

Diffuse cerebral microhemorrhages in a patient with adult-onset Pompe's disease: a case report

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Abstract

Background—Pompe's disease is a glycogen storage disease that manifests as progressive neuropathy, and myopathy. There are a few reports of vasculopathy in this disease, thought to be from small- and medium-vessel arteriopathy. We present a case of late-onset Pompe's disease with microhemorrhages and review of the pertinent literature.

Methods—We describe a case of microhemorrhages in a patient with known late-onset Pompe's disease.

Results—Our patient was noted to have numerous microhemorrhages concentrated in the posterior circulation distribution in what can best be described as central microhemorrhages, distinct from the pattern seen in amyloid angiopathy. Previous autopsy studies have found vacuoles in the vessel wall, resulting in small aneurysms as a part of the Pompe syndrome.

Conclusions—There is an accumulating body of evidence that suggests cerebral vasculopathy as one of the primary manifestations of adult-onset Pompe's disease. This is manifested as dolichoectasia of basilar artery, aneurysms, and microhemorrhages that are central in distribution. The primary pathology is thought to be glycogen deposition in small- and medium-sized intracranial vessels. Controlling blood pressure aggressively and screening intracranial vascular imaging are recommended. Further definition of the syndrome is continuing from phenotypic and genotypic dimensions.

Introduction

Pompe's disease or glycogen storage disease type II is a rare (incidence 1 in 40,000 births) [1,2] autosomal recessive metabolic disorder characterized by excessive lysosomal glycogen deposition. It is caused by mutations in the gene encoding for acid alpha glucosidase, a hydrolyase, responsible for glycogen degradation in lysosomes [3]. Lack of the enzyme causes excess glycogen deposition, resulting in progressive myopathy and neuropathy. Depending on the age of onset, Pompe's is divided into two distinct variants, infantile and adult onset [4]. The common manifestations in the infantile form include cardiomyopathy and severe generalized muscular hypotonia. The late-onset variant is characterized by skeletal myopathy of limb girdle distribution. Neither form is associated with significant cognitive impairment.

There are a few case reports describing dilative arteriopathy and basilar artery dolichoectasia in patients with late-onset Pompe's disease [5,6]. Intraparenchymal hemorrhages [7] and microhemorrhages are also reported [8]. These are more central in nature than peripheral as is typical of amyloid angiopathy [8].

We report a case of a young patient with late-onset Pompe's disease with microhemorrhages. We present the literature review and elaborate on possible pathophysiology of vasculopathy in Pompe disease.

Patient case presentation

A 25-year-old man with Pompe disease, receiving treatment with Alglucosidase alfa (Lumizyme) replacement, presented with several days of right-sided mouth, shoulder, and hand numbness and one day of vertigo. Physical examination revealed an emaciated 25-year-old with mildly dysmorphic facies and severe generalized muscle wasting. Neurological examination revealed normal cognition, normal cranial nerve examination except a subtle loss of pinprick sensation over the right angle of the mouth, generalized muscle wasting and hypotonia, 2/5 strength with pronounced proximal weakness and hypoactive reflexes. Sensory examination showed patchy loss of pinprick sensation on the right side. His systolic blood pressure (SBP) was in the 160–170 mmHg range, and intravenous nicardipine was used to control it.

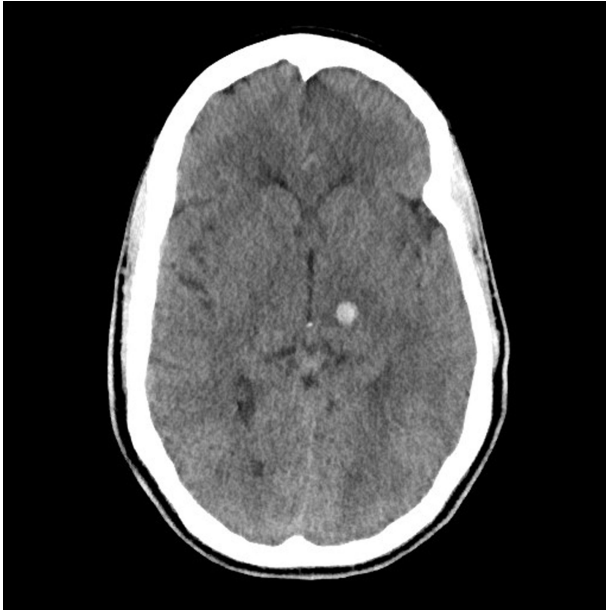


Figure 1. Pompe CT

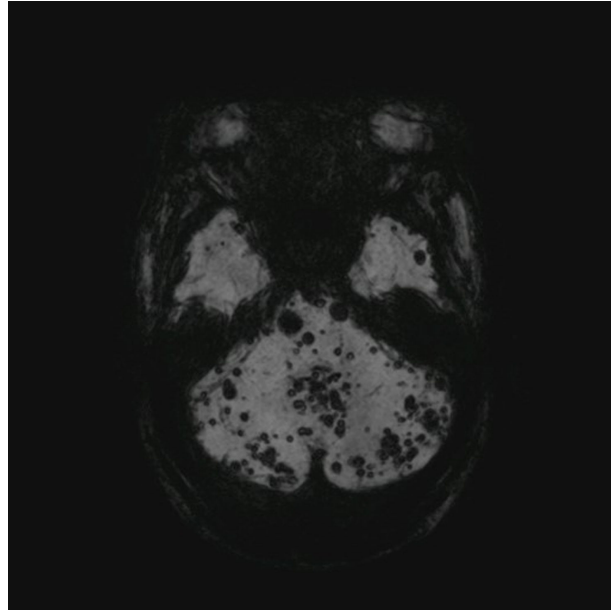


Figure 3. Pompe bold2

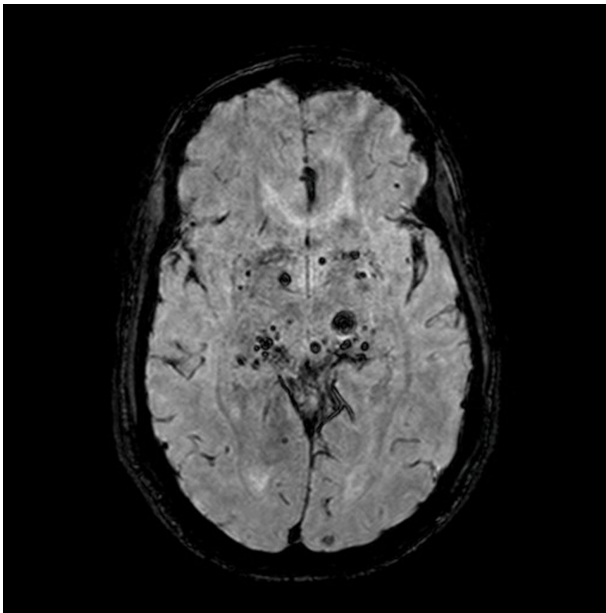


Figure 2. Pompe bold1

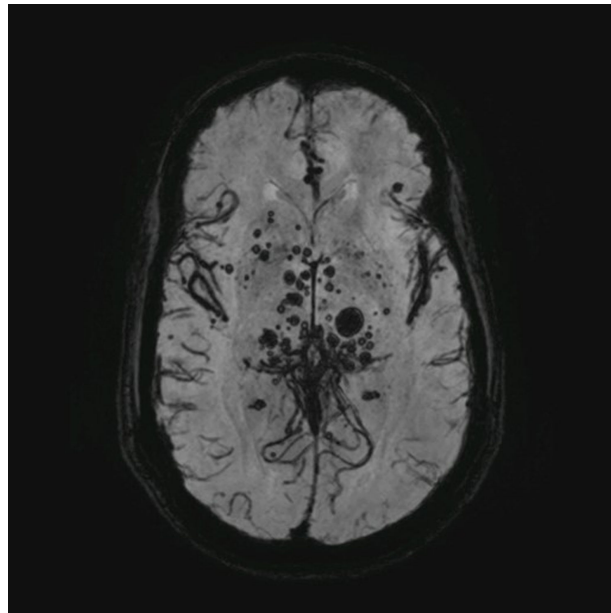


Figure 4. Pompe SWI 1

Angiotensin-converting enzyme inhibitor was started as the maintenance therapy to target SBP less than 120 mmHg. Laboratory investigations included comprehensive metabolic profile, complete blood count with differential, calcium magnesium level, international normalization ratio, prothrombin time, and activated partial

thromboplastin time. All of his laboratory values were within normal range. Computed tomography showed a prominent left thalamic hemorrhage (Figure 1). His symptoms resolved during the hospitalization, except for mild numbness in the right perioral area.

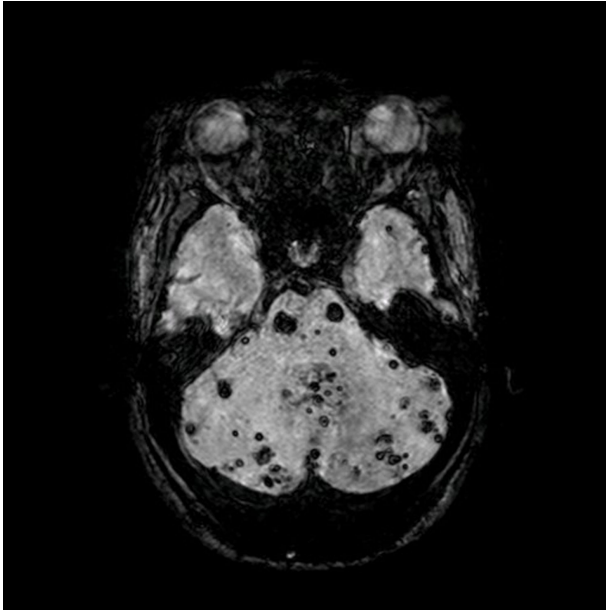


Figure 5. Pompe SWI 2

Given the patient's young age, further imaging was carried out to look for any vascular pathology. MRI revealed numerous foci of low signal intensity scattered throughout the brain parenchyma on susceptibility-weighted images, consistent with microhemorrhages, at different stages of evolution (Figures 2–5). Most of these microhemorrhages were located in the posterior circulation distribution. There was a focus of high signal intensity in the left thalamus on the T1-weighted images, consistent with subacute hemorrhage. Magnetic resonance angiography of head and neck revealed diffuse ectasia of the intracranial vessels (Figures 6 and 7).

He had an uneventful stay in the hospital and was discharged home on ACE inhibitor with a blood pressure goal of less than 120/80 mmHg.

Discussion

Arteriopathy is clinically important but as yet under-described and -recognized manifestation of late-onset Pompe's disease [4–6]. Our case adds to the slowly accumulating body of evidence that intracranial vascular pathology is an integral part of late-onset Pompe's disease. Systemic vascular pathology has been described in late-onset Pompe's disease [9]. Intracranial vascular pathology so far reported in late-onset Pompe's disease includes basilar dolichoectasia [5,6], cerebral micro-



Figure 6. Pompe MRA 1

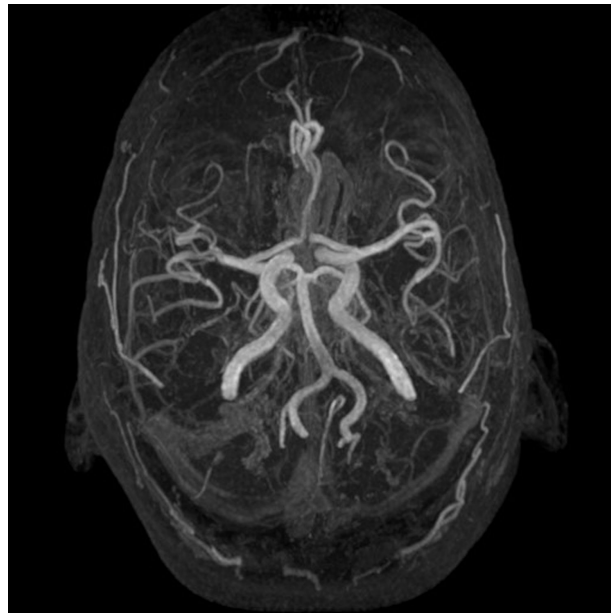


Figure 7. Pompe MRA 2

bleeds [7], aneurysms [10,11], intraparenchymal hemorrhage [7], and aneurysmal thrombosis [12].

Arteriopathy in Pompe's disease predominantly affects small- and medium-sized vessels [8]. As in our case, most of this pathology is found concentrated in the posterior circulation territory. Microscopic glycogen-laden

molecules have been demonstrated as expected and are thought to be the cause of intracranial arteriopathy [5].

In our opinion, tighter blood pressure control may benefit these patients and reduce the risk of microhemorrhages. Screening intracranial vascular imaging may detect vascular pathology like aneurysms, microhemorrhages, and dolichoectasia early. Neurological symptoms should prompt urgent evaluation and close monitoring.

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