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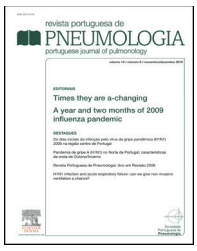

CASE REPORT

A new case of Job's syndrome at the clinic: A diagnostic challenge

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KEYWORDS
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Abstract Job's syndrome or Hyperimmunoglobulin E syndrome (HIES) is a rare primary immunodeficiency characterized by recurrent soft tissue infections, coarse face, skeletal and vascular abnormalities, and markedly high levels of Immunoglobulin E. Eczema that resembles atopic dermatitis but is refractory to traditional treatment and severe and recurrent bacterial pneumonias often recognized during childhood. Early diagnosis and treatment prevent progressive pulmonary sequellae and increase survival. About 200 cases of HIES has been reported worldwide. The authors report a new case of HIES with one of the worst pulmonary sequellae found in the literature on this subject and review this infrequent topic.

PALAVRAS-CHAVE
Síndrome de Job;
Síndrome de hiperimunoglobulina E;
Bronquiectasia;
Relatório de caso;
Eosinofilia;
Imunodeficiência primária

Um novo caso de síndrome de Job na clínica: um desafio de diagnóstico

Resumo A síndrome de Job, ou síndrome de Hiperimunoglobulina E (HIES), é uma rara imunodeficiência primária caracterizada por infecções recorrentes de tecidos moles, anomalias grosseiras faciais, esqueléticas e vasculares, e níveis visivelmente elevados de Imunoglobulina E. O eczema semelhante à dermatite atópica, mas refractário ao tratamento tradicional e pneumonias graves e recorrentes são frequentemente reconhecidas durante a infância. Um diagnóstico e tratamento precoces impedem sequelas pulmonares progressivas e aumentam a sobrevivência. Foram relatados cerca de 200 casos de HIES em todo o mundo. Relatamos um novo caso de HIES com uma das sequelas pulmonares mais extensas encontradas na análise bibliográfica sobre este assunto, conjuntamente com uma revisão sobre esta patologia pouco frequente.

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Introduction

The prevalence of primary immunodeficiency (PI) is underestimated worldwide. In the United States, the calculated prevalence of diagnosed PI is 1 in 1200 people of all ages.[1] Hyperimmunoglobulin E syndrome (HIES) is among the earliest described syndromes of immunodeficiency characterized by recurrent and severe pneumonia, eczema, and markedly high levels of immunoglobulin E (IgE). Both male and female are affected and familial or sporadic cases have been reported worldwide. The authors present a new case of HIES, lately diagnosed, with severe pulmonary sequellae.

Case history

A 25-year-old man came to the hospital complaining of mild shortness of breath, cough with a yellowish expectoration, weakness and profuse unexplained sweating without fever. The first symptoms had started three month before. He was a nonsmoker and had no history of environmental exposure to chemicals or dust. His medical history was positive for dermatitis since the first 24 h of his life, recurrent severe staphylococcal pneumonias with empyema, chronic external otitis, sinusitis and dermatitis. He also showed pathological fractures of the seventh left rib, intercostal herpes-zoster at two years of age. Frequent episodes of severe infectious diarrhea were also reported. His family history was unremarkable.

On physical examination, the patient's body size was smaller than normal for his age and sex. His face was coarse, with prominent forehead, broad nasal bridge, and facial asymmetry. Marked joint hyperextensibility and scoliosis was found. Chest examination showed a respiratory rate of 24 breaths/min with crackles in the left base. His skin showed signs of pruritic chronic dermatitis spread all over, mainly at his legs, arms, and axillae. Onychomycosis was present at his fingernails with clubbed fingers. The rest of the vital signs and physical examination were unremarkable.

Laboratory findings included: Hb: 11.0 g/dL, WBC count: 15.0×10^9/L with 10% eosinophils and 52% neutrophils, erythrocyte sedimentation rate: 80 mm/h, alkaline phosphatase: 211 U/L [reference range (RR): 35–150 U/L]. No other metabolic abnormalities were observed. Alfa-1 antitrypsin, serum IgA and IgM levels were within normal limits. IgG: 17.0 g/L (RR: 6.4–13.5 g/L) and IgE: 21,300 U/mL (RR: 10–179 U/ml) were high. A chest radiograph performed on admission showed multiple thin-walled cysts with air-fluid level consistent with superinfection (Fig. 1). The thorax CT scan alterations are showed in Fig. 2.

Topical antibiotic and steroids creams, oral ketoconazole, and ceftriaxone and azithromycin were initially used without a significant improvement. On the fifth day of treatment a sputum culture with meticillin resistant *S. aureus* was received and vancomicin was initiated with excellent results. No other germs were isolated on blood or sputum cultures. The diagnosis of sporadic form of HIES (Job's syndrome) was made based on clinical and laboratory findings. Skin lesions improved and prophylactic treatment with trimethoprim-sulfamethoxazole was recommended.

Discussion

There are two forms of HIES: an autosomal-dominant form caused by mutations in signal transducer and activator of transcription (*STAT)3* (gene location 17q21),[2] and a recessive form frequently associated with dedicator of cytokinesis (*DOCK)8* mutations (9p24) or tyrosine kinase (*TYK)2* (19p13.2) mutations. The dominant form (familial or sporadic) is characterized by skeletal, connective tissue, recurrent pulmonary infections and eczema. Autosomal-recessive HIES is present with recurrent viral and staphylococcal skin infections, frequent central nervous system abnormalities and vasculitis. This form exhibits a higher mortality and a lack of tendency to pneumatoceles formation.[3,4] Inheritance usually follows an autosomal dominant pattern with variable penetrance being the autosomal recessive pattern infrequent.

Pathogenesis is complex and not very well understood. Originally, HIES was consider to be due to a defect in neutrophil chemotaxis but this is not a constant feature. Leucocytes of HIES patients have defective cytokine-mediated signal transduction through the Janus Kinase (*JAK*)-*STAT* pathways. *STAT3* is a major signal transduction protein involved in diverse pathways including wound healing, angiogenesis, immune pathways, and cancer. HIES patients have impaired differentiation of Th17 T cells from mutations in *STAT3*.[5] Experimental models in which Th17

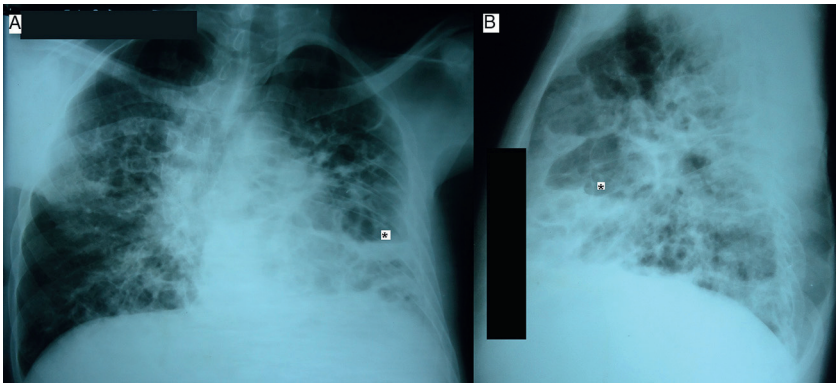

Figure 1 Chest radiograph on admission (A: posteroanterior and B: lateral view) showing multiple thin-walled cyst (pneumatoceles) with air-fluid level (*).