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Case report

Myalgic phenotype and preserved muscle strength in adult-onset acid maltase deficiency

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Abstract

Adult-onset acid maltase deficiency is a rare disorder characterized by progressive proximal muscle weakness and early respiratory insufficiency. We present a case of a 53-year-old woman who presented with several years of severe, diffuse myalgia and no evidence of weakness on examination. Further testing revealed a mildly elevated serum creatine kinase, a subtle vacuolar myopathy, decreased skeletal muscle α-glucosidase activity, and causative mutations in the responsible *GAA* gene. While likely very uncommon, adult-onset acid maltase deficiency may present with diffuse strength-sparing myalgia.

Keywords: Acid maltase deficiency; Glycogen storage disease II; Pompe disease; Myalgia; Myofascial pain

1. Introduction

Acid maltase deficiency (AMD, Pompe disease, or glycogen storage disease II [GSD II]) is a rare recessively-inherited lysosomal storage disorder whose phenotype displays wide variability in severity and age of onset. AMD was initially recognized in infants, in whom the natural history is characterized by organomegaly, progressive hypotonic weakness and early demise [1]. Numerous responsible mutations in the gene encoding acid α-glucosidase (*GAA*) have been described [2], and enzyme replacement therapy has demonstrated improved functional outcomes in children and adults [3,4].

Initially described decades after the infantile form [5], adult-onset AMD typically presents as a slowly progressive proximal myopathy with early neuromuscular respiratory insufficiency [6]. While muscle pain and generalized fatigue are frequent and likely under-recognized symptoms associated with adult-onset AMD [7,8], weakness is the clinical hallmark of this disease. We report here a patient with adult-onset AMD presenting with longstanding severe myalgia and preserved muscle strength.

2. Case report

A 53-year-old woman presented for evaluation of approximately 5 years of slowly progressive diffuse axial and limb muscle pain. For 1 or 2 years she had experienced intermittent painful distal lower limb muscle cramps. Her myalgia was present at rest and exacerbated with activity. Her discomfort had resisted extensive attempts at pharmacologic management, and exacerbation of her muscle pain with movement was her primary source of functional limitation. As a result of her muscle pain and the associated worsening with exertion, she had greatly limited mobility (she ambulated without assistance within her household but preferred a wheelchair for excursions away from her home), and she experienced difficulty completing some activities of daily living such as dressing and bathing without the assistance of her husband.

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On examination her limb strength was normal. The neurologic examination was performed by two different neurologists (LKJ and RHG) on two occasions separated over a 3 month period, with no significant interval change or interrater differences. Muscle strength was assessed in conventional clinical fashion with confrontational manual muscle testing, with all strength graded on a scale ranging from 0 (normal) to −4 (plegic). All limb, bulbar, and axial muscles were consistently graded 0, corresponding to an MRC grade of 5 in all muscles examined. She stood from a seated position and ambulated with apparent discomfort but without other outward limitation. Limb and axial muscles were diffusely tender to palpation. There was no macroglossia or other muscular hypertrophy and limb and axial muscle tone were normal. Muscle stretch reflexes, sensation, and coordination were normal. There was no contraction myotonia or any muscle contraction with direct percussion. She was mildly overweight (weight of 65.4 kg with a body mass index [BMI] of 26.2), and her general medical examination was otherwise unremarkable.

Serum studies were notable for a mildly elevated serum creatine kinase (CK) of 420 U/L (normal range 38–176 U/L). Blood counts, serum electrolytes, sedimentation rate, antinuclear antibodies, and serum markers of liver, renal and thyroid function were all normal. An electrodiagnostic evaluation demonstrated normal nerve conduction studies. Needle electrode examination revealed brief myotonic discharges and short-duration, low-amplitude, complex motor unit potentials in most lower limb, upper limb, and axial muscles examined. There were no fibrillation potentials or complex repetitive discharges. On the basis of these findings, mutation analysis for types I and II myotonic dystrophy (DM1 and DM2) was performed at a diagnostic reference laboratory and was found to be normal.

Subsequent muscle biopsy of the biceps brachii (Fig. 1) was performed with the site chosen on the basis of the most prominent contralateral electromyographic abnormality. It demonstrated extremely rare muscle fibers containing unrimmed vacuoles, some of which demonstrated increased acid phosphatase activity. Increased acid phosphatase activity was also noted in other vacuolated and rare non-vacuolated muscle fibers. Periodic acid-Schiff (PAS) staining demonstrated no glycogen accumulation. Lysosome-associated membrane protein-2 (LAMP-2) was immunolocalized with a monoclonal antibody and found to have normal reactivity. Subsequent measurement of muscle α-glucosidase activity was performed at a diagnostic reference laboratory, demonstrating significantly reduced enzyme activity (0.37 μmol/min/gram, normal reference mean of 5.86 +/− 2.06 μmol/min/gram). Assays for neutral maltases were normal. Sequencing of *GAA* demonstrated the very common "leaky splice" IVS1-13T>G mutation [9] and a previously unreported c.1396_1397insG mutation, which creates a frame shift starting at codon Val466 and a stop codon 39 positions downstream.

Additional testing revealed normal intracranial magnetic resonance angiography, electrocardiography, and surface echocardiography. Pulmonary function testing performed in the seated position only demonstrated a reduced vital capacity (1.54 L, 50% of predicted) and intermittent desaturations on overnight oximetry. She had not complained of frank exertional dyspnea (though admittedly she had

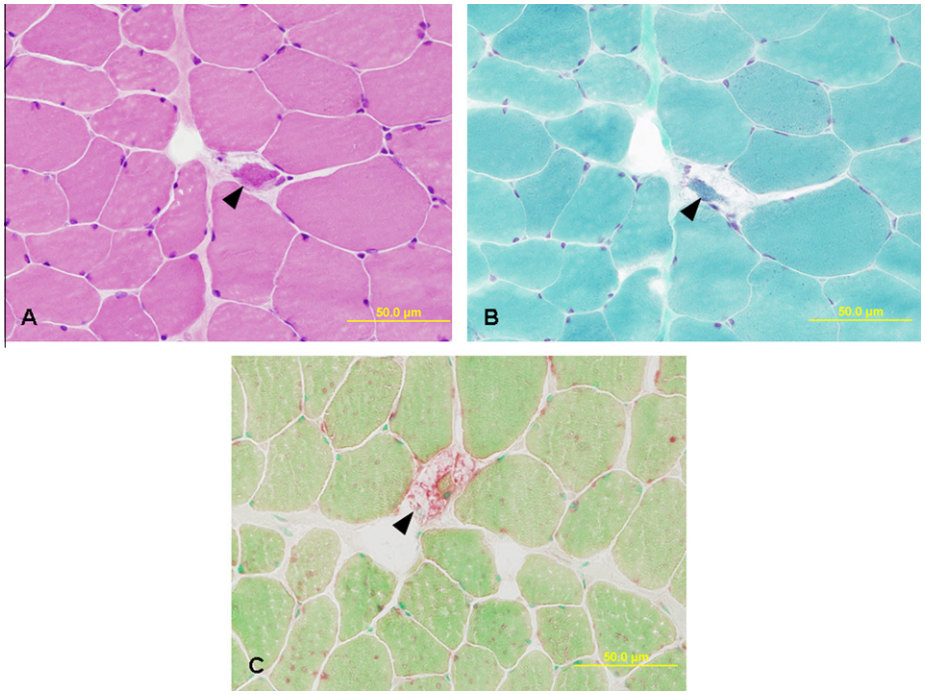

Fig. 1. Consecutive sections of a vacuolated fiber (A and B). (A) Hematoxylin and eosin section shows a single fiber harboring vacuoles (arrowhead). (B) In modified Gomori trichrome section, the vacuoles are not rimmed by membranous material. (C) Acid phosphatase activity is increased in the vacuoles (arrowhead) as well as in non-vacuolated fibers. Bar: 50 μm.