inheritance. CGD is characterized by neutrophils and monocytes capable of normal chemotaxis, ingestion and degranulation, but unable to kill catalase-positive microorganisms due to defects in one of the 5 major subunits of NADPH oxidase.

Method and material: The medical records of 38 patients diagnosed with CGD were reviewed and analysed with respect to demographic data, age at presentation and diagnosis, clinical features, laboratory investigations, organisms isolated, treatment & prophylaxis given and clinical course.

Results: Our study had 28 males and 10 females with 13 having history of consanguinity. Their mean age at presentation and diagnosis was 1.32yr and 2.5yr respectively. The most common manifestations at presentation were failure to thrive (100%) and lymphadenopathy (100%) followed by hepatomegaly (72%) and splenomegaly (48%). The commonest infection was pneumonia (84%) followed by abscesses (55%) involving lungs, liver, subcutaneous tissue; osteomyelitis (15%); urinary tract infections; otitis media and CNS infections. Organisms isolated from blood, stool and pus of infected lesions included bacteria- Mycobacterium tuberculae (50%), Staphylococci (24%), Klebsiella (16%) and fungi- Aspergillus (13%), Candida (26%). Biopsies done in 36% patients from lymph node, skin, lung and liver showed non caseating granulomatous inflammation. Diagnosis was based on reduced nitroblue tetrazolium test (NBT) between 0-5% in all patients and confirmed by dihydrorhodamine (DHR) assay in 84% patients. 18 families were screened. All patients received antibiotics, 80% received AKT, 76% received Antifungals and all received antifungal and antibacterial prophylaxis. 4 patients have succumbed to the illness and 13 patients are lost to follow-up. 7 patients inherited CGD in an X-linked recessive fashion. Genetic mutation analysis has been done in 22 patients.

Conclusion: CGD is a not uncommon in India. The commonest mode of presentation was Pneumonia, skin and subcutaneous abscesses, lymphadenitis and osteomyelitis. Mycobacteria, Staphylococcus Aureus, Klebsiella, Aspergillus, Candida, and Gram negative bacilli were the commonest organism isolated in our series. Infection with Aspergillus, Burkholderia Cepacia, Serratia Marcescens, Nocardia should prompt work up for CGD. All children with CGD should be given routine chemoprophylaxis with Septran and Itraconazole. Families should be screened and counselled during future conceptions.

PID_ALP_ID-1_V1.4
AN INTERESTING CASE OF FEVER-NEONATAL ONSET MULTI SYSTEMIC INFLAMMATORY DISORDER

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Background: Neonatal onset multisystem inflammatory disease (NOMID) is the most severe phenotype in spectrum of Cryopyrin (NLRP3/NALP3) associated periodic syndromes (CAPS) associated with chronic IL-1B over production. Mutated NLRP3 causes constitutive activation of NLRP3 Inflammasome which over produces IL-1B. The role of IL1 B in NOMID has been demonstrated in clinical trials using IL1 blocking agents that cause rapid resolution of disease manifestations.[1]

Case Summary: A 16 months old male child presented with complaints of fever and rash since day 1 of life and delayed development. Fever is almost always associated with rash. Rash is urticarial, truncal with itching. At 7 months child was noticed to have anemia with hepatosplenomegaly and neuroimaging was s/o mild cerebral atrophy with communicating hydrocephalus. Patient had h/o 3-4 episodes of pneumonia too. Examination revealed overhanging forehead, hypertelorism, depressed nasal bridge. Child had pallor, rash, hepatosplenomegaly with generalized hypotonia. A differential of primary immune deficiency disease v/s inflammatory disorder v/s mastocytosis v/s storage disorder was evaluated. His baseline investigations were within normal range. MRI was s/o mild generalized atrophy with dilated lateral ventricles. Bone marrow aspiration was done to r/o mastocytosis. Liver biopsy had no evidence of storage disease. Lymphocyte subset and DNT cell analyses were within normal range. After ruling out the above differentials a periodic inflammatory syndrome was suspected. Cryopyrin mutation analysis at NIH suggested mutation in CIAS1 G755R region. This mutation is interesting as it is exon 4, which is not a common mutation.

Discussion: A basic innate response to any pathogen is Inflammasome formation.[2] In CAPS, mutated NALP3 is constitutively activated resulting in increased assembly of NALP3 infalmmasome and active caspase 1. Active caspase 1 cleaves inactive pro IL 1 B to its active form. NOMID has onset in neonatal or early infancy. It has continuous flares with involvement of skin (rash), eye (conjunctivitis), joints, ears, and meninges.[1] Distinguishing features being chronic meningitis, SNHL and a characteristic facies. IL 1 receptor antibodies (Anakinra) are used in the treatment. With treatment, systemic inflammation, conjunctivitis, arthritis and cochlietis can be prevented. Leptomeningitis can be fully reversible.

Conclusion: NOMID is a CAPS presenting with fever since early life. The cardinal features are fever with rash since day 1 of life with continuous flares. The present case of NOMID had an exon 4, rather than exon 3 where most of the identified mutations are seen. After differentiating it from immunodeficiency disorder and since the pathophysiology of NOMID involves IL-1 B over production, IL1 antibodies are used in treatment, which cause prevention of end organ damage.

PID_ALP_ID-1_V1.6
TOPIC: LEUKOCYTE ADHESION DEFICIENCY TYPE 1 – A TERTIARY CARE CENTRE EXPERIENCE

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Introduction: Leukocyte adhesion defect (LAD) is a rare, autosomal recessive primary immunodeficiency disorder of phagocytes with defective aggregation at the site of infection due to the absence of surface integrins. Diagnosis is based primarily on flow cytometric analysis of neutrophils for the surface expression of CD11, CD18 and CD15s. More than 300 cases have been described for LAD 1 worldwide, while for LAD 2 and LAD 3; there are less than 10 cases each.

Materials and methods: Analysis of clinical and laboratory profile of 6 cases of LAD type 1 seen at our institute over a period of 5 years (2011-2016) Demographic data was collected with respect age, consanguinity, community and residence. Taking an average of WBC count on presentation, mean WBC count was calculated. Microorganisms identified from respective in situ sites were documented. The CD 11, CD18 and CD15s expression identified with flow cytometry analysis. The data obtained being tabulated and expressed in graphical form.

Results: The age of presentation was from 1 to 6 months. Five were born of consanguineous marriage. 4 patients were from Maharashtra and 2 from Gujarat. 3 patients belonged to Hindu Maratha, 2 to Muslim Sunni and one to Hindu Kathiawadii community. All had delayed separation of umbilical cord on questioning. Average neutrophil count at presentation was 67,788/mm^3. Of the 6 cases, 4 had gram negative septicemia. Pseudomonas was isolated from blood culture in two cases and ET culture in one. In one patient, Klebsiella was isolated in urine and enterococci in blood. Axillary and inguinal ulcers were seen in one and necrotizing otitis externa in the another patient. All cases were severe LAD type 1 with CD 18 and CD11 a, b and c ranging from 0% in 4 and 1.6% in one. 3 patients expired from septicemia and one was lost to follow up. One case is hospitalized with necrotizing otitis externa with LMN facial palsy. One case is posted for transplantation at AIIMS, New Delhi.

Conclusion: LAD is a rare disease characterized by lack of cell surface expression of integrins, which are essential for adhesion of leukocytes to endothelial cells and chemotaxis. LAD-1 caused by lack of CD-18 integrins on the neutrophil surface has the worst prognosis and most patients die within 1st year due to severe infections;< 1% expression are clinically severe, whereas those with 2.5-10% expression are moderate to mild. In LAD-II, the neutrophils lack the membrane carbohydrate Sialyl-Lewis X required for adherence to activated endothelial cells. LAD-III is associated with defect in activation of Rap 1 protein.

LAD-I is characterized by delayed shedding of umbilical stump, recurrent bacterial infections of the skin, leucocytosis, absence of pus and poor wound healing. All patients in present study had delayed separation > 10 days (Mean 5.8-10.9). Commonest organisms isolated are Staphylococcus aureus and enteric gram negative bacilli and in our study pseudomonas was in majority.

Confirmation of diagnosis in LAD-I requires demonstration of absence of CD18 and associated alpha subunit of CD11a, CD11b, CD11c on flow cytometry. 4 of 6 patients had complete absence of the integrins. Differential diagnosis include Interleukin-1 receptor associated kinase deficiency, Hyper IgE syndrome and leukemoid reaction. The only corrective treatment is hematopoietic stem cell transplantation. Reported survival in a largest series is5 years after follow up was 75%. These patients die in childhood if transplantation is not done and if the transplantation is carried out before serious infections, the prognosis is very good.
LAD is a rare form of congenital immune deficiency to be suspected in a child with delayed fall of umbilical cord, high WBC count with neutrophilia and consanguineous marriage. High index of suspicion and early diagnosis before infection sets in is important as mortality rate is high. Pseudomonas was most common organism isolated in the present study.

RBC Disorders

RBC-1_V1.1

ACQUIRED APLASTIC ANAEMIA IN CHILDREN – OPTIMAL OUTCOMES DEPEND ON OPTIMAL DELIVERY OF IMMUNOSUPPRESSIVE THERAPY

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Background: Acquired aplastic anemia (AA) is a haematological emergency in children and we have gained enormous knowledge about the pathogenesis and immune mediated self-destruction of stem cells and immunosuppressive therapy. Due to its rarity, we have limited data of this entity, especially, its course and outcome in resource limited countries.
Patients and methods: The case records of children who had been diagnosed to have AA since 2002 at our centre were reviewed. The diagnosis of AA was made in children with pancytopenia without organomegaly and confirmed by hypocellular bone marrow showing decreased expression of all three hematopoietic lineages. Clinical findings including dysmorphism, thumb abnormalities, congenital malformations and skin hyperpigmentation were noted down. Mitomycin C induced chromosomal instability to rule out Fanconi anaemia, Ham's test to look for paroxysmal nocturnal haemoglobinuria and chromosomal analysis to look for complex karyotypic abnormalities seen in myelodysplastic syndrome were documented in all patients.
After initial stabilization, the option of haematopoietic stem cell transplantation (HSCT) was offered to all those who had matched related donors. If not, immunosuppressive therapy was delivered within two months from diagnosis after the child was infection free. A combination of 40mg/kg/day of Horse derived antithymocyte globulin (ATGAM) and methylprednisolone at 2 mg/kg/day were started for the first 4 days through a central venous catheter. Oral cyclosporine and G-CSF were started on the fifth day and since 2015 Eltrombopag was added to the IST regimen. Revolade and GCSF were continued for about 8 to 12 weeks and cyclosporine from 6 to 12 months. All patient received Voriconazole and Acyclovir prophylaxis till neutrophil recovery to 1000.
Results: A total of 109 children had been diagnosed as AA, of whom, 42 had acquired AA. The mean age of children with acquired AA was 8.16 years (2-15 yrs). Boys were twice more commonly affected (ratio M: F = 2:1). Details are listed in table 1.
Of the 41, 21 underwent HSCT as they had fully matched related donor and 20 children received IST. Of the 20 children who received ATG, 10 children (70%) had complete remission in a median duration of 78 days. Two of the three non responders were treated with second IST and all three succumbed to the illness. One child developed acute myeloid leukaemia after achieving partial remission and was salvaged with HSCT, and 1 more non responder had an unrelated HSCT and is doing well. One child has suffered a relapse after a durable remission of over 18 months off immunosuppression. The 21 children who have been transplanted have an overall survival rate of 77 %.
Conclusion: Immunosuppressive regimen including Horse ATGAM, Methyl prednisolone, Cyclosporine, GCSF and Eltrombopag along with adequate and meticulous supportive care including neutropenic care, prompt infection management and the use of irradiated and leukodepleted blood products results in a 70% response rate and should be offered to all children with aplastic anaemia with no matched family donor. The addition of Elthrombopag has resulted in early recovery of all three cell lines and must be added to the IST protocol in children.

RBC-1_V1.2

DISCORDANT BEATS – A PROSPECTIVE STUDY OF CARDIAC MRI TO ASSESS IRON OVERLOAD IN PATIENTS WITH THALASSAEMIA MAJOR

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Introduction: Advances in blood banking has ensured optimal delivery of monthly transfusion needed to save the lives of about 10,000 new thalassaemia children born each year in our country. The burden of iron chelation has now increased as these children survive into their second and third decade of life. Cardiac failure secondary to myocardial haemosiderosis is the most common cause of mortality in these patients. Our study has been done to evaluate the prevalence and severity of cardiac ironload in children with beta thalassemia major and the effectiveness of serum ferritin as a marker of iron overload.
Patients and Methods: We conducted a prospective study from the year 2015-2016 where we performed T2* cardiac magnetic resonance (CMR), serum ferritin levels and pulmonary artery pressures by echocardiography in 100 patients with transfusion dependent beta thalassaemia major. The study had been approved by IRB at the VHS centre and informed consent was obtained from all of these families. The median age of our patients was 14 (range 7 TO 33 years) with 51% of them being female. The mean serum ferritin level was 2520.78 +-223.454 ng/ml. High iron overload with a serum ferritin of over 2500 was seen in 37% of our patients. The 29% patient group that had less than 1000 ferritin were considered to be chelated optimally as per international guidelines. A cardiac T2*of over 20 milliseconds was taken as a marker of heart free of iron overload.
The mean cardiac MRI T2* was 12.73 +-2.436 milliseconds. About 70% of our patients had moderate myocardial iron overload (T2* 10-20 ms) and 24% had severe iron overload (T2* <10ms). The mean pulmonary arterial pressure was 35.96+-8.3 mm of Hg. About 76% of the patients were on a single drug chelation therapy at the time of evaluation. Following the cardiac iron status they have been started on combination chelation therapy consisting of deferasirox and deferiprone.
We found no significant correlation (r=0.014, p=0.23) between the serum ferritin levels and myocardial ironload. The most significant finding was that 38 % (11/29) of our patients with serum ferritin < 1000 had severe cardiac iron load. A significant correlation could also be established between pulmonary arterial pressures and cardiac MRI T2 *(r=1.2, p =0.0024).

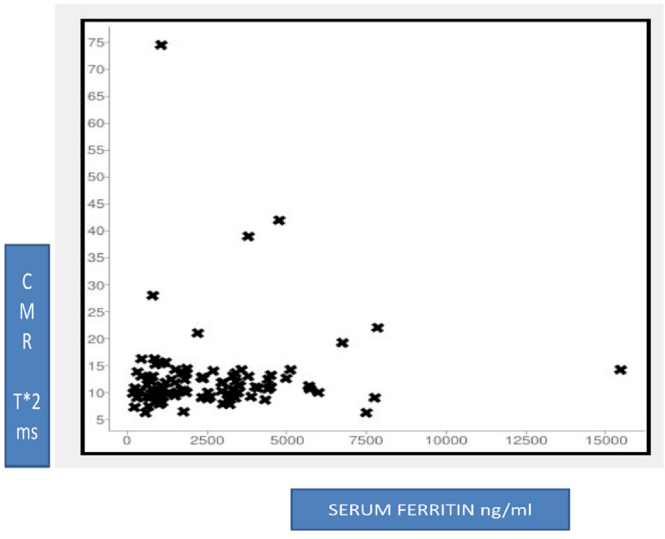

Figure 1. No correlation between serum ferritin and cardiac ironload.