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CASE REPORT

Jobs Syndrome (Hyper IgE Syndrome: HIES): Case Report and Literature Review

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ABSTRACT

Jobs syndrome or hyper IgE syndrome is a heterogenous group of immunodeficiencies characterized by recurrent skin and pulmonary infections, high serum IgE levels (> 2000 IU/ml) and eczematous dermatitis. Other features involve coarse facial features and skeletal abnormalities. There are two types depending on the genes involved: autosomal dominant (AD-HIES) and autosomal recessive (AR-HIES). Approximately 250 cases of Jobs syndrome have been reported worldwide. Hereby we present a case of 2-year-old male child who presented to our hospital with cutaneous abscesses, dry skin and fever.

Key Words: *Hyper-immunoglobulin syndrome E syndrome, Recurrent infections, Eczema*.

INTRODUCTION

Hyper IgE syndrome is a rare immune disorder which was first described by Davis et al. in 1966 in two girls suffering from cold abscesses, skin eczema and pneumonia.[1] In 1972 high IgE levels were found in these patients by Buckley et al.[2] It usually presents in early childhood or late in adulthood. Both males and females are affected, and this syndrome is mostly inherited as autosomal dominant and recessive autosomal.[3] Autosomal dominant (AD-HIES) is mostly caused by mutations in STAT 3 gene while etiology of autosomal recessive (AR-HIES) is still debatable but DOCK8 gene is linked with it. It is characterized by recurrent soft tissues bacterial and fungal infections, eczematous dermatitis, skeletal abnormalities and vascular abnormalities. In pediatrics very few cases have been published till date leading to diagnostic challenge.[4]

CASE REPORT

A 2 years old boy was admitted in Jinnah Hospital, Lahore with complaints of recurrent skin abscesses and pustular lesions on limbs, upper chest and head for last 6 months, dry skin, intermittent fever for last 15 days and decreased appetite. He took oral and intravenous antibiotics for abscesses in the past, but no workup was done. There was no history of loose stools, ear discharge, cough or bleeding from any site. Family history was not significantly related to condition. His parents were cousins, and his birth history was uneventful. The child was breastfed, vaccinated and developmentally normal.

On physical examination he was small for his age and sex, with weight of 9 kg, height 76 cm and head circumference 46 cm. He was irritable, febrile (103 F) with heart rate 118/min, respiratory rate of 32/min. He was pale and having cervical lymphadenopathy of less than 1cm. BCG scar was present. The skin examination revealed multiple abscesses on body involving both shoulders and left thigh with signs of cellulitis. The skin was dry and scaly with post inflammatory scarring. The rest of the systemic examination and skeletal examination was unremarkable.

His labs showed hemoglobin of 8.4 g/dl, total leukocyte count of 41400/cmm with neutrophils

71.6%, lymphocytes 23% and ESR was 30mm/hour, CRP was 109.03 and serum immunoglobulins level were IgE 6300 IU/ml (reference range ≤49 IU/ml), IgA 0.93 IU/ml, IgG 23.8 IU/ml and IgM 1.77 IU/ml (table 1). Mantoux test negative and CXR was normal. Further investigations with swellings ultrasound (back of right and left shoulder) showed thick debrinous pus/abscess with streak of synovial fluid (table 2). while USG of right thigh abscess showed well defined thick-walled hemorrhagic collection (fig 1). Pus culture showed Staphylococcus aureus sensitive to vancomycin, linezolid, meropenem, amoxicillin-clavulanic acid combination and teicoplanin.

TABLE 1: Serum immunoglobulin levels showing raised IgE levels

	Reference value	Measured
Serum IgE	10.1-49 IU/ml	6300
Serum IgA	0.21-2.91 g/dl	0.93
Serum IgG	5.4-18.22 g/dl	23.8
Serum IgM	0.41-1.83 g/dl	1.77

TABLE 2: USG showing pus/abscess and debrinous collection on back of right and left shoulder back along with right thigh

Areas	Findings
Right shoulder	Back of right shoulder shows the debrinious pus/abscess approx. 49×47mm with streaks of synovial fluid in shoulder.
Left shoulder	Similar looking abscess / pus in the front of left shoulder approx. 40×45 mm.
Right thigh	Front of right thigh shows well defined rounded thick walled hemorrhagic collection approx.. 35×38 mm along with streaks of fluid in right knee joint.

From the above findings the diagnosis of hyper IgE syndrome (Jobs syndrome) was made. His abscesses were drained and the child was started on vancomycin along with meropenem according to bacterial sensitivity pattern. During the course of treatment, his condition improved, fever subsided and no new lesions were seen. The child was discharged on prophylactic syrup amoxicillin-clavulanic acid combination and parents were advised to bring the child for follow up after 2 weeks in outpatient department

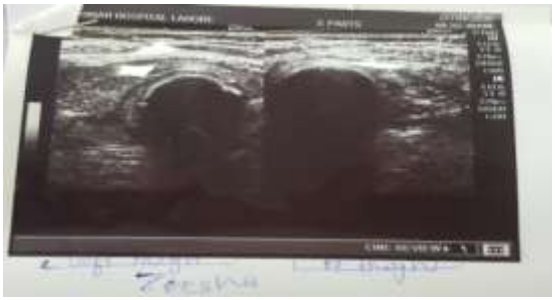

Fig 1: Ultrasound of the patient's thigh.

DISCUSSION

Hyper-immunoglobulin E syndrome also known as Job's syndrome is a rare multisystem primary immunodeficiency disorder which is characterized by recurrent staphylococcal infections, skin abscesses, eczematous dermatitis and high serum IgE levels. It is often accompanied by abnormalities of skeleton, connective tissue and dentition.[5] These patients also have prominent facial and oral findings e.g. Prominent forehead, deep eyes, broad nose, facial asymmetry and primary teeth retention. It affects both males and females of all ethnic backgrounds and usually presents in early childhood.

Job's syndrome is mostly inherited as autosomal dominant (AD-HIES) however autosomal recessive and sporadic cases are also reported.AD-HIES is a multisystem disorder with vascular and skeletal abnormalities and develops due to STAT3 gene while autosomal recessive AR-HIES is caused by DOCK8 gene mutations.[6] Pathogenesis is not very well understood and still debatable but it is considered to be a defect in neutrophil chemotaxis. STAT3 gene is signal transducer and its mutation leads to diminished Th 17 response and absent IL-17.[7] This results in decreased chemotaxis and recurrent infections. Severe and recurrent bacterial pneumonias are often present during childhood. The cold abscesses without signs of inflammation are common. Frequent pathogens isolated in HIES are Staphylococcus aureus, H. influenza and streptococcus pneumoniae.

Diagnosis of HIES is based on clinical findings (typical facial features, recurrent infections and abscesses) laboratory investigations (markedly high IgE levels and eosinophilia) and genetic testing. Our patient had multiple features suggestive of hyper IgE syndrome; recurrent staphylococcal infections, eczema, high IgE levels.[8] There was also absence of dental, skeletal, connective tissue and pulmonary findings which indicate autosomal recessive AR-HIES pattern however genetic analysis could not be done due to economic consideration.

There is no cure of hyper IgE syndrome. The therapeutic strategy is mainly directed towards management and prevention of infections. Systemic bacterial and fungal infections can be severe and correct antibiotic drug selection is crucial.[9] Long term prophylactic therapy with anti-staphylococcal antibody such as cotrimoxazole, oral cephalosporin and semisynthetic penicillin are used. Intravenous immunoglobulin is the most frequent immunomodulator and may be used to decrease the number of infections. Other options like interferon gamma and hematopoietic stem cell transplantation has also been used in some cases.

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