

Late-onset Pompe disease in a 54 year-old sportsman with an episode of syncope: a case report

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Abstract. – Pompe disease is an extra-rare metabolic storage disease with deficiency of acid-alpha-glucosidase (GAA) enzyme activity, which leads to the pathologic accumulation of glycogen in target tissues (skeletal muscles, heart, brain). Clinical features and severity vary by the age of onset, rate of extent of organ involvement. In the late-onset Pompe disease (LOPD) form, essential cardiomyopathy seems to be uncommon. Muscles weakness and respiratory failure are the main symptoms of adult patient with Pompe disease. In presented case LOPD coupled with patient's regular sporting activity and healthy diet, which may explain the low intensity of the symptoms and the slow progress of the disease, lack of skeletal muscles weakness and lack of brain manifestation. Myocardial storage deposits are the only abnormalities found.

Key Words:

Pompe disease, Cardiomyopathy, Hypothyroidism.

Introduction

Pompe disease is a metabolic storage disease with deficiency of acid-alpha-glucosidase (GAA) enzyme activity, which leads to the pathologic accumulation of glycogen in target tissues (skeletal muscles, heart, brain). Age of onset, rate of extent of organ involvement and severity, are the basis of classification of Pompe disease¹. In 1932 the Dutch pathologist Joannes Cassianus Pompe described the disease in a 7 month-old girl with severe muscle weakness who also had hypertrophic cardiomyopathy and generalized glycogen accumulation in various tissues throughout the

body². An estimated frequency of the disease is about 1/40,000 with a higher incidence in certain populations such as African Americans (1/14,000), Northern Europeans of Dutch origin and South East Asians. Interest in Pompe disease has grown significantly since the first specific enzyme replacement therapy (ERT) with recombinant human GAA was implemented in the treatment of this metabolic myopathy in 2006³. In the late-onset Pompe disease (LOPD) (individuals with onset after the age of 12 months) form, essential cardiomyopathy seems to be uncommon. Muscle weakness and respiratory failure are the main symptoms in adult patient with Pompe disease⁴⁻⁶. In contrast to the LOPD, severe cardiomyopathy with progressive heart failure is present in the infantile-onset Pompe disease (IOPD) (individuals with onset before the age of 12 months) form. In IOPD with no ERT, one-year survival is extremely rare⁷. In this report we present an adult case of a 54-year-old sportsman with a LOPD who showed atypical symptoms and slow progress of the disease due to his regular sporting activity and healthy diet.

Case

A 54 year-old Caucasian sportsman was admitted to the Internal Disease Clinic after an episode of syncope. From youth he has performed regular sports activity with 7-8 low carbohydrate meals per day. There was no history of falls, syncope, chest pain, or neurological deficiencies. His medical history was notable and he had been treated for hypothyroidism and mixed hypercholesterolemia. His blood pressure was 134/91 mmHg, his heart rate was 68/min with no cardiac mur-

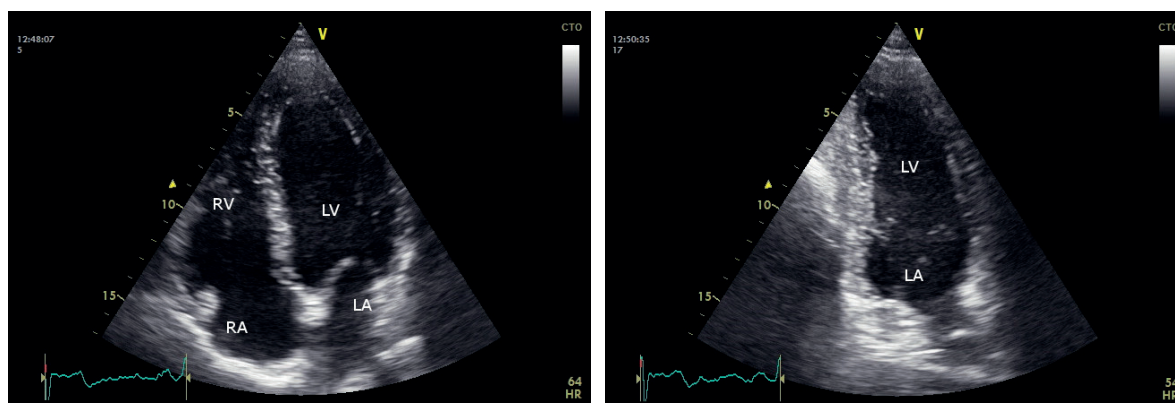


Figure 1. TTE *A*, Apical four-chamber view, *B*, Apical two-chamber view.

murs on auscultation, and no muscles weakness was reported. ECG, 24-hour Holter monitor and brain magnetic resonance (BMR) revealed no abnormalities. During diagnosis, transthoracic echocardiography (TTE) revealed multiple storage materials located in the left ventricle (LV) wall of heart without myocardial hypertrophy, with decreased ejection fraction (EF) below 50%. Cardiovascular magnetic resonance (CMR) confirmed heart-muscle infiltration. Pompe disease was diagnosed based on dried blood-spot (DBS) testing.

Discussion

Pompe disease is caused by mutations that result in absent or reduced GAA enzyme activity, which lead to glycogen accumulation in its target tissues (skeletal muscles, heart, and brain)⁸. It is

a heterogeneous, progressive storage disease with individual patient outcomes⁹. Patients with LOPD often develop skeletal muscle weakness, cardiomyopathy is rare. A minority of LOPD patients demonstrate mild LV hypertrophy^{10,11}. The differential diagnosis in presented case included other storage diseases like Danon disease or Fabry disease, but there were no Wolff-Parkinson-White (WPW) pattern, no massive LV hypertrophy, no early indications for heart transplantation characteristic for Danon disease¹², neither restrictive cardiomyopathy, nor neurological disturbances which are observed in Fabry disease^{13,14}. Schneider et al¹⁵ suggest that there may be a higher prevalence of hypothyroidism in patients with LOPD compared to the general adult population, which was registered in presented case. Some studies^{16,17} showed that Pompe disease and hypothyroidism have some common biochemical features at a cellular level. Because it is an insidious disease,

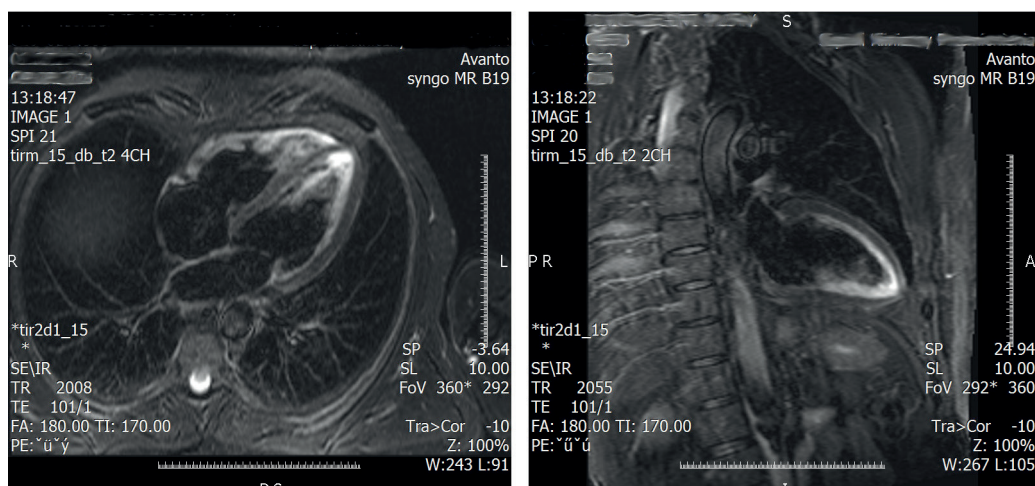


Figure 2. CMR *A*, 4-chamber view, *B*, 2-chamber view.

with no obvious clinical features, muscle biopsies presenting acid phosphatase positive inclusions and rimmed vacuoles, might be helpful tool in diagnosis of Pompe disease¹⁸. Few recent studies have now revealed and confirmed the role of SUMOylation in congestive heart disease such as cardiac hypertrophy by promoting cardiac cell death¹⁹. We believe that further studies might be needed to explore the SUMOylation mechanism in the development and the course of storage diseases. Early diagnosis is extremely important since timely implemented ERT can restrain the progression of the disease²⁰.

Conclusions

In our case, LOPD coupled with the patient's regular sporting activity and healthy diet may explain the low intensity of the symptoms and the slow progress of the disease. The lack of typical muscle weakness, storage material located in the left ventricle (LV) wall and presence of hypothyroidism, make this case unique.

Conflict of interest

The authors declare no conflicts of interest.

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