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A case of late diagnosis of Gaucher disease with lung involvement (case study)

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ABSTRACT

The present authors report the case of an adult male with no medical history, who developed prolonged fever of unknown cause, progression of anemia and lung fibrosis. A hematological disease was suspected and further investigations were done. The bone marrow aspirate raised the suspicion of Gaucher's disease. The positive diagnosis was Gaucher's disease with lung involvement (pulmonary fibrosis and pulmonary hypertension), and cardiac involvement (restrictive cardiomyopathy). Clinical evolution was unfavorable, and the patient died of cardiorespiratory failure.

In conclusion, the present case report illustrates a late diagnosis of Gaucher's disease with lung and cardiac involvement resulting in death in a short period.

Keywords: Gaucher disease, pulmonary fibrosis, pulmonary hypertension.

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Introduction

Gaucher's disease, the most frequent lysosomal storage disease, is caused by mutations in the glucocerebrosidase gene, leading to decreased enzymic activity and accumulation of glucocerebroside within the macrophages of the reticuloendothelial system [1]. Despite the heterogeneity of Gaucher's disease, three basic clinical forms have been distinguished based on the degree of neurological involvement [2, 3]. Most patients with Gaucher's disease have the non-neuronopathic form (type I) and the most common symptomatic presentation includes hepatosplenomegaly, anemia and thrombocytopenia due to hypersplenism, and often, skeletal involvement [4].

Symptomatic lung involvement in Gaucher's disease is relatively rare, being restricted to patients with other severe manifestations. Pulmonary involvement includes Gaucher cell infiltration of the alveolar or interstitial spaces, peribronchial or vascular infiltration, or arterio-venous shunting,

most often as a complication of long-standing liver disease (hepatopulmonary syndrome) [5]. Cardiac involvement in patients with Gaucher's disease is also uncommon.

The present authors describe a relatively rare case of Gaucher's disease with severe cardiopulmonary involvement, with pulmonary fibrosis and pulmonary hypertension, and restrictive cardiomyopathy.

Case report

A 47-yr-old male, was evaluated at the present author's hospital for progressive asthenia, weight loss (10 kilograms during the previous 8 months), irritative dry cough (lasting for 8-9 months), fever and exertional dyspnea. The patient also complained of generalized bone pain, especially of the lumbar spine, aggravated during the last year.

The patient had smoked 18 packet-years (20 cigarettes/day since the age of 18).

The symptoms started 9 months previously to his admission in our hospital. He was admitted in a different hospital, where a slight anemia associated with a biological inflammatory syndrome was found. He was readmitted after 6 months in the same hospital, due to worsening symptoms, prolonged fever of unknown cause, progression of anemia (Hb=7g/dl), and of the inflammatory syndrome (ESR=125mm/h). A hematological disease was suspected and the patient was sent to our hospital for further investigations.

The initial clinical examination revealed an ill-looking patient, with cachexia, skin and mucosal pallor and acrocyanosis; bilateral fine crackles at the lung bases, SaO₂ =88%(aa), hypotension (BP=80/50mmHg), tachycardia (HR=110/min), hepatomegaly (vertical diameter=18cm), and splenomegaly (grade II).

1. Laboratory tests: normocytic, hypochromic, hyposideremic anemia (Hb=7.4g/dl, MCV=83fl, MCHC=30,6g/dl; serum iron=13µg/dl); leucopenia=2.700/mm³; inflammatory

syndrome (ESR=80mm/h, fibrinogen=540 mg/dl); hypoproteinemia (5.6g/dl) with hypoalbuminemia (2.11g/dl); hypergammaglobulinemia (2.18g/dl) with polyclonal increase in IgA (8.05g) and IgM (8.05g); hyponatremia (129mmol/l), hyperkalemia (5.5mmol/l), hypocalcemia (7.6mmol/l); negative HIV test; negative hepatitis virus blood tests (HBsAg, AntiHCV); negative immunological tests (cryoglobulins, rheumatoid factor, antinuclear antibodies); direct microscopic examination of sputum with no Koch bacilli; sputum cultures with normal flora, no Koch bacilli; repeated hemocultures: sterile.

2. Abdominal ultrasound confirmed hepatomegaly and splenomegaly: an anteroposterior diameter of the liver's left lobe of 8cm, a heterogeneous structure with increased echogenicity; portal vein diameter=11mm; splenic vein diameter=9mm; the long diameter of the spleen=13.4cm.

3. Chest radiograph showed polymorphic opacities with medium density in the superior half of the right lung and all over the left lung.

4. Chest CT revealed multiple soft tissue masses, of low intensity, in the medio-anterior left lung field and fewer in the peripheral right lung field, suggestive for congestive infiltrates (figure 1 and 2).

Figure 1 - Chest CT – multiple soft tissue masses, of low intensity, in the medio-anterior left lung field and fewer in the peripheral right lung field, suggestive for alveolar infiltrates.

Figure 2 - Chest CT – multiple soft tissue masses, of low intensity, in the medio-anterior left lung field and fewer in the peripheral right lung field, suggestive for alveolar infiltrates.

5. Pulmonary function tests: restrictive syndrome: FVC=2.80l (66%); FEV1=2.38l(68%); FEV1/FVC=85.1%; PEF=3.99l/s (46%); FEF25%=3.99l/s (53%); FEF50%=2.69l/s (58%); FEF75%=1.68l/s (89%).

6. Video-bronchoscopy showed no proliferative masses in the evaluated areas, including at the level of the first order segmental bronchi; moderate quantity of mucous secretions (figure 3); the bronchoalveolar lavage revealed no Koch bacilli; the biopsy taken at the level of the right superior lobar bronchus revealed Gaucher cells.

Figure 3 - Bronchoscopy - without proliferative mass, moderate mucous secretions.

7. Echocardiography showed restrictive presentation with normal function, mild pulmonary hypertension, endomiocardial fibrosis and pericardial calcifications. LV was slightly hypokinetic; normal cardiac output (>50%); high subendocardial

echogenity, especially at the level of the inferior and posterolateral walls of the LV; pulmonary time to peak velocity=80-90 ms; atrial reverse flow=89-90 ms; Δ PRV-RA=25 (max 27).

8. Bone marrow aspirate: normocellular BM, with a G/E ratio=2.5, and a 60% infiltration with Gaucher cells.

9. Dorso-lumbar spine and sacroiliac joints radiographic examination: L5 sacralization; superiorly closed left sacroiliac joint, with reduced transparency of the joint space in the superior 1/3rd part.

10. Flexible upper GI endoscopy showed no esophageal varices.

11. The enzyme assay confirmed the glucocerebrosidase deficiency (2.9 nmol/h/mg; normal=30-100) and increased chitotriosidase activity (34.500 nmol/h/ml; normal=170-5700).

Discussion

Our patient is a 47 year old cachectic male with predominant pulmonary symptoms and hepatosplenomegaly, with laboratory findings like polyclonal gammopathy, hypoalbuminemia, high ESR, and fever, implied malignancy at first. The presence of Gaucher cells in the bone marrow was surprising for us because of the low incidence of Gaucher's disease at such an old age.

The present case report describes a patient with no medical history, but with a previously unreported infiltrative lung disease with pulmonary hypertension. Histologically, this interstitial pulmonary disease was characterized by infiltration of Gaucher cells. Clinical signs and symptoms of pulmonary disease have been reported in Gaucher patients [6,7]. Signs consist of airway obstruction with reduced expiratory flow; reduced lung volume and reduced alveolar-capillary diffusion [8]. Lung involvement can be investigated through chest X-ray, pulmonary function tests, high-resolution CT of the chest and oxygen saturation in arterial blood. Pulmonary hypertension is the most

severe lung complication in Gaucher patients. Its exact pathophysiology is still debated [9,10]. Most of the described cases with severe lung disease, characterized by recurrent pulmonary infections and progressive dyspnea culminating in fatal respiratory insufficiency, were children. Kerem et al have demonstrated that type I patients with pulmonary function abnormalities have significantly more severe disease than those with normal pulmonary function [11].

The restrictive lung function pattern, hepatosplenomegaly, anemia, skeletal involvement, and restrictive cardiomyopathy, all support the diagnosis of Gaucher's disease with lung and cardiac involvement. Cardiac involvement in patients with Gaucher's disease is uncommon. Pericardial effusion resulting in constrictive pericarditis, valvular calcifications, and focal infiltrations of Gaucher's cells in the ventricular myocardium have been reported [12].

The clinical evolution was not favorable, and the patient died of cardiorespiratory failure.

The present authors have concluded that the case is particular due to the lack of previous medical history, the late diagnosis, in adulthood, at the time when the disease was in an advanced stage, with multivisceral involvement, and the presence of rare manifestations of Gaucher's disease such as lung and cardiac involvement.

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