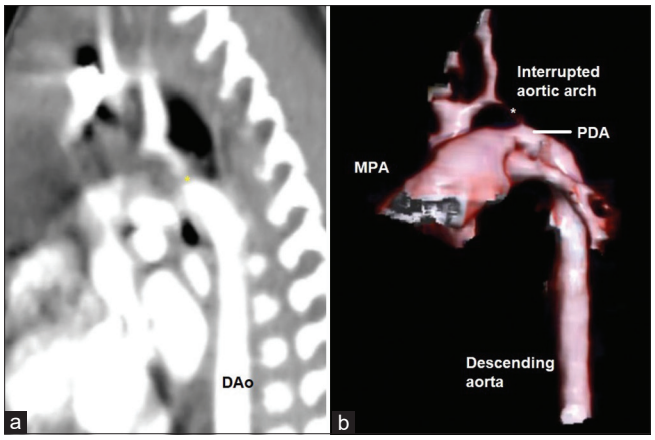

Figure 2: (a) Two-dimensional computerized tomographic aortogram (sagittal view) showing interrupted aortic arch; (b) three-dimensional volume-rendered image (anterior view) showing interrupted aortic arch and patent ductus arteriosus continuing as descending aorta. (* - location of aortic arch interruption, DAo: Descending aorta, MPA: Main pulmonary artery, PDA: Patent ductus arteriosus)

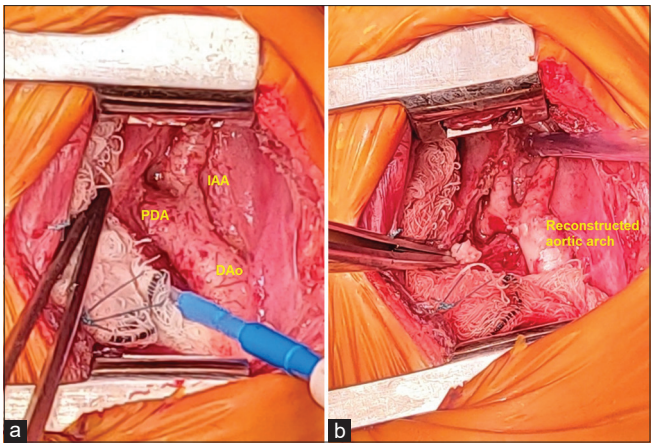

Figure 3: (a) Left thoracotomy preoperative image showing thread-like interrupted segment and large patent ductus arteriosus continuing as descending aorta (b) Left thoracotomy postoperative image showing good-sized reconstructed aortic arch with neck vessels (DAo: Descending aorta, IAA: Interrupted aortic arch, PDA: Patent ductus arteriosus)

unobstructed blood flow and no residual PDA [Figure 1c]. The VSD and ASD repair has been planned in the follow-up within the next few months.

Discussion

Screening for CCHD means early detection and planned elective surgical management. A combination of antenatal ultrasound with postnatal physical examination misses CCHD in one-third babies.[6] Prenatal detection rates are lower in low- and middle-income countries due to limited resources and as many mothers do not receive proper antenatal care.[7] CCHD screening with pulse oximetry can prevent this common cause of neonatal mortality.[4]

The sensitivity of CCHD screening is 77%, while the specificity is 98%.[5,8,9] These values can increase further if pulse oximetry is combined with an antenatal ultrasound and a postnatal physical examination.[8] There are many case reports describing false-positive results, but few reporting false-negative ones.[5,7,10] This is probably because false-positive cases get evaluated during hospital stay, whereas false-negative screens get discharged. They may go unreported due to acute deterioration and expiry at home, or being mis-diagnosed as septicemia, especially in low- and middle-income countries where access to echocardiography and pediatric cardiology facilities is limited.

CCHD screening works on the principle of identifying systemic desaturation or differential saturation in upper and lower limbs. Once detected, a detailed evaluation by pediatric cardiologists and cardiac-directed investigations are warranted. Hoffman described anomalies that are missed by pulse oximetry; very small right to left shunt, CCHD with relatively high cardiac output and high mixed venous saturation, and those without systemic desaturation.[10]

Although this infant had an IAA with duct-dependent systemic circulation, no upper and lower limb discrepancy in oxygen saturation was found. The baby escaped detection by the CCHD screening and customary neonatal examination before discharge, probably due to the following reasons: first, the large size and nonrestrictive nature of the VSD resulted in mixing of oxygenated and deoxygenated blood and thus increased the oxygen saturation of right ventricular blood that was being pumped into the descending aorta through the ductus arteriosus. The upper limbs received blood from left ventricle through the ascending aorta and the lower limbs received mixed blood through the PDA. This probably resulted in equalization of upper and lower limb oxygen saturation. Second, the large PDA resulted in the equal upper and lower limb BP. Third, a cardiac murmur was not heard due to the combination of a large VSD and large PDA.

IAA is one of the main CCHDs for which CCHD screening was devised. A difference in upper and lower limb saturation is the clinical alert for suspecting its presence. It is important to emphasize that complex CHDs although described individually in literature are in actuality a constellation of separate independent lesions that may not fit into the predefined expected clinical repertoire. A clinician who practices universal CCHD screening must be cognizant of its intrinsic limitations and be able to counsel parents regarding the screening results accordingly.

Lessons learnt

- Complex CHDs are combination of different independent lesions that may display unusual hemodynamics and clinical manifestations
- Care provider practicing universal CCHD screening should be aware of basic cardiac physiology and hemodynamics for understanding and interpreting CCHD screening results
- Care provider should know the limitations of CCHD screening protocol.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Congenital Hyperinsulinism: A Case Report and Challenges in Management

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Abstract

Background: Congenital hyperinsulinism (CHI) is a rare condition that usually presents in the newborn period. It is characterized by hypoketotic hypoglycemia due to excessive insulin secretion. We describe below a case of CHI due to a paternally inherited mutation of the ABCC8 gene and the challenges in its management. **Clinical Description:** A term female appropriate for gestational age baby with an uneventful antenatal period and delivery presented at 46 h of life with fever, decreased oral acceptance, lethargy, and hypoglycemic seizures. On examination, the baby was febrile but hemodynamically stable with no other clinical evidence of sepsis. **Management:** Child had recurrent episodes of hypoglycemia and required a glucose infusion rate of 12 mg/kg/min for maintaining euglycemia. The baby required diazoxide and octreotide for maintaining euglycemia. The hypoglycemia was nonketotic and associated with hyperinsulinism. 18-fluoro-dihydroxyphenylalanine positron emission tomography-computerized tomography scan showed diffuse uptake in the pancreas suggestive of diffuse hyperinsulinism. However, genetic testing showed heterozygous mutation for paternally transmitted pathogenic ABCC8 splicing variant. The child was stabilized and discharged on oral diazoxide and long-acting octreotide. **Conclusion:** CHI is an important cause of persistent hypoglycemia in neonates. Early diagnosis and management are important to prevent long-term sequalae. Establishing a correct molecular diagnosis is essential to decide about appropriate line of management (surgical/conservative) and provide genetic counseling to the family.

Keywords: Hyperinsulinism, neonate, octreotide, refractory hypoglycemia

Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoketotic hypoglycemia in neonates and infants.[1] The clinical manifestations of hyperinsulinism are due to hypoglycemia and include features such as floppiness, jitteriness, poor feeding, lethargy, irritability, and later as seizures, coma, and even neonatal death. Timely identification of hypoglycemia and its cause and initiation of treatment are essential to prevent neurological complications and long-term neurodevelopmental deficits.[2]

This case report describes the challenges faced in the diagnosis and management of CHI such as need for nuclear radio imaging such as18-fluoro-dihydroxy phenylalanine (18F-DOPA) positron emission tomography-computerized tomography (PET-CT) scan and genetic tests to determine etiology. Along with intensive clinical monitoring, transfer of care to parents before discharge is an important part of management. CHI due to monoallelic paternally transmitted recessive KATP pathogenic variant (ABCC8 splicing) predicts focal hyperinsulinism with 97% sensitivity and 90% specificity.[3] This case was unique as baby had a diffuse insulinoma on PET scan which changed the line of management from surgical to medical conservative therapy.

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Clinical Description

A female baby was born out of nonconsanguineous marriage to 26-year-old primigravida at 38 weeks of gestation. The antenatal period was uneventful with no history of drug intake during pregnancy. The child was delivered vaginally with APGAR score of 8, 9. Baby was appropriate for gestational age with birth weight of 3000 g and age-appropriate length and head circumference. She had normal systemic

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examination with no apparent congenital abnormalities at birth. Baby started taking breast feeds soon after birth. Baby was well till 46 h of life when she presented with complaints of fever (38.5°C), decreased oral acceptance, lethargy, and one episode of seizure in the form of uprolling of eyeballs and tonic–clonic movements. On examination, the baby was hemodynamically stable, febrile (38.5°C), and hypoglycemic (37 mg/dL). Keeping a provisional diagnosis of early onset sepsis, sepsis screen, and lumbar puncture were done which showed no evidence of sepsis or meningitis. Ultrasound cranium was normal.

Management and outcome

The baby was given a bolus of 10% intravenous dextrose and started on glucose infusion rate (GIR) @6 mg/kg/min which had to be gradually increased to a GIR of 12 mg/kg/min in view of recurrent episodes of hypoglycemia on lower GIRs. Whenever GIR was stepped down and oral feeds were started, baby had episodes of hypoglycemia. In view of persistent hypoglycemia, differential diagnosis of inborn errors of metabolism such as galactosemia, causes of hyperinsulinism, endocrine disorders such as hypopituitarism and adrenal insufficiency were kept, and further workup was done.

Critical samples at the time of hypoglycemia were negative for plasma ketones and showed hyperinsulinism (insulin = 3.2 uIU/mL). Metabolic workup including lactate, ammonia, urine for reducing substances, tandem mass spectroscopy, gas chromatography–mass spectrometry, and Galactose-1-Phosphate Uridyltransferase (GALT) assay were within normal limits. Cortisol, thyroid profile, and growth hormone levels were normal. Glucagon challenge test showed a glycemic response of >30 mg/dL on administration of 0.03 mg/kg of glucagon injection intravenously which supported the diagnosis of hyperinsulinism. The baby was given oral diazoxide at 5 mg/kg/day in three divided doses which was gradually increased to 15 mg/kg/day to maintain blood sugars. As sugars could not be controlled on the same, injection octreotide was introduced at 10 mcg/kg/day and increased to 20 mcg/kg/day every 6 hourly. Once blood sugar levels were stabilized on injection octreotide, diazoxide was stopped. In view of labile blood sugar levels even on diazoxide, nuclear imaging and genetic studies were planned.

18F-DOPA PET-CT scan showed diffuse uptake in the pancreas suggestive of diffuse hyperinsulinemia. Genetic studies done on child and parents using next-generation sequencing – targeted (tNGS) gene panels showed a heterozygous pathogenic mutation for a paternally inherited pathogenic ABCC8 splicing variant [Figure 1]. Sequence analysis includes the coding exons and flanking intronic regions (50 bp upstream–10 bp downstream of each exon). Confirmation of mutations identified by tNGS is undertaken by Sanger sequencing. Both the parents were fine and did not have any significant history of similar illness.

Magnetic resonance imaging Brain done at 1 month of age showed cystic encephalomalacia with surrounding gliosis in bilateral parieto-occipital lobes and frontal lobes suggestive of brain injury due to hypoglycemia.

Final diagnosis was made as congenital diffuse hyperinsulinism with paternally inherited pathogenic heterozygous ABCC8 splicing variant mutation with neonatal hypoglycemic brain injury.

Once the baby was able to maintain blood sugar levels (till 4–5 h postinjection) on subcutaneous injections of octreotide, the mother was taught to monitor blood glucose by glucometer and technique of giving octreotide injection subcutaneously. Baby was discharged on monthly intramuscular injection of 2 mg Octreotide long-acting Release (LAR). Parents were counseled regarding frequency of feeding, daily home blood glucose monitoring, medicine delivery, and possible side effects of hypoglycemia or infection at home. Baby was followed up till 9 months of age when she was maintaining euglycemia on the same. She had started sitting without support, developed stranger anxiety, and able to speak bisyllables with palmar grasp present. Hearing and vision were normal. Baby's weight and length were 7.5 kg, 67 cm, respectively (appropriate as per the WHO growth charts) at 9 months of age.

Discussion

CHI in young infant usually results from inappropriate, excessive secretion of insulinor deficiency of one of the hepatic glucoregulatory enzymes. CHI may have devastating consequences in this age group and demands early recognition and effective treatment. Signs and symptoms are mostly nonspecific such as lethargy, poor feeding, jitteriness, apnea, and seizures, but the associated hypoglycemia can be easily diagnosed with a glucometer. The challenge lies in maintaining euglycemia, which requires very high GIR. The diagnosis of CHI is suspected if there is the presence of persistent/recurrent hypoglycemia on a GIR >8 mg/kg/min. Increased levels of serum insulin and/or serum c-peptide levels at the time of hypoglycemia are diagnostic of CHI. Glucagon challenge test supports the diagnosis. The goal of management is to maintain euglycemia to prevent brain damage and sudden deaths due to hypoglycemia. The recommended levels of blood glucose level

Variant details

Gene	Zygosity	Inheritance	HGVS description	Location: GRCh37 (hg19)	Classification
ABCC8	Heterozygous	Paternal	NM_001287174.1:c.3871-1G>A, p.(?)	Chr11:g.17418861	Pathogenic

Figure 1: Details of genetic mutation

for babies with suspected CHI is >3.9 mmol/L (70 mg/dL).[4] Medical management consists primarily of frequent feeding, nasogastric feeding may be required to be given by infusion and highintravenous GIR to maintain blood sugar levels.[5] The main drugs for treatment are diazoxide (a potassium ATP channel agonist), octreotide (somatostatin analog), glucagon, glucocorticoids. Diazoxide keeps K_{ATP} channel found across cell membranes in the beta cells of the pancreas open, thereby inhibiting insulin secretion. The dose of diazoxide used is 5–20 mg/kg/day 8 hourly. Octreotide causes activation of somatostatin receptors 5, stabilizes K_{ATP} channel, and inhibits calcium channels, thereby inhibiting insulin release. Dose used is 5–25 mcg/kg/day subcutaneous injections three or four times a day. Glucagon injections (0.5–1 mg, subcutaneous) in episodes of acute symptomatic hypoglycemia or as a continuous intravenous infusion @ 1–20 mcg/kg/h for short-term maintenance of glucose levels along with octreotideare also used.

CHI has a strong genetic basis and mutations in the key genes (ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, HNF4A, HNF1A, and UCP2) regulating insulin secretion have been identified.[6] The ABCC8 gene provides instructions for making the sulfonylurea receptor 1 protein, subunit of the K_{ATP} channels found across cell membranes in the beta cells of the pancreas. The K_{ATP} channel controls the secretion of insulin from beta cells into the bloodstream. Recessive inactivating mutations in ABCC8 and KCNJ11 genes, which alter the function of K_{ATP} channels causing unregulated insulin secretion unresponsive to diazoxide, are the most common causes of severe CHI found in 50% of the patients.[5] CHI can be focal, diffuse, or atypical but clinically indistinguishable.[7] Confirmed cases of CHI can be differentiated into focal and diffuse forms using 18F-DOPA-PET scan.

CHI with a paternally inherited heterozygous mutation mostly suggests focal hypersecretion of insulin.[3] On review of literature, very few case reports with similar associations were found; however, none of them was reported from India.[8-10]

Follow-up of all cases should be done to look for any neurodevelopment delay, cerebral palsy, epilepsy, vision issues, and to initiate early intervention. Genetic counseling is an important part of management. It includes genetic testing of both the parents and discussion about the risk of recurrence and need for prenatal testing in future pregnancies.

Early and prompt diagnosis of CHI with aggressive management to maintain euglycemia is crucial for an intact survival of baby. Genetic studies especially in babies unresponsive to diazoxide therapy are important in finding out the mutations and genetic defects. These help in decision of definitive management and counseling of the parents for prognosis of this baby as well as for future pregnancies.

Lessons learnt

- CHI is a rare but important cause of refractory hypoglycemia in neonates and infants
- Somatostatin analogs may be required to maintain euglycemia in these patients. And long-acting somatostatin analogs can be used for management at home
- Nuclear radio imaging and genetic tests are important for diagnosis, providing management options and for genetic counseling.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Fructose 1,6 Bisphosphatase Deficiency Mimicking Glycogen Storage Disease as Recurrent Hypoglycemia

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Abstract

Background: Fructose 1,6 Bisphosphatase (FBPase) deficiency is a rare and treatable cause of ketotic hypoglycemia in children. Affected children present in the postneonatal period with recurrent episodes of early morning hypoglycemia typically triggered by an infection. We present a child with recurrent hypoglycemic seizures who was initially considered as glycogen storage disease (GSD) type 1, but on further evaluation, was diagnosed with FBPase deficiency. **Clinical Description:** A 2.5-year-old developmentally normal boy presented with the second episode of hypoglycemic seizure. He had a similar episode following a fasting time of 10 h at 2 years of age. Critical sample analysis revealed ketosis, lactic acidosis, hyperuricemia, and raised triglycerides. He was diagnosed with probable GSD type 1. At 2.5 years of age, he had another episode of hypoglycemic seizures following a similar fasting spell, and critical sample evaluation revealed similar findings. However, he did not have the classical cherubic facies associated with GSD type 1, and a repeat ultrasound abdomen showed normal-sized liver. **Management:** The clinical presentation and critical sample evaluation were suggestive of gluconeogenesis defect. However, the child did not have any other end-organ involvement. Hence, a possibility of FBPase deficiency was considered. The genetic testing confirmed compound heterozygous mutations involving the FBP1 gene. **Conclusion:** Fructose 1,6 bisphosphonate deficiency is a close mimicker of GSD 1.

Keywords: Fructose 1,6 bisphosphatase deficiency, gluconeogenesis defect, glycogen storage disease 1, recurrent hypoglycemia

Hypoglycemia in children is a heterozygous condition with different possible etiologies. Thorough clinical examination with analysis of critical samples is essential to clinch the diagnosis. Despite this, there is considerable overlap in clinical presentation between the various etiologies that pose challenges in making an accurate diagnosis. We present a child with recurrent ketotic hypoglycemia, initially suspected to have glycogen storage disease (GSD) type 1, where genetic evaluation revealed fructose 1,6 bisphosphatase (FBPase) deficiency.

Clinical Description

Two and half-year-old developmentally normal boy, firstborn to nonconsanguineous marriage, was admitted and evaluated elsewhere for early morning hypoglycemic seizure at the age of 2 years. Critical sample analysis revealed elevated lactate, uric acid, and triglycerides with 2+ urine ketones. Ultrasound abdomen showed enlarged liver with altered liver echotexture. He was diagnosed with probable GSD type 1, and his parents were counseled regarding the same. Further evaluation was not done as parents could not come following COVID 19 pandemic-associated lockdown.

Management and outcome

Six months later, he presented to our hospital with a second episode of early morning hypoglycemic seizures following approximately 10 h of fasting. A dietary history revealed that he was on exclusive breast feeds till 6 months of age following which weaning was started. He was a strict vegetarian with a preference for sweets and fruits and had his regular meal the night earlier with an extra half apple. On examination, his anthropometric measurements were normal and he did not have the cherubic facies typically observed in

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GSD. There was no hepatomegaly, and his external genitalia was normal. Critical sample evaluation revealed similar findings: ketosis, lactic acidosis, hyperuricemia, and normal A repeat ultrasound abdomen revealed a normal-sized liver without any altered echoes. The occurrence of recurrent early morning hypoglycemia with ketosis, lactic acidosis, and hyperuricemia suggested a disorder of gluconeogenesis, the most common of which is GSD type 1. However, without the classic cherubic facies, hepatomegaly, or any other end-organ involvement, the possibility of FBPase deficiency was considered. A molecular genetic evaluation revealed a compound heterozygous missense mutation of the FBP1 gene (c. 841G>A p. Glu281 Lys and c.472C>T p. Arg158Trp) gene, which was reported as pathogenic for FBPase deficiency. Parents were counseled to avoid a fructose-rich diet and advised to undergo sanger sequencing for risk stratification for the next pregnancy.

Discussion

In otherwise healthy children, dietary glucose utilization takes over 3–4 h after a feed[1]. Any starvation beyond this causes a fall in insulin levels and a rise in counter-regulatory hormones such as glucagon, cortisol, and growth hormone. This causes a switch from glycolysis to glycogenolysis and gluconeogenesis, which maintains glucose levels in the serum. Thus, GSDs and disorders of gluconeogenesis present during the postneonatal period when infants are exposed to prolonged fasting of 3–6 h.

Gluconeogenesis is the reverse reaction to glycolysis which involves the synthesis of glucose from the various substrate (pyruvate, lactate, glycerol, and gluconeogenic amino acids). Disorders of gluconeogenesis include GSD type 1, pyruvate carboxylase deficiency, phospho-enol-pyruvate carboxykinase deficiency, and FBPase deficiency. Gluconeogenesis mainly occurs in the liver and kidneys, and some of these disorders result in the accumulation of toxic metabolites resulting in liver and kidney injury[2].

FBPase is a critical enzyme in gluconeogenesis. It catalyzes the conversion of fructose 1,6 bisphosphate to fructose-6-phosphate[2]. FBPase deficiency is a rare autosomal recessive disease with an estimated incidence between 1/350,000 and 1/900,000[3]. Children present with recurrent hypoglycemia with lactic acidosis, triggered by prolonged fasting or an intercurrent illness. These children develop hypoglycemia following a fructose-rich diet. This is because of the accumulation of fructose-1-phosphate in the liver, which inhibits glycogen phosphorylase[2]. Hypoglycemic episodes can rarely present in the neonatal period, as neonates have lower glycogen stores, but commonly occur in older infants[4]. These episodes are associated with hyperventilation, tachycardia, and seizures. Our child had a normal neonatal period and infancy, with the first symptoms occurring at 2 years. Like other gluconeogenetic defects, critical sample evaluation reveals ketosis, lactic acidosis, hyperuricemia, pseudo hypertriglyceridemia (due to elevated glycerol) with appropriately suppressed insulin and elevated levels of counter-regulatory hormones. Treatment is tailored to the prevention of hypoglycemia. This includes dietary restriction of fructose and sorbitol and intake of uncooked starch to maintain fasting sugar levels. This is especially important during intercurrent illness as the overall intake is reduced[5]. Dietary restrictions include a reduction in the number of fruits such as apples, apricots, bananas, processed dates, grapes, and raisins. All commercially available ready-to-eat foods such as jams, jellies, hard-boiled candies, chocolates, sweetened yogurt, bakery items, breakfast cereals, energy drinks, and bottled juices/sodas should be avoided as well. Medications in syrup formulation should be avoided as there have been case reports of hypoglycemic episodes triggered by fructose-sweetened syrups[6]. Differential diagnoses include gluconeogenesis defects such as GSD-1, pyruvate carboxylase, and phosphor enoyl pyruvate carboxykinase deficiency as well as mitochondrial disorders, all of which will present with ketotic hypoglycemia and lactic acidosis. Unlike those diseases, children with FBPase deficiency do not have end-organ involvement[2]. Previous case reports have also noted its similarity in presentation between with GSD 1[7,8]. Children with FBP1 deficiency can have mild transient hepatomegaly during the metabolic crisis, in contrast to GSD1 where they present with huge firm hepatomegaly. With proper prevention and management of hypoglycemic episodes, these children tend to have normal growth and development.

To conclude, FBPase deficiency can mimic GSD type 1 and should be considered in any child who presents with recurrent ketotic hypoglycemia with lactic acidosis. It is a benign disease without any end-organ involvement, and children have normal growth. Management typically involves long-term dietary modification. The long-term prognosis of FBPase deficiency is excellent, and preventive long-term dietary modification is recommended.

Lessons learnt

- FBPase deficiency is a close mimicker of GSD type 1
- It is a benign disease without any end-organ involvement, and children have normal growth. Managementtypically involves long-term dietary modification
- Syrup formulation contains fructose-based sweeteners and should be avoided in children with FBPase deficiency

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Splenic Abscess: A Rare Complication of Scrub Typhus in a Child

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Abstract

Background: Scrub typhus is endemic in the various parts of the world and especially in the Indian subcontinent. Splenic infarcts and abscess are largely unknown in scrub typhus. These can be a source of persistent abdominal pain in the left hypochondriac region. **Clinical Description:** A 9-year-old child presented with a 7-day history of fever, loose stools, respiratory distress, and abdominal pain. On examination, she was febrile, had tachypnea, tachycardia, pallor, and facial puffiness. Systemic examination showed pleural effusion and hepatomegaly. Acute febrile illness with third spacing led to differentials of tropical infections (dengue, scrub typhus, enteric fever, and malaria). **Management:** Dengue, enteric fever, and malaria were ruled out on investigations. Scrub IgM enzyme-linked immunosorbent assay was positive. Ultrasound of the abdomen showed multiple splenic anechoic lesions suggestive of abscesses. Contrast-enhanced computed tomography (CT) confirmed the findings. Ultrasonography-guided aspiration of the lesion revealed blood-stained pus. The gram stain was negative, and culture was sterile. The final diagnosis was scrub typhus with splenic abscess. Her symptoms resolved with doxycycline therapy. **Conclusion:** Involvement of the spleen resulting in infarct and abscess is a rare complication in scrub typhus and can lead to persisting abdominal symptoms. Splenic infarction is not a well-known complication in patients of scrub typhus; hence, it may lead to under diagnosis of the condition. An abdominal ultrasound or if required, CT scan of the abdomen might be needed in cases with persistent abdominal symptoms to rule out this rare complication.

Keywords: Abscess, child, scrub typhus, splenic infarct

Scrub typhus is caused by a bite of trombiculid mite, and the causative agent is orientia tsutsugamushi. The disease in endemic in the Indian subcontinent and is prevalent in the months of June through November. If left untreated, the mortality rate of scrub typhus is about 30%.[1] The typical manifestation is multiorgan dysfunction secondary to endothelial damage. Involvement of the abdomen, liver, central nervous system, and respiratory system is well-known. The common abdominal imaging findings include hepatomegaly, splenomegaly, gall bladder wall thickening, and lymphadenopathy.[2] Splenic infarcts have been reported infrequently. These usually manifest as diffuse or left hypochondriac abdominal pain and are likely secondary to either direct invasion of the organisms or immune mediated vasculitis seen in scrub typhus and may get complicated by abscess formation. To the best of our knowledge, this is the first case report of scrub typhus with splenic abscess, which is one of the rare complications of scrub typhus.

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We report a case of scrub typhus in a child who presented with multi-organ involvement that resolved but was followed by persistent left hypochondriac pain. She was evaluated for the abdominal pain, and on abdominal ultrasonography (USG), multiple splenic infarcts with likely abscess formation of different sizes were detected.

Clinical Description

A 9-year-old girl presented with a history of high grade fever for 7 days, loose stools for 5 days, and increased respiratory rates for 3 days. She also had abdominal pain, which was dull

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aching and diffuse for 3 days with no aggravating or relieving factors. There was no history of cough, rash, vomiting, or decreased urine output. She was treated at a nearby local hospital conservatively with intravenous (IV) fluids for 3 days and was referred to our center when the respiratory distress worsened.

Vitals revealed fever (103°F), tachypnea, tachycardia, and normal blood pressure. In view of tachypnea with oxygen saturation in room air at 95%–96%, she was started on nasal prong oxygen. She had pallor, facial puffiness, pedal edema, and ascites. There was no lymphadenopathy, icterus, rashes, petechiae, or joint involvement. No eschar was found. Respiratory system examination showed dullness on bilateral inframammary and infra-axillary regions with decreased air entry suggestive of bilateral pleural effusion. On abdominal examination, she had hepatomegaly (3 cm below right costal margin in the mid-clavicular line) and no splenomegaly. The rest of the systemic examination was normal. Considering the clinical phenotype of an acute febrile illness with hepatomegaly and features of third spacing, the differential diagnoses of common tropical infections (enteric fever, scrub typhus, dengue, and malaria) were kept, and investigations planned accordingly.

Management and Outcome

Dengue fever was kept as the first differential diagnosis; however, the rapid test for IgM and NS-1 antigen was negative. The child had microcytic hypochromic anemia (Hb: 10.3 g/dL; no hemoconcentration) with thrombocytopenia (platelet count 34,000/mm^3) and leukocytosis (total leukocyte count 11400/mm^3; differential leukocyte counts P51, L43, M5, E1). Serum electrolytes (sodium: 140 mEq/L, potassium: 4.1 mEq/L, and chloride: 95 mEq/L) and transaminases (aspartate aminotransferase: 28 mg/dL, alanine aminotransferase: 17 mg/dL) were normal. Renal function test at admission was 17 mg/dL and serum creatinine 0.24 mg/dL. Enteric fever was excluded by sterile blood culture and negative Widal test. Malarial parasite smear was negative. IgM enzyme-linked immunosorbent assay for scrub typhus was positive (optical density >4). Scrub typhus polymerase chain reaction kit was not available at the time in our center.

At the time of admission, she was started on IV ceftriaxone and doxycycline along with other supportive measures. She became afebrile after 48 h of starting doxycycline, pleural effusion resolved, and she was made off oxygen support by day 6 of hospital stay. However, on day 7 of hospital stay, the child had abdominal pain predominantly in the left hypochondriac region. Physical examination was inconclusive. Ultrasound of the abdomen showed multiple well-defined anechoic lesions with internal echoes within, suggestive of abscesses in the spleen [Figure 1a and b]. Contrast-enhanced computed tomography (CT) image showed splenomegaly with peripheral wedge shaped as well as lobulated nonenhancing hypodense lesions of varying sizes within the splenic parenchyma [Figure 2].

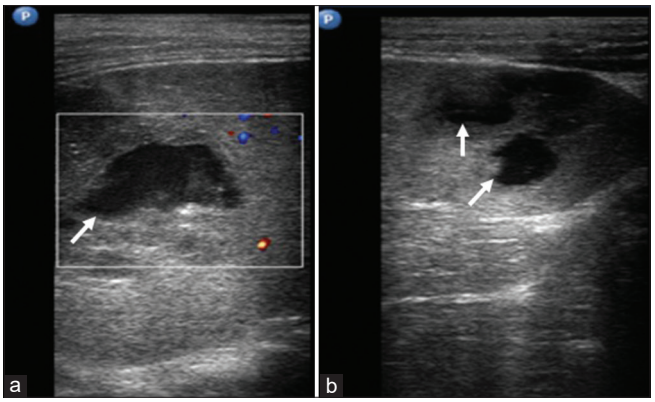

Figure 1: (a and b) Ultrasound of the abdomen showing multiple well-defined anechoic lesions with internal echoes within suggestive of abscesses

USG-guided aspiration of the lesions revealed blood-stained pus. The gram stain was negative, and culture was sterile. Doxycycline was given for 7 days and ceftriaxone for 14 days. At the time of discharge, the platelet count was 204,000/mm^3. The final diagnosis was scrub typhus with splenic infarcts and splenic abscess. At the time of discharge, she was symptom-free.

Discussion

Scrub typhus is one of the most common tropical infections in children and adults and one million new cases occur each year. It is estimated that 1 billion are at risk of contracting the infection.[3] The incubation period of scrub typhus is 10–12 days (range: 6–21 days). The symptoms most commonly include fever and rash with or without the characteristic eschar. Scrub typhus manifests with multiorgan involvement in some cases with myriad of symptoms. The complications of scrub typhus can be seen in almost all major organ systems and the associated findings, not limited to those mentioned, include: cardiovascular, respiratory, neurologic, gastrointestinal, renal injury, and complications such as hemophagocytic lymphohystiocytosis.[4]

Splenic abscesses are rare complication, and the exact incidence or prevalence is unknown. The autopsy reports of all age groups found prevalence to be around 0.05%–0.7%.[5] Splenic abscesses are usually seen with infective endocarditis, acquired immunodeficiency syndrome, diabetes mellitus, immune deficiencies, and others. The formation of splenic abscess in these conditions can be explained by septic embolization, splenic infarcts (secondary to vasculitis) as the starting point for abscess, and contagious spread from surrounding organs. Abscess development in a splenic infarct secondary to the generalized vasculitic processes seen in scrub typhus seems plausible. If left untreated, splenic abscess can lead to severe morbidity and mortality.[5] It is difficult to comment on the exact prognosis of splenic infarcts/abscess in scrub typhus as many cases probably go undetected. Abscess formation may lead to persistence of symptoms or occurrence of new

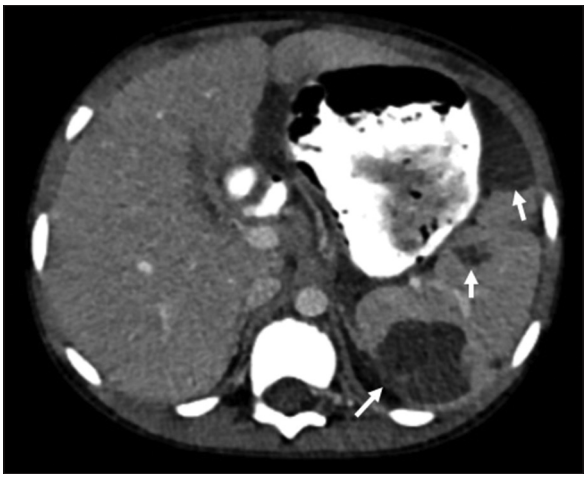

Figure 2: Contrast-enhanced computed tomography image of the abdomen shows splenomegaly with peripheral wedge shaped as well as lobulated nonenhancing hypodense lesions of varying sizes within the splenic parenchyma

symptoms. Antibiotics may be required for longer duration in the presence of abscess and the abscess may require drainage in some cases for symptom and source control. Ultrasound and computerized tomography scans are both sensitive modalities for the diagnosis of splenic infarcts and abscess, although both have a slightly lower specificity. The presence of liquid material inside the cavity characterizes necrosis or abscess formation. In this case, since the radiologist was unable to unequivocally characterize the lesions on USG, as they were multiple, we had to proceed with a CT scan.

Splenic infarcts have been mentioned as a presenting feature[6] or as a complication[7] of scrub typhus in isolated case reports.[2,6-12] A case report from South India of a 4-year-old girl who presented with acute febrile illness and encephalopathy showed the presence of eschar and splenomegaly.[12] USG abdomen showed fluid in the peritoneal cavity and multiple splenic infarcts which were confirmed on CT scan. The child was treated with anti-raised intracranial pressure measures, ceftriaxone, and doxycycline. She showed improvement in sensorium from day 4. The splenomegaly regressed and repeat USG abdomen was normal. A similar case from North India was reported in an 8-year-old boy who presented with acute febrile illness and had tachycardia and tachypnea at presentation. On examination, he had eschar on his inner thigh. He complained of persistent left hypochondriac pain and abdominal CT revealed splenic infarction. He was treated with doxycycline and his symptoms resolved.[11] A retrospective study by Park *et al*.[2] evaluated abdominal imaging findings in scrub typhus in 94 Korean patients presenting with abdominal complaints over 5 years (2008–2013). The findings in the descending order of frequency were as follows: enlarged lymph nodes (53.2%), hepatomegaly (47.9%), splenomegaly (46.8%), and ascites (28.7%). The prevalence of splenic infarction was only 6.4%. A similar study by Kim *et al*.[8] in 78 Korean patients revealed splenic infarcts in 3.8% patients. Both these studies were planned based on the imaging profile rather than the clinical profile, and neither included children. Thus, splenic infarcts and abscesses are rare complications in scrub typhus and can lead to persisting abdominal symptoms, particularly localized to the hypogastrium region. Abdominal imaging may be needed in these cases.

Lessons learnt

- Splenic infarct and splenic abscess are a rare complication of scrub typhus
- In case of left upper abdominal pain, an abdominal ultrasound or if required, CT scan of the abdomen might be needed to rule out this rare complication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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There are no conflicts of interest.

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Alopecia Areata during the Convalescent Phase of Kawasaki Disease

A 4-year-old boy presented with high-grade fever for a week and generalized rash for 5 days. Examination revealed cheilitis, a "strawberry" tongue, nonpitting edema over the dorsum of both hands, left anterior cervical lymphadenopathy, and an erythematous maculopapular rash on the trunk. There was no conjunctival injection. The child had anemia (hemoglobin: 8.9 g/L), leukocytosis (total leukocyte count: 27,000/L), thrombocytosis (850,000/L), and elevated values of erythrocyte sedimentation rate (60 mm in the 1st h), C-reactive protein (112 mg/dL), and pro B-type natriuretic peptide (5249 ng/ml, normal <194 ng/mL). Normal coronary artery *Z*-scores were reported on two-dimensional echocardiography. A diagnosis of Kawasaki disease (KD) was kept as four out of five diagnostic criteria were met. The child was started on intravenous immunoglobulin and aspirin as per protocol. He became afebrile within 24 h and was discharged on low-dose oral aspirin (3 mg/kg/day) on day 4. He presented at 4 weeks with patchy loss of hair since a few days. There was no history of self-mutilation. The nonscarring occipital scalp lesion was typical of alopecia areata [Figure 1a]. Common causes (hypothyroidism, autoimmunity, and tinea capitis) were ruled out. Beau's lines were also noted [Figure 1b]. Both were considered secondary to KD. The alopecia resolved within 2 months and the Beaus lines disappeared as the nails grew out.

KD is a medium-vessel vasculitis affecting young children.[1] It has been reported with autoimmune disorders such as celiac disease, autoimmune hemolytic anemia, and others. KD-associated alopecia has been reported in children previously: a 26-month-old boy with diffuse hair loss[2] and a 10-year-old boy with alopecia areata.[3] In both cases, the alopecia resolved with recovery from KD. Diffuse hair loss is often seen during acute stress or illnesses. This results in a large proportion of hair follicles rapidly converting from the anagen phase to the telogen phase (telogen effluvium) resulting in hair loss. This is often seen with the appearance of Beau's lines, which are nonspecific transverse grooves that develop within the nail plate. These may be due to a transient arrest of or dystrophic production of the nail matrix due to interference with the blood supply. High-grade fever and a variety of systemic, infectious (including KD) cutaneous disorders and medication may result in these.

Figure 1: (a) Alopecia areata over occipital area in the index patient noted at 4 weeks after discharge. (b) Beau's line over the finger nails at 4 weeks of follow-up

The pathogenesis in alopecia areata is more specific and autoimmune related. Affected follicles are infiltrated with T-lymphocytes with resultant release of cytokines. Alopecia areata has often been reported concurrently with Hashimoto's thyroiditis and other autoimmune disorders. The role of monocyte chemoattractant protein-1 (MCP-1) has been implicated in KD. Not only does it regulate the recruitment of monocytes around hair follicles,[4] but also it is associated with the pathogenesis of coronary artery abnormalities in KD[5] due to polymorphisms found in the regulatory region of MCP-1 gene. Thus, alopecia areata, an innocuous finding in itself, can be helpful in understanding and exploring the underlying autoimmune etiopathogenesis of KD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the guardian has given consent for images and other clinical information to be reported in the journal. The guardian understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Gratification Disorder – A Seizure Mimicker

A 1.5-year-old developmentally normal girl presented with paroxysmal movements lasting for 1–2 min, every 2–3 days for a few weeks. The neurodevelopmental examination was normal. The events [Figure 1 and web video 1 (video available from: *https://www.ipcares.org/articles/2021/1/2/images/IndianPediatrCaseRep_2021_1_2_135_317370_sm2.mp4*)] revealed posturing of the lower limbs with asymmetrical adduction and flexion of the hips, flexion and fisting of the left arm, intermittent neck flexion, and right striatal toe. Consciousness remained intact and the movements could be aborted by distraction. The differential diagnoses included gratification behavior, seizures, and dystonia. Unimpaired consciousness, absence of typical semiology, and distractibility ruled out seizures. The following features were in favor of a gratification disorder, instead of a movement disorder: presence of neck flexion, rather than tonic extension; continued exertion of perineal pressure in the absence of lower limb dystonias on sitting upright; and cessation with distraction.

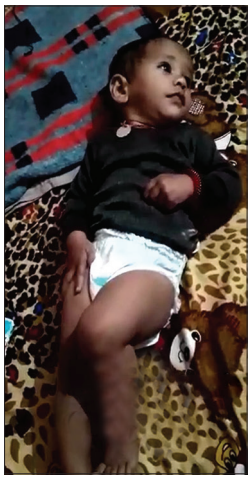

Figure 1: Typical posture of the child during the event

This disorder is often misdiagnosed as seizures, dystonia, or abdominal pain leading to unnecessary investigations and treatment.[1] It peaks between 3 and 36 months of age and presents with stereotyped episodes encompassing vocalizations, grunting, facial flushing, diaphoresis, and perineal pressure with characteristic posturing of the lower extremities. Masturbatory activity may be difficult to recognize in young children as manual genital stimulation is usually absent.[2] The child is distractable[3] and may express displeasure when interrupted.[2] Examination and investigations are normal.[3] Video recording helps in understanding the nature of the event.[1-3] Sexual abuse and perineal irritation should be ruled out.[3]

Parental education is the cornerstone for management. Most children outgrow gratification behavior by 7 years of age.[1] Behavior modification strategies such as distraction and firm instruction to avoid such behavior without reprimand or harsh discipline have successful outcomes.[1]

Declaration of patient consent

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The Night Wanderer: Microfilaria in Peripheral Blood Smear

Lymphatic filariasis (LF) is caused by *Wuchereria bancrofti* (90%), *Brugia malayi* (<10%), and *Brugia timori*. Over 250 million children are exposed to LF worldwide. Common pediatric manifestations in endemic areas are asymptomatic infection or acute clinical manifestations by 11–15 years of age.[1]

A 13-year-old boy presented with painless swelling over the medial aspect of his left arm that was initially diagnosed as evolving cellulitis and treated with antibiotics. A possibility of LF was considered on finding high total leukocyte counts (10,480/mm^3) with 25% eosinophilia. A provocative dose of diethyl carbamazine (DEC) was given, following which a nocturnal blood sample was collected and peripheral smears made. The diagnosis was clinched by identification of the *W. bancrofti* microfilaria (mf) based on the large size (>200 μm), presence of sheath, short head space, and anucleate tail [Figure 1 and web video 1 (video available from: *https://www.ipcares.org/articles/2021/1/2/images/IndianPediatrCaseRep_2021_1_2_136_317374_sm2.mp4*)]. The child was treated with DEC (6 mg/kg/day).[2]

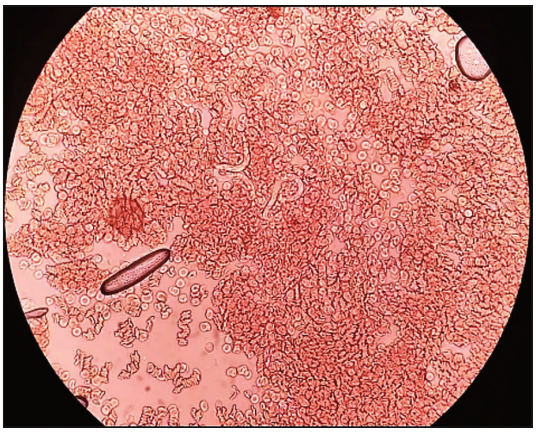

Figure 1: Nocturnal peripheral smear showing presence of microfilaria

Microfilariae usually circulate between 10 PM and 2 AM at night, coinciding with the usual feeding timing of mosquitos.[3] the prevalence rate of mf is 30% in children < 10 years and almost 69% in adolescents < 19 years. Two thin and two thick smears are made and stained with Giemsa or Hematoxylin. Species can be determined by the aforementioned morphological characteristics. An entire blood film should be scanned at ×10 before being reported as negative. Other diagnostic modalities include the detection of mf antigen by immune-diagnosis, Doppler sonography, lymphoscintigraphy, and histopathology.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Management of an Adolescent Boy with a Congenital Heart Disease: The Value of Care Coordination

Editors Comment: We have introduced this section to focus on the various social and systemic aspects of child health care that exists in the less developed parts of the country. Attainment of the Sustainable Developmental Goals and ensuring health equity will only be possible when these issues are successfully addressed. And as you all know, the first step is not just creating awareness but also triggering reflection. We present this case-based series from a network of not-for-profit primary health-care facilities (AMRIT Clinics) that provide preventive, promotive, and curative health care to remote, rural, and high migration communities in remote Udaipur district, about 100 km away from the nearest tertiary hospital.

In 2014, two tribal teenagers (17 and 18 years old, respectively) with congenital heart disease presented to our clinic within a span of 2 weeks. Their late presentation was not due to the mild nature of their disease, but rather a reflection of the challenges, they had faced to get a diagnosis and proper treatment since early childhood. We describe the history, management, and outcome of one of them to illustrate the kind of care coordination required for vulnerable children with medical conditions that warrant advanced health care but who lack access to health facilities that can provide it.

Case Study

Ramlal (*name changed*) was born in Manpur village of Salumbar tehsil of Udaipur district. More than 90% of the population of the village is tribal. The nearest town is 30 km away and the nearest tertiary hospital is 100 km away. Ramlal was 16 years old at initial presentation and complained of breathlessness and easy fatigability from as far back as he could remember. When he arrived, he looked visibly breathless. His weight was 35 kg and height was 54 cm. His pulse rate was 92/min, respiratory rate was 28/min, and blood pressure was 110/72 mmHg. He had central and peripheral cyanosis, Grade III clubbing, and an oxygen saturation of 84% in room air. On auscultation, his chest was clear. The rest of the examination performed by the health worker (HW) was unremarkable. His hemoglobin level was ascertained to be 18% g by a Sahli's hemoglobinometer.

Ramlal was born at home. His father tills a small piece of land and his mother is a homemaker. He has two sisters, both of who were healthy. He had attended school till class 5 but then had to drop out due to his illness. From early childhood (about 2 years of age), Ramlal's parents had taken him to various health-care providers, including the local primary health center and even faith healers and local quacks. They had never learned that he had a heart disease. Finally, when there was no improvement, they resigned to fate and believed that his disease was due to supernatural causes. About 6 years earlier, Ramlal's condition deteriorated with acute worsening of his usual breathlessness. At that time, his parents conferred with other villagers, borrowed money, and took him to the nearest hospital 100 km away, where he was admitted. At discharge, he was informed that he has a severe heart defect since birth, which could be corrected by an operation, but the facilities for that were available only in Jaipur. His father took another loan and got him admitted in the medical college in Jaipur. An echocardiogram confirmed that he had a heart disease. He was told that the operation carried a "high risk to life" would cost about Rs. 50,000, and he should apply to the Chief Minister Relief Fund for reimbursement of the costs of surgery. Not knowing how to proceed further, and unable to get any more guidance, father and son returned disheartened to their village.

Ramlal continued to silently harbor a desire to get relieved from his misery. He kept all his papers and reports carefully, hoping against hope that his desire to get operated would be fulfilled someday. When he was 17 years old, he chanced upon the male HW from our clinic during a community outreach visit to his village and they got talking about his health issues. The HW brought him to the clinic to see if we could help him. We reviewed his studies and discovered that the echocardiography report showed a tetralogy of Fallot, adequately sized confluent pulmonary arteries, and severe infundibular and valvular pulmonary stenosis. While we were searching for options, we learned of the UN Mehta government run Institute of Cardiology in Gujarat that offered free cardiac surgery for tribal patients and reportedly had good surgical outcomes. However, documents confirming tribal status and proof of residence of the patient were required. The primary health-care team assisted the family in collecting and collating these documents. Since the family had never visited Ahmedabad, they were extremely apprehensive about going there by themselves. The PHC team was also concerned that Ramlal and his parents would not be able to navigate the process of hospitalization on their own. It was decided that the PHC physician and HW would accompany them to Ahmedabad, help with the formalities of admission, liaise with the cardiologist and cardiothoracic vascular surgeon, and arrange for blood transfusion and other prerequisites.

After getting admitted, Ramlal underwent a series of investigations to assess the preoperative state – echocardiography, cardiac catheterization, and a multiple slice pulmonary computerized

The patient, his family, and his Care Coordinators

tomography. These confirmed the earlier findings and revealed other intricate vascular details: the right pulmonary artery measured 8.3 mm, there was a large aortopulmonary collateral (measuring 2.8 mm) that emerged from the descending aorta at T5/T6, had a tortuous course, and ascended to T-3 level, bifurcating into two branches at the right upper lobe and right hilum. There were a few other smaller ill-defined collaterals. Based on this, surgery was planned and a week later, a trans-right atrium intracardiac repair was performed successfully. This was followed by cardiac catheterization and coiling of the major aortopulmonary collaterals a day later. The postsurgical period was uneventful and he was discharged after a week. He returned to the village a different person, pink, with abated breathlessness and no longer constantly fatigued.

At present, 6-year postsurgery, he is healthy, symptomless on accustomed work and his clubbing is reversed. He does get breathless still on heavy exertion. The community HW helped him get enrolled in a vocational training course on tailoring. After completion, he started his own shop and earns about Rs. 9000 every month. He also got married a year ago.

Discussion

Most children with critical congenital heart diseases in developed countries that require surgical intervention within the 1st year of life are detected during pregnancy or in the early neonatal period. In low- and middle-income countries like India, antenatal and neonatal identification is low, many children succumb to their cardiac disease in the first few weeks of life without getting diagnosed, there are few and inequitably distributed pediatric cardiothoracic centers, and the costs of surgery are often beyond the means of a person belonging to the lower socioeconomic strata. This means that only a small proportion of all critical congenital heart diseases (CHDs) is detected in time, and fewer still are operated.[1] Those from the hinterland are even less likely to be diagnosed, operated, survive, or lead a normal life. While there are program initiatives for early detection of defects at birth like the Rashtriya Bal Suraksha Karyakram, and state-funded insurance schemes, public awareness is poor and the coverage is low. It is estimated that in India, about a million children with CHDs remain unoperated.

Many families with children from the hinterland affected with congenital disorders seek medical attention and move to and fro primary and tertiary health-care centers if they survive. They have limited resources, lack awareness, and exposure and are very fearful of visiting hospitals in the city. In the process of seeking optimal care, they may end up spending a lot of money, getting indebted, and having to sell the few assets that they have like pieces of silver jewelry, or small pieces of land. In the absence of an informed person or institution to help them navigate the complex and often unresponsive systems of health care, insurance, and social support, they often recede into oblivion, without receiving medical attention. Ramlal was indeed fortunate to have gained access to a responsive primary health-care system that coordinated his care from diagnosis till the completion of treatment and even beyond.

Care coordination is increasingly recognized as an important function or service for managing children with chronic diseases and those with special needs. Such children and their families often require assistance in negotiating advanced and expensive medical care, social support, and vocational or educational support. A care coordinator assists the family in coordinating care across systems (i.e., health care and social service) and across primary, secondary, or tertiary levels of health care.[2] To enable them to function effectively and efficiently, they should be aware of the resources (institutions, schemes, and entitlements) that are available for the care of these children and how to tap them if required. The care coordinator needs to be in essence, first of all, an advocate of the child, especially when the family has limited means and resources to do the needful themselves.

People living in remote rural areas are financially burdened and have limited education and need enormous help at all levels. In this particular case, the primary care clinic acted as the care coordinator, assisting the child to connect with the tertiary clinical care, and linking them with the entitlement that provided care free of cost. This required assisting with the documents, physical accompaniment, and negotiating care on behalf of the family. The care coordination role also extended to linking the individual with vocational training that helped the boy integrates with the social and economic life like his peers in the village. Primary care providers, especially pediatricians, should be exhorted to play the role of care coordination. The health systems and insurance mechanisms need redesigning to allow care coordination to become incentivized so that more primary care physicians and pediatricians will be motivated to assume lead roles and advocate for making systems responsive to their needs. Operational and implementation research is required to understand the pathways of care that children from disadvantaged families with reversible congenital conditions need to traverse.

It was Rudolf Virchow who stated that "A physician is a natural attorney of the poor."[3] By extension, a pediatrician is a natural attorney of children. Coordinating care of children, especially those from poor families, and with chronic health needs, would be one step in playing that role.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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The Tale of a Diagnostic Conundrum

Recreation of the scene of the crime...

A 12-year-old boy presented to the emergency with a history of low-grade, intermittent fever for 4 days. He had painful swelling of both knees for the same duration that was causing painful restriction of movements. No other joints were involved. He also had breathlessness for 2 days that had initially been on exertion but was now occurring at rest and worsened on lying supine. Swelling had appeared around his eyes and over his feet for 2 days. There was decreased frequency of urination, but no discoloration had been noted. There was no history of any chest pain, palpitations, rashes, appearance of small nodules, or abnormal movements. There was no history of skin lesions or sore throat in the recent past. He gave a significant history of a previous episode of migratory, asymmetrical painful joint swellings involving both knees, elbows, left wrist, and right ankle 2 years earlier, for which he was treated and the medication was still continuing.

On examination, he was febrile (39.4°C), had tachycardia (104 beats/min), and increased respiratory rate (26/min). All pulses were well felt, with no particular character. The jugular venous pressure was elevated (6 cm above the sternal angle). The blood pressure was 140/90 mmHg (>95th centile). His weight was 36 kg (0 to −1 Z score), height was 150 cm (0 to −1 Z score), and body mass index was 16 (0 to −1 Z score). General physical examination revealed pallor, periorbital puffiness, and bilateral pedal edema. Both knees showed features suggestive of arthritis. No skin lesions, rashes, erythema marginatum, or subcutaneous nodules were noted. Examination revealed a hyperdynamic apex with high-pitched Grade 2 pansystolic murmur best heard in the mitral area and bilateral basal crepitations.

*Dr Watson: Could this be congestive heart failure (CHF), secondary to rheumatic heart disease? (**RHD**) Let me elicit some more pertinent clinical details.*

It was discovered that the child had been diagnosed with acute rheumatic fever (ARF) and treated with oral steroids and aspirin for 12 weeks in the previous episode. There had been a rapid therapeutic response, with the joint pain and swelling abating within 48–72 h, any no residual deformities. On follow-up, the child had developed moderate mitral regurgitation, deemed secondary to RHD. He had been advised prophylactic therapy with oral penicillin. However, compliance had been poor in the past 3 months.

Dr Watson: Hmm, but what could be the cause of oliguria in this case?

In a setting of CHF, oliguria could be due to left ventricular dysfunction leading to peripheral circulatory failure. However, the absence of hypotension made this unlikely. Instead, he had hypertension, periorbital puffiness, and pedal edema, all features of fluid overload. These suggested that an intrinsic acute kidney injury (AKI) superimposed on an underlying cardiac abnormality be considered.

Dr Watson: If this is AKI, what could be the cause?

AKI in ARF could be due to infective endocarditis (IE) associated with glomerulonephritis (GN). *Let me order an Echocardiogram and other supportive investigations.*

The hemoglobin level was 6.6 g/dL, total leukocyte count of 19.4 × 10 ^{9}/L (77% polymorphs, 10% lymphocytes, and 11% monocytes), and platelet count of 5.5 × 10 ^{9}/L. Peripheral smear showed microcytic hypochromic anemia with no evidence of hemolysis. Erythrocyte sedimentation rate (ESR) was elevated (120 mm/h). The renal function tests were grossly deranged (blood urea 166 mg/dL and serum creatinine 3.6 mg/dL). When compared with reports available from 3 months ago, the rise in serum creatinine was thrice the baseline (0.7 mg/dL), which confirmed AKI stage 3.[1] Serum Na+ was 136 mEq/L and K+ was 6 mEq/L. C-reactive protein was negative. Antistreptolysin 0 (ASLO) was raised (430 IU/mL). Serial blood cultures were sterile and throat swab culture negative for *Streptococcus pyogenes*. A renal ultrasonogram revealed normal kidney sizes (right 8.5 cm and left 8.6 cm) with mildly increased echogenicity. Chest X-ray showed cardiomegaly, electrocardiogram was normal, and echocardiogram showed severe mitral regurgitation with anterior mitral leaflet thickening and no restriction of leaflet movement, or vegetations.

Dr Watson: Let me synthesize the clinical findings and investigation reports

Clinical diagnosis of recurrence of ARF in an established RHD is made in the presence of either 2 major or 1 major and 2 minor or 3 minor criteria with evidence of preceding Group A streptococci (GAS) infection. In this case, two major (arthritis and carditis) and two minor criteria (fever >38.5°F and ESR >30 mm) are satisfied with increased ASLO titers.

Dr Watson: Do I need to order any other investigations?

Urinalysis is an indispensable investigation in AKI for delineating etiology. The child's urinalysis revealed microscopic hematuria (100 dysmorphic red blood cells (RBCs)/ High power field (HPF) with RBC casts) and proteinuria 1+. The urine protein to urine creatine ratio was 0.4. These findings suggested acute GN (AGN) as the cause for AKI. Severe AKI in a setting of AGN means that rapidly progressive GN (RPGN) could be a likely diagnosis, the histopathological hallmark of which is crescentic GN.

Dr Watson: Could this be IE-associated GN?

The child had fever but no other clinical correlates of IE including splenomegaly, Janeway lesions, Roth spots, splinter

hemorrhages, or Osler's nodes. Serial blood cultures were sterile, and the echocardiogram revealed no vegetations. These ruled out IE-associated AGN.

Dr Watson: This needs further workup. I believe a renal biopsy is also in order.

Renal biopsy reveals crescentic GN. Out of 25 glomeruli, 50% had crescents that were predominantly cellular [Figure 1], in addition to 1 fibro cellular, 1 fibrous crescent, and 1 globally sclerosed glomeruli with immune complex deposition (IgG-2+ and C3-3+). The serum C3 levels were 204 mg/dL (normal 90–180 mg/dL); antineutrophilic cytoplasmic antibodies were negative. The final diagnosis is crescentic GN (immune complex mediated).

Dr Watson: Early treatment of crescentic GN is crucial to prevent progression to end-stage renal disease. Let's start prompt immunosuppression.

The child is given intravenous (IV) methylprednisolone pulses for 5 days followed by IV, as per standard treatment protocol. The urine output and symptoms improved with diuretics and immunosuppressive therapy. Dialysis is not required.

Dr Watson: Let me check the diagnostic algorithm for RPGN to ascertain etiology.

Dr Watson reviews Figure 2. The lack of respiratory symptoms, sinusitis, negative ANCA, and presence of immune deposits rules out Wegener's granulomatosis. Antiglomerular basement membrane disease (GBM) is excluded by the absence of anti-GBM antibodies and rapid improvement in symptoms without need for plasmapheresis. Among the immune-mediated GN, immunoglobulin (IgA) nephropathy is ruled out in the absence of mesangial IgA deposits. Lupus nephritis is eliminated by the absence of symptoms and signs of systemic lupus erythematosus and the absence of full house immune positivity. Poststreptococcal GN (PSGN) could be considered, especially since the biopsy showed crescentic GN with IgG and C3 deposits in the glomerular capillary walls.

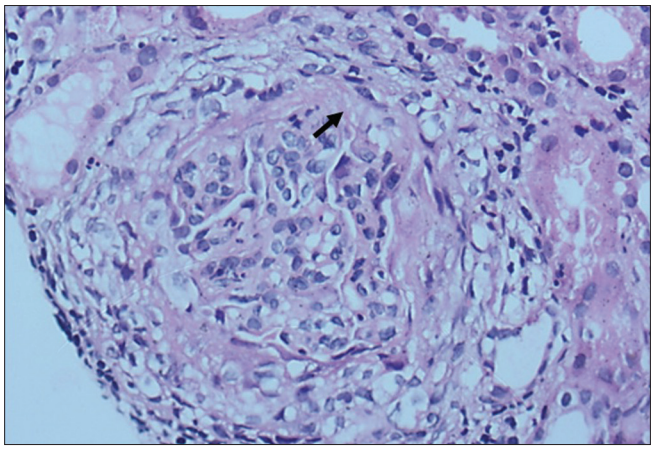

Figure 1: Figure section shows glomerulus with circumferential cellular crescent, with mesangial matrix expansion, hematoxylin and eosin stain, ×200

However, PSGN is characterized by hypocomplementemia and in this case, the C3 levels were normal. Hence, PSGN becomes less likely.

Dr Watson: Could this be membranoproliferative glomerulonephritis (MPGN)?

Since the aforementioned causes of crescentic GN were excluded, MPGN is definitely likely in the presence of globally sclerosed glomeruli on the light microscopy and immune complex deposits on immune fluorescence, since normal C3 levels are described in 30% cases of MPGN.[1] Features such as basement membrane splitting and lobular accentuation of the glomeruli may not always be appreciated in early stages of MPGN.

Dr Watson: Let me complete my case diary by adding the details of the follow-up.

After the initial IV pulse of steroids, the child was put on tapering doses of oral prednisolone (2 mg/kg/day daily to 0.3 mg/kg/day on alternate days). He has received 6 pulses of monthly IV Cyclophosphamide so far. The estimated glomerular filtration rate (eGFR) at the end of 6 months is 82 ml/min/1.73 m^2, implying residual renal injury and chronic kidney disease stage 2. This clinical course further favors MPGN.

If Holmes was here, I would have been the one saying 'Elementary, my dear Sherlock!'.

Discussion

We have described a case of RHD with ARF in a child, complicated by RPGN. The most common cause of GN in RHD is IE, which is seen in 18%–25% cases of IE.[2] However, it is mostly asymptomatic. When symptoms do occur in IE, it is usually due to acute nephritic syndrome, rarely as RPGN.[3,4] ARF and GN have been reported in RHD in the absence of IE,[5] although in adults. It was postulated that the causative organism would be a common rheumatogenic and nephritogenic Group A streptococcal strain, possibly strain M1, that is known to trigger both ARF and PSGN, since both are pathogenetically distinct entities. While ARF is speculated to be due to molecular mimicry, PSGN is proposed to be due to the binding of nephritis-associated plasmin receptor and streptococcal pyrogenic exotoxin B to glomeruli, inducing immune complex deposits.[4]

MPGN has been reported in an adult with ARF.[6] To reiterate, MPGN is the likely cause of crescentic GN in our patient, since 30%–40% of MPGN may have normal complement levels at presentation, and distinction of early MPGN from infection-related GN is difficult on light microscopy. The concurrent occurrence of immune complex-mediated MPGN and ARF is very rare. We were unable to isolate GAS strain M1 due to logistic constraints. Another limitation was absence of electron microscopy which could have established the diagnosis of MPGN by demonstration of subendothelial and intramembranous immunoglobulin G and C3 deposits.

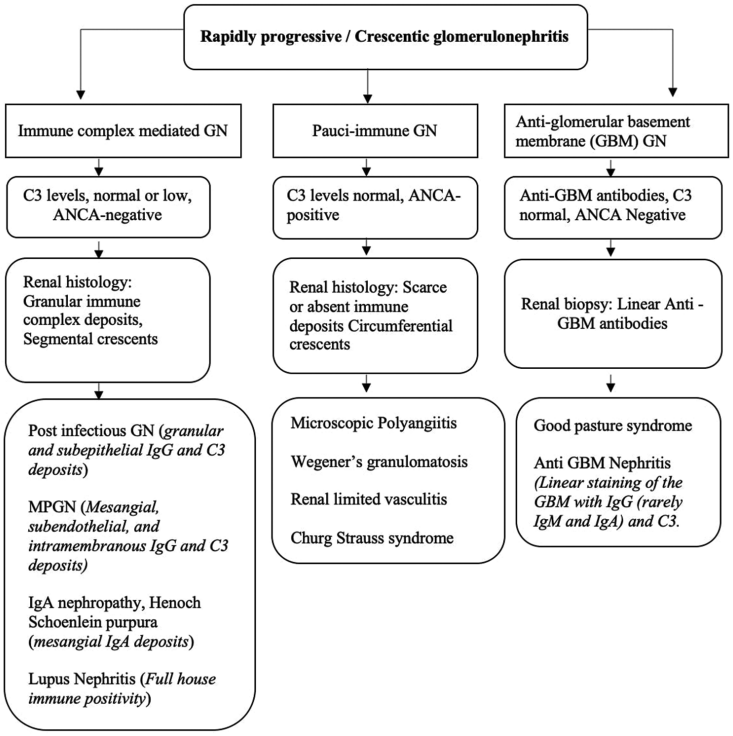

Figure 2: Algorithm for differential diagnosis of rapidly progressive glomerulonephritis

Declaration of patient consent

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Conflicts of interest

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Attempted Suicide by Poisoning: A Growing Challenge in Adolescence

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Editor's comment: Medico-legal cases (MLC) are medical cases with legal implications for the treating doctor, whence after examination of the patient, it is opined that investigation by law enforcement agencies is essential for establishing and fixing criminal responsibility according to the laws of the country. We have introduced this section to acquaint our readers with the appropriate protocols related to MLC's that require knowledge of Forensic Sciences.

Suicidal behavior is one of the leading causes of injury and death, globally. Suicide, defined as the act of intentionally causing one's own death, accounts for the second most common cause of death amongst adolescents aged 15–19 years[1]. Attempted suicide or parasuicide is any form of nonfata, serious, deliberate, self-harm, with or without suicidal attempt. The exact estimate of parasuicide in adolescents is unknown, but the World Health Organization estimates it to be 40–100 times higher than the number of reported suicides, annually[2]. In the United States, completed suicide is thrice as common in adolescent boys than girls, while attempted suicide is twice as high in teenage girls, compared to boys. In India, a country with the largest adolescent population worldwide, suicides and suicidal attempts present a grave issue with a 15-year-old individual in India having a 1.3% cumulative risk of dying before the age of 80 years by suicide.[3] Suicidal attempts are 25 times greater than suicide, with self-poisoning the most common mode of parasuicide[4]. Poisoning (usually with pesticides or drug overdose) is an act of impulsiveness commonly seen in adolescent girls, in India and globally.

Poisoning, whether accidental or suicidal, is one of the most common situations encountered in a pediatric emergency department. As practicing pediatricians, we should be competent enough to suspect, identify, and manage such cases efficiently to save the patient's life, as well as fulfill our basic medicolegal responsibilities and duties. This can be done by timely and appropriate management that encompasses sensitively collecting and documenting legal evidence, ensuring medical and psychiatric intervention, and notifying the competent authorities. This article aims to sensitize our readers to these critical aspects of attempted suicidal poisoning by describing a true but anonymized case.

Case Report

A 15-year-old girl was brought to the emergency department of our hospital by her family, with an alleged history of ingestion of 2 caps (around 10 mL) of floor cleaner 2 h earlier, followed by loss of consciousness within 15 min. There was no history of any vomiting, loose motions, abnormal odor, seizures, visual disturbances, bleeding from any site, or respiratory difficulties. On reviewing the history for a precipitating event, it was revealed that she had been scolded by her mother immediately before ingestion. The nature of the floor cleaner was probably phenyl, though it was kept in an unlabeled bottle, since it was apparently milky white in color and diluted with water.

On examination, she was found to be normothermic, with normal heart rate, respiratory rate, and blood pressure for her age. General physical examination revealed no frothing or burns in or around the oral cavity. There was no abnormal odor coming from her mouth or clothes. Multiple healed cut marks were noted on her left wrist. The patient regained consciousness almost as soon as the examination started, which

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was approximately an hour post ingestion. She complained of a mild headache and pain and burning sensations in her throat. The resident on duty registered an MLC and informed the police constable posted in the hospital police station. Her pupils were of normal size and reaction. The level of consciousness, higher mental functions, and neurological examination were normal. The rest of the systemic examination was unremarkable.

After obtaining informed consent from the child and her mother, external decontamination was done and the contaminated clothes were kept in a large bag for toxicological sampling. Gastric lavage was not done since the amount ingested was small and there had been a delay of about 2 h before reaching the health facility. Samples for toxicological examination including blood and urine were collected and sealed. Supportive management was provided in the form of intravenous fluids and antacids. Baseline investigations were normal.

On probing further, it was learned that she had tried to cut her wrist 10 months earlier following a scolding by her brother, but no medical intervention had been sought. There was no history of drug/substance abuse, psychiatric illnesses, or similar suicidal attempts in the family or circle of friends and acquaintances. She was a student of class 10 in a government-run school and average in studies. Her father was a painter and her mother a homemaker. She had a 20-year-old elder brother (who worked with their father) and an 18-year-old elder sister, who was married. The family belonged to the lower socioeconomic Class A referral was sent for a psychiatry evaluation. She was reported to have normal affect and mood with no active suicidal ideation. The current incident was deemed as an impulsive act with low lethality. A final diagnosis of parasuicide (by probable phenyl poisoning) was made. The patient and her family underwent counseling and she was discharged after drawing up a plan for follow-up with the outdoor psychiatry services.

Let's ask the experts

How common is suicide and parasuicide in Indian adolescents? In 2019, 7% of the total number of suicides were individuals <18 years of age. Poisoning (26%) was the second most common modality, in which 17.3% consumed insecticides[5].

What are the causes of suicidal ideation in Indian adolescents? The main causes of suicides in this age group include family problems, failure in examinations, love affairs, and illnesses[5]. Although nonsuicidal self-injury does not include an intent to die (as in this case), it is a strong risk factor for suicidal attempts. Social and environmental risk factors are exacerbated by an immediate trigger like agitation, intoxication, or an acute stressful event in most circumstances.

How does one manage a case of suspected poisoning? The approach is given in Table 1.

What are the legal duties of a doctor in case of poisoning? This entails the following proper medicolegal documentation and preservation of samples[6]:

1. Inform the nearest police officer/magistrate in all cases of poisoning, whether accidental, suicidal, or homicidal
2. If the patient is critically sick, inform the magistrate to record the dying declaration, or record the dying declaration in person in the presence of an independent witness. This has to be recorded irrespective of the age. The admissibility is decided later by the court, on the basis of assessment of maturity of understanding of the individual or his/her mental competence to be a witness
3. Prepare a medicolegal report with details of history and examination findings and nature of poison, if known. Preserve relevant samples (given below) and hand over to the investigating officer in a sealed condition for forensic analysis
4. In case of death with suspected poisoning or a patient brought dead, do not issue a death certificate but send for a medicolegal postmortem after informing the police.

What samples need to be preserved in case of a suspected poisoning? In cases of suspected poisoning, the following samples need to be collected:

1. Blood sample: 10 mL each in 2 containers, one with preservative (EDTA or sodium fluoride) and one without preservative
2. Urine sample: Preferably two samples of 20 mL should be collected, one immediately on arrival, and the second after ½ an hour
3. Gastric lavage fluid: This should be preserved with pure NaCl (4 g/100 mL)
4. Vomitus/feces/any other fluid available
5. Clothes stained with vomitus/spilled poison
6. Suspected material recovered from possession of the victim/accused and from circumstantial environmental materials such as food and drink.
7. Properly seal, label, sign and hand over all the samples to the investigating officer.

Is it Phenyl or phenol poisoning – a diagnostic dilemma and implications? Household floor cleaners are frequently used for attempted suicide due to ease of availability. They can be broadly categorized into white phenyl (predominantly pine oil with a very small percentage of phenolic by-products) and black phenyl (an emulsified blend of coal tar acids in an anionic soap base). The former has relatively low toxicity with small doses and only causes skin irritation, mild respiratory discomfort, and occasionally central nervous system (CNS) depression. In contrast, phenol is highly toxic/corrosive with a fatal dose as low as 50 mg. It causes nausea, vomiting, diarrhea, chemical burns, CNS manifestations, hemolytic anemia, methemoglobinemia, pulmonary edema, and hypotension. Thus, it is critical to determine the nature of the floor cleaner, as the prognosis and outcome differs markedly.

Table 1: Medical duties in case of suspected poisoning

Procedure	Description
Emergency stabilization	Quick assessment for detection of life-threatening conditions and appropriate measures to stabilize airway, breathing, and circulation
Clinical assessment and diagnosis	Comprehensive history taking and examination to give idea about the type of poison and the system involved/toxidrome
Active removal of toxic substance	External decontamination-removal of clothes and washing of exposed parts like skin and eyes with water
	Gut decontamination - using either syrup of ipecac, gastric lavage, activated charcoal or whole bowel irrigation depending on the type of poison consumed, clinical presentation and time since ingestion
	Gastric lavage/activated charcoal are most commonly used and are usually done when the physician thinks a sufficiently high dose of toxin has been ingested and the patient presents within one hour of ingestion
Specific antidote	Administration of specific antidotes wherever available promptly can be a life saving measure in cases of poisoning. The local hospitals should look into the common poisonings presenting to their hospital and keep a ready stock of relevant antidotes with them
Psychiatric care and supportive therapy	Good nursing and supportive care helps in improving the outcome tremendously, especially as antidotes are available for very few poisons. Psychiatric assessment and counseling of both patient and family helps in preventing repeated episodes and identifying patients who require follow-up care for mental health

Legislature

In India, attempted suicide was an offense punishable under Section 309 of the Indian Penal Code (IPC) which stated "Whoever attempts to commit suicide and does any act towards the commission of such offence, shall be punished with simple imprisonment for a term which may extend to 1 year or with fine, or with both." However, this was decriminalized by the Mental Health Act in 2018, which states "Notwithstanding anything contained in section 309 of the IPC, any person who attempts to commit suicide shall be presumed, unless proved otherwise, to have severe stress and shall not be tried and punished under the said code."

Doctors are legally bound to inform all cases of poisoning to the competent authority after initiating life-saving measures and stabilizing the patient. If not done, the doctor may be held liable under section 176 IPC (omission to give notice or information to a public servant by a person legally bound to give). If the doctor intentionally fails to collect, preserve, and seal the evidence related to the case of poisoning, he is liable to be punished under section 201 IPC. The doctor may need to take a dying declaration in impending death if a district magistrate is unavailable. Through this case, we have tried to highlight the standard protocols for management of an adolescent with attempted suicide by poisoning. These cases are on a rise in recent years due to various changes in societal and family dynamics and increasing expectations. Doctors should be aware of the medical, psychosocial, and legal aspects of such cases to help improve their competency in management.

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Reye's Syndrome, Still an Enigma after 50 Years: Have the Curtains Finally Been Drawn?

Despite tremendous advances in the understanding of the pathophysiology of diseases that plague humankind, a few diseases still remain poorly understood. Reye's syndrome (RS) is an exemplar of such entities. It is a rare and potentially fatal pediatric illness characterized by acute noninflammatory encephalopathy and fatty liver failure. Our quest for reviewing this condition was inspired by a case report published in Indian Pediatrics in April 1971 by Joseph and John[1] that described three affected children from the same family. We present a brief review of RS, beginning from its discovery, to the present understanding and future prospects.

Clinical Case Description

The case report revolves around three siblings living in Nagari, Andhra Pradesh, who were sequentially admitted with acute febrile illnesses in a local hospital of repute. The first, the eldest sibling, a 10-year-old girl developed fever, headache, and seizures. On the 2nd day of illness, she was brought to the hospital in an unconscious state. Examination revealed hypertonia, a distended bladder, and dilated, nonreacting pupils. She succumbed within 2 h of admission. The very same day, the youngest sibling, a 6-year-old boy, also developed features of febrile encephalopathy but without any seizures. At admission, he had irregular breathing and was comatose and hypotonic, with dilated, nonreacting pupils. Despite supportive management, he deteriorated rapidly and expired within 30 min of hospitalization.

Both the children had similar investigation results. These included slightly elevated total leukocyte counts with a neutrophilic differential count, slightly elevated cerebrospinal fluid (CSF) cell count (7 and 13 cell/mm^3 respectively), and postmortem liver histopathological findings of microvesicular fatty degeneration within preserved hepatic architecture. The same day the second issue, an 8-year-old boy also developed a fever and was immediately hospitalized. The child did not develop any neurological symptoms and had normal leukocyte counts. He remained febrile for 4 days and was discharged uneventfully on the 5th day. None of the children had any history of exposure to drugs, poisons, or chemicals. Other children, including their cousins who resided nearby and with whom they played, remained healthy.

In their discussion, the authors cite three reports of siblings with similar presentations reported from across the globe, including one from Vellore. The first article described nonlethal encephalopathy occurring 2 weeks after smallpox vaccination in a child, with severe and fatal encephalopathy developing in the elder sibling, who did not got vaccinated. The second described three siblings who developed varicella infection. Out of them, two developed encephalopathy and one expired. The third report was about two siblings who developed febrile encephalopathy without any identifiable preceding events and died within a week of each other. Joseph and John opined that the sequential and temporally close involvement observed in their case report indicated a common source epidemic that was more likely an infection than poisoning, given the varying incubation period. This was supported by the intrafamilial involvement and lack of similar presentation in the extended family and community.[1]

Brief Review

Historical background and past knowledge

In 1954, an epidemic of febrile encephalopathy affected children of Uttar Pradesh, Bihar, and erstwhile Bengal. Common clinical features were hypoglycemia; fatty changes in the liver (found on post mortem analysis); inability to isolate any bacterial, protozoal, viral agent, or chemical poison; and high mortality. This mystery illness was named "Jamshedpur Fever" by Khan in 1954 and was probably the first report of the yet to be recognized RS.[2]

RS was named after the Australian pathologist Ralph Douglas Kenneth Reye, who described 21 Australian children presenting with encephalopathy and fatty degeneration of viscera between 1951 and 1962.[3] All of them exhibited anicteric firm hepatomegaly, neutrophilic leukocytosis, hypoglycemia, elevated hepatic transaminases, elevated prothrombin time, negative blood cultures, and low CSF sugar levels. The pathological hallmark was fatty degeneration of the liver and kidneys accompanied by cerebral edema without inflammatory changes. Mortality was high; out of 21 patients, 17 died.[3]

What was known in the 70s

The national surveillance for RS was started by the Centers for Disease Control and Prevention (CDC), Atlanta, in 1973 to monitor RS during an epidemic of influenza B in America. Closer home, cases of acute encephalopathy with fatty visceral infiltration were also reported from Vellore and Chandigarh in the 1970s. In those days, RS was considered a biphasic illness that started with premonitory viral symptoms like upper respiratory tract infection, diarrhea, or the development of chickenpox, followed by encephalopathy, seizures, posturing, and irregular respiratory pattern. An infectious cause was suggested when it was noted that a few cases were occurring in siblings. The proposed etiology was an overwhelming viral infection, with superadded exposure to an unidentified toxin.

Limited diagnostic modalities were available to determine underlying causes. Management was largely supportive and the outcome poor, largely due to late hospitalization.

Advances in the last 50 years

Various diagnostic criteria have been formulated for RS over the years. The most commonly used one is the CDC case definition. This requires fulfillment of the following criteria: (1) acute noninflammatory encephalopathy demonstrated clinically by an alteration of consciousness, CSF containing <8 leukocytes per mm^3, or brain histology demonstrating cerebral edema without perivascular or meningeal inflammation; (2) hepatopathy demonstrated by either a liver biopsy/autopsy considered diagnostic of RS, or ≥ threefold rise in levels of Aspartate aminotransferase and Alanine aminotransferase, or serum ammonia; and (3) no other explanation for the cerebral and/or hepatic abnormalities.

It is now recognized that RS is not a single illness but a syndrome that has a seasonal variation and is due to multiple causes. Antecedent viral infection is a sine qua non. Implicated infections include influenza, varicella, measles, and that caused by coxsackie B or respiratory syncytial viruses. The postulated mechanism is that viral RNA diverts the host endoplasmic reticulum to synthesize viral proteins. This disturbs Kupffer cell function, triggering a cytokine cascade, especially tumor necrosis factor (TNF), which inhibits fatty acid oxidation. The increased levels of plasma ammonia and free fatty acids result in mitochondrial damage and fatty infiltration.[4]

Toxins and drugs such as salicylates, paint thinner, aflatoxin, valproic acid, paracetamol, antiemetics, and insecticides can also induce RS. The association with aspirin and other salicylates has been extensively studied since the 1980s. These drugs enhance the *in vitro* release of TNF by macrophages and inhibit the release of the antiapoptotic nuclear factor, kappa B, causing rapid death of target cells. Aspirin metabolites inhibit the long-chain 3-hydroxyacyl-CoA dehydrogenase component of the mitochondrial trifunctional enzyme involved in β-oxidation.[4] The characteristic neurologic features are probably due to hyperammonemia resulting from the hepatic mitochondrial dysfunction. This induces astrocyte edema, diffuse cerebral edema, and elevated intracranial pressure.[4]

The growing body of evidence of an association between aspirin and RS led government and health agencies to issue various advisories: placement of warning labels on drug containers, avoiding aspirin in febrile children, and promotion of acetaminophen as a safer antipyretic. Following these steps, the incidence of RS fell so significantly that it was declared a "public health triumph." However, there were arguments that favored a more complex etiology. For instance, countries such as Australia where aspirin was infrequently used continued to report cases, while countries such as France and Belgium which continued using aspirin did not.

As knowledge and diagnostic modalities have advanced over the years, many cases of RS have been reclassified and are referred to as "Reye's like syndrome." A large proportion (148/598) of the RS surveillance data generated in the United Kingdom (1981–1996) underwent revision.[5] Almost half of these included metabolic disorders such as medium chain acyl coenzyme A dehydrogenase deficiency, fatty acid oxidation defects, urea cycle disorders, organic aciduria, and carnitine deficiency. This led to another hypothesis emerging that of an underlying metabolic disease being triggered by unknown insults.

Timely hospitalization and intensive monitoring in RS are essential. Neurological assessment should be frequent as deterioration can be rapid. Investigations include hemogram, coagulogram, blood sugar, ammonia, hepatic enzymes, electrolytes, CSF analysis, antibodies against varicella and measles (when suspected), and a toxin screen (for salicylate, paracetamol, valproate, and organophosphate if indicated by history). A metabolic workup should include tandem mass spectrometry and gas chromatography/mass spectroscopy for amino acid and urinary organic acids, respectively. Management is supportive; consisting of maintenance of euglycemia (10% dextrose containing intravenous fluids), temperature and perfusion, correction of coagulopathy, initiation of measures to reduce cerebral edema, acidosis and hyperammonemia, and anticonvulsants where necessary. The prognosis improves with appropriate management; complete recovery, lesser probability of permanent hepatic damage, and fewer recurrence.

The future

Incidence of RS has decreased over the last three decades, and cases are now scarce. The United States Food and Drug Administration Drug Event Reporting System and Japanese Adverse Drug Event Report databases have reported only 186 and 30 cases of RS, respectively, from 2004 to 2020. Most of these were due to the use of aspirin, 80 and 5 in America and Japan, respectively.[6] Caregivers of children who require long-term salicylate therapy (i.e., Kawasaki disease, juvenile idiopathic arthritis, rheumatic arthritis, and thrombotic ischemic stroke) should receive customized counseling: information about the risks of influenza and varicella, and vaccination offered accordingly; recognition of symptoms of RS so that aspirin can be promptly stopped and the child hospitalized without delay.

To reiterate, the prevalence of RS varies geographically. It results from a complex interaction between a wide repertoire of known and unknown factors. Sporadic and epidemic cases should be investigated thoroughly. RS should be considered as a diagnosis of exclusion in children with acute febrile encephalopathy, or acute toxic-metabolic encephalopathy.

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Neo-Quiz 2

1. A baby boy was born at 36-week gestation to a primigravida with a history of polyhydramnios but otherwise normal antenatal period. He was delivered by a cesarean section due to cephalopelvic disproportion (birth weight is 4.1 kg). Apgar scores were normal. The baby is dysmorphic with a large protruding tongue, dysplastic ears, bilateral auricular pits and tags [Figure 1], hemihypertrophy of the left upper and lower limbs, umbilical hernia, and bilateral palpable abdominal masses (identified as kidneys on ultrasonography). The baby had hypoglycemia (blood sugar 32 mg/dl) at 2 hours of birth which normalized only after reaching a glucose infusion rate of 10 mg/kg/min. What syndrome does the baby have?
2. Which maternal antibodies are responsible for most cases of neonatal lupus?
3. A 28-week female baby was born with a birth weight of 980 g. The baby is discharged after a stay of 56 days in the neonatal intensive care unit. Which growth chart should be used to interpret her anthropometric parameters (i) at birth and (ii) at discharge? Till what gestational age can these charts be used?
4. A pregnant woman comes for a routine antenatal checkup at 34-week gestation. Hypertension is noted for the first time, and her abdominal ultrasonography shows the estimated fetal weight at 7th centile for gestational age. Figure 2 shows a Doppler image of the umbilical artery. What does this finding signify?
5. A 14-day-old female term appropriate for gestational age (AGA) baby is born with these skin lesions [Figure 3]. Identify the disorder. What is the most common gene responsible for this, and what is the mode of inheritance?
6. What is Quintero staging, and why is it used during twin pregnancy?
7. Which intravitreal drugs are used in the management of aggressive posterior retinopathy of prematurity?

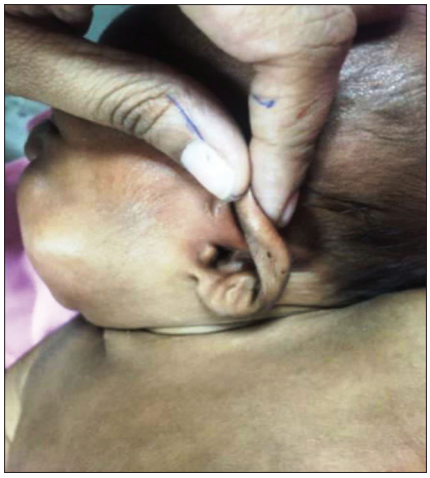

Figure 1: Question 1

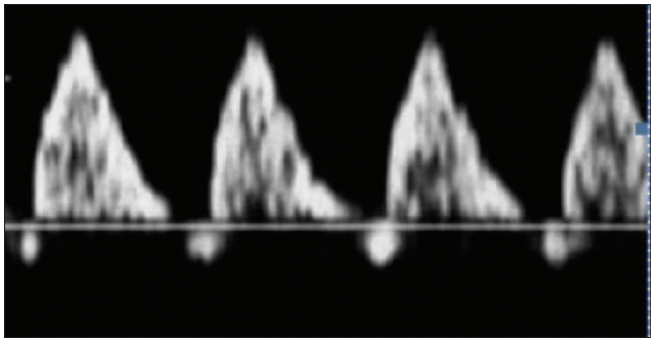

Figure 2: Question 4

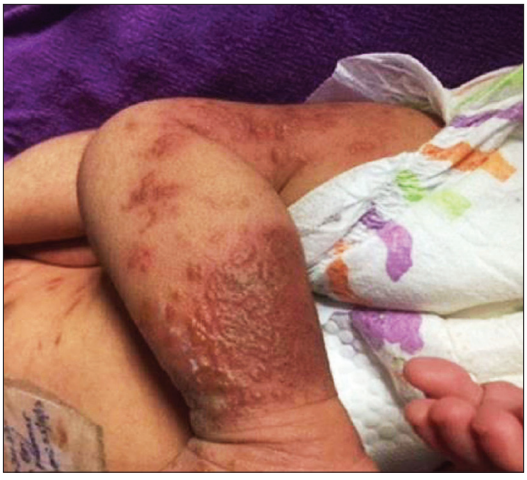

Figure 3: Question 5

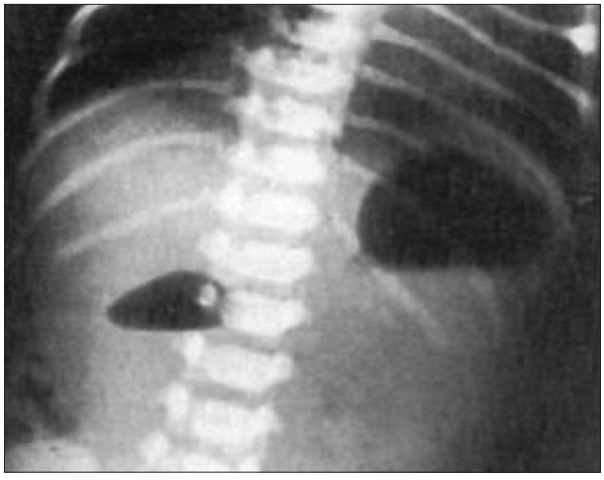

Figure 4: Question 9

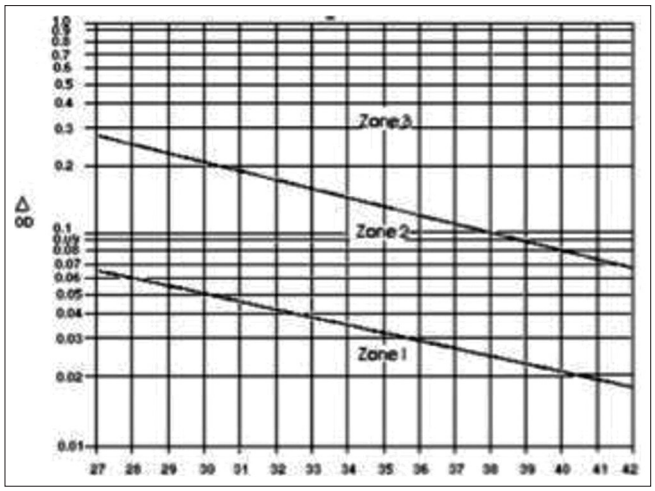

Figure 5: Question 10

8. What is the most common genetic cause of hearing loss in neonates?
9. A 38-week male AGA neonate noted to have mongoloid facies, simian crease, and sandal gap presents with recurrent bilious vomiting on the second day of life. The abdominal X-ray picture is given in Figure 4. What is the radiological finding called and what condition will you suspect? What conditions will you suspect if this sign is seen in the presence of distal bowel gas?
10. What is the name of the following graph [Figure 5], and what is it used for? If a value falls in zone 3, what does that indicate?

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Uncommon Causes of a Common Presentation: Respiratory Distress in Children

Respiratory distress is a common presentation in pediatric patients. All of us are familiar with the usual underlying causes of distress and their management, with children responding to standard care in most cases. Occasionally, one may find a patient who does not respond and poses a diagnostic dilemma. We hereby present some case reports of uncommon causes of respiratory distress from the neonatal period to adolescence.

Healey D, Ron N, Hromada A, et al. Perinatal/neonatal case presentation: Pulmonary artery sling associated with respiratory distress. Springer Plus 2016;5. DOI 10.1186/s40064-015-1656-5.

A 34-week appropriate for gestational age male baby was born to fourth gravida and para one mother who had been covered with steroids before birth. The Apgar score was normal. The baby was admitted in neonatal intensive care unit for respiratory distress that developed immediately after birth and was associated with decreased air entry on examination. A chest X-ray showed left-sided pneumothorax and bilateral opacities suggesting respiratory distress syndrome. The baby was initiated on noninvasive positive pressure ventilation. His clinical status gradually improved over the next 72 h, and he was subsequently discharged in the next few days. At 2 months of age, the baby developed cough and wheezing which were diagnosed as a viral lower respiratory tract infection and treated as an outpatient. At 4 months, the child required admission for another episode of respiratory distress and wheezing. This time the diagnosis was made as bronchiolitis, due to respiratory syncytial virus infection. In-depth probing of history revealed that the baby had persistent tachypnea and feeding difficulties since birth. The X-ray showed hyperinflation, increased peribronchial markings and focal infiltrates in the right infrahilar region, suggestive of atelectasis. A barium contrast esophagogram was planned that displayed subtle contour change in the esophagus, above the level of carina. Careful re-examination identified a systolic murmur at the left upper sternal border. An echocardiography revealed a pulmonary artery sling with the left pulmonary artery arising from right pulmonary artery. The ventricular function was good with mild hypoplasia of the left pulmonary artery.

Disu EA, Kehinde OA, Anga AL, et al. Congenital pulmonary airway malformation: A case report of a rare cause of neonatal respiratory distress and review of literature. Niger J Clin Pract 2019;22:1621-5.

A newborn was referred to a hospital on the 13th day of life as a case of persistent pneumonia for the 3rd day after birth. The baby was born to a 34-year-old primigravida with no significant antenatal or perinatal history. The birth weight was 3.1 kg. On examination, the baby had a respiratory rate of 100/min, severe respiratory distress with intercostal and subcostal recessions, bulging anterior chest wall, hyperresonant right hemithorax, and bronchovesicular breath sounds which were reduced in the lower half of the right posterior hemithorax. All other systems were normal. X-ray chest showed leftward shift of the mediastinum, hyperlucency of the right lower lobe with reduced lung markings, and haziness of the right upper and middle lobes. Differentials of congenital lobar emphysema and congenital pneumonia were kept. A computed tomography scan of chest done showed a multicystic mass in the right lower lobe suggestive of congenital cystic adenoid malformation. Other tests including abdominal ultrasound scan and barium meal with follow-through were normal.

Thakur N, Agarwal D, Narayan S, et al. Recurrent pneumonia in an infant with an esophageal lung. Indian Pediatr 2020;57:266-7.

A 7-month-old girl baby presented with respiratory distress for a week that had not responded to a short course of antibiotics. There was a significant history of episodes of choking during feeding recurrent lower respiratory infections. At admission, the infant had tachypnea, tachycardia, chest retractions, and decreased breath sounds on the right side of the chest. The apex beat was localized to the right, suggestive of dextrocardia. Investigations revealed neutrophilic leukocytosis and a positive C-reactive protein. Chest X-ray showed hazy right hemithorax with right side mediastinal shift. This prompted a computed tomography chest which demonstrated right lung hypoplasia with cystic bronchiectatic changes and nonvisualization of the right main bronchus, hypoplastic right main pulmonary artery, and an abnormal bronchoesophageal communication. A barium swallow study showed filling of right main bronchus directly from the esophagus. Rigid bronchoscopy showed a blind-ended right bronchial stump. The final diagnosis was esophageal lung. Ultrasound abdomen and echocardiography were normal. The patient improved on antibiotics and supportive care. Parents were advised surgical intervention for the underlying condition.

Ahmed H, Ndiaye C, Barry MW, et al. A rare cause of upper airway obstruction in a child. Case Rep Otolaryngol 2017;2017265.

A 4-year-old girl was hospitalized with a history of difficulties in breathing for a year. The nature of dyspnea had progressively changed from intermittent episodes to persistent respiratory distressed that had worsened for a week before presentation. Salient examination findings included a hyperextended neck and Stage 4 laryngeal obstruction. Direct laryngoscopy showed a round cyst, with vascular markings on the wall, originating in the left ventricle, encroaching on the root of the epiglottis, and completely blocking the vocal cords. Thick mucoid fluid was seen on incision of the cyst, which was then marsupialized. The final diagnosis was a ductal ventricular band cyst. Epiglottic and ventricular band cysts are retention-type cysts that occur due to chronic inflammation and lead to blockage of mucus glands. Such type of chronic inflammation happens during episodes of superinfection or laryngeal trauma in sick patients requiring multiple intubations.

Powell AW, Hanke S, Tweddell JS, et al. A 14-year-old boy with unusual presentation of respiratory distress. Case Rep Pediatr 2016;7313942.

A 14-year-old boy was hospitalized with sudden episode of respiratory distress for 6 h before admission. There was a history of associated cough, congestion, high-grade fever, fatigue, myalgia, and vomiting. He was a known case of mild persistent asthma who usually responded to albuterol/salbutamol by metered-dose inhalers. However, this time there had not been any response. Oxygen saturation was low, varying from 70% to 80%. Air entry was decreased bilaterally. There was no audible wheeze. Suspecting an acute exacerbation of asthma, initial management included albuterol-ipratropium nebulization and injection methylprednisolone, to no avail. Chest X-ray revealed extensive airspace disease bilaterally which appeared such as multifocal pneumonia or pulmonary edema. Salient investigations revealed respiratory acidosis, leukocytosis with left shift, negative blood culture, and respiratory viral testing. Despite initiation of noninvasive respiratory support by BiPAP with 100% FiO2, the child developed hypotension and shock. He was intubated and started on inotropes, antibiotics (vancomycin and ceftriaxone), and antiviral agents (Tamiflu). Frothy drainage in the endotracheal tube and requirement of high ventilator pressures were noted, consistent with diffuse pulmonary edema. An echocardiogram revealed cor triatriatum with a membrane separating the left atrium into two chambers. Doppler flow demonstrated the pulmonary veins entering the left atrium on the proximal side of the atrial membrane. Right ventricular hypertension (pressure estimated to be greater than half the systemic blood pressure) was noted. A transesophageal echocardiogram confirmed the presence of severely restrictive cor triatriatum for which was emergent resection of the cor triatriatum membrane was done.

Duke C, Alexander K, Hageman JR. An unusual cause of respiratory distress in a 17-year-old boy. Pediatr Ann 2014;43:20-3.

A 17-year-old boy was being treated as a viral syndrome in view of frontal headache, body aches, neck pain, and stiffness for 5 days and fever for 4 days. Worsening, in the form of nonbilious emesis and nonbloody diarrhea, with notable increase in neck pain, prompted the parents to get him hospitalized. He was dehydrated and appeared ill. There was no history of sore throat, chest pain, or abdominal pain. An urgent chest radiograph was done which was suggestive of bilateral lower lobe pneumonia. The patient was treated empirically with ceftriaxone, vancomycin, and azithromycin. Subsequent blood culture was negative. Lumbar puncture result showed only few red blood cells in cerebrospinal fluid. In spite of the above child developed hypoxia, following day for which oxygen support was escalated and the patient was referred to higher center. Subsequently, as the child did not maintain 10 l of oxygen, he was shifted on BiPAP. Respiratory examination revealed decreased breath sounds at bases bilaterally and coarse breath sounds in remaining lung fields with intermittent crackles. Transverse leukonychia was noted. Repeat chest radiograph showed bilateral lower lobe opacities more than the previous one. Laboratory reports showed neutrophilia, thrombocytopenia, highly raised CRP (229 mg/L), and hypoalbuminemia. Complement levels C3 (30 mg/dL) and C4 (5 mg/dL) were low. Respiratory viral panel was negative. Additional laboratory studies included tuberculosis interferon release test, cytomegalovirus polymerase chain reaction, Epstein–Barr virus capsid antibody, HIV antibody, histoplasma serum/urinary antigen, Bartonella antibody, and pneumococcal urinary antigen which came negative on follow-up. A computed tomography of the head, neck, and chest done which showed bilateral partial thrombosis of the internal jugular veins, more extensive on the right than the left; opacification of the right ethmoid air cells and sphenoid sinus (air-fluid level in the maxillary sinus was consistent with acute sinusitis); adjacent broken molar with a periodontal abscess; and images of the lung apices showed bilateral multifocal air space opacities and mediastinal lymph nodes. The child was intubated due to worsening status. Some other rheumatology tests done including anticardiolipin, antiextractable nuclear antigens, anti-SSA or B antibodies, vascular antineutrophil cytoplasmic antibodies, antinuclear antibodies, and anti-DNA native double-stranded antibodies were all negative. The patient was given anticoagulant therapy with enoxaparin to treat the internal jugular venous thromboses. Laboratory studies of antithrombin III, lupus anticoagulant (double-Russell's viper venom time), activated protein C resistance, factor V Leiden, protein C, protein S, and homocysteine were all within normal limits. The patient was diagnosed with atypical Lemierre's syndrome; however, an organism was not isolated from the blood culture, and the periodontal abscess was the most likely source of infection.

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An Adolescent with Mediastinal Lymphadenopathy: What Lies Within?

Sachin Singh, Joseph L. Mathew, Sahajal Dhooria[1], Kushaljit Singh Sodhi[2], Parikshaa Gupta[3], Pankaj Vaidya, Meenu Singh

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Editors Comment: As the name of this section suggests, we will be discussing important aspects of clinical-radiological correlation. Through a series of cases in which radiological investigations played an important role in clinching the diagnosis.

We report a child who was referred to us with a history of fever and cough for 1 month but whose physical examination yielded no abnormalities. However, mediastinal widening was evident on the chest X-ray. Therefore, the major clinical differential diagnoses considered were thoracic tuberculosis (TB), Hodgkin lymphoma, or sarcoidosis. The learning objectives of this case are to highlight a stepwise approach to establish etiological diagnosis in a case of mediastinal lymphadenopathy, so that specific (rather than empiric) therapy can be instituted. Investigations that can confirm the diagnosis should be preferred over those that may be less helpful, even if they are easier to perform. This case also highlights the necessity of diligent efforts to confirm TB before starting treatment.

Clinical Description

An 11-year-old boy presented to a private practitioner in the month of January, with fever and cough lasting a month. The fever occurred daily, was of moderate intensity, peaking to 102°F, and without any diurnal variation. It was associated with a dry, intermittent cough, without diurnal variation, postural variation, or sleep disturbance. There was no history of breathing difficulty, chest in drawing, or limitation of activity. There were no specific aggravating or relieving factors or history suggesting postnasal drip. There was no history of decreased appetite, weight loss, night sweats, joint pains, rash, or redness of the eyes. There was no history of contact with TB. The child was immunized as per the National Immunization Schedule. He had received treatment with oral antibiotics, oral bronchodilators, and two different cough syrup mixtures but did not improve. Therefore, he was referred to our institution for further evaluation.

On examination, the heart rate was 90/min, respiratory rate 20/min, temperature 101°F, SpO_2 98% in room air, and blood pressure 117/75 mmHg. The body mass index was 23.9 corresponding to +1.62 Z-score. General physical examination did not reveal pallor, cyanosis, icterus, edema, or significant lymphadenopathy. Throat and sinus examinations were normal. Respiratory system examination showed symmetric chest expansion, centrally positioned trachea, no mediastinal shift, normal percussion note in all areas, and bilaterally equal vesicular breath sounds without crackles or wheeze. Examination of the other systems was unremarkable.

A screening chest X-ray was done in view of the persistent cough [Figure 1].

What are the salient findings in the chest X-ray?

The striking finding was the mediastinal widening, which suggested significant right paratracheal lymphadenopathy. There was no significant pulmonary parenchymal involvement or pleural effusion. The trachea, bones, and soft tissues appeared normal. It was difficult to comment on subcarinal nodes from this X-ray film.

What are the clinical possibilities based on the clinical history and radiograph?

We considered thoracic (mediastinal) TB and also sarcoidosis as well as lymphoreticular malignancy (especially Hodgkin lymphoma). These differential diagnoses were considered

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because the clinical symptoms of 1-month duration, normal physical examination including respiratory examination, and mediastinal widening on the chest X-ray could occur in any of these conditions.

What should be the line of investigations?

We investigated the child as per the differential diagnoses considered. First, we investigated for TB. Since there was no sputum even after induction, we collected gastric lavage after overnight fasting. This was processed by Ziehl–Neelsen (ZN) staining for acid-fast bacilli (AFB), cartridge-based nucleic acid amplification test (GeneXpert), and liquid medium mycobacterial culture. ZN staining and GeneXpert were negative. In addition, a tuberculin skin test was done, which was reactive (26 mm × 18 mm).

Investigations performed for Hodgkin lymphoma showed normal blood counts, differential count, peripheral smear, and erythrocyte sedimentation rate. Noninvasive biomarkers for lymphoma and germ-cell tumors were assessed. Lactate dehydrogenase was 417 U/L (normal range: 60–170 U/L), alpha-fetoprotein was 0.988 IU/mL (normal range: 0–5.8 IU/mL), and human chorionic gonadotropin was 0.5 mIU/mL (normal <1 mIU/mL).

We also explored the possibility of sarcoidosis by analyzing serum calcium, creatinine, alkaline phosphatase, alanine and aspartate aminotransferases, serum level of angiotensin-converting enzyme, 24-h urine calcium–creatinine ratio, and eye fundus examination. These were all normal.

What other investigations can be planned?

At this stage, we proceeded with fiber-optic bronchoscopy and bronchoalveolar lavage (BAL) to examine the airway for extrinsic compression and analyze BAL fluid for evidence of TB, malignant cells, and sarcoidosis. Airway anatomy was normal. BAL fluid was negative for TB on ZN staining and GeneXpert. A sample was processed for liquid medium culture. The BAL lymphocyte count and CD4:CD8 ratio were normal which made sarcoidosis unlikely, a ratio of >2 being suggestive, and a ratio of >4 being consistent with sarcoidosis.

Recognizing the need for a tissue diagnosis, we then performed a computed tomography (CT) scan of the thorax to localize a site for mediastinal lymph node aspiration. It is pertinent to note that CT scans are associated with significant radiation dosage and do not offer a confirmatory diagnosis in most cases. Hence, it was performed after bronchoscopy and BAL in this case. The representative sections of the CT scan are shown in Figure 2.

What are the salient findings in the computed tomography scan images?

The CT scan showed a hypodense mass lesion (measuring 4.2 cm × 3.2 cm) in the right paratracheal location, extending beyond the paratracheal region, to the precarinal and subcarinal locations as well. These appeared to be multiple lymph nodes of variable sizes, the largest measuring 14 mm. The lung parenchyma was normal.

The next option for a tissue diagnosis was either a CT scan-guided mediastinal lymph node aspiration or endoscopic bronchial ultrasound (EBUS)-guided lymph node aspiration. We proceeded with the latter because the age of the child, size and position of the lymph nodes, and experience of the operator made it feasible in this case. It also avoided the need for additional radiation. Examination of the lymph node aspirate showed a reactive population of lymphoid cells with occasional histiocytic collection and few necrotic fragments without granulomas. ZN stain was positive, confirming the presence of AFB. However, GeneXpert of the sample was negative. There were no abnormal cells suggesting lymphoma. This suggested the diagnosis as mediastinal TB, although culture was awaited for confirmation.

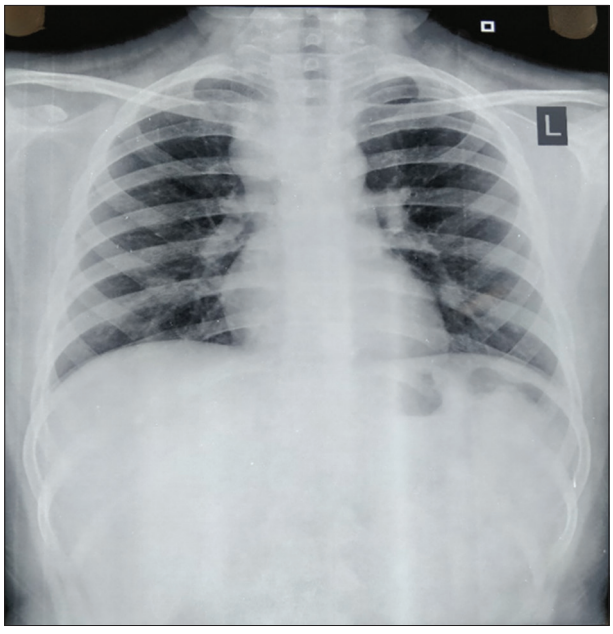

Figure 1: Chest X-ray PA view.

Management and Outcome

Standard antituberculosis treatment (ATT) was started using four drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol), administered daily along with pyridoxine. The child was discharged. On follow-up after 1.5 months, he was afebrile, had no cough or breathing difficulty, had increased appetite, and had gained 2-kg weight. Mycobacterial culture reports of gastric lavage samples, BAL, and mediastinal

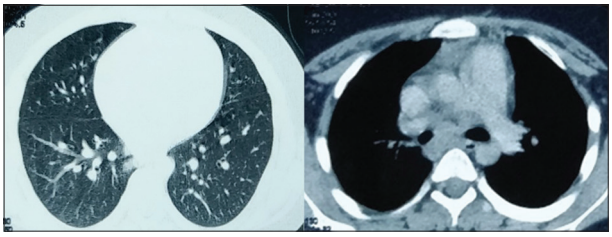

Figure 2: Representative Computed tomography sections

lymph node aspirate were all negative. The child was administered first-line ATT for 6 months and remained well. As mediastinal lymph node resolution may take longer, a follow-up chest X-ray is planned 6 months after cessation of therapy.

Discussion

TB is one of the most common infectious diseases worldwide. Due to the paucibacillary nature of the illness in children, confirming the diagnosis is a great challenge. Mediastinal lymph node involvement is one of the forms of extrapulmonary TB.

Mediastinal lymph node TB without parenchymal lesions poses an even greater diagnostic challenge due to the relative inaccessibility of tissue specimens.

In the majority of children with mediastinal lymphadenopathy, involvement occurs in more than one location.[1] In a study conducted on 100 children, the mediastinal lymph node involvement was mostly in the subcarinal (90 patients), hilar (85 left, 72 right, and 61 bilateral), axillary (79 cases), precarinal (64 cases), and right paratracheal (63 cases) locations.[2] Plain radiography is not reliable to confirm the etiology of mediastinal lymphadenopathy. CT scans have an advantage over plain X-ray chest, as lymph node necrosis is suggestive of TB, whereas sarcoidosis and lymphoma lack necrosis. The absence of lymph node necrosis in the index child necessitated invasive tissue diagnosis. In cases with lymphoma, there is a homogeneous enhancement of lymph node. For confirmation of the diagnosis, lymph node sample using EBUS-guided transbronchial needle aspiration[3] is required for histopathology; CT scans help in the localization of the site for aspiration or biopsy.

AFB can be positive in nontubercular mycobacterial (NTM) infections and also nocardiosis and actinomycosis. However, establishment of NTM pulmonary disease requires clinical, radiographic, and microbiologic confirmation by culture.[4] Clinically, these usually occur in immune-compromised patients. Typical radiological features are fibrocavitary lesions or regions of bronchiectasis, nodular infiltrates, consolidation, and tree-in-bud opacities on CT scan.[4]

The prognosis of mediastinal lymphadenopathy depends on the underlying etiology, location, and associated parenchymal lesions. The assessment of response to antituberculosis therapy does not require a chest X-ray on completion of the intensive phase, if there is clinical improvement. It may only be indicated when there is persistence of symptoms or the desired response seems to be slow. An X-ray may be done on completion of the continuation phase to document response, although lymph node resolution may take longer.[5] If there is airway compression by enlarged lymph nodes, corticosteroids are prescribed for 4 weeks followed by tapering over the next couple of weeks before omission.[6]

Conclusion

This child with fever, cough, normal physical examination, and mediastinal widening on chest X-ray underwent a stepwise approach to confirm the diagnosis. Ultimately, invasive tissue diagnosis by endoscopic bronchial ultrasound (EBUS)-guided mediastinal lymph node aspiration confirmed TB. This case highlights several learning points for clinicians.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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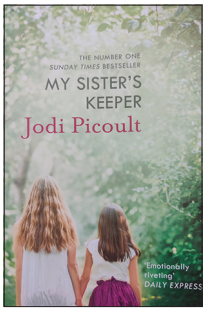
My Sister's Keeper

Editor's comment: This section will focus on books and movies that tell us the stories of patients with medical illnesses and their journeys. The reader may wonder why such a section has been included in a medical journal. It is the modus operandi that we have employed to highlight how and why the world of clinical medicine is changing. If you go through the 2017 CARE guidelines recommended for writing a case report, you will come across an element entitled' "patients' perspective" that deepens the dimensions of the clinical condition that is being described.



About the Author

Jodi Lynn Picoult is an American writer. Picoult has published 26 novels, accompanying short stories, and has also been awarded the New England Bookseller Award for fiction in 2003. Her brand of fiction is characterized by the fact that she usually portrays moral dilemmas which pit family members against each another. She has not shied away from controversy, many of her books having as their theme contentious current issues such as abortion, assisted suicide, race relations, eugenics, and school shootings. She is also, as one discovers, the mother of a child who needed 10 surgeries for cholesteatoma-a circumstance she credits as being the reason she holds the medical profession in such high regard.

About the Book

"My Sister's Keeper" is set against the backdrop of the gut-wrenching diagnosis of Acute Promyelocytic Leukemia and how the family copes in the shadow of the interventions needed to keep their second born, Kate, alive. The story is written in first person, a master stroke as one gets an intimate look at the inner workings and motivations of each character.

The primary protagonist is Anna, the third and youngest child. Anna initially comes across as a disgruntled teenager who like all adolescents is looking to find her own identity. In her case though, there is a unique situation, in that Anna was genetically designed to be her older sister Kate's bone marrow match-a fact that seems to have contributed to her sense that she did not really belong in this family. All of thirteen, she decides at the start of the novel that she has had enough of subsuming her needs and life to the needs of the older sibling and decides to take her parents to court to medically emancipate herself.

This decision changes everyone and everything that come into her path and the ensuing drama has been masterfully, sensitively recounted. The passages sharing the view of the world and its happenings from the perspective of the kids as they are growing up are particularly appealing. Anna is portrayed sensitively, showcasing all the inevitable confusion and yet passion of the teenage years. Her need to be seen and validated as also the growing realization that her parents are unable to understand things from her perspective, is moving and emotionally charged.

Anna's father, Brian, is a fire fighter, an intensely metaphorical profession, given that in many ways that's what his role is in the family. His interest in astronomy (Anna is short for Andromeda) seems to have started as a hobby and is now an attempt to maintain perspective through the shambles of his life and marriage. His perspective is that of a sincere father and husband who is trying his best to keep his family afloat amidst the catastrophe his family is going through. His life seems to be a balancing act between managing medical and financial issues, as well as the emotional needs of his wife and kids. He is particularly concerned about Anna, who he considers to be the stable one as compared to the rest of his brood.

Brians wife, Sara, is a lawyer who has given up practicing Law to take care of her three children. The story of her life is recounted in flashbacks interspersed with present day rendition. Her story is that of a young mother intent on saving the life of her daughter since the age of 2 years, when she was first diagnosed. Picoult lets the reader gradually uncover the making of a woman who is pushed emotionally to the limit, time and again. Sara seems to have lost herself through the 14 demanding years since her daughter's diagnosis was made. She is the backbone, and also paradoxically also the weakest link in the family's structure. In the present, she finds herself defending all the decisions she has ever made, in a court of law against her own daughter. A process that forces her to see herself and her life's work from the perspective of all her children.

Anna's teenage brother, Jesse, is a druggie teenager bordering on delinquency. Jesse's angst seems a manifestation of all the unacknowledged pain that the other members of the family are experiencing. His use of substances and predilection for causing mayhem hides feelings of worthlessness stemming from a childhood spent in the shadow of his younger sister's disease.

Perhaps the most poignant passages are assigned to Kate, the victim of the devastating disease and harrowing treatments. In addition to being a survivor of leukemia and now chemotherapy-induced chronic renal failure, she is also a teenager who desperately longs to lead a "normal" life. The parts of the book that deal with Kate would appeal the most to the "pediatrician" within our readers. Picoult describes, in sometimes excruciating detail, the nontherapeutic effects of life-saving interventions that are used in children with leukemia, This perspective is almost never factored in the vision of the treating medical personnel, who are completely focused on saving lives, preventing relapses and decreasing morbidity.

Picoult succeeds in making the reader feel torn. One veers to feel support toward Anna, and other times Sara, the poor mother in this situation. The courtroom scenes are full of conflict and yet since one has been made aware of each character's unique points of view, there is a much deeper conflict to have a straight-forward verdict. The book ends in a rather emotionally unsatisfying way, but given the fact that by the end, one has developed an attachment to all the main characters, perhaps that was intentional on part of the author.

The greatest strength of this novel is in the descriptions of the inner workings of each character. Each of the protagonists, in their own way, is looking for redemption and the author manages the tall task of fleshing out their individual voices beautifully. The medical portions have been dealt with robust research and the emotion with depth, yet scant sentimentality. The medical themes that keep one engrossed are ethical dilemmas at the very cusp of life and death. The author manages to bring alive the complex and contradictory world of this family and make it entirely relatable to all readers, but especially pediatricians. The gray areas of Medicine, the controversial subjects, as also the sheer pace of the book, make it difficult to put down. Do keep aside time (and a box of tissues!) before picking up this gem.

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Conflicts of interest

There are no conflicts of interest.

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Clinical Crossword: 2

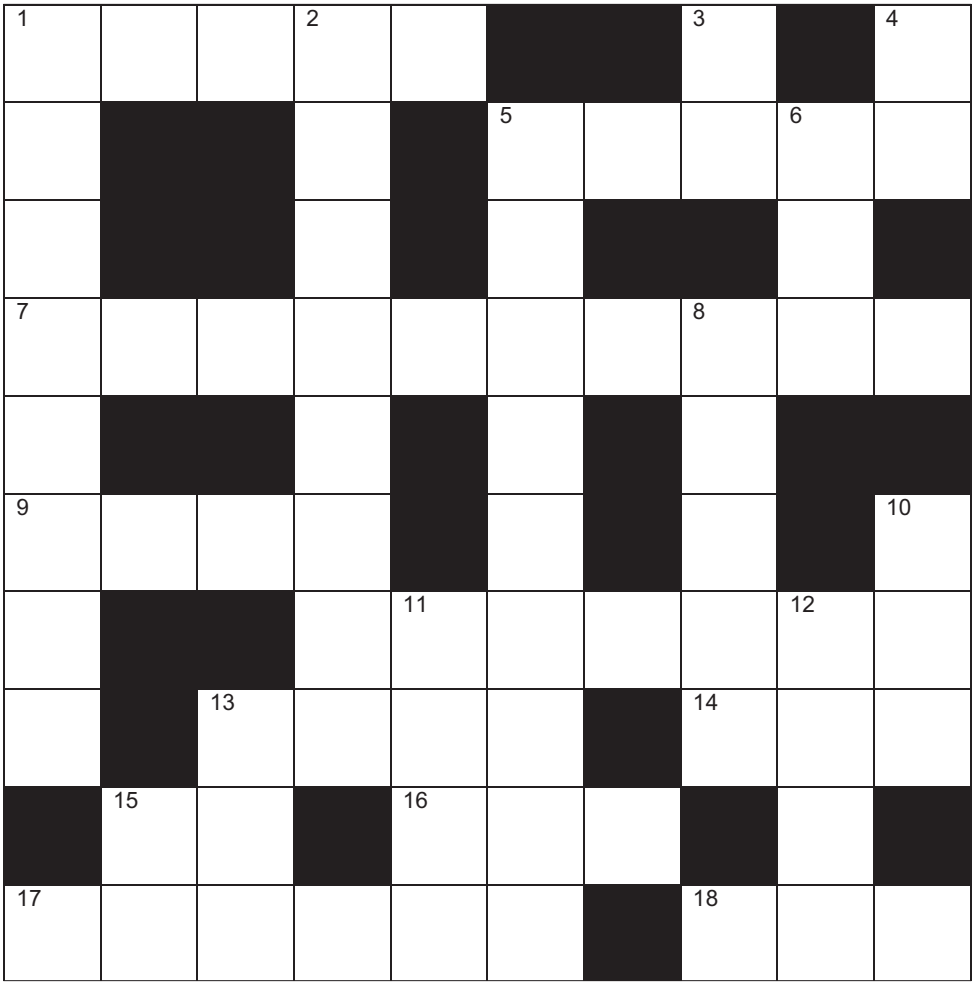
Dear crossword lovers, I hope to have as much fun solving these clues, as I had in making them. Please send your answers to ipcares2020@gmail.com. We shall post the answers and the names of the first 10 readers who solve the crossword on our website.

Across

1 The group that proposed a unified definition of the medical condition in 6 Down; abbr. (1,1,1,1,1)
5 Clinical criteria used to approach a child with congenital heart disease (5)
7 Necrotizing, ulcerative lesions caused by fusiform bacteria and spirochetes (10)
9 An abnormal sound heard in the lungs on auscultation (4)
11 The pH of lacrimal gland secretions
14 The minimum frequency of which contributes to minimum acceptable diet
15 Mature female reproductive cells
16 The echocardiography that is superior to the transthoracic modality; abbr. (1,1)
17 A bag-like organ or structure (3)
18 A classical radiological sign is seen in the spine in ankylosing spondylitis (6)
19 Retrograde flow of urine; abbr. (1,1,1).

Down

1 A marsupial that inspired a strategy for keeping neonates warm (8)
2 Dead tissue (8)
3 The parameter that is estimated of amniotic fluid in the Liley Curves; abbr. (1,1)
4 An orifice of the body (2)
5 Stress fractures are common in this bone in athletes (9)
6 The clinical syndrome graded by serum creatinine and



urine output; abbr. (1,1,1)

8 The prefix used to describe the butterfly-shaped endocrinal gland (5)

10 A flat wing-like structure (3)

12 Analgesics are used to do this to pain

13 A clinical scale that assesses the sensorium; abbr. (1,1,1,1)

14 A neuroimaging technique for mapping brain activity; abbr. (1,1,1)

16 The synonym for giant cell arteritis; abbr. (1,1).

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Skills That Pediatricians Cannot Learn From Books or Databases

I recount this incident from the early years of my pediatric residency. I had recently started attending the Genetics Clinic in my institute and found dysmorphology fascinating.

One day I was allotted a 5-year-old boy with developmental delay and dysmorphism. After taking a detailed history and performing a thorough clinical examination, I presented the patient to my senior. After an in-depth discussion, we entered the salient clinical features into a dysmorphology database and got a list of differentials, the topmost being Coffin–Lowry syndrome. The clinical description and images of this disorder matched the clinical phenotype of our patient. I felt very proud of myself for contributing to the establishment of diagnosis and felt sure that I would be able to make many more diagnoses, now that I had learned how to operate the database. My senior chalked out the management plan. The family would be counseled about the disorder, prognosis, and other details by my senior as soon as he got time. In the meantime, I was to facilitate the referrals to multiple departments that were required in the workup of such a case.

Diligently, I wrote down all the places that the mother was expected to take her child and started explaining where they were located. After a first few minutes, she interrupted me and asked "Why do I need to go to so many places?" I replied, "Your child needs some important investigations." Her next question was, "When will you give my son some medicine to cure him?" When I said, that I could not prescribe any medicine, she asked me whether we were waiting for the investigation reports to start the treatment. After telling her that the condition in question had no cure, I started to explain that the investigations were important for assessing the child holistically and providing supportive care. Suddenly she burst out, "What kind of a doctor only gets investigations done, but does not prescribe any medication? What do you have to gain from getting these done?" Luckily, my senior intervened and started to calm the mother by asking her to sit down and offering her a glass of water. The father was called and the next hour was spent counseling the family about the condition and how we would all be working together to support and optimize her child's physical and mental well-being. I was completely taken aback and then started to feel angry. Here, I was with her child's best interests at heart, and I was being accused of malintent!

Later my senior told me in detail how counseling was supposed to be done, and how to recognize the steps of grief in a parent and pace the content accordingly, among others. But I was still miffed. It was only much later that I realized how insensitive I had been. That day, the only thing I had been keen on learning was how to operate the dysmorphology database to enable myself to deduce a rare diagnosis. I did not treat the child as a person but as a medical condition. I did not pay any attention to the mother's body language or care about how she must be feeling when I broke the news so insensitively. I did not wait for the parents to be properly counseled. I was just bothered in getting the tasks assigned to me, completed.

In those days, and till date, the top priority of most residents is gaining clinical knowledge and experience, learning examination skills, and performing exotic procedures. Learning how to empathize, and communicate with the patient and family is never a priority for residents, or taught or demonstrated proactively by the departments. These skills are somehow expected to develop magically just by themselves. Such close encounters can be quite dangerous during the early years of training. The art of communicating sensitive information and dealing with anxious parents is an essential competency for all pediatricians. It has to be a shared two-way process, not a didactic monolog. Competency-based medical education has been introduced in the undergraduate curriculum. However, postgraduate residents do not receive any formal instruction. This should be included as a part of their curriculum, and sensitization activities should be carried out right from the start of residency. Empathy and communication cannot be learned from any database or textbook.

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