Case report

Two cases of Pompe's disease: case report and review of literature

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KEY WORDS

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A B S T R A C T

Glycogen storage disease type II (also called Pompe's disease or acid maltase deficiency) is an autosomal recessive metabolic disorder which causes an accumulation of glycogen in the lysosomes due to deficiency of the lysosomal acid alpha-glucosidase enzyme. It is the only glycogen storage disease with a defect in lysosomal metabolism, and the first glycogen storage disease to be identified in 1932. The build-up of glycogen causes progressive muscle weakness (myopathy) throughout the body and affects various body tissues, particularly in the heart, skeletal muscles, liver, and nervous system.

We are presenting two cases of infantile form of Pompe's disease with secondary hypertrophic cardiomyopathy (CMP). The first case was a 1-year-old female child who presented with Ross Class III heart failure (HF) of 3 months duration. Echocardiography (ECHO) showed concentric left ventricular (LV) hypertrophy, with the posterobasal segment more hypertrophic than the interventricular septum and moderate pericardial effusion. The second case was a 2-month-old male child who presented with Ross Class II HF. His ECHO showed eccentric hypertrophy of the posterobasal left ventricle, with thickening of the mitral valve leaflets and the chordae with Grade I mitral regurgitation (MR). Both children were diagnosed to have Pompe's disease by blood alpha-glucosidase assay.

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Introduction

Pompe's disease or glycogen storage disease type II, is a lysosomal storage disorder in which deficiency of alpha-glucosidase leads to accumulation of glycogen and finally to destruction of muscle tissue.^{1–3} Complete deficiency of alpha-glucosidase causes a progressive lethal cardiac and skeletal muscle disorder known as infantile Pompe's disease. Partial deficiency leads to a milder late onset phenotype.^{4,5} The latter condition may present at any age and is subdivided into non-classical infantile, childhood, juvenile, and adult Pompe's disease. Infantile Pompe's disease is a rapidly progressive disease, characterised by prominent cardiomegaly, hepatomegaly, weakness and hypotonia, and death due to cardiorespiratory failure in the first year. Patients with the infantile variant form⁴ (non-classic infantile Pompe's disease) show slower progression and less severe cardiomyopathy (CMP) but present in the first year of life. Echocardiogram (ECHO) typically reveals a hypertrophic

CMP with or without left ventricular (LV) outflow tract obstruction in the early stages of the disease. In the late stages of infantile disease, patients may have impaired cardiac function and a dilated CMP.

We present two cases of infantile Pompe's disease, both with ECHO features of hypertrophic CMP. In addition, the second case also showed thickening of mitral leaflets and chordae.

Case history

Case 1: The first case was a 1-year-old female child who had presented with features of Ross Class III heart failure (HF) at 9 months of age, treated at another hospital with diuretics and angiotensin-converting enzyme inhibitors (ACEI) and was referred to our hospital. She presented to us with cough of 10 days' duration. On examination, the patient was acyanotic and comfortable at rest. Her pulse rate was 110/min, respiratory rate was 30/min, with BP of 106/86 in the upper limbs and 120/86 in the lower limbs. Her cardiovascular system examination was clinically normal. She had mild hepatomegaly.

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Figure 1 Case 1: (A) Electrocardiogram showing short PR interval and left ventricular (LV) hypertrophy. (B) Chest radiograph. (C) Electrocardiogram image: parasternal long axis view, showing eccentric LV hypertrophy of posterior wall. (D) M-mode image at mitral valve level, showing thickened mitral valve and chordae.

Routine blood investigations were normal. Electrocardiogram (ECG) showed a PR interval of 0.10s and features of LV hypertrophy. The ECHO examination revealed concentric LV hypertrophy (Figures 1A, B) with Grade I diastolic dysfunction and no evidence of LV outflow tract obstruction. The assay for alpha-glucosidase from whole blood using dried blood spot filter paper was done. The activity of the alpha-glucosidase in the patient was 0.108 pmol/punch/hr (normal range: 0.75–7.23) and the ratio of neutral alpha-glucosidase/acid alpha-glucosidase (with inhibitor)⁶ was 76 (normal range: 9.8–43.37), consistent with the diagnosis of Pompe's disease.

Case 2: The second case was a 2-month-old male child who presented with Ross Class II HF. On examination, the child was tachypnoeic and acyanotic. His cardiovascular system examination showed Grade II ejection systolic murmurs at the left second inter costal space. Wet lung signs were present. Moderate hepatosplenomegaly (HSM) was present. Serum aspartate transaminase and alanine transaminase were mildly elevated. Serum creatinine phosphokinase (total) was 1123 U/dL. The ECG showed short PR interval and features of LV hypertrophy. The ECHO examination revealed concentric LV hypertrophy, global hypokinesia of left ventricle, moderate LV systolic dysfunction and Grade II mitral regurgitation. Quantitative blood alpha-glucosidase level was 24 nmol/hr/mg (normal >60), suggestive of Pompe's disease.⁶ Patient improved with diuretics and ACEIs. Ten months later, ECHO examination revealed eccentric LV hypertrophy involving posterobasal wall (Figure 2B).

Mitral valve leaflets and chordae were thickened (Figures 2A, C, D). Grade I MR (Figure 2E) was present. No evidence of LV outflow tract obstruction was observed.

Discussion

In infantile Pompe's disease, the effects of glycogen accumulation are very pronounced in the heart.^{1–3} Lysosomal glycogen accumulation results in a significant amount of cardiac hypertrophy that may begin in utero and that is significant even at 4–8 weeks of age.³ The cardiac response to glycogen accumulation can result in hypertrophic or hypertrophic and dilated CMP.³ In the earlier phases of the disease, infants generally present with severe ventricular hypertrophy with or without LV outflow tract obstruction and normal or even hyperdynamic LV function.^{1–3,8} Both our cases had presented early in infancy with decompensated HF and improved with symptomatic treatment with diuretics and ACEIs. Both cases showed LV hypertrophy on ECHO. Neither of them showed evidence of LV outflow tract obstruction. Our second case, during the course of the disease also showed thickening of both mitral leaflets and chordae, which has not so far been described in literature.^{2,9}

Beyond infancy, there is variable involvement of the heart in Pompe's disease, and a spectrum of disease among children with partial enzyme activity, ranging from unaffected to

Figure 2 Echocardiogram images of Case 2. (A) Three-dimensional images showing left ventricular (LV) hypertrophy. (B) M-mode image at papillary muscle level showing eccentric LV hypertrophy involving postero-basal wall. (C) M-mode image at mitral valve level showing thickened mitral leaflets. (D) Parasternal long axis view, showing thickened mitral valve leaflets. (E) Colour Doppler image showing Grade I mitral regurgitation.

moderate cardiac hypertrophy, and cardiac dysfunction has been described.^{4,5}

Interference with specialised conducting tissues produces a shortening of the atrio-ventricular (PR) interval on the ECG, seen in both our cases. The mechanism of accelerated atrio-ventricular conduction in Pompe's disease may be related to the insulator effect of glycogen in conduction tissue.⁹ The conduction abnormalities, in conjunction with the hypertrophic CMP, place these patients at a high-risk of tachyarrhythmia and sudden death, especially in situations of stress such as infection, fever, dehydration, and anaesthesia.⁹

Thus, the diagnosis of hypertrophic CMP in infancy and childhood should be considered with the possibility of being a secondary form, and should be screened for Pompe's disease.

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