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Case Report

Hyper IgE syndrome with congenital hypothyroidism: a rare association

Anjana Annie George, Ashwini Chinagundi, Meghashree S. B., Vishwanath B.*

Department of Pediatrics, VIMS Ballari, Karnataka, India

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***Correspondence:**
Dr. Vishwanath B.,
E-mail: drvishubee@gmail.com

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ABSTRACT

Hyper IgE syndrome (HIES) is a rare immunodeficiency syndrome, with autosomal dominant inheritance, caused mainly due to STAT 3 mutation. The affected children usually present with atopic dermatitis, recurrent staphylococcal infections, phenotypic characteristics and increased IgE levels. Though, there is a case report of autoimmune thyroiditis in HIES, congenital hypothyroidism is not reported. Here we report a case of HIES with typical phenotypic features with congenital hypothyroidism that presented to us with recurrent infections, atopic dermatitis and pneumatocele of right lung. Child was subsequently managed with antibiotics, levothyroxine and lobectomy.

Keywords: Congenital hypothyroidism, Hyper IgE syndrome, Pneumatoceles

INTRODUCTION

Hyper IgE syndrome (HIES) earlier known as Job's syndrome is a rare primary immunodeficiency syndrome. It is very rare disorder with annual incidence of 1:1,0 00,000.

The disease is characterized by atopic dermatitis, recurrent staphylococcal infections and increased IgE levels, with an onset in early childhood. It was first described in 1966 by Davis and coauthors and named the disease as Job's syndrome.[1] Later on Bukley found increased IgE levels in similar patients as described by Davis and reported subsequently some specific physical characteristics which he named as HIES.[2] Two types have been described:

Autosomal dominant type which associated with recurrent skin and sinopulmonary infections, pneumatoceles, eczema, mucocutaneous candidiasis, eosinophilia, and characteristic facies. Retained primary teeth, minimal trauma fractures and scoliosis may be present in older children. This type occurs due to mutation in STAT 3 gene (signal transducer and activator of transcription 3) in 70% cases. This gene acts a regulator of inflammatory response by regulating differentiation of naive CD4+ cells into T helper Th17 cells. Autosomal recessive type associated with recurrent pneumonia without pneumatoceles, sepsis, enzyme, boils, mucocutaneous candidiasis, neurologic symptoms, eosinophilia.[3] This type occurs mainly due to DOCK8 gene mutation.

Even though a case of autoimmune thyroiditis in HIES has been reported, no case of congenital hypothyroidism in HIES is reported so far. Here, we report a case of Autosomal dominantly inherited HIES with classical features including pneumatocele with congenital hypothyroidism.

CASE REPORT

A 1 year 6-month-old girl, born to 3rd degree consanguineous parents, presented with history of cough, cold, fever and hurried breathing. There was past history of repeated hospitalizations. Child was admitted at 2 months of age for septic arthritis. Later on child was admitted with recurrent pneumonias at 5 months, 6 months, 9 months and 10 months of age. In view of

repeated episodes of infections, primary immunodeficiency panel was sent which showed high IgE levels (844 IU/ml) with normal IgM, IgG and IgA. NBT, DHR tests, lymphocyte subsets were within normal limits and HIV was negative. CBC was showing eosinophilia (6.6%). Child was diagnosed as a case of HIESand was later discharged on cotrimoxazole prophylaxis. In spite of prophylaxis, child was again admitted at 1 year 3 months and 1 year 5 months of age with pneumonia.

On examination, the patient was found to have coarse facies, prominent forehead, deep set eyes, broad nose, fleshy nasal tip, high arched palate and hyperextensibility of joints (Figure 1). Large solitary well defined hyperpigmented plaque of size 14×8 cm was seen over the posterior aspect of thigh and calf having a raised border scaling, oozing and areas of healing with hypopigmentation (Figure 2). KOH examination of the scrapings from nail and skin lesions was unremarkable.

Figure 1: HIES child with typical facial and physical features.

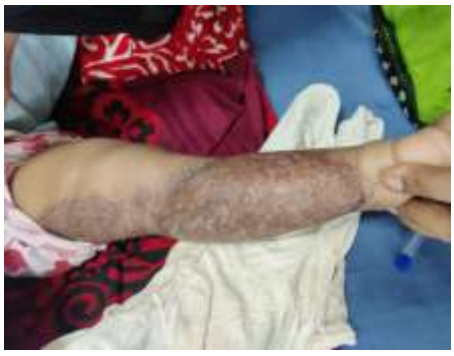

Figure 2: Atopic dermatitis in a child with HIES.

Respiratory system examination was showing features suggestive of bilateral pneumonia with decreased breath sounds on the right side. Child was started on first line antibiotic therapy. As there was no response to regular antibiotics, antibiotics were switched to second line. In view of history of constipation, thyroid profile was done, which was suggestive of congenital hypothyroidism. (TSH: 40 mcIU/ml, T4: 2.1 mcg/dl, FT4: 0.3 ng/dl). TPO antibodies were done and was negative (5 IU/ml). X-ray was suggestive of cystic lesion in the right upper lobe of lung. HRCT chest was done which showed multiple thin walled, regular walled air filled cysts with adjacent pneumonitis changes suggestive of pneumatocele in the right lung. Along with antibiotics and supportive care, child was started on thyroxine supplementation (levothyroxine 12.5 µg). In view of pneumatocele with recurrent infections, thoracotomy with right middle lobectomy was done for the child. Postoperative period was uneventful.

DISCUSSION

The autosomal dominant HIES is caused by heterozygous mutations in the gene encoding signal transducer and activator of transcription 3 (STAT-3). These mutations result in a dominant negative effect. The many clinical features are caused by compromised signalling downstream of the interleukin (IL)-6, type I interferon, IL-22, IL-10 and epidermal growth factor (EGF) receptors. The autosomal recessive form is associated with neurological involvement but not with pneumatocele formation

The characteristic clinical features are staphylococcal abscesses, pneumatoceles, osteopenia, and unusual facial features. There is a history from infancy of recurrent staphylococcal abscesses involving the skin, lungs, joints, viscera, and other sites. Persistent pneumatoceles develop as a result of recurrent pneumonia. Patients often have a history of sinusitis and mastoiditis. *Candida albicans* is the 2nd most common pathogen. There can be a prominent forehead, deep-set wide-spaced eyes, a broad nasal bridge, a wide fleshy nasal tip, mild prognathism, facial asymmetry, and hemihypertrophy, although these are most evident in adulthood. In older children, delay in shedding primary teeth, recurrent fractures, and scoliosis occur. These patients demonstrate an exceptionally high serum IgE concentration, an elevated serum IgD concentration, usually normal concentrations of IgG, IgA, and IgM. They also exhibit pronounced blood and sputum eosinophilia and poor antibody and cell-mediated responses to neo-antigens. Traditionally, IgE levels >2000 IU/ml confirm the diagnosis. But this may not hold true for neonates and infants with the pruritic pustular dermatosis, where IgE levels will be elevated for age and are usually in the 100s. Peripheral blood eosinophilia is present in as many as 93% of the patients. Recurrent pneumonias occur that may heal to form pneumatoceles and bronchiectasis.

It was found in a study that about 77% of the patients with HIES had pneumatoceles.[4] However, another study from India found pneumatoceles and bronchiectasis in only one out of six patients of HIES, though pneumonia was present in all patients.[5] Our patient had recurrent skin, pulmonary infections and persistent pneumatocele. HIES has been related with a heightened risk for autoimmune diseases such as systemic lupus erythematosus and dermatomyositis. Even autoimmune hypothyroidism was

noticed in Hyper IgE syndrome.[6] Our patient had congenital hypothyroidism as well as pneumatocele and it is a rare association in HIES.

CONCLUSION

HIES is a rare immunological disorder characterised by clinical trial of atopic dermatitis, recurrent staphylococcal infections, and increased IgE levels with an onset in early childhood. The characteristic facial and physical features along with presence of pneumatocele in radiological imaging in a child with recurrent infections should arouse a suspicion in treating clinician the possibility of HIES. Congenital hypothyroidism is a rare association seen in children with HIES.

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