

Atopic Dermatitis or Hyper IgE Syndrome ?

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Abstract

Eczema and skin infections are commonly encountered in children in the outpatient department. However, presence of both recurrent dermatitis and skin infections should alarm one to consider Hyper IgE syndrome (HIES) as a differential. Here we present a case of HIES in a two and a half year old female child with history of recurrent dermatitis and skin infections in the form of cold abscesses. Laboratory investigations showed markedly elevated IgE levels and high absolute eosinophils counts. Patient was treated with trimethoprim-sulfamethoxazole and supportive care. The current report highlights the fact that HIES can present in early childhood with just skin manifestations and without any significant pulmonary manifestations.

Key words: Hyper IgE syndrome, Eosinophilia

Introduction

Eczema and skin infections are commonly encountered in children in the outpatient department. However, presence of both recurrent dermatitis and skin infections should alarm one to consider Hyper IgE syndrome (HIES) as a differential. Hyper IgE syndromes are a group of rare primary immunodeficiency disorders characterized by marked elevations in IgE levels, recurrent staphylococcal skin infections, recurrent pneumonia and chronic eczematoid dermatitis¹. The skin infections are in the form of boils and furuncles which typically lack the signs of inflammation, hence referred to as "cold abscesses".

Hyper IgE syndrome is a complex immune deficiency with diverse clinical manifestations and heterogenous genetic origins². HIES are mostly sporadic but two inherited forms are recognized, a dominant form (Type 1), caused by mutations in *STAT3* (Signal transducer and activator of transcription 3), and a recessive form (Type 2) is due to mutation in *Dock-8* or cytokine *sis-8* and *TYK2*³. This report highlights the fact that HIES can be suspected on the basis of the key features observed in early childhood like chronic recurrent dermatitis and skin infections.

The Case

This two and a half year old girl was born to non-consanguineous parents with uneventful perinatal events at term gestation with a

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birth weight of 3 kgs. She was exclusively breast feed till six months of age. The child presented to the paediatric outpatient department with complaints of severe pruritis over face, hands, abdomen, ears and face since the age of 18 months and cold abscesses on buttock and thighs. The child also had frequent upper respiratory tract infections requiring hospital outpatient visits. She was admitted once with acute lower respiratory infection needing intravenous antibiotics, however the chest radiograph did not reveal any significant findings. On physical examination, the child had a dry eczematous scaly rash with crusting predominantly on cheeks, abdomen, forearm, and buttock (Fig 1 and 2) and cold abscess over peri-anal region

which was fluctuant cyst like lesion, neither hot nor tender with no signs of any local or generalized inflammation (Fig 3). Vital parameters were in the normal range. Respiratory, cardiovascular, abdominal, and nervous system examination was unremarkable. On investigation, hemoglobin was 10.6 gm%, total leukocyte count was 15700/ μ L (polymorphs 32%, lymphocytes 49%, eosinophils 10%, monocytes 8%), platelets 9.54×10^9 /L, absolute eosinophil counts were 1531/ μ L and IgE level was 18,403IU/ml. Chest radiograph was normal.



Fig 1: Dry eczematous scaly rash over wrist and lower limbs



Fig 2: Dry eczematous scaly rash over lower limbs



Fig 3: Cold abscess over peri-anal region

Discussion

Dermatitis and skin infections with abscesses are quiet often seen in paediatric age group leading to significant morbidity and adverse affects. Although the skin rash of HIES resembles atopic dermatitis, Hochreutener et al emphasized the importance of clinical differentiation of the HIE syndrome from atopic dermatitis because the treatment and prognosis are different⁴. As atopic dermatitis is the commonest cause of recurrent dermatitis in children, clinicians think of AD as the likely possibility in this scenario, and often overlook the skin infections. AD is a chronic relapsing hypersensitive manifestation of skin, itching being a significant feature. An increasing trend of AD is seen in India. Around 10-20% of children and 1-3% of adults are affected in developed countries with this type of skin manifestation⁵. In addition to atopic dermatitis, the differential diagnosis of HIE syndrome includes DiGeorge syndrome, Wiskott -Aldrich syndrome and chronic granulomatous disease. It is therefore necessary to consider these possibilities whenever a child with dermatitis and skin infections is evaluated.

To identify patients with HIES, NIH (National Institute of Health) scoring system is used, which is based on certain clinical and laboratory findings. Patients with an NIH score of 40 or more are likely to have a STAT3 mutation. Grimbacher et al prospectively evaluated patients with suspected HIES according to the NIH scoring system⁶. They also scored cases of atopic dermatitis and other immune deficiencies for comparison. The maximal score obtained for each age group was 25 for 0-2 years, 60 for 3-6 years, 76 for 7-12 years, and 96 for more than 18 years. The study suggested that points more than 40% of the maximal score was significantly associated with a diagnosis of HIES, points less than 20% were not observed in HIES, and diagnosis can't be ruled out for points between 20-40%. In our case, the score obtained was 31, which was well above the maximal score obtained for that age group by Grimbacher et al⁶.

HIES has an incidence of 1 in 500,000 live births⁷ and occurs in both males and females of all ethnic groups with equal frequency⁸. Type 1 is a dominant form caused by heterozygous mutations in the transcription factor STAT3 involving skin, connective tissue, skeleton and characteristic facial appearance. The locus for familial autosomal dominant (AD)-HIES, STAT3 is located on chromosome 17q21⁵. Thus, a deficiency in STAT3 is a cause of sporadic and familial HIES. Type 2 HIES is an autosomal recessive (AR) syndrome⁷. The patients with type 2 HIES do not have skeletal and dentition abnormalities.

In HIES, IgE levels exceeds 2000 IU/ml and may decrease with age or remain within normal range in about 20 % of cases⁹. IgE anti staphylococcal antibodies are common and are specific. The NIH score correlates with the severity of disease and it is a useful tool to diagnose of AD- HIES rather than AR-HIES. Definitive diagnosis is established by genetic study.

As there is no definitive therapy available, so the strategy in HIES is towards prevention and management of bacterial infections. Good skin care and hygiene is necessary to prevent skin infections. Antimicrobial prophylaxis to prevent *Staphylococcus aureus* skin and lung infection is among the most widely used treatments options. Lifelong antibiotics and antifungals as required reported to be safe and effective. Trimethoprim-sulfamethoxazole is a safe and effective alternative to penicillin; importantly, it has anti-MRSA properties¹⁰. High-dose IV Immunoglobulin shown to lead to marked clinical improvement in patients with HIES¹¹.

Our report highlights the fact that possibility of HIES should be considered in children presenting with recurrent eczema and skin infections. The NIH scoring system can be used in establishing the diagnosis.

Conclusion

HIES is a rare primary immunodeficiency syndrome which occurs in early childhood with triad of symptoms. This case highlights high suspicion rate to be considered for HIES in patients with recurrent chest infections with skin infections. Early diagnosis and treatment is life saving and can reduce morbidity. Trimethoprim-sulfamethoxazole is safe, effective and should be given for long term as prophylactic therapy.

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