Hyperimmunoglobulin E (Job's) Syndrome: A Rare Cause of Recurrent Pneumatocele, Lung Abscess and Empyema in Childhood

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Abstract

The hyperimmunoglobulin E (HIE) or Job's syndrome is a rare and complex disorder characterized by recurrent staphylococcal lung infections with abscess and pneumatocele formation and chronic eczematoid dermatitis in childhood. Laboratory evaluation reveals consistent elevation of circulating immunoglobulin E levels. This article describes a case of HIE (Job's) syndrome as a cause of recurrent lung infections with abscess, pneumatocele formation and empyema necessitating tube thoracostomy.

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Key words: *hyperimmunoglobulin E, Job's syndrome, recurrent lung abscess, pneumatocele, empyema, eczematoid skin lesions, bone fractures*
Abbreviations: HIE: *Hyperimmunoglobulin E*, **Ig:** *Immunoglobulin*, **PMN**: *Polymorphonuclear*

Introduction

Hyperimmunoglobulin E (HIE) syndrome or Job's syndrome is a rare and complex disorder characterized by extremely high levels of serum immunoglobulin (Ig) E, recurrent severe staphylococcal lung infections with pneumatocele formation, staphylococcal skin abscess or chronic eczematoid dermatitis (1-6). Patients may also have coarse facial features (5), mild eozinophilia, mucocutaneous candidiasis (7), empyema (8), recurrent bone fractures that may be seen with osteoporosis (9) and variable polymorphonuclear (PMN) leukocyte chemotactic abnormalities have also been reported in this syndrome (3,6). The syndrome was first described in 1966 by Davis et al. (1). Since then, over 150 cases have been described, mainly children (5). We report a case of hyperimmunoglobulin E (Job's) syndrome who presented with recurrent staphylococcal lung abscess, pneumatoceles and empyema during childhood necessitating recurrent antistaphylococcal antibiotic therapy and drainage by closed tube thoracostomy.

Case Report

A 9-year-old girl was referred to the thoracic surgery unit for evaluation of recurrent bilaterally staphylococcal lung abscess, pneumatoceles and right thoracic empyema. History revealed that she had a lung infection and pustular skin lesions localized on the neck at the age of 6 months. The patient was treated

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with an antibiotic. During the succeeding 7 years she had multiple episodes of bronchitis or pneumonia, eczematoid skin lesions on the face, back, buttocks, arms and legs, middle ear infections, sinusitis and candidal infections of the mouth and groin. She was allergic to a wide variety of environmental agents including soap, fur, toys, fuzzy, dust, and feathers. Neither his parents nor her sibling had the same problem. At 4 years of age, she was hospitalized because of bilaterally distal humerus fractures, resulting from a mild trauma.

At the age of 8 years she had a high fever with chills, generalized malaise, fatique, dyspnea and a productive cough. Cultures of sputum and thoracentesis identified *Staphylococcus aureus* as the offending organism. The patient was treated with intravenous administration of an antistaphylococcal antibiotic and drainage by closed tube thoracostomy with complete resolution of the empyema.

Three months later the diagnosis of Hyper-Ig E was established with a large pneumatocele in the right upper lobe (Fig-1). The serum Ig E level was 20.000 U/mL (normal: 0.0-60 U/mL). Sputum specimens grew *Staphylococcus aureus*. Initial attempts at another institution to manage the infection by antistaphylococcal antibiotic and subsequently by percutaneous catheter drainage of the pneumatocele were succesful.

On admisson (at the age of 9 years) physical examination revealed a girl with dark brown hair and normal growth for her age. Patient had 39 °C fever with productive cough. There were multiple skin scars over the face, back, buttocks and extremities (Fig-2). There was no adenopathy appreciated on physical examination. Breath sounds over the right lower lung markedly diminished and had bilaterally diffuse coarse ronchy. The liver and spleen were not enlarged. Complete blood count yielded a white blood cell count 30.1/mL with 64.7% neutrophils and 4.5/mL eosinophilia (normal:0.0-0.2). Hemoglobin and hematocrit 98 g /L and 0.32 respectively, with hipochromic anemia. Serum electrolytes were normal. Tests for cystic fibrosis (sweat cloride) were negative. The serum Ig E level was

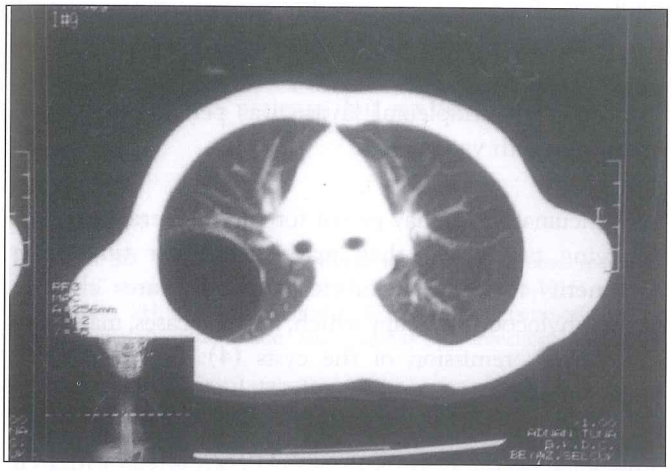

Figure 1. *Chest CT scan demonstrating large pneumatocele in the right upper lobe.*

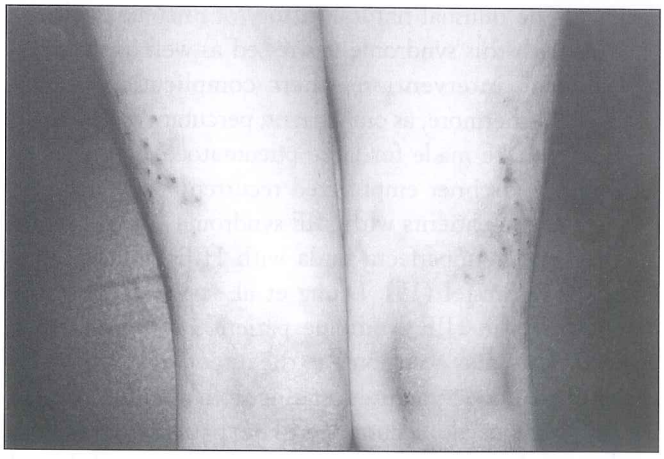

Figure 2. *Showing eczematoid skin lesions of the lower extremities.*

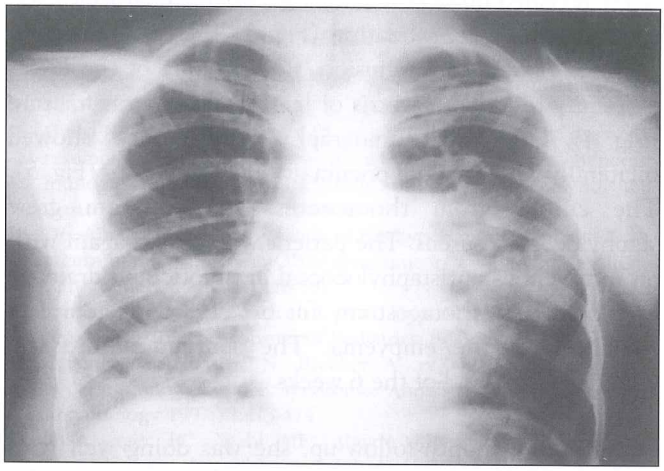

Figure 3. *Chest X-ray on admission showing bilaterally lung abscess, pneumatoceles and patcy areas of consolidation.*

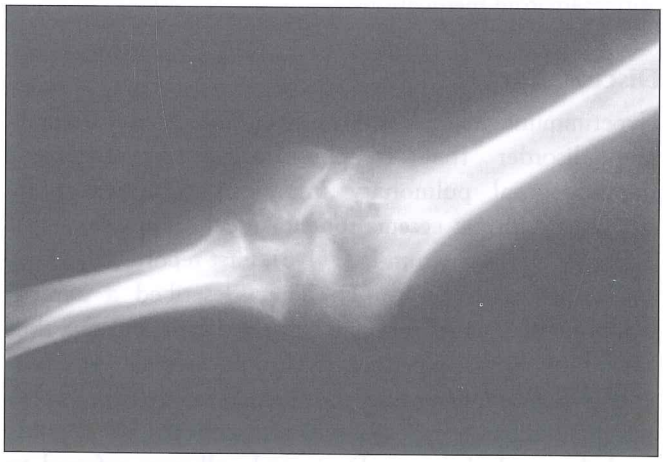

Figure 4. *Radiography of the left upper extremity revealing scatris of distal humerus fracture.*

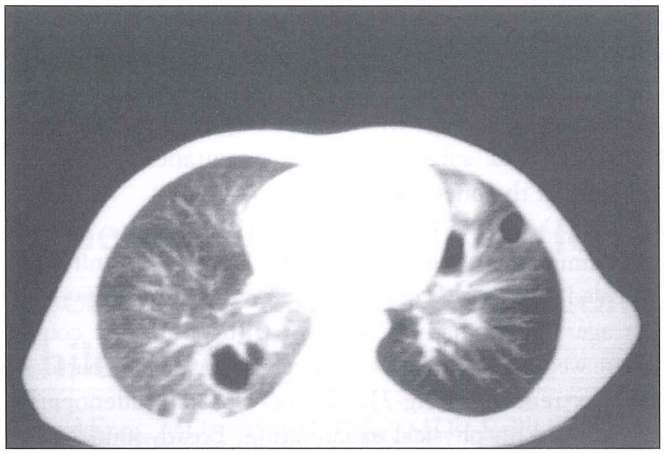

Figure 5. *Computed tomography of chest showing bilaterally abscess and pneumatoceles formation.*

19.300 IU/ml. Other serum immunoglobulin levels were within normal limits and a normal result for nitroblue tetrazolium reduction test (NBT), thus suggesting normal leucocyte chemotaxis. Based on the clinical history and the elevated level of Ig E, the diagnosis of hyperimmunoglobulin E (Job's) syndrome was made. Chest X-ray revealed bilaterally lung abscess, pneumatoceles and patchy areas of consolidation (Fig. 3). Thorax ultrasound revealed right pleural effusion. Radiography of the upper extremity revealed a scatris of left distal humerus fracture (Fig 4). Computed tomography of the chest showed bilaterally abscess and pneumatocele formation (Fig 5). The culture from thoracentesis and sputum grew staphylococcus aureus. The patient was treated again with an intravenous antistaphylococcal antibiotic and drainage by closed tube thoracostomy for 6 weeks with complete resolution of the empyema. The sputum culture was negative at the end of the 6 weeks.

During the 3-month-follow-up, she was doing well with intermittant prophylactic antibiotic therapy except for intermittant eczamatoid skin dermatitis although antieczematoid medications.

Discussion

Hyperimmunoglobin E (Job's) syndrome is an extremely rare disorder that is characterized by recurrent staphylococcal pulmonary infections complicated by empyema, chronic eczema, pneumatoceles formation, and markedly elevated serum Ig E (1-6). First reported by Davis and colleques in 1966 (1). They described a clinical syndrome in 2 unrelated girls with red hair and fair skin who, from birth, experienced chronic eczema, recurrent staphylococcal infections of the sinopulmonary tract, and in abnormal inflamatory response with the formation of "cold" staphylococcal abscesses. Davis and colleques referred to this syndrome as Job's syndrome because of its resemblance to the affliction of the biblical figure. Buckley and co-workers (2) linked these clinical findings with markedly elevated serum Ig E levels and coarse facies. Hill and co-authors (3) reported hyperimmunoglobulinemia E and defective chemotaxis of polymorphonuclear leukocytes in the 2 original girls with Job's syndrome. In addition to elevations in Ig E levels, defects in neutrophil chemotaxis have been reported by several authors (3,10,11). It is possible that the patient described by Swim et al. (12) had the clinical manifestatios of the hyperimmunoglobulin E syndrome but with normal neutrophil chemotaxis. Our patient was found to have a normal neutrophil chemotaxis. It is not possible to infer from currently available data whether an abnormality of neutrophil chemotaxis has a prominent role in the pathophysiology of the recurrent infection in this syndrome. A primary defect in the function of polymorphonuclear lekocytes as evaluated by chemotaxis is not always demonstrated in these patients (8).

A review of the National Institute of Health experience of 13 patients with Job's syndrome suggested that recurrent bronchitis is a common pulmonary complication of the syndrome. Empyema developed in many of these patients (6). Our patient also had a reccurent tharocic empyema which required a chest tube placement for 6 weeks. Additionally, intrapleural lavage was performed through chest tube with vancomisin.

The pneumatoceles may persist for varying period of time, enlarging rapidly, or they may regres over time. The treatment for this condition is adequate chronic antistaphylococcal therapy which, in some cases, may cause spontaneous remission of the cysts (4). In our patient, pneumatoceles were present with gradual decrease in their size, therefore, surgical intervention was not required n a remarkable series, 11 patients with HIE reported by Merten and associates (14) all had 'lung cysts' were reported to have spontaneously resolved after continuous antibiotic therapy. The unusual natural history of pneumatoceles in patients with this syndrome is stressed as well as the need for surgical intervention when complications occur (22,23). Furthermore, as our patient, percutaneous catheter drainage can be made for large pneumatoceles to remove succesfully. Kirchner emphasized recurrent bone fractures in some of the patients with HIE syndrome (9) and a case of osteogenesis imperfecta tarda with HIE syndrome was reported by Brestel (15). Leung et al. suggested that the monocytes from HIE syndrome patient cause osteopenia and osteclasts, may contribute to the osteoporosis (16). Our patient had a bone fracture resulting from a mild trauma at age of four but no recurrence. The patients with Job's syndrome also seem to be preposed to unusual fungal infections such as cryptococcosis and histoplasmosis of the

esophagus (21) and colon (22). Our patient also had a fungal infection of the mouth and groin, which treated easily.

The primary defect in HIE syndrome is unknown, therefore, definitive therapy is not possible. Several investigators have studied the effects of normal plasma transfusions, histamine-2-receptor blocking agents, transfer factor, levamisole, ascorbic acid and interferon-alpha in the treatment of HIE syndrome (3,11,20). Normal plasma transfusions, cimetidine and ascorbic acid said to improve the chemotactic abnormalities of neutrophils and did not observed any severe infections in their patients (11,20). We used levamisole, ascorbic acid and histamine-2-receptor blocking agents in our patient which proved useful. Our patient had no any important lung disease except recurrent mild skin lesions on regular controls. Etzioni et al. reported that a small dose of cyclosporin A (3 to 5 mg/kg/d) is beneficial in patients with HIE syndrome (21). It should be considered in severe cases where other therapeutic modalities have failed.

The long-term outcome of this disease is unknown. Life long antistaphylococcal antibiotic therapy seems to be most succesful treatment and useful in preventing infections in these patients, but no definitive therapy is available.

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