Job Syndrome

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Introduction
Job syndrome, also known as hyperimmunoglobulin E syndrome (Hyper IgE), is a rare autosomal dominant disorder. It is characterized by recurrent staphylococcal skin abscesses, eczematous dermatitis and extreme elevation of serum IgE. Other common manifestations include mucocutaneous candidiasis, several connective tissue and skeletal abnormalities. It is named after the Biblical character Job (Hazrat Ayub A.S) whose faithfulness was tested by an affliction with draining skin sores and pustules. People with this condition have long-term severe skin infections.

Case Report
A 22 years old male, resident of Jhelum, having positive family history of job syndrome, presented with complaints of multiple punched out skin ulcers, bruises, striae and generalized itching for 8 months. He also had shortness of breath, generalized edema and ear discharge. His dermatological problems started at the age of 3 months, and since then he had been on topical steroids. There was no history of fever, bleeding diathesis, bone pains, numbness, weight loss, orthopnea or urinary complaints.

On physical examination, he was short statured with broad face, coarse facial features, deep-set eyes, depressed nasal bridge, wide inter-alar distance, high arched palate, deformed teeth and nails, dermatitis, pruritic marks and cutaneous candidiasis. Laboratory evaluation revealed significantly raised serum IgE levels (1276.7 IU/ml). Rest of the investigations were unremarkable. He was given antibiotics (Amoxicillin clavulanate, Fusidic acid), anti-pruritic (Calamine lotion), analgesic (codeine) and Tetanus prophylaxis. He improved and was sent home with advice of follow up.

Discussion
Job syndrome is a primary immunodeficiency disorder, reported in 1966 for the first time by Davis et al. It is a rare condition affecting fewer than 1 per million people. About 250 cases of Job syndrome have been reported in the medical literature. No sex predilection is reported.

Job syndrome-STAT3 deficient hyper IgE syndrome is caused by mutation in STAT3 gene located on human chromosome 17q21. This results in impaired induction and signaling of key cytokines, including interleukins IL-6, IL-10, IL-17, IL-22, and IL-23, which explains susceptibility to various infections. Mutations in STAT3 gene have been identified in almost all clinically verified cases. Although the diagnosis of Job syndrome is usually delayed until the individual reaches childhood or adolescence, symptoms may start appearing in infancy. It typically manifests as neonatal rash and also affects skeleton, connective tissue and dental development with variations in severity. These individuals have characteristic facial features. Oral thrush may be seen and tympanic membrane may be scarred due to recurrent otitis. Children with this disorder are more prone to opportunistic infections. Diagnostic hallmark is very high serum immunoglobulin E levels. A definitive diagnosis is provided by heterozygous mutations in the STAT3 gene. Therapeutic strategy in Job syndrome is directed mainly towards the prevention and management of infections for which the patient requires interdisciplinary care. Surgery is sometimes needed to drain the abscesses.

Kimata et al reported positive results of high-dose intravenous immunoglobulins, leading to the decrease in IgE concentration and effective protection against severe infections. A review of reported cases of lymphoma in Job’s Syndrome indicates an increase in relative risk, mainly mature B cell lymphomas and class C Hodgkin lymphomas. Few data is available on the prognosis of patients with Job syndrome. Many patients who are receiving appropriate treatment and undergoing regular monitoring may live beyond the age of 50 years. Death is often due to infectious complications.

Job syndrome, a multisystem disorder with heterogeneity of underlying genetic defects, is a broad spectrum constellation of clinical manifestations which puts a great challenge for clinicians to establish a diagnosis in suspected cases. This makes it an interesting case to be studied.
References