

Huge aneurysm of the ascending aorta in a patient with adult-type Pompe's disease: histological findings mimicking fibrillinopathy

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Received 9 May 2012; received in revised form 6 July 2012; accepted 10 July 2012

Abstract

Adult-type Pompe's disease (glycogen storage disease type II) has rarely been shown to present with dilatative arteriopathy, suggesting potential smooth muscle involvement in addition to lysosomal glycogen deposits usually restricted to skeletal muscle tissue. We report the case of a middle-aged man under enzyme replacement therapy presenting with an exceedingly large thoracic aortic aneurysm. Surprisingly, the histological work-up of resected aortic tissue revealed changes mimicking those observed in patients with classic connective tissue diseases. Enzyme replacement therapy, in addition to musculoskeletal and pulmonary treatment for patients with Pompe's disease, may prolong survival and lead to patients presenting with vascular alterations that may pose surgical and potential diagnostic challenges in the future.

Keywords: Adult-type Pompe's disease • Glycogen storage disease • Aortic aneurysm • Fibrillinopathy

INTRODUCTION

Pompe's disease, also known as glycogen storage disease type II (GSD II) is a rare autosomal recessive disease with an incidence of roughly 1:40000 [1]. Adult-type Pompe's disease typically presents with lysosomal glycogen deposits restricted to skeletal muscle tissue [1]. Several previous studies have however reported the presence of dilatative arteriopathy [2], with rare evidence of aortic involvement leading to increased aortic wall stiffness [3], suggesting possible smooth muscle cell involvement. In the following, we report the case of a male patient diagnosed with adult-type Pompe's disease who presented with massive annulo-aortic dilatation. Histological findings revealed similarities with aortas of patients with classic connective tissue diseases.

CASE PRESENTATION

A 48-year-old male patient presented with severe aortic valve regurgitation secondary to massive annulo-aortic dilatation (max. diameter 96 mm, max. diameter of the aortic arch 30 mm) and consecutively a dilated and hypertrophic left ventricle (Fig. 1). The patient's family history was negative for connective tissue disorders or aneurysms. Scoring for Marfan's syndrome according to the new Ghent nosology was negative for a connective tissue disease.

The patient was known for manifest adult-type Pompe's disease (GSD II), diagnosed 30 years previously. At the current presentation, the patient had received enzyme replacement

therapy for 4 years twice a week, using recombinant α -glucosidase. In addition, he was on nocturnal bi-level positive airway pressure-therapy. Treatment markedly stabilized the patient's musculoskeletal and pulmonary function, enabling him to independently transfer to and from the wheelchair, despite moderate tetraparesis. Preoperative pulmonary tests showing a vital capacity of 1.5 l and a forced expiratory volume of 1.0 l/s were not considered as an absolute contraindication to surgery. Because of the anticipated progression of cardiac failure and the high risk of aortic rupture, the patient was scheduled for elective aortic root replacement.

The operative procedure was performed through median sternotomy, using moderate hypothermic cardiopulmonary bypass. A composite-graft (mechanical bi-leaflet 29 mm aortic valve, ATS/Medtronic® Valved Conduit) was implanted with the classic technique according to the Bentall procedure. Weaning from cardiopulmonary bypass was uneventful and the patient was extubated on postoperative day 1. However, he suffered from atelectasis of the left inferior lobe and right-sided pneumothorax requiring a thoracic drainage. The patient was subsequently discharged 2 weeks postoperatively with stable respiratory and cardiac functions to a rehabilitation unit.

The specimen of the resected aortic tissue was formalin-fixed and processed according to standard histopathological procedures. Examination on haematoxylin-eosin and special stains revealed minimal intimal fibrosis and a generalized increase in mucinous extracellular substance (Fig. 2A), without evidence of medial necrosis. Widespread, pronounced fragmentation and loss of elastic fibres were noted, comparable in severity to

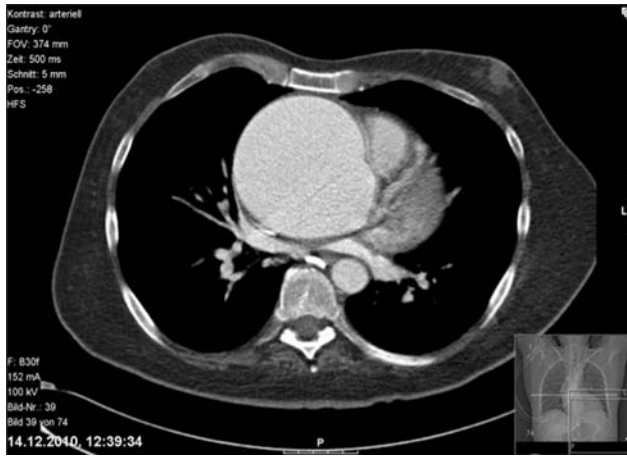


Figure 1: CT-scan showing a very large aneurysm (96 mm) of the aortic root and ascending aorta, without signs of rupture.

changes observed in the setting of fibrillinopathies e.g. Marfan's syndrome (Fig. 2B). Focally accentuated globular glycogen deposits were observed in smooth muscle cells within the media (Figs 2C and D), which were significantly enhanced when compared with an aortic specimen from an age- and gender-matched control patient with a large aortic aneurysm due to hypertension (Fig. 2E and F).

DISCUSSION

Pompe's disease, or GSD II (OMIM ID: 232300) is a rare autosomal recessive inherited disease caused by various mutations in the gene of the lysosomal hydroxylase acid α -1,4-glucosidase [4]. The adult-type of this disease is believed to cause intralysosomal glycogen depositions restricted to skeletal muscle tissue [1], thus differing from the infantile and juvenile type by the lack

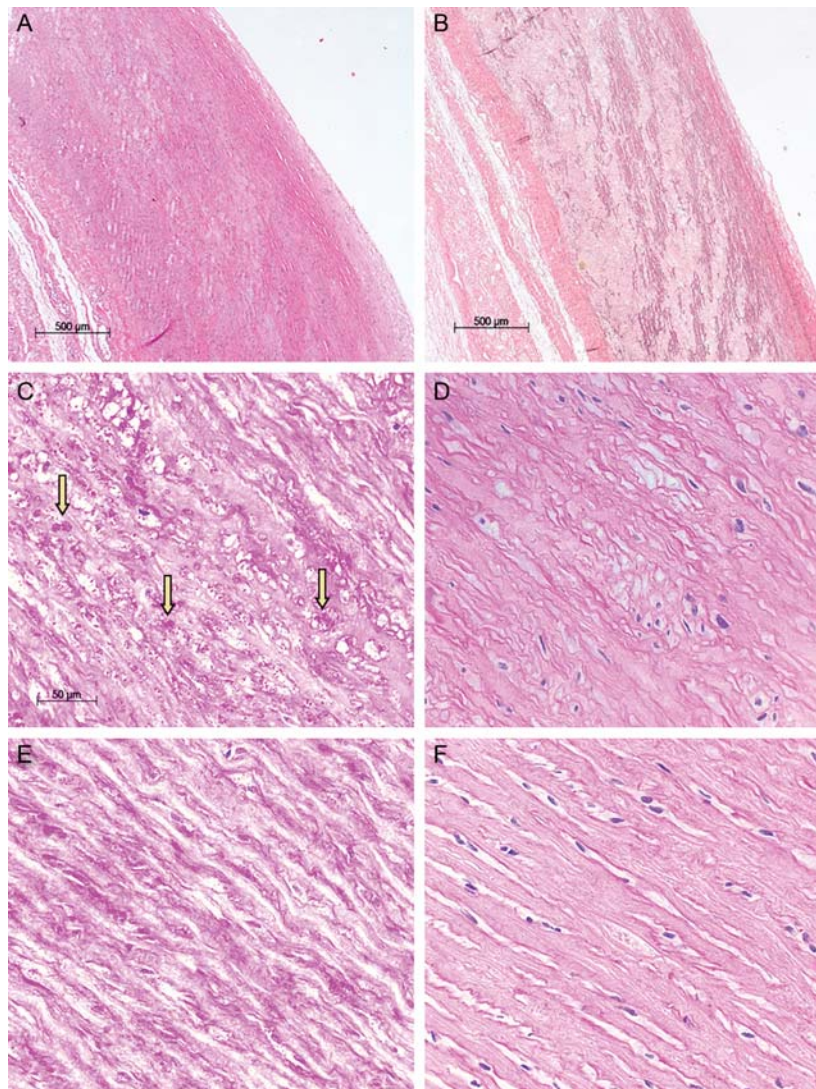


Figure 2: Haematoxylin-eosin (A) and Elastica Van-Gieson (B) staining of representative sections of aortic tissue. Slightly hyperplastic and fibrosed intima (right side of image). Increased deposition of mucinous substance (grey-blue) within the media, accompanied by extensive fragmentation and loss of elastic fibres (stained grey-black in B). Periodic acid-Schiff (PAS, C and E) as well as PAS-dia (D and F) staining of representative sections of aortic tissue. Index patient's aorta shown in the top row (C and D) and for comparison the aorta of an age- and sex-matched control in the bottom row (E and F). The arrows highlight larger accumulations of PAS-positive globules within smooth muscle cells in the aortic media (C). Glycogen digestion (PAS-dia) shows complete negativity, indicating that the PAS-positive globules represent glycogen. Essentially no or only small glycogen globules revealed in the control aorta (E).

of involvement of other organ systems, the rate of progression to death, the age at onset and the lower degree of skeletal myopathy.

Adult Pompe's disease is defined by onset at or after the second decade of life, causing proximal-accentuated skeletal myopathy with progressive muscle weakening. Our patient was diagnosed at 20 years of age, and presented with progressive impairment of pulmonary function in addition to skeletal myopathy. This clinical presentation raises the suspicion of a variant of the disease-sharing features of both the juvenile as well as the adult form and may be explained by persistently low residual enzyme levels when compared with other GSD II patients.

Recent reports have documented several cases of cerebral aneurysms as well as other vascular involvement in patients with adult-type Pompe's disease [2]. Sacconi *et al.* [5] reported an unexpectedly high number of patients with adult-type Pompe's disease and intracranial artery abnormalities and dilatative peripheral arteriopathy as well as one case of increased aortic wall stiffness [3] have been reported. Increasing evidence suggests an involvement of smooth muscles cells in adult-type Pompe's disease in the urinary bladder, gastrointestinal tract and in the wall of blood vessels. Interestingly, the computed tomography-scan of our patient also revealed an ectatic left vertebral artery (7 mm), a dilated and tortuous basilar artery (5 mm) and bilateral marked elongation of the neck vessels in addition to the huge aortic aneurysm. In this case, composite graft replacement was performed in a standard fashion.

Since the natural course of Pompe's disease may be improved through musculoskeletal and pulmonary treatment as well as through enzyme replacement, older patients may present with alterations of the vasculature, including large aortic aneurysms. This case showed unexpected histological findings. In addition to increased glycogen stores, disturbances of the aortic wall architecture with excessive fragmentation of elastic fibres within the

media were observed—changes similar to those observed in patients with fibrillinopathies, e.g. Marfan's syndrome. This case, to the best of our knowledge, most probably summarizes the first patient with adult onset of Pompe's disease presenting with a huge aneurysm of the aortic root and histological changes mimicking Marfan's disease.

ACKNOWLEDGEMENTS

The authors would like to thank Eva Roost and Mario Stalder for their input and involvement with the case.

Conflict of interest: none declared.

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