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Paediatrics

RARE CASE OF JOB SYNDROME (HYPER-IGE SYNDROME)- A CASE REPORT

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ABSTRACT Job's syndrome is a rare disease characterized by recurrent skin and/or lung abscesses, dermatitis, and bone and tooth defects, in addition to significantly increased serum IgE levels. A six years old female presented to us with recurrent "cold" abscesses on her face with a history of recurrent bronchitis, eczema on buttocks, antecubital fossa and back and oral thrush. She had coarse facial features, a prominent forehead, deep-set eyes, a broad nasal bridge, and a wide, fleshy nasal tip. With prominent eosinophilia and significantly increased serum IgE levels, a diagnosis of Job's Syndrome was suspected. The patient was managed with incision and drainage of abscesses, appropriate antibiotics, good skin care and regular follow-up visits. The objective of this report is to create awareness about this disease and its management as its diagnosis is very difficult, so a high degree of clinical suspicion is needed.

KEYWORDS : Job's syndrome, STAT3 mutation, Hyper-IgE syndrome

INTRODUCTION

The hyperimmunoglobulin E syndrome (HIES), or Job's syndrome, is a rare multisystem disease in which the immune and somatic systems are affected, including neutrophils, monocytes, T cells, B cells, and osteoclasts. Autosomal *dominant* mutations in STAT3 lead to inhibition of normal STAT signaling leading to characteristic facies with broad nose, kyphoscoliosis, eczema, recurrent sinopulmonary and cutaneous infections ("cold abscesses"). Characteristically, pneumonias cavitate leading to pneumatoceles. IL-17–producing T cells (responsible for protection against extracellular and mucosal infections) are profoundly reduced in Job's syndrome.[1]

We are reporting a case of Job's syndrome presented to us in the Pediatric out-patient department of Civil Hospital, Amritsar to create awareness about this rare disease and its management.

CASE REPORT

A six years old female presented to us in Civil hospital, Amritsar with recurrent abscesses on her face (Fig. 1) for the past 8 months. These fluctuant masses lacked the typical signs of infection (pain, heat, or redness). The patient had also had high grade fever for the past 4 days. There was a history of recurrent bronchitis, eczema on buttocks, antecubital fossa and back and oral thrush in the preceding years.

On physical examination, the patient had coarse facial features, a prominent forehead, deep-set eyes, a broad nasal bridge and a wide, fleshy nasal tip. Retained primary teeth were present (Fig. 2) without eruption of permanent teeth. Mild cervical lymphadenopathy could also be appreciated.

On work up, Hemoglobin was 7 g%, Total leucocyte count was 19,000/ cubic mm, and Differential leucocyte count showed eosinophilia. From the symptoms, the typical physical features and the prominent eosinophilia, Job's syndrome was suspected and IgE testing was done, which came out to be significantly elevated (2122 IU/ml). The abscesses were incised and drained and the pus and exudates in the abscesses were sent for culture and sensitivity. It came back positive for S. aureus and S. epidermidis. The patient was treated with vancomycin and ceftriaxone as per sensitivity results.

Follow-up was scheduled for 2 weeks at which the patient showed improvement of her symptoms. Patient's parents were advised good skin care of the patient to prevent skin infections in the future. Emollients were prescribed for eczema and regular follow-up was scheduled every month.

DISCUSSION

Hyper-IgE syndrome (Job's Syndrome) is a rare, primary immunodeficiency distinguished by the clinical triad of atopic dermatitis, recurrent skin staphylococcal infections, and recurrent pulmonary infections. Furthermore, there are elevated IgE levels of early onset in primary childhood. The annual incidence of Job syndrome is estimated at around 1: 1,000,000. Although initially described in female subjects, both genders are affected, with no ethnic factor.[2]

The name Job's Syndrome came from the biblical character Job, whose faithfulness was tested by an affliction with draining skin sores and pustules just like the ones that happen in this disease. The symptoms are most often present in childhood, but because the disease is so rare, it often takes years before a correct diagnosis is made.[3]

Autosomal dominant mutations in STAT3 or autosomal recessive mutations in DOCK8 are the primary causes of this disease leading to slight difference in manifestations.[1,2]

Mishra S *et al* has described the clinical features of this disease. Autosomal dominant form appears early in life with recurrent staphylococcal and candidal infections, pneumonias, lymphadenitis, and eczematous skin. Patients have delay or failure in shedding of primary teeth. Typical facial features include facial asymmetry, a prominent forehead, deep-set eyes, broad nasal bridge, wide, fleshy nasal tip, mild prognathism, and craniosynostosis. Some patients have scoliosis, as well as bones that fracture easily and chronic dermatitis. "Cold" abscesses are pathognomonic for this, but are not a diagnostic feature. Upper airway infections manifest as paranasal sinusitis, exudative otitis media, otitis externa, and mastoiditis. *S. aureus* is the most frequently isolated organism. Pneumonia is frequently followed by pneumatocele or bronchiectasis, bronchopleural fistulas, lung abscesses. Pulmonary cause leads to chronic respiratory insufficiency resulting in death. Autosomal recessive form possesses similar features, but the patients have fatal neurological abnormalities and early presentations.[4]

On work up, eosinophilia is the most prominent feature and usually accompanies the IgE. The serum IgE is typically >2000 IU/mL, while other immunoglobulin levels are normal. However, IgE level normalizes in adulthood in about 20% of cases. Culture and sensitivity of the pus, after incision and drainage of the skin abscesses, should always be done to identify the causative organism in order to treat them properly. When lung infection is present, sputum should be obtained through routine collection, sputum induction, or bronchoscopy. *STAT3* mutation analysis should be performed to confirm a high clinical suspicion of HIES.[5]

The therapeutic strategy in HIES is directed mainly toward the prevention and management of infections with systemic antibiotics and antifungals. This can prevent serious, overwhelming infections

and prevent lung parenchymal damage. Most frequent choices of antibiotics are trimethoprim-sulfamethoxazole and amoxicillin-clavulinic acid[6,7] but culture-sensitivity should always be used a guide to prevent resistance.

Although immunomodulatory agents in HIES have not been well-studied, intravenous immunoglobulin may decrease the number of infections for some individuals and is the most frequent immunomodulator used, if needed.[8]

Periodic chest imaging and high clinical suspicion assist in early detection of infections. Culture of skin lesions and sputum samples helps direct therapy. Routine dental care is necessary to ensure timely removal of primary teeth to allow eruption of secondary teeth. Routine screening of adolescents for early signs of scoliosis is recommended. Prenatal diagnosis for pregnancies at increased risk is possible if the pathogenic variant in the family is known.[9]

CONCLUSION

Job syndrome is a rare disease and so its diagnosis is very difficult as high degree of clinical suspicion is needed. Regular use of prophylactic antibiotics and emollients, maintenance of skin hygiene to prevent infections and regular follow-up visits with the physician are the way-to-go in this disease's management.

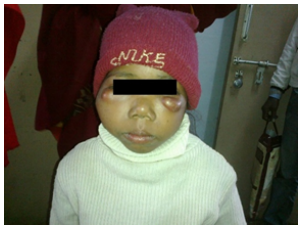

Fig 1: Child with facial abscesses

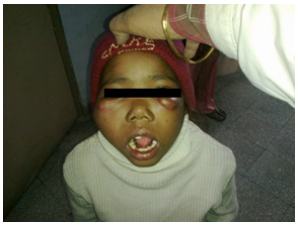

Fig 2: Retained primary teeth

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