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CONTENTS

TOPIC OF INTEREST - "HEMATO-ONCOLOGY "

Nutritional anemia - Strategy for prevention and management **245**
- Elizabeth KE

Megaloblastic anemia - An update **252**
- Sunil Gomber, Mukesh Yadav

Autoimmune hemolytic anemia **258**
- Pandiarajan Vignesh, Sanjib Mondal

Childhood acute lymphoblastic leukemia - An update **266**
- Srinivasan Peyam, Amita Trehan

Thrombocytopenia - Case vignettes **276**
- Nita Radhakrishnan, Ravi Shankar

Automated analyzer based approach to anemia **288**
- Abhishek Sharma, Reena Das, Prashant Sharma

Clotting factor replacement therapy **298**
- Shanthi S

Hematopoietic stem cell transplantation - Where we are and the way forward **312**
- Ramya Uppuluri, Venkateswaran VS, Revathi Raj

DRUG PROFILE

Drugs in pediatric rheumatology **317**
- Jeeson C Unni, Ranjit Baby Joseph, Sagar Bhattad

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SURGERY

Acute pain management - Review of current concepts **328**
- Jayanthi R, Gopa Das Majumdar

ADOLESCENCE

Office mangement of substance use in adolescence **337**
- Jayashree K, Preeti M Galagali

RADIOLOGY

Radiological evaluation of gastrointestinal foreign bodies **343**
- Raveendran J, Balaji S, Vijayalakshmi M

CASE REPORT

Herbs and hemolysis **351**
- Shyamala Jayamoorthy, Revathi Raj

Allgrove syndrome with a novel mutation - Case report in two siblings **353**
- Anish A, Riyaz A, Nisha M, Najeeba R, Roshin RA, Jitesh P

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HEMATO-ONCOLOGY

NUTRITIONAL ANEMIA - STRATEGY FOR PREVENTION AND MANAGEMENT

*Elizabeth KE

Abstract: *This review elucidates the prevalence of anemia in various age groups in India and existing strategies for prevention and management of anemia. The inadequacies of existing strategies and their solutions are discussed. Multi-pronged approach incorporating delayed cord clamping, iron folic acid supplementation, dietary diversification and food fortification is recommended. Besides, there is a need to address iron refractory anemia, infections like malaria, worm infestations, Helicobacter pylori infection and also genetic causes like hemoglobinopathies.*

Keywords: *Anemia, Prevalence, Digital testing for hemoglobin, Anemia mukt bharat, National iron plus initiative.*

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Points to Remember

- ***There is high prevalence of anemia in all age groups including women of reproductive age, in our country which is a serious public health problem.***
- ***Anemia Mukt Bharat is an updated version of National Iron Plus Initiative (NIPI) campaign.***
- ***For operational convenience, double the dose of IFA recommended for prophylaxis is given for treatment of iron deficiency anemia, followed by monitoring after 2-4 weeks.***
- ***Currently the tolerable upper limit of elemental iron is estimated as 60 mg.***
- ***If there is no improvement in hemoglobin, alternate causes should be considered.***
- ***Multi-pronged approach like delayed cord clamping, iron folic acid supplementation, dietary diversification and food fortification is recommended.***
- ***Behavioral Change Communication aims at dietary diversification.***
- ***Iron fortified rice and other cereals, double fortified salt and home fortifications are recommended.***
- ***WHO 2001 recommends that children between 6 - 59 months must be prescribed daily iron if the prevalence exceeds 40%.***
- ***Dietary diversity and ideal phytate to iron ratio (< 0.4 :1) and vit C to iron ratio (4:1) are recommended for better absorption.***

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HEMATO-ONCOLOGY

MEGALOBLASTIC ANEMIA - AN UPDATE

***Sunil Gomber**
****Mukesh Yadav**

Abstract: *Megaloblastic anemia is a multisystem disorder, which can easily be diagnosed with high index of suspicion. A complete blood count and review of blood and bone marrow films reflect the typical pathognomonic cytologic appearance of megaloblastic anemia. Assessment of metabolites like serum homocysteine and methylmalonic acid in the serum or in the urine is considered to be more sensitive and specific whereas serum cobalamin and folate levels are of limited value. It is highly amenable to therapy once the primary cause is established. Appropriate replacement therapy of deficient nutrient, cobalamin or folate or both, easily corrects the anemia.*

Keywords: *Anemia, Megaloblast, Replacement therapy, Children.*

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Points to Remember

- ***Vitamin B12 and folic acid deficiencies are the leading causes of megaloblastic anemia.***
- ***Vitamin B12 deficiency may present with pancytopenia, hemorrhagic manifestations and fever, thus mimicking diseases like aplastic anemia or acute leukemia.***
- ***Homocysteine is increased in both folate and vitamin B12 deficiency but serum MMA is increased in vitamin B12 deficiency only.***
- ***Apart from an anemic syndrome, patients with vitamin B12 deficiency may also present with neurologic symptoms.***
- ***Treatment of folate deficiency with folic acid supplements should be initiated after ruling out concomitant vitamin B12 deficiency as it increases the risk neurological and neuropsychiatric disorders.***
- ***Hypokalemia and iron deficiency can occur during treatment of severe megaloblastic anemia.***

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HEMATO-ONCOLOGY

AUTOIMMUNE HEMOLYTIC ANEMIA

** Pandiarajan Vignesh*
*** Sanjib Mondal*

Abstract: *Autoimmune hemolytic anemia (AIHA) is caused by autoantibodies to red blood cells resulting in excessive destruction of erythrocytes. AIHA is either idiopathic or associated with infections, malignancies and autoimmune diseases. AIHA is classified into warm, cold and mixed types.Warm AIHA is marked by anemia, jaundice and spherocytes, due to extravascular hemolysis. Cold agglutinin disease results after infections and causes red cell agglutination at colder temperatures. Positive direct antiglobulin test (DAT) in the setting of hemolytic anemia is diagnostic of AIHA. Immunosuppression is the main basis of management.*

Keywords: *Auto antibody, Extravascular hemolysis, Intravascular hemolysis, Hemoglobinuria, Direct Coomb's test, Immunosuppression.*

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Points to Remember

- ***AIHA is either idiopathic or associated with infections, malignancies, autoimmune diseases, and lymphoproliferative syndrome. AIHA is classified into warm, cold and mixed types.***
- ***Warm AIHA is marked by the presence of anemia, jaundice and spherocytes, due to extravascular hemolysis.***
- ***Cold agglutinin disease results after infection with Mycoplasma pneumoniae or Epstein-Barr virus and causes red cell agglutination at colder temperatures. Features of cold antibody AIHA and PCH include features of intravascular hemolysis and microvascular occlusive episodes.***
- ***Primary immunodeficiency diseases associated with AIHA include common variable immune deficiency, autoimmune lymphoproliferative syndrome (ALPS) and Wiskott Aldrich syndrome.***
- ***Positive DAT in the setting of haemolytic anaemia is diagnostic of AIHA. Other laboratory parameters include increased reticulocyte count, indirect bilirubin, and LD, decreased haptoglobin and presence of hemosiderin in urine sediments.***
- ***Bone marrow examination is indicated, in cases of clinical suspicion of hematological malignancy or bone marrow failure syndromes.***
- ***Blood transfusion in AIHA is indicated in case of severe anemia. Immunosuppression is the main basis of management.***
- ***Splenectomy or plasmapheresis are indicated in refractory cases.***

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HEMATO-ONCOLOGY

CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA - AN UPDATE

*Srinivasan Peyam
**Amita Trehan

Abstract: *Acute lymphoblastic leukemia (ALL) comprises 75% to 80% of all childhood leukemias. ALL occurs commonly between 2 and 5 years of age with 80-85% being of B-lineage, T-lineage accounting for 10-15% and around 5% being uncommon variants. An improved understanding of the biological heterogeneity of the disease has led to marked improvement in outcome, with current 5-year event-free survival (EFS) being 85% and overall survival (OS) rates being around 90%.*

A diagnosis of leukemia is confirmed by doing a bone marrow examination which ideally includes morphology, flowcytometry, cytogenetics and molecular genetics. Current day therapy is dependent on the risk assessment and the response of the disease to therapy. Precursor B ALL is stratified into standard, intermediate and high risk disease with minimal residual disease assessment at the end of Induction therapy being the most important indicator of prognosis. T-ALL is treated with a protocol similar to HR ALL. Combination chemotherapy consisting of drugs acting at different phases of the cell cycle is the cornerstone of therapy. Treatment broadly consists of 4 phases: Induction, consolidation, delayed intensification or re-induction and maintenance therapy.

A hematopoietic stem cell transplant is required in very few with contemporary treatment. Targeted therapy/ immunotherapy are the newer approaches for refractory/ relapsed leukemias. Supportive care which includes treatment and prophylaxis for infections, transfusion support, nutritional support and psychological support are vital to the management of disease.

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Keywords: *Childhood ALL, Risk, Response, Treatment, Genetics.*

Points to Remember

- ***Childhood ALL has a good prognosis.***
- ***B-lineage ALL constitutes around 80% and T lineage around 15% cases, 5% being mixed lineage/others.***
- ***Childhood ALL management is risk (clinical/ cytogenetic/molecular analysis) and response (prednisolone response/minimal residual disease) based, indicating the need for adequate cytogenetic and molecular analysis at diagnosis.***
- ***Children who are low risk can be treated with less intensive therapy, while high risk children require intensive therapy.***
- ***Ph-like ALL is a major missed entity among B-other-ALLs, with scope for their identification by molecular diagnostics.***
- ***HSCT is needed in very few children as upfront therapy in the management of childhood ALL.***
- ***Supportive care is important and it includes infection control, transfusions and good nutrition.***
- ***Precision medicine in the future will include immunotherapy and pharmacogenomics of anti-metabolites to improve survival in the small percentage who still relapse and to decrease treatment related morbidity.***

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HEMATO-ONCOLOGY

THROMBOCYTOPENIA-CASE VIGNETTES

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Abstract: *Platelets play a vital role in coagulation and hemostasis. Thrombocytopenia is a common hematological concern in pediatric practice, the etiology of which can vary from mild viral illnesses to critical illnesses. Understanding the pathogenesis of each of these conditions is crucial as decisions such as 'to treat or not to treat' and 'how to treat' are based on this. For the same platelet count, the decision to treat varies based on the pathogenesis. In this article, we explore the common causes of thrombocytopenia in children, their pathogenesis and logic for treatment.*

Keywords: *Thrombocytopenia, Bone marrow suppression, Immune thrombocytopenia, Approach.*

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Points to Remember

- ***Thrombocytopenia is a vital clue to the diagnosis of many acute and chronic illnesses.***
- ***Management of thrombocytopenia is decided based on the underlying etiology.***
- ***It is important to focus on the clinical condition of the child than on platelet counts.***
- ***Mean platelet volume ranges from 7-9 fL which is expressed in automated hematology analyzers. In conditions where platelets are destroyed, megakaryocytes produce large platelets. In bone marrow pathology, where megakaryopoiesis is affected, usually platelets are of normal size except in certain inherited conditions.***
- ***Immature platelet fraction is a measure of reticulated platelets or "reticulocyte" equivalent of platelet series. They are physiologically more active. IPF >8% predicts platelet recovery within the next 24 to 48 hours in dengue infection.***
- ***Bone marrow failure syndromes and leukemias should not be missed while evaluating thrombocytopenia.***
- ***Inherited causes of thrombocytopenia like Fanconi's syndrome, thrombocytopenia absent radius syndrome, dyskeratois congenita, Wiskott Aldrich syndrome should be suspected when there are suggestive features on physical examination.***

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HEMATO-ONCOLOGY

AUTOMATED ANALYZER BASED APPROACH TO ANEMIA

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Abstract: *Anemia represents an extremely common clinical problem among children in India. Automated hematology analyzers yield a wealth of data that can aid etiological diagnosis and follow-up of anemic children. Conventional approaches include the use of parameters indicating cell volume and size variability in conjunction with the reticulocyte count to classify anemias. Recent advances range from reliable enumeration of schistocytes, enhanced precision in nucleated RBC counts, multiple approaches for detection of spherocytes, improved parameters for identification of anemias due to iron deficiency and iron restriction to hematopoiesis and improved prediction of hematopoietic recovery by identifying immature reticulocyte populations. This review discusses interpretation of the analyser data and their relevance to practicing paediatricians managing anemia.*

Keywords: *Anemia, Automated analysers, Automation, Erythrocytes, Laboratory test.*

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Points to Remember

- ***Automated hematology analyzers yield a wealth of data that can aid etiological diagnosis and follow-up of anemic children.***
- ***Conventional approaches include the use of parameters indicating cell volume and size variability in conjunction with the reticulocyte count to classify anemias.***
- ***Recent advances include precise schistocyte and nucleated RBC enumeration, improved parameters for iron deficiency and iron-restricted hematopoiesis, increasing utility of immature reticulocyte populations and detection of spherocytes and other poikilocytes.***
- ***Future advances in the field are likely to include digital image analysis and artificial intelligence to analyse patterns indiscernible to the human mind and eye.***

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HEMATO-ONCOLOGY

CLOTTING FACTOR REPLACEMENT THERAPY

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Abstract: *Inherited disorders of clotting factor deficiency are known to occur with all coagulation factors. Of these, Von Willebrand disease, hemophilia A and B are the commoner conditions. Fresh frozen plasma contains all coagulation factors and hence in the past it was used as the major therapy for all inherited clotting factor deficiencies presenting with bleeds. Later cryoprecipitate was discovered and used for deficiency of fibrinogen, factorVIII, factor XIII and Von Willebrand disease. Both these blood products have to be administered in large volumes and they also carry a high risk of transfusion transmitted infections. This led to the discovery of clotting factor concentrates. Good manufacturing practices have resulted in the availability of products with high degree of purity and safety. Plasma derived single factor concentrates are available for all factors except for factor II and factor V. Advances in genetic engineering led to the discovery of recombinant factors which have very high safety profile. Currently recombinant forms of factor VIIa, factor VIII, factor IX and factorXIII are available. The standard of care for factor deficiencies is to replace the missing factor using clotting factor concentrates to enable patients to lead a completely normal life. This article deals with factor replacement therapy for the common and rare bleeding diatheses.*

Keywords: *Factor replacement therapy, Clotting factor concentrates, Fresh frozen plasma,Cryoprecipitate.*

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Points to Remember

- ***Clotting factor concentrates are available for almost all factor deficiencies except FV and they are the drug of choice for congenital factor deficiencies.***
- ***FFP contains all coagulation factors and hence can be used in a coagulopathic child with bleeds if specific factor concentrates are not available.***
- ***Cryoprecipitate contains fibrinogen, FVIII, FXIII and von Willebrand factor and can be used in deficiencies if specific factor is not available.***
- ***Recombinant FVIIa and activated prothrombin complex concentrate (aPCC) are useful in arresting bleeding in hemophilia children with inhibitors.***
- ***Prophylaxis using continuous factor replacement is recommended as the standard of care in haemophilia patients.***
- ***Tranexamic acid should be avoided in patients receiving prothrombin complex concentrates (PCC).***

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HEMATO-ONCOLOGY

HEMATOPOIETIC STEM CELL TRANSPLANTATION - WHERE WE ARE AND THE WAY FORWARD

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Abstract: *Hematopoietic stem cell transplantation is potentially curative in several stem cell disorders. The process involves HLA typing, donor selection, conditioning, harvesting stem cells , infusion , supportive care, engraftment and immunosuppression to prevent graft versus host disease and graft rejection. A team of experienced pediatric intensivists, dedicated nurses, antibiotic stewardship and infection control measures are essential components for providing optimal care. With advances in molecular diagnosis and whole-exome sequencing, the indications for hematopoietic stem cell transplantation=are expanding and several hitherto unrecognized life-threatening conditions have a potential for cure. Pediatricians are the key personnel to maintain the shared care and follow up for late effects, thus ensuring intact and quality survival.*

Keywords: *HSCT, Children, Survival, Cure.*

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Points to Remember

- ***Hematopoietic stem cell transplantation (HSCT) is potentially curative in several congenital and acquired stem cell disorders including thalassemia major, primary immune deficiency disorders, Fanconi anemia and malignancies.***
- ***HLA typing of Class I (A, B, C) and Class II (DP, DQ, DR) antigens is the key to determining the compatibility of the donor and in planning the type of HSCT namely matched related, matched unrelated, mismatched related or unrelated and haploidentical stem cell transplantation.***
- ***Although 30% of patients can find a compatible match within the family, alternative donor transplantation is an option in the remaining 70%, including unrelated and haploidentical transplants.***
- ***The source of stem cells could be peripheral blood, bone marrow or cord blood and donation of stem cells is safe for the donor.***
- ***Supportive care is the key to ensuring optimal outcomes.***
- ***Teamwork between experienced pediatric intensivists and nursing groups, antibiotic stewardship and infection control measures are the essential components of care.***
- ***Immunosuppression is only for a short duration of one year on average unlike solid organ transplantation where the children are on lifelong medications. However, follow up for late effects of chemotherapy utilizing shared care with pediatricians is essential for optimal outcomes.***

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DRUG PROFILE

DRUGS IN PEDIATRIC RHEUMATOLOGY

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Abstract: *Various factors, including disease activity and severity, co-morbidities and patient preference (including cost, route of administration and frequency of monitoring) need to be factored in deciding the optimal treatment of various rheumatic diseases in children. Non-steroidal anti-inflammatory drugs and steroids may be used to provide symptomatic relief whereas the arrest of progression of disease is achieved using disease modifying drugs. Treatment goals include achievement of remission or low disease activity, and the prevention of radiographic progression of the disease.*

Keywords: *Juvenile idiopathic arthritis, Rheumatic, NSAIDs, Steroids, Disease modifying anti rheumatic drugs, Methotrexate, Biologicals, Children.*

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Points to Remember

- ***Numerous medications are currently available for the treatment of rheumatic diseases apart from NSAIDs and steroids.***
- ***NSAIDs and steroids can be used as a stopgap measures till optimum effects of disease modifying drugs start appearing.***
- ***Methotrexate is the most commonly used agent for initial treatment of juvenile idiopathic arthritis.***
- ***Combination therapy has been shown to have better outcome than monotherapy but the choice of medications should be tailored for each patient.***
- ***Most of these medications require periodic monitoring by specialists for possible major adverse effects.***

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SURGERY

ACUTE PAIN MANAGEMENT - REVIEW OF CURRENT CONCEPTS

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Abstract: *Perception of pain in children is complex and often remains underrated and untreated. It entails many physiological, psychological, behavioral and developmental factors. Pain management requires identification of the source and assessment of the intensity of pain.*

This review article discusses some of the common age specific pain assessment tools used in practice to grade the severity of pain and how to plan the patient specific analgesic regimes. It has also reviewed the different methods currently used for acute pain management and the pharmacological aspects of various analgesics used in children.

Keywords: *Acute pain, Management, Children.*

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Points to Remember

- ***Pain in children is underrated and undertreated.***
- ***The source of pain must be identified, followed by assessment of severity.***
- ***Analgesic drugs can be broadly divided into-opioid, non opioid analgesics and adjuvant drugs.***
- ***Optimal combinations of opioid and non opioid analgesics are used to maximise pain control with minimal drug induced side effects.***
- ***Paracetamol either alone or along with NSAIDS form the mainstay of treatment for mild to moderate pain and weak opioids (codeine, oxycodone, hydrocodone and tramadol) for outpatient management of moderate pain.***
- ***Severe pain is ideally treated with opioids like morphine in the hospital setting where it can be used with precautions.***
- ***Opioids may be largely grouped as agonist, partial agonist and agonist-antagonist. The latter agents have less potential for side effects like respiratory depression and lesser potential for abuse.***
- ***Adjuvant analgesics derived from diverse pharmacologic classes like antispasmodics, clonidine etc. are now used to manage non-malignant pain.***
- ***Local anaesthetics are widely used nowadays for topical analgesia, intraoperative pain management and post operative pain.***
- ***Non-pharmacological techniques of pain management should be utilized in children in appropriate situations.***

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ADOLESCENCE

OFFICE MANAGEMENT OF SUBSTANCE USE IN ADOLESCENCE

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Abstract: *Substance use in adolescents begins in the critical phase of growth. Adolescents are "biologically wired" to seek new experiences and take risks, as well as to carve out their own identity. Substance use during adolescence has been associated with a greater risk of substance use disorders in adulthood. Efforts should be focused on early identification, awareness and prevention programs, and routine monitoring of adolescent health. Pediatricians should screen for nonspecific flag signs and specific indicators of substance use and underlying mental health disorders should be diagnosed in these adolescents. Behavioural interventions, family, school and community support groups need to be created for their management*

Keywords: *Substance use, Drug addiction, Adolescence, Adolescent behaviours, Screening.*

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Points to Remember

- ***Substance use in adolescents begins as a result of curiosity or peer pressure.***
- ***The primary care pediatrician plays an important role and has an unique opportunity to screen adolescents for SUD.***
- ***Creating awareness among adolescents, parents and teachers is the need of the hour.***
- ***Pediatricians should screen every adolescent for substance use.***
- ***Treatment requires a multidisciplinary approach along with parental and peer support.***
- ***Behavioural interventions help in prevention of substance use.***

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CASE REPORT

HERBS AND HEMOLYSIS

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Abstract: *Glucose 6 phosphate dehydrogenase is an important enzyme preventing oxidative damage to red blood cells. While hemolysis induced by exposure to various medications in G6PD deficient individuals is well recognized, less well known is the same phenomenon triggered by exposure to herbs. We present here an infant with this rare clinical presentation.*

Keywords: *Hemolysis, G6PD deficiency, Herbs, Acalypha indica.*

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CASE REPORT

ALLGROVE SYNDROME WITH A NOVEL MUTATION - CASE REPORT IN TWO SIBLINGS

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Abstract: *Allgrove syndrome (AS/Triple A syndrome) is a rare, familial, multisystem, potentially fatal autosomal recessive disorder characterized by achalasia, alacrimia and ACTH-resistant adrenal failure. There is significant heterogeneity in the clinical features and the types of mutations reported in families with Allgrove syndrome. Two siblings (ten- year-old girl and her six-year-old brother) presented with adrenal insufficiency, hyperpigmentation and alacrimia. Genetic exome sequencing revealed a homozygous variant of uncertain significance in exon 6 of the Triple A syndrome (AAAS) gene in the proband which was further confirmed by Sanger validation.*

The parents were found to be heterozygous, and the sibling homozygous for the tested variant of the Achalasia, Adrenocortical insufficiency, Alacrimia Syndrome AAAS gene. There was good response to replacement therapy with hydrocortisone.

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Keywords: *Adrenal insufficiency, Alacrimia, AAAS gene, ALADIN.*

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