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Job's syndrome

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In 1966, Davis et al. described two unrelated girls with red hair, chronic generalized eczema, repeated Staphylococcal skin infection and respiratory infection[1]. They suggested the name of "Job's Syndrome" for this clinical condition due to its resemblance to the sufferings of Job (Hazrat Ayyub A.S.). Main features of Job Syndrome include recurrent respiratory infections, eczema and very high serum IgE levels. Since then, more than 100 cases have been reported in literature including two from India[2,3] To our knowledge, no case has yet been reported from Pakistan. Recently we admitted a six month old boy with repeated chest infection and eczema and found high serum IgE levels. We are reporting this case along with review of literature.

Case Report

A six-month-old boy presented to emergency room of the Aga Khan University Hospital on 17 March 1999 with history of fever and cough for seven days. He had no history of vomiting, diarrhea or any other significant illness. He was born by normal vaginal delivery at term after an uneventful pregnancy, to consanguineous parents. He had two elder siblings who were normal. In the past he has had several episodes of respiratory illnesses and skin rash. Initially he remained well for about a month after birth, when lie got his first attack of respiratory illness. This was treated with antibiotics and bronchodilators. At the age of three months, he developed generalized eczema that was diagnosed as seborrheic dermatitis and managed with steroids, emollients and antibiotics by a dermatologist. Skin biopsy was also done which remained inconclusive.

On examination the boy bad normal anthropometric measurements (weight = 6.0 kg; height 63 cm; OFt = 43 cm), blond skin and hair (unlike his parents) and generalized eczema over face, trunk and limbs. He looked anemic and had a temperature of 3 8°C, respiratory rate 60/mm and heart rate 120/mm. His respiratory examination revealed subcostal indrawing and wheezing. His skin showed lesion compatible with eczema. Rest of the physical examination including ENT, abdomen etc was unremarkable. Investigations revealed hemoglobin of 12.0 G/d and a white cell count of 6.8 x 109 /L with 27% polymorphs and 13% lymphocytes. Eosinophils were 55% with an absolute count of 3.7 x 109 /L. The smear showed mild hypochromic anemia and severe eosinophilia. Bone marrow examinations were normal. Serum sodium was 130 meq/L, serum potassium 4.2 meq/L , chloride was 98 meq/L and bicarbonate was 19.3 meq/L. Serum creatinine was 0.4 mg/dl and SGPT was 34 lU/L. Serum zinc was 150 ug/dI (normal range 50 - 150 .ugldl). Blood, urine and stool cultures did not grow any organisms. Serum IgE was 1098 1U/ml (95th centile for age 29 lU/ml). IgA was 0.164 G/L (0.08-0.68 G/L); IgM was 0.02 G/L (0.03-0. 10 GIL) and IgG svas 1.55 G/L (0.2 1-0.7 GIL). X-ray chest revealed bilateral pneumonia. He was treated with antibiotics (Cefotaxime and Cloxacillin) and nebulized salbutamol for 10 days. He was discharged on 27-3-1999 on oral salbutamol and theophyllin. He was readmitted on April 1, 1999 with fever, cough and respiratory distress with wheezing, exacerbation of skin eczema and diarrhea. Repeat investigations revealed persistence of eosinophilia i.e., 1.21 x 109/L .The blood culture grew Staphylococcus aureus and stool examination showed Giardia lamblia cysts. He was treated with cloxacillin, gentamicin and metronidazole. He improved and was sent home on April 4, 1999. Since this boy had come from another province, the parents took him back to his hometown and never brought him for follow up. The boy's uncle was contacted after a few months who informed that the boy died a month after discharge due to pneumonia at a hospital in Islamabad.

Discussion

Job Syndrome is a rare immuno-deficiency disorder that comprises essentially of generalized eczema and susceptibility p to skin and Sinn-pulmonary infections. Characteristic facial features comprising of broad-based nose, broader alae nasi and prominent eyebrows are seen in majority of cases[4]. Symptoms of recurrent skin and sinu-pulmonary infections usually start during the first two years of life. they may be delayed up to 17 years[5]. Skin and lung infections are tile commonest but infections of the sinuses. middle ear and 01 tract also occur. Patients are usually infected by Staphylococcus aureus, Haemophilus influenzae and Streptococcus pneumoniae and Group A beta heniolytic streptococcus[5]. Buckley et al[6] described its association with elevated levels of IgE. This was also confirmed by Hill and Quie[7] and is now considered a cardinal feature of the disease. Donabedian et al. laid two criteria for the diagnosis of Job's syndrome: (1) recurrent skin and sinu-pulmonaty infections and (2) a 10-fold increase in the IgE level (2000 lU/ml). Though our patient did not fulfill the second criterion, this may be due to early presentation of the case. Majority of the cases reported in the literature was older than our case. It seems that IgE levels in Job's Syndrome increases with age as reported by Posic et al[8]. In their patient, the IgE levels were 348 lU/mi at the age of 2 months and increased to 2050 lli/ml at 9 months. In one of the cases reported by Donabedian and Gallian the IgE level was 72 LU/mi in cord blood, 1600 lU/ml at the age of 19 months and 4100 lU/mi at the age of 3 years[5]. The exact mechanism of the immune defect is unknown, although defective neutrophil chemotaxis is frequently reported[9]. There are conflicting reports about its association with the occurrence of the Interleukin 4 receptor variant Q576R[10]. Job's Syndrome is now recognized as a multi-system disorder, with nonimmunologic abnormalities of the dentition, bones and connective tissue. Job's Syndrome can be transmitted as an autosomal dominant trait with variable expressivity. Multipoint analysis and simulation testing confirmed that the proximal 4q region contains a disease locus for Job's Syndrome[11].

Though no specific satisfactory treatment is available for the illness but antibiotics are the mainstays of therapy during infective episodes. The role of prophylactic antibiotics for longer duration is more controversial though some benefit has been shown by use of cotrimoxazole[12]. Intravenous immunoglobulins have also been used with disappointing results[5]. Similarly gamma interferon has been used in some patients[13]. Till date only one patient with Job's Syndrome complicated by lymphoma received bone marrow and stem cell transplantation with resulting remission of symptoms as well as normalization of the elevated lgE levels[14].

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