CASE REPORT
Volume - 10 | Issue - 08 | August - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

JOB'S SYNDROME: A RARE CASE REPORT

Paediatrics

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ABSTRACT

Hyper IgE Syndrome (HIES) or Job's Syndrome is a complex primary immunodeficiency disorder characterized by elevated serum IgE levels, recurrent skin rashes, eosinophilia, skeletal and connective tissue abnormalities. The patients also exhibit features of specific facies, retention of deciduous teeth and susceptibility to infections. HIES is a rare genetic disorder where some cases are inherited as autosomal dominant or autosomal recessive but most cases are supposedly sporadic. Hereby we present a case of 12-year-old male child admitted in the hospital with complaints of fever, skin rashes, intermittent abdominal pain and generalised lymphadenopathy. As there is no definite cure for HIES, the approach was directed towards conservative management. Due to the extreme paucity of reported cases in literature, this case report can help shed light on a syndrome of such rarity.

KEYWORDS

Hyper IgE syndrome, skin rashes, generalised lymphadenopathy, eosinophilia

INTRODUCTION:

Hyper IgE syndrome (HIES) or Job's Syndrome is a rare primary immunodeficiency disorder which apparently manifests during childhood. The incidence of HIES is < 1:1000000.[1] Only 300 cases of Hyper immune IgE Syndrome have been reported in literature till date. The disorder is generally characterized by repeated Staphylococcal infections of the skin, recurrent pneumatoceles, skeletal abnormalities and characteristic facial features. It was first described by Davis *et al.* in 1966 and named after the biblical character Job who was "smote with sore boils". In 1972, the raised IgE levels was documented as a cardinal feature of the syndrome and the name HIES was subsequently proposed. Mutations in the Signal Transducer and Activator of Transcription 3 (STAT 3) gene has been found to cause over 60% of the HIES cases.[2] Most cases of HIES occur as the result of a new mutation in this gene. Defects of the immune system and elevated levels of immunoglobulin E (hyper IgE) in the blood are the major diagnostic findings.

CASE REPORT:

A 12-year-old male child presented to our institute with complaints of fever, skin rashes, intermittent abdominal pain and generalised lymphadenopathy for a duration of 5 years. The abdominal pain was spontaneous, moderate to severe, dull which was non-radiating. He had bilateral pitting pedal oedema upto the level of groin. His medical history was significant for bronchial asthma, recurrent oesophageal candidiasis and retention of primary teeth. The patient appeared cachectic and had poor appetite for the past few months. There was no relevant family history.

General examination revealed mild pallor and generalised lymphadenopathy. Eczematous skin rashes and dystrophic nails were observed (Fig.1). The patient also had broad nasal bridge, deep set eyes and mild scoliosis. Palpation of the abdomen revealed tenderness over the epigastrium. Bilateral crepitations were heard in the lower part of the lungs.

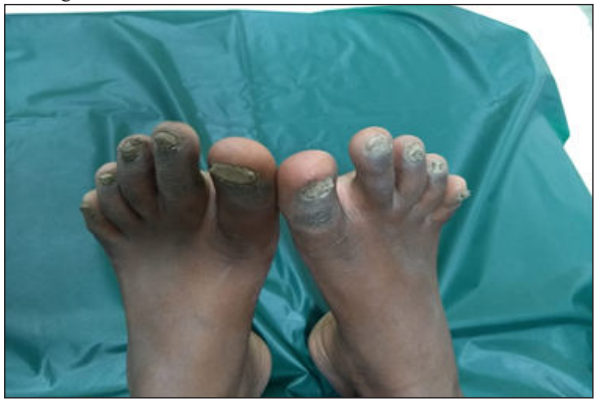

Fig.1 Dystrophic Nails And Eczematous Rashes

Further procedures were done after parental counselling about the condition. Complete blood count revealed decreased RBC count of 3.5 million cells/mm^3 and WBC count of 11,800 cells/mm^3. Haemoglobin was 11.2 gm%. Peripheral blood smear showed mild microcytic hypochromic anaemia with moderate eosinophilia. Immunoglobulin assay revealed IgE levels of 13800 IU/ml in contrast to a normal reference value of less than 200 IU/ml and increased IgG levels of 2200 IU/ml. Ultrasonography (USG) of the abdomen revealed mesenteric, para aortic, bilateral iliac, para caval lymphadenopathy. Colonoscopic biopsy showed mild chronic colitis with eosinophils and skin biopsy indicated eosinophilic infiltration. Correlating these findings with the National Institute of Health (NIH) scoring system developed by Grimbacher *et al.* led to the diagnosis of HIES with a final score of 127 (>40 is significant). Genetic testing and sequencing revealed a heterozygous STAT 3 mutation and confirmed the diagnosis.

A multidisciplinary approach under the guidance of different specialities were instituted for the management. Bacterial skin infections were treated with cotrimoxazole and steroids were used to alleviate the immune response. A conservative line was adopted with appropriate drugs (fluconazole) for fungal infections. During the course of treatment, symptoms subsided and the skin lesions were healing. The parents were then asked to bring the child for routine follow-up in the paediatrics out patient department.

DISCUSSION:

Hyper IgE Syndrome (HIES) is a multisystem disorder distinguished by Staphylococcal cold abscesses, high serum IgE levels, recurrent lung infections and chronic dermatitis. There are two types of the inherited disease: autosomal dominant (AD-HIES) caused by mutation in the STAT 3 gene and autosomal recessive (AR-HIES) caused by mutation in the DOCK 8 gene. Dominant-negative mutations of STAT 3 were found to be the most common cause of AD-HIES.[3] The pathophysiology is still unclear to a large extent. It is believed that a defect in the STAT 3 gene causes impaired T_H17 cells differentiation which in turn leads to decreased transcription of the interleukins Il-17 and Il-22.[4] Hence, there is a downregulation of immune responses especially against bacterial and fungal infections.[5]

The clinical features of HIES encompasses a wide range of systems and conditions. Immunological features cover eczematoid rashes, recurrent sinopulmonary infections, marked increase in serum IgE levels, eosinophilia and increased susceptibility to infections.[6] Non immunological features are multifold - Craniofacial abnormalities such as prominent forehead, prognathism, increased inter-alar width, craniosynostosis and high arched palate; musculoskeletal defects like osteopenia, scoliosis and joint hyperextensibility; abnormal dentition includes delay in exfoliation of primary teeth and presence of buccal mucosal defects; vascular abnormalities like tortuosity, aneurysms as well as lacunar infarcts.[7] Uncommonly, autoimmune disorders like membranoproliferative glomerulonephritis (MPGN), systemic lupus erythematosus (SLE) and dermatomyositis can occur.[8]

The principal therapeutic approach is to manage infections and take proper skin care. Systemic antibiotics and antifungals are of great use in treating the respective infections. Prophylactic therapy is given to prevent future infections. The exact role of bone marrow transplantation and immunoglobulin therapy remains to be studied.

CONCLUSION:

There are many questions about HIES that are yet to be answered. Thus, there is a dire requirement of case reports and studies regarding recent advances in management of this condition. Early diagnosis and prophylactic therapy to prevent future infections can go a long way in having a good prognosis.

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