



JOBS SYNDROME A RARE CASE REPORT

KEYWORDS

Job's syndrome, Growth Retardation, Staphylococcal abscesses, Raised serum IgE levels.

Dr Nita R Sutay

Professor and Head of The Department, Grant government medical college and Sir JJ Group Of Hospitals Mumbai, Maharashtra India.

Dr Devanand gulab Chaudhari

Assistant Professor, Grant government medical college and Sir JJ Group Of Hospitals Mumbai, Maharashtra India

Dr. Yugesh Kumar Agrawal

Resident, Department Of Pediatrics, Grant government medical college and Sir JJ Group Of Hospitals Mumbai, Maharashtra India

ABSTRACT

Background:- Job's syndrome (Hyper IgE Syndrome (HIES) or Buckley syndrome) is a rare primary immunodeficiency syndrome characterized by recurrent severe staphylococcal infections like skin abscesses, severe lung infections that result in pneumatoceles and multi organ dysfunction. The hallmark finding in Job's syndrome is very high concentrations of serum IgE. Incidence is less than 1 per million people. We report here a case of 1 1/2 year old female child who had history of swelling of left thigh following a thorn prick. She was diagnosed to be having Job's syndrome on the basis of classical triad ie Raised serum IgE, recurrent staphylococcal abscesses and recurrent respiratory infections.

Case Report:- We present here a case of 1 1/2 year old female child who had history of swelling over left thigh following a thorn prick. After this the child gradually developed multiple swellings all over the body. There was also history of fever and peeling of skin involving multiple sites. On examination the child was malnourished and stunted. There were multiple fluctuant swellings over chest and abdomen with ulceration over left thigh. Multiple abscesses over knee, left wrist and elbow joints with restricted, painful movements of involved joints were also seen. Skin biopsy was suggestive of features of atopic dermatitis. The diagnosis of Jobs syndrome was made on the basis of presence of staphylococcal abscesses, history of recurrent respiratory tract infections and finally demonstration of abnormally high serum IgE levels.

Conclusion:- The classical triad of recurrent respiratory tract infections, multiple abscesses and raised IgE levels is diagnostic of Jobs syndrome. Any patient having these signs and symptoms should be investigated by estimation of serum IgE levels for confirmation or ruling out Job's syndrome. Recurrent respiratory tract infections and pulmonary complications are the common causes of mortality in these children. Late diagnosis is associated with growth abnormalities. Early diagnosis and institution of prophylactic treatment reduces complications and ensures proper growth.

Introduction:

Job's syndrome, also known as Hyper IgE Syndrome (HIES) or Buckley syndrome is a rare primary immunodeficiency syndrome first described in Jobs in 1966 [1]. It is characterized by recurrent severe staphylococcal infections like skin abscesses, severe lung infections that result in pneumatoceles and very high concentrations of serum IgE. The incidence of Jobs syndrome is less than 1 per million people. Only about 250 people with Jobs syndrome have been reported in medical literature. The most common form of inheritance is autosomal dominant [2]. Rarely autosomal recessive pattern can also be seen. It is caused by mutation in *STAT 3* gene, which is involved in many cellular functions like cell growth and division, cell movement and apoptosis. Mutations lead to impaired cellular functions such as immune system impairment making patient highly susceptible to infections. The common clinical features consist of recurrent staphylococcal abscesses, Pneumatoceles, osteopenia, coarse facial features like prominent forehead, wide spaced eyes, broad nasal bridge & mild prognathism [3]. In older children, delayed shedding of primary teeth, recurrent fractures and scoliosis may occur. The other type autosomal Recessive form may present with severe atopic dermatitis, eczema, asthma, food allergies and anaphylaxis. Recurrent skin infections caused by herpes simplex, herpes zoster, molluscum contagiosum and papilloma viruses are common. Abscess and mucocutaneous candidiasis secondary to immunosuppression is also common [4]. Uncommon manifestations include stroke, meningitis, and coronary aneurysms. A complex scoring system that weights both the immunologic and somatic features of the syndrome was designed to aid in the clinical diagnosis of these patients. Notwithstanding this system the hallmark finding of Jobs syndrome is Elevated IgE levels which if greater than 2,000 IU/L is considered diagnostic. However, younger patients may have low levels and are usually in 100s. Eosinophilia, lymphopenia, low T- cell number and impaired T-

cell function can also seen. The most effective treatment is long term administration of antibiotics to protect the patient from staphylococcal infections. IVIG should be administered to antibody deficient patients and to those with severe eczema or atopic dermatitis. Autosomal recessive form is being increasingly treated with allogenic bone marrow transplantation but its efficacy is yet to be established [5].

Case Report

A 1 ½ year old female child was brought with history of swelling over left thigh with intermittent fever since 1 ½ months following history of thorn prick. The swelling has increased gradually and was associated with tenderness and local redness. Child was taken to a private hospital where Incision & drainage was done. But in due course of time, child developed ulceration at the wound site. At the same time, child also started developing multiple swellings all over the body. This entire episode was associated with fever which was mild to moderate grade, intermittent and not associated with chills. It got relieved on taking medication. On general examination, vitals were stable. The child was underweight and stunted for age. There was evidence of bilateral pedal edema. On local examination there were multiple fluctuant swellings over chest, abdomen, right shoulder and behind ears. They were tender on palpation and associated with local rise in temperature. Ulcerations were present over posterior aspect of thigh, back and abdomen. Diffuse hypopigmented patches over back and abdomen were also noted. Peeling of skin and scaling was present on Palms & soles. Oral cavity and External genitalia was normal.

Abscesses over left knee, left wrist and elbow region with restricted movements were seen. The restrictions of movements were due to intense pain. (Figure 1).



Figure 1 : Multiple abscesses and ulcerations over chest, abdomen, back and thighs.

Systemic Examination was normal. Routine blood investigations showed anemia (Hb- 5.8 g%) with leucocytosis (WBC count-26,400/mm³). Liver and kidney function tests were normal. Serum IgE levels were significantly raised. Serum IgE levels and absolute eosinophil counts were found to be significantly raised (219.20 IU/ml (Normal < 60) and 206/cu mm respectively). Pus from the abscess was sent for gram stain and culture sensitivity. On culture there was growth of multiple organisms including Gram +ve cocci in pairs and chains (streptococci) and Gram -ve bacilli (E-Coli) sensitive to sensitive to Clindamycin and piperacillin tazobactam respectively. Skin biopsy showed mild hyperkeratosis, spongiosis and hypergranulosis in epidermis with small vessel proliferation in dermis and periadnexal lymphoplasmacytic inflammatory infiltrate s/o atopic dermatitis. Chest X-Ray showed homogenous opacity in left lower lobe suggestive of consolidation (Figure 2).



Figure 2 : X-Ray chest PA view showing inhomogeneous radiopacities in bilateral lower zones and left middle lobe.

Computed tomography of chest revealed patchy consolidation in bilateral lower and left middle zones and left pleural abscess. Baby was treated with IV antibiotics (Based on sensitivity patterns). Skin biopsy showed f/s/o atopic dermatitis. Incision & drainage of abscesses and daily dressing of wounds was done. USG guided aspiration of pleural abscesses was tried but it was non- tappable. Packed cell transfusion was also given. Baby responded well to above treatment and his wounds decreased significantly (Figure 3).



Figure 3: Improvement in general condition of the baby. Note markedly reduced abscesses and ulcers.

Pruritic symptoms also decreased and there was visible improvement in general condition of the baby. Intravenous antibiotics were continued and multivitamins and other symptomatic management was given

Discussion:

Jobs syndrome was first described by Davis SD et al in 1966. It was named after the biblical character Job, who was "smote with sore boils". It was only in 1972 that the characteristic finding of Elevated IgE level was recognized as a cardinal feature and the name hyperimmunoglobulin E syndrome (HIES) was proposed for Jobs syndrome [6]. More recently vascular anomalies like coronary aneurysms and intracranial anomalies like chiari malformation and altered signal intensity areas on magnetic resonance imaging involving CNS are found to be associated with HIES. The molecular basis of this disease is identified to be signal transducer and activator of transcription-3 (STAT3) gene [7]. This mutation is responsible for impaired IL-6 and IL-23 signaling, the crucial T cell transcription factor retinoid-related orphan receptor gamma (ROR-gt) is also diminished, impairing IL-17 expression and Th17 differentiation. All these changes are responsible for impaired cell mediated immunity and increased susceptibility of individuals affected with this disease to fungal and extracellular bacterial infections [8]. HIES is associated with decreased life-expectancy. The average life span is reported to be 25-30 years though some patients may survive up to 4th or 5th decade. The mortality is usually due to pulmonary infections like staphylococcal pneumonias, fungal infections like aspergillosis and in minority of cases development of malignancies like Hodgkins and non-hodgkins lymphoma. Facial features of patients with Jobs syndrome are broad nose, deep seated eyes and generalized coarse appearance. Dermatological involvement usually manifests as eczematous or erythematous pruritic rash. Patient commonly present with eczema, recurrent respiratory tract infections caused by staphylococci, streptococci and H. Influenza. Fungal infections like Aspergillosis, Scedosporium, Pneumocystis jiroveci pneumonia, disseminated histoplasmosis, cryptococcosis, and coccidioidomycosis may also be seen in these patients. Invasive fungal infections if not treated promptly may rapidly prove fatal. Osteoporosis, scoliosis, hyperextensible joints and pathological fractures are some of the common forms of musculoskeletal involvement seen in HIES.

Investigations reveal eosinophilia with raised serum IgE levels. In many patients serum IgE levels are more than 2000 IU/ml but in pediatric patients the rise may be subtle and Sr IgE level may be in 100s [9]. ESR and CRP are raised in majority of the patients but this rise is not essential for the diagnosis of Jobs syndrome. Mutation analysis can be done for the molecular diagnosis but this is a complex procedure with considerable cost. Moreover facilities for molecular analysis may not be present everywhere. Imaging studies may be undertaken to know the extent of respiratory involvement. Since osteoporosis is silent till there is pathological fracture these patients should carefully be screened for development of osteoporosis.

The management basically consists of prevention and prompt treatment of bacterial infections. The prophylactic antibiotics therapy consists of trimethoprim-sulphamethoxazole administration. Management of dermatitis is essential part of management. Pruritic symptoms are controlled with anti-histaminics. Fungal infections like candidiasis, aspergillosis and onychomycosis are treated with appropriate systemic anti fungal therapy. Bone marrow and stem cell transplantation have been done in few cases but there value and safety in Jobs syndrome is yet to be established [10].

Conflict Of Interest: None

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