Abstracts

Infections in Patients with Immunodeficiency Syndromes

01
Primary Sclerosing Cholangitis as a First Manifestation of Hyper IgM Syndrome

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Background: Primary sclerosing cholangitis (PSC) is a chronic liver disease characterized by inflammation, destruction and fibrosis of the intrahepatic and extrahepatic bile ducts that leads to cirrhosis of the liver. PSC is often complicated by recurrent episodes of bacterial cholangitis (infection of the bile ducts with bacteria). The cause of PSC is unknown but many investigators suspect that it is an autoimmune disease. Other etiologies, such as infectious agents, toxins or recurrent infections of the bile ducts are also possible causes. About 30% of patients with PSC have elevated serum gamma-globulin concentrations and about half have elevated serum IgM concentrations. About half of patients have serum antibodies against a perinuclear antigen in neutrophil cytoplasm (ANCA) and fewer have anti-smooth muscle (actin) or antinuclear antibodies. Although primary sclerosing cholangitis may be asymptomatic, the most common symptoms are fatigue, jaundice, pruritus, and abdominal pain. Primary sclerosing cholangitis is said to progress relentlessly to cirrhosis, although a patient's condition may remain stable for years.

Report: We report a 12 year old female diagnosed as a case of hyper-IgM syndrome that presented with recurrent infections and sclerosing cholangitis. She developed also Evans syndrome (autoimmune hemolytic anemia and thrombocytopenia). Immunological evaluation showed decreased levels of serum IgG and IgA with elevated levels of IgM. She also presented elevation of alkaline phosphatases and mild elevation of liver enzymes.

Outcome: Liver biopsy demonstrated the presence of idiopathic sclerosing cholangitis. The patient was started on monthly IVIG therapy at 4000 units/kg and also prophylactic antibiotics, prednisolone and vitamin E with normalization of her IgG and IgM levels and a decrease in the incidence of infections and normalization of liver function.

02
Allogeneic Bone Marrow Transplantation with Reduced Intensity Conditioning for Chronic Granulomatous Disease Complicated by Invasive Aspergillus Infection

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Background: Chronic granulomatous disease (CGD) is a rare disorder characterized by recurrent infections which can result in impaired quality of life, frequent hospitalization, end-organ damage and often death. Allogeneic BMT provides a definitive cure for CGD but carries a significant risk of mortality and morbidity, and hence it is often delayed until the patient is chronically ill and disabled. Reduced intensity conditioning (RIC) is associated with less toxicity from the conditioning agents and so presents an attractive option for non-malignant diseases such as CGD.

Objectives: We aim to report a case of successful allogeneic BMT after RIC for a case of X-linked CGD complicated by severe invasive aspergillus infection.

Methods & Results: A nine year old boy who had been diagnosed with X-linked CGD at age 3 weeks developed invasive aspergillus infection involving lungs and bones at age 8 years. This was treated with various antifungal agents and required surgery to control the infection. He underwent an allogeneic matched sibling BMT from his sister after reduced intensity conditioning. He successfully engrafted with neutrophils >500 on day 26 platelets >50,000 on day 29. He had several complications during both early and late post BMT periods but has made a full recovery from these and is now 3 years post BMT off all immunosuppressive therapy. He remains on antifungal therapy and has shown no evidence of reactivation of fungal infection.

Conclusions: Successful allogeneic BMT for a case of X-linked CGD complicated by severe invasive...
Aspergillosis was possible after effective antifungal therapy to control his infection and RIC to limit myelosuppression which aided rapid recovery of normal donor granulocytes to eliminate his infection.

03 Altered Immune Response from C4 Hypocomplementemia

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Background: C4 deficiency seems related to the development of autoimmune diseases, probably because it causes a reduction in clearance of immune complexes and a deficit in pathogens processing with a subsequent alteration in the organization of specific immune response with reduction in specificity of antibody formation.

Objectives: We analyzed in a clinical setting the presence or absence of immune function's alteration in patients with hereditary or acquired C4 complement deficit and with or without immune related pathology in order to identify possible alterations of secondary immune response.

Methods: We analyzed 12 subjects with immunity-related diseases and low levels of serum C4 and their relatives. We considered presence or absence of pathology, C3 and C4 serum concentration, genetic C4 polymorphism, and granulocyte functionality. Subjects were grouped on the basis of the presence or absence of disease and of the genetic polymorphism (not Q0 = they expressed all the C4 alleles; Q0 = they did not express one or more C4 alleles).

Results: C4 levels are related with the presence or absence of the disease, not with the C4 genes: C4 levels are higher in healthy subjects (H) in regard to ill (I) patients (Q0-H vs Q0-I: 20.35±6.1 mg/dl vs 14.61±5.8 mg/dl, p < 0.05; notQ0-H vs notQ0-I: 23.14±7.3 mg/dl vs 14.97±6.3 mg/dl, p < 0.05). IgM serum level is the same in Q0-H and Q0-I but higher concentration in notQ0-H in regard to notQ0-I. IgG were higher in Q0-H in regard to Q0-I but were lower in notQ0-H in regard to notQ0-I: Q0 appear less efficient in isotopic switching; they continue, even in case of disease, high production of IgM, less specific than IgG. Neutrophil chemotaxis tested with autologous serum is a few higher in healthy subjects in regard to ill patients.

Conclusions: C4 level assessment is useful for monitoring the activity of pathology. C4 deficiency causes alterations of immune system that can predispose to autoimmune diseases. C4 genes polymorphism study supplies the best indication of the real deficiency of the factor.

04 Reduced Bone Mineral Density and Minimal Trauma Fractures in Hyper IgE Syndrome

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Background: Hyper IgE with recurrent infections syndrome (HIES) is an immunodeficiency characterized by eczema, recurrent skin and pulmonary infections, and elevated levels of serum IgE. In addition to these immunologic features, skeletal and connective tissue abnormalities include characteristic facies, hyperextensibility, osteopenia/osteoporosis, scoliosis, minimal trauma fractures, and retention of primary teeth.

Objective: We aimed to further understand the minimal trauma fractures in individuals with HIES through determination of bone mineral density (BMD), examination of markers of bone turnover, and correlation of these findings with other connective tissue and skeletal features of HIES.

Methods: Sixty patients with HIES enrolled in a natural history prospective protocol at the NIH were examined yearly with history and physical, dental examinations, bone dual x-ray absorptiometry (DEXA) scans, and laboratory studies.

Results: Reduced BMD was seen in 37 of 60 (62%) patients with HIES including 57% of 37 adults and 70% of 23 children. Only 16 adults (43%) had BMD within normal range, while 11 (30%) and 10 (27%) had BMDs within osteopenic range and osteoporotic ranges, respectively. While 22 (59%) of the HIES adults had experienced minimal trauma fractures, neither the presence of, nor increase in number of minimal trauma fractures correlated with a decrease in BMD. However, an increase in minimal trauma fractures did correlate with retained primary dentition, but not with scoliosis or hyperextensibility. Of the children with HIES, 7 (30%) had normal BMD, while 11 (48%) were osteopenic and 5 (22%) osteoporotic. Ten children (43%) had experienced minimal trauma fractures, which were not associated with reduced BMD. Biochemical bone markers, osteocalcin and N-telopeptide, were within normal ranges in all patients. BMD improved in 7 patients, 5 adults and 2 children, after treatment with bisphosphonate therapy.