Hyper IgE syndrome: Report of two cases with moderate elevation of IgE

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ABSTRACT

Hyper IgE syndrome with recurrent infection (Job's syndrome) is a rare idiopathic primary immunodeficiency disease characterized by the triad of elevated serum IgE (>2000 IU/ml), recurrent cutaneous abscesses and recurrent sinopulmonary infections. The bacteria which commonly infect these patients are Staphylococcus aureus and Haemophilus influenzae. Therapy should include prolonged antibiotic therapy and early surgery. Non-specific agents like levamisole and ascorbic acid may reduce recurrent infections. We are reporting two girls, six and twelve years of age, presented with recurrent cutaneous and respiratory infections and moderately elevated levels of serum IgE.

KEY WORDS: Hyper IgE syndrome, Job's syndrome

INTRODUCTION

Hyperimmunoglobulin E syndrome with recurrent infections (HIES) or Job’s syndrome is a primary phagocytic disorder characterized by atopic-like dermatitis which first manifests during infancy, 'cold' soft tissue abscesses, recurrent pneumonias, pneumatoceles and craniofacial and skeletal abnormalities. In 1966, Davis, Schaller and Wedgwood first reported Job’s syndrome. The nomenclature is derived from the similarity of the condition to the Biblical Prophet Job ‘who was afflicted with sore boils from the sole of his feet unto his crown.’ The first case from India was reported in 1994 by Pherwani et al. In 2001, Pherwani and Madnani reported six patients with prominent cutaneous and respiratory features, but only one had familial involvement.

An elevated IgE level (>2000 IU/ml) and peripheral eosinophilia are the most constant findings in this disorder. We report two girls with the disorder, whose IgE levels were only moderately elevated.

CASE REPORTS

Case 1
A 6-year-old girl born of non-consanguineous parentage and uneventful pregnancy was brought on several occasions with fever, severe impetiginous lesions and multiple abscesses that each time subsided with systemic antibiotics like...
cefadroxil. From early childhood onwards, there was a history of atopic-like eczema, an episode of lung abscess and empyema. No family members were affected.

The tip of the nose was fleshy and the inter-alar distance was increased, with a coarse facies. The scar of drainage of empyema was still present on the chest wall. There were also multiple scars on the face, trunk and limbs. No bony abnormalities were detected.

An X-ray chest showed fibrosis in the right midzone. She had peripheral eosinophilia and the serum IgE was raised (420 IU/ml). ELISA for HIV was negative.

Oral vitamin C was started 500 mg daily with reduction in the recurrence of infections. However, after two years she died following a prolonged respiratory infection.

**Case 2**

A 12-year-old girl born of a non-consanguineous marriage presented with multiple discrete and confluent erythematous scaly papules and plaques with follicular prominence over the face, trunk and limbs with accentuation in the retroauricular area. The rash had been treated with topical betamethasone dipropionate. The girl had been admitted previously in the pediatrics ward for the treatment of staphylococcal pneumonia.

She had a coarse facies with a fleshy tip of the nose and increased inter-alar distance. Multiple scars that had followed furuncles were present over the limbs and trunk. All fingernails and toenails showed discoloration, dystrophy, loss of cuticle and subungual hyperkeratosis. Two tender cystic swellings of size 10 x 6 cm were present in the left inguinal region above and below the inguinal ligaments. On incision and drainage these discharged thick creamy pus.

*S. aureus* sensitive to cloxacillin was grown from the discharged pus. Nail clippings showed dermatophyte hyphae. Blood investigations showed only eosinophilia with raised ESR. The serum IgE was raised (564 IU/ml). Blood ELISA for HIV was negative. A chest radiograph showed multiple pneumatoceles (Figure 1).

**DISCUSSION**

HIES is a rare multisystem primary phagocytic disorder that affects the dentition, skeleton, connective tissue and immune system. It is inherited as a single locus autosomal dominant trait with variable expressivity. Our two patients had typical features of HIES.[5-6] There was no family history of a similar illness in our patients. HIES may be caused by the mutation of a single gene, mutation in different genes in different families or deletion of contiguous genes in a short chromosomal region.[5] The disease focus for HIES had been mapped to the proximal region of chromosome 4q.[7] Recently, an autosomal recessive variant has been described,[8] in which the IgE level is lower than reported earlier.[4,6]

Usually IgE levels in HIES exceed 2000 IU/ml. However, IgE levels may decrease with age, may fall within the normal range (0.1-90 IU/ml) in about 20% of the cases,[1,5] and do not correlate with disease severity.[9] IgE antistaphylococcal antibodies are common and are relatively specific for the syndrome.[1] Both the cases
being reported here showed only moderate elevation in serum IgE levels, viz. 420 IU/ml in the first case and 564 IU/ml in the second case. This further supports the view that if other features of HIES are present, a normal IgE level should not exclude the presence of HIES in older children.[5]

Dermatitis is present in more than 80% of the patients of HIES and usually begins at 2 months to 2 years of age.[1] It resembles atopic dermatitis, but is accentuated in retroauricular and hairline areas in addition to flexural involvement.[1] The skin and soft tissue infections present as cellulitis, furunculosis, paronychia, suppurative adenitis and deep soft tissue ‘cold’ abscesses. Constitutional symptoms like fever may be absent or blunted. Severe pulmonary infections caused by either *S. aureus* or *H. influenzae* are common. Empyema may complicate pneumonia and there is a high propensity for bronchiectasis and pneumatoceles.

Primary phagocytic disorders like HIES are rare and usually first manifest during childhood. A phagocytic disorder should be considered in patients with unusually severe and recurrent infections by common pathogens. Patients usually die prematurely due to pulmonary infections. Early diagnosis of phagocytic disorders can be lifesaving and can lead to a significant reduction in morbidity.

**REFERENCES**