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

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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 dilative 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...
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 hydroxylasis 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 of involvement in other tissues.
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 im-
pairment of pulmonary function in addition to skeletal myop-
athy. 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 un-
expectedly high number of patients with adult-type Pompe’s
disease and intracranial artery abnormalities and dilative peri-
pheral 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 archi-
tecture 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.

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Abnormalities of cerebral arteries are frequent in patients with late-onset
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