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Case report

Metabolic cardiomyopathy in GM1 gangliosidosis: Worse prognosis factor?

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Abstract

GM1 gangliosidosis is an autosomal recessive lysosomal storage disorder due to deficiency of the β-galactosidase enzyme which hydrolyzes the terminal β-galactosyl residues from GM1 ganglioside, glycoproteins, and glycosaminoglycans. Patients with infantile GM1 gangliosidosis present at birth or shortly thereafter with visceral changes and severe neurological deterioration leading to early death. In this report, we presented a case of infantile GM1 gangliosidosis associated with multiple organomegaly.

Keywords:
Infant; cardiomyopathy; GM1 gangliosidosis.

Introduction

Three clinical forms of GM1 gangliosidosis are recognized: infantile-, juvenile-, and adult-onset forms. The β-galactosidase activity in affected individuals correlates with disease onset. The infantile form is usually fatal within the first 2 years of life.
Metabolic cardiomyopathies develop as a result of impaired energy-producing pathways concerning carbohydrate, fat, and mucopolysaccharide metabolism [1]. However, cardiomyopathy due to infantile GM1 gangliosidosis is related to disturbed elastogenesis and elastin-binding protein defects [2].
Metabolic infantile GM1 gangliosidosis cardiomyopathy has been rarely reported [3]. Herein we report a new case of in 4-month-old boy. The aim is to highlight clinical, pathological and prognostic characteristics of this entity.

Observation

A 4-month-old boy was referred to us for hepatosplenomegaly, nephromegaly, and cardiomegaly. The infant was born from consanguineous marriage after 38 weeks of unremarkable gestation. On his family history, we noted high rate of cardiac-related child death among first-degree siblings. Physical examination on admission revealed a height of 75 cm (at 97th percentile), weight of 7400 g (75th -90th percentile) and head circumference was 43 cm (50th -75th percentile for age).
The baby had tachycardia, mild tachypnea with shortness of breath. He had a coarse facial feature, hepatosplenomegaly, scrotal angiokeratoma, bilateral hydrocele and large gluteal Mongolian spots. Neurological examination revealed hypotonia, with a lack of head control, could not sit with support. The fundoscopic examination was normal.
Laboratory analyses revealed mild anemia, elevated liver transaminases, high alkaline phosphatase, and lactate dehydrogenase values. Blood lactate, pyruvate, and amino acid values were normal. Thyroid function test, creatinine kinase, blood gas, and urine analysis were normal. Tandem mass spectrometry of blood was negative for amino acid and acylcarnitine abnormalities. Peripheral blood smear findings were normal. Bone marrow aspiration was normocellular with foamy cells (Figure a). Lysosomal enzymes (sphingomyelinase and glucosylceramidase) were normal except for β-galactosidase, which showed only 1.48 nmol/hr/mg protein activity in the lactates (normal range 107.3±35.8).

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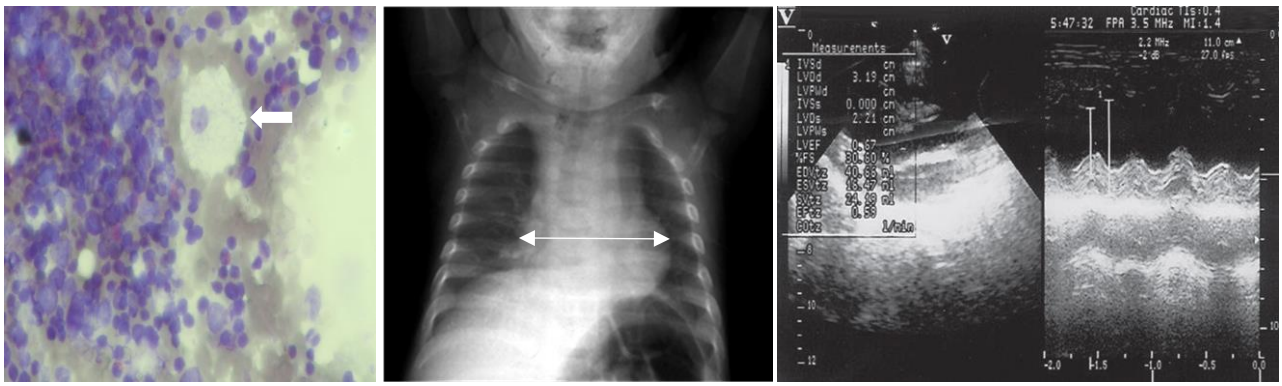
Chest X-ray showed a cardiac/thoracic ratio of 0.8 and pulmonary congestion (Figure b). Anterior beaking of the vertebral bodies was noticeable. Abdominal ultrasonography revealed hepatosplenomegaly and bilateral nephromegaly. Echocardiography showed dilatation of all four cavities specially the left ventricle with poor contractility and ejection fraction of 57% (Figure c). Electrocardiography revealed hypertrophy of the left ventricle and left axis deviation. Treatment for cardiac failure was initiated. The patient died 10 months later due to severe congestive decompensation.



a b c

Figures:
a: Bone marrow examination showing foamy cell proliferation.
b: Chest X-ray showing visible anterior beaking of the vertebral bodies.
C: Echocardiography showed dilatation of the four cardiac cavities with poor contractility

Discussion

GM1 gangliosidosis is a neuronopathic lysosomal storage disorder caused by a deficiency in the enzyme β-galactosidase related to GLB1 gene mutations. This enzyme is responsible for the degradation of GM1 ganglioside, oligosaccharides, and keratan sulfate. This disorder leads to lysosomal accumulation of the GM1 ganglioside and other galactose-containing glycoconjugates [4,5]. GM1 gangliosidosis is ultra-rare disease with an estimated incidence of 1 in 100,000-200,0000 live births [6]. The residual activity of the mutant β-galactosidase enzyme, organ distribution and the importance of material accumulation determine the clinical classification of infantile (type 1), juvenile (type 2), and adult (type 3) forms. The infantile form is characterized by absent mutant enzyme activity with progressive neurologic deterioration, sensorimotor and psycho-intellectual dysfunction. The evolution is usually fatal within 3 years of life [7]. The prenatal diagnosis of GM1 gangliosidosis is still difficult because of the non-specificity of the related ultrasonographic abnormalities [8]. typically, cherry-red spots at the macula, facial dysmorphism, hepatosplenomegaly, neurologic degenerative disorder, and generalized skeletal dysplasia are hallmarks of the disease. Diagnosis is confirmed by the assessment of the β-galactosidase activity [9].
Cardiac involvement rarely associated with GM1-gangliosidosis. Some mutations of the GLB1 are common to the lysosomal enzyme and the elastin binding protein (EBP). Consequently, this form of the disease may present more musculoskeletal and cardiac specific manifestations [10]. The cardiac involvement may worsen the prognosis and accelerate the fatal evolution by hemodynamic disorder and bronchopulmonary recurrent infections.

Conflict of Interest: None

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