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An unusual form of Gaucher's disease: pulmonary and cardiovascular involvement and cholelitiasis

Research Article

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Abstract: Gaucher's disease is an inherited storage disease caused by a deficiency of the enzyme glucocerebrosidase. Although the hepatic manifestations are seen frequently, pulmonary and cardiovascular involvements are known to be very rare in Gaucher's disease. This report presents these rare findings made by conventional radiography, computerized tomography (CT), and High-resolution CT (HRCT) of a 16-year-old female patient with fatal Gaucher's disease.

Keywords: *Gaucher's disease • Cardiovascular calcification • Pulmonary interstitial involvement*

1. Introduction

Gaucher's disease is an autosomal recessive disorder. A deficiency of the enzyme glucocerebrosidase leads to the accumulation of the enzyme substrate glucosylceramide in reticuloendothelial cells throughout the body, primarily in the liver, spleen, lymph nodes and bone marrow. In this report, in addition to these frequent manifestations, pulmonary and cardiovascular involvement together with cholelitiasis in a 16-year-old female patient with Gaucher's disease and her CT findings are presented.

2. Case Report

A 16-year-old female patient with the diagnosis of Gaucher's disease was hospitalized with complaints of palpitation and dyspnea. Her initial diagnosis of Gaucher's disease was established outside of our center at early childhood and her routine follow ups and treatments were conducted at another testing facility. In her initial physical examination in the emergency department, crepitant rales in the bases of both lungs and grade 1/6 systolic ejection murmur on the mitral area and hepatosplenomegaly were defined. Laboratory routine studies revealed normal hemoglobin, hematocrit, WBC count, but decreased platelets count of 76500/mm³ (normal range: 180000-360000/mm³) and high values of liver enzymes [(AST: 195 IU/mL) (normal range: 0-40 IU/mL) and ALT: 104 U/L (normal range: 0-35 IU/mL)]. Serum calcium, phosphorus, total cholesterol and BUN levels were within the normal limits. C-reactive protein was negative. Respiratory samples were tested for tuberculosis and smear for acid-alkali resistant bacteria and Polymerase Chain Reaction studies for *M tuberculosis* complex and revealed negative results. Posteroanterior chest radiography showed a mild cardiomegaly and interstitial involvement affecting both lungs diffusely (Figure 1). A moderate hypertrophic cardiomyopathy and a mild mitral insufficiency were detected by echocardiography. Despite an empirical intensive antibiotic treatment, no improvement was seen in her lung symptoms, and her breathing problems increased. The thorax CT demonstrated severe calcification on ascending aorta, aortic arch and thoracic

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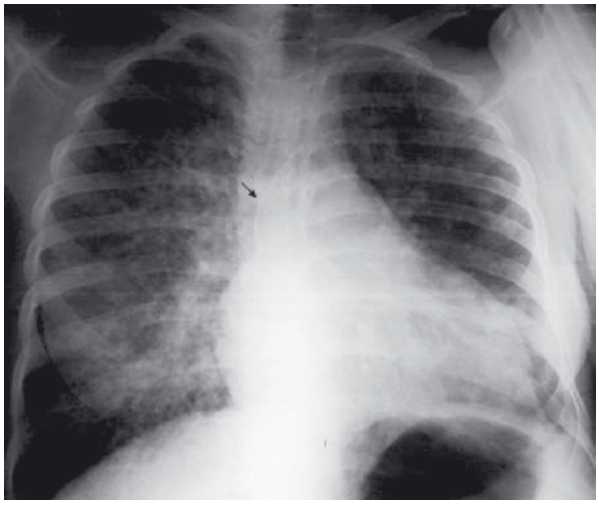
Figure 1. PA chest radiography. Reticular interstitial involvement pattern in both lungs, especially in the right and calcification of aortic arch (Black arrow).



aorta. Calcifications of mitral and aortic valves were also observed (Figure 2a-b-c). In addition to these, the gall bladder seen in the lower CT section was remarkable for stone densities (Figure 2d). High-resolution CT (HRCT) of the chest revealed extensive bilateral reticulonodular pattern and peripheral ground-glass opacities (Figure 3). She died on the 40th day of the hospitalization because of right ventricle failure developed due to the refractory pulmonary symptoms. The family did not approve the postmortem study due to religious beliefs.

3. Discussion

Gaucher's disease is the most common form of the lysosomal storage diseases and is clinically characterized with hepatosplenomegaly, anemia and thrombocytopenia because of an accumulation of the fatty substance, glucocerebroside in liver, spleen and bone marrow. However, in Gaucher's disease chest radiography is mostly normal [1], but typical reticular, nodular or reticulonodular interstitial involvement has been demonstrated in case of pulmonary involvement with conventional radiography [1-3] and HRCT [4,5]. The patient presented here was not only supported the previous descriptions of interstitial disease in HRCT but also had peripheric ground-glass appearance. In this respect, our patient presented similar radiological findings previously described by others [4,5]. The only difference was the ground-glass appearance was previously defined for the adult patients over the age of 50, the patient presented here was 16 years old. In the cyto-pathological examination of the lung biopsy tissue, lipid-laden macrophages (Gaucher cells) which

Figure 2. Axial CT images. Aortic and mitral valve calcification (a,b), aortic arch calcification (c). Two stones in the gall bladder and calcification on the descending aorta anterior wall (d).

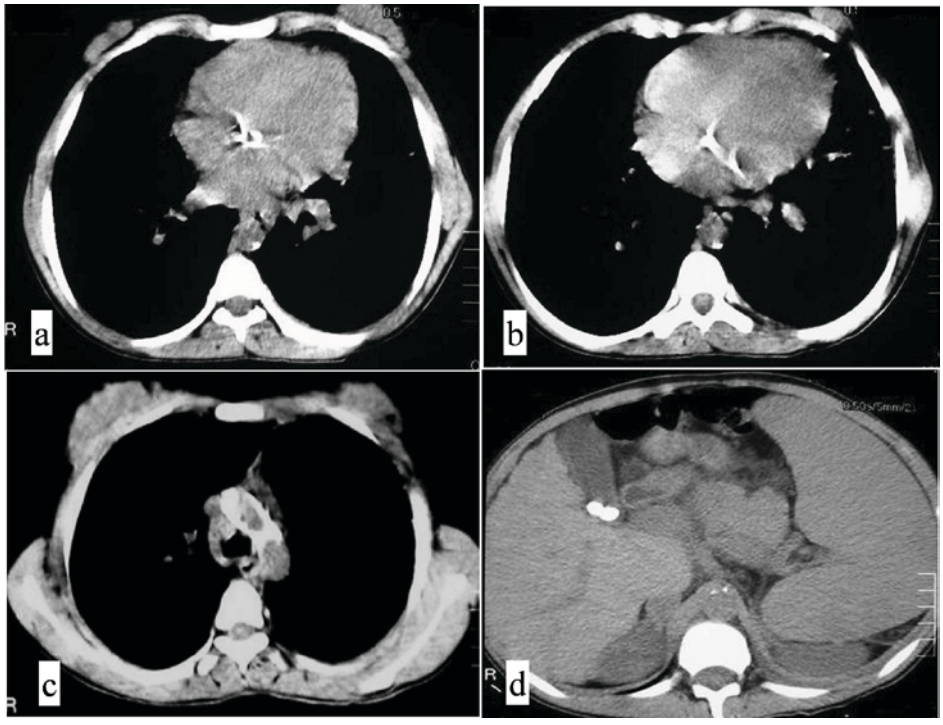
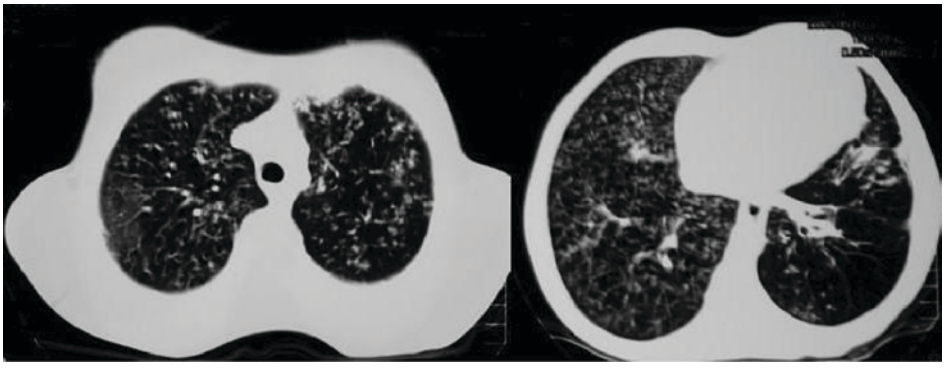


Figure 3. HRCT images. Diffusive reticulonodular involvement in the lungs and ground-glass appearance in the peripheral areas on the HRCT sections taken from various slices.



aggregate within the alveolar spaces and infiltrate to the alveolar walls, perivascular and pulmonary septa have been defined [2,6]. In some cases, Gaucher cells can occlude precapillaries and capillaries, which in turn leads to perfusion defects and pulmonary hypertension [3]. The ground-glass appearance on radiological imaging may reflect the interstitial or intra-alveolar processes described in the pathological examinations of the lungs of the adult Gaucher's disease [2]. Persons affected most seriously may also be more susceptible to infections, particularly air-borne respiratory infections. Direct pulmonary and cardiovascular involvement in Gaucher's disease is very rare. The most commonly reported involvements in the literature are those of pericardium (constrictive pericarditis or pericardial calcification) [7,8] or mitral, aortic valves and ascending aorta calcifications [9-11]. Similarly, the 17-year-old patient reported by George *et.al* had also calcification not only on the ascending aorta but also on the aortic arch and thoracic aorta [9]. It is considered that this calcification formation may be due to the recurrent valvulitis attacks triggered by the deposition of Gaucher cells or by the release of excessive cytokines [11]. Additionally, there are studies which indicate the relation between the calcification of aortic and mitral valves and D409H Gaucher's disease [9,11].

There are several studies which show that there is a significant increase in the prevalence of cholelitiasis in Gaucher's disease patients compared to normal populations [12,13]. These studies include only the adult patients with Gaucher's disease. There has been no study on children or adolescents. Although the etiology is not well known, biliary stone disease suggested to a mechanism secondary to hemolytic anemia, hepatic involvement, increased biliary secretion or immune reactions to glycolipid accumulation [12,13].

As a conclusion in this report we presented some typical radiological findings of a 16-year-old female patient with the pulmonary and cardiovascular involvements and also with cholelitiasis. According to our knowledge this co-incidence has not been reported before and it may indicate the most unfavorable prognosis.

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