SYMPTOMATIC POMPE DISEASE: CAN MUSCLE MAGNETIC RESONANCE IMAGING FACILITATE DIAGNOSIS?

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Glycogen storage disease (GSD) type II, or Pompe disease (PD), is a lysosomal storage disorder caused by acid a-1,4-glucosidase deficiency. Its clinical spectrum varies greatly depending on the age of onset, rate of disease progression, and extent of tissue involvement. Late-onset PD (LOPD) can be asymptomatic for years, causing diagnostic delay. Muscle biopsy may be uninformative, because muscle fiber involvement can be patchy.1 Dried blood spot testing (DBS) has been suggested as an initial diagnostic tool.2 Although we are unsure whether patients diagnosed at an asymptomatic stage should be treated with enzyme replacement therapy (ERT) to prevent disease progression, there is an increasing need for early disease markers to monitor closely for overt myopathy.3 Muscle magnetic resonance imaging (MRI) has become an established and validated non-invasive technique for assessment of selective muscle involvement, mainly in the hereditary myopathies,4–6 using imaging protocols7 that highlight fatty infiltration using T1- weighted (T1-w) sequences. There is increased interest in short-tau inversion recovery (STIR) and T2 fatsaturation techniques, which both highlight muscle "edema." These techniques have been used mainly in inflammatory myopathies8 or in selected dystrophies, such as dysferlinopathy and facioscapulohumeral dystrophy.9 Here we present the case of an asymptomatic patient with LOPD who showed a distinctive muscle MRI pattern that helped us make an early diagnosis. A 16-year-old asymptomatic Italian boy was evaluated at our center for persistent incidental creatine kinase (CK) elevations (600 IU/L). He exhibited mild, generalized hyporeflexia. Cardiac and respiratory function tests were normal. DBS was not performed for temporary technical problems, so he underwent a quadriceps muscle biopsy, which showed normal histochemistry and immunohistochemistry. He also underwent muscle MRI with T1-w and STIR sequences on the lower limbs. T1-w sequences did not show any pattern of selective muscular adipose substitution, with the exception of mild involvement of the adductor magnus muscles bilaterally. However, both proximal adductor magnus muscles were altered with an "edema-like" signal on STIR sequences (Fig. 1). Selective adductor magnus involvement in T1-w sequences is the earliest manifestation of juvenile LOPD.10 However, mildly increased signal intensity on STIR images has been described in leg muscles in only a small percentage of LOPD cases. The meaning of this is still unknown, although it is probably partially related to the high glycogen content found in muscle biopsies and described in other GSDs.11,12 The MRI findings prompted us to test a-glucosidase muscle activity, which proved to be low (9.75 pmol/min/mg, reference range 113 6 41). Molecular analysis of the gene encoding acid a-1,4-glucosidase (compound heterozygosity: IVS1-32-13T>G; c.1670T>G) confirmed a diagnosis of PD. T2 quantification is lacking, and further studies are needed to confirm this finding on a larger sample to define its specificity and explain its meaning. However, this case highlights the usefulness of muscle MRI with both T1-w and T2-STIR sequences in the diagnosis of LOPD, particularly when clinical and muscle biopsy findings are uninformative.

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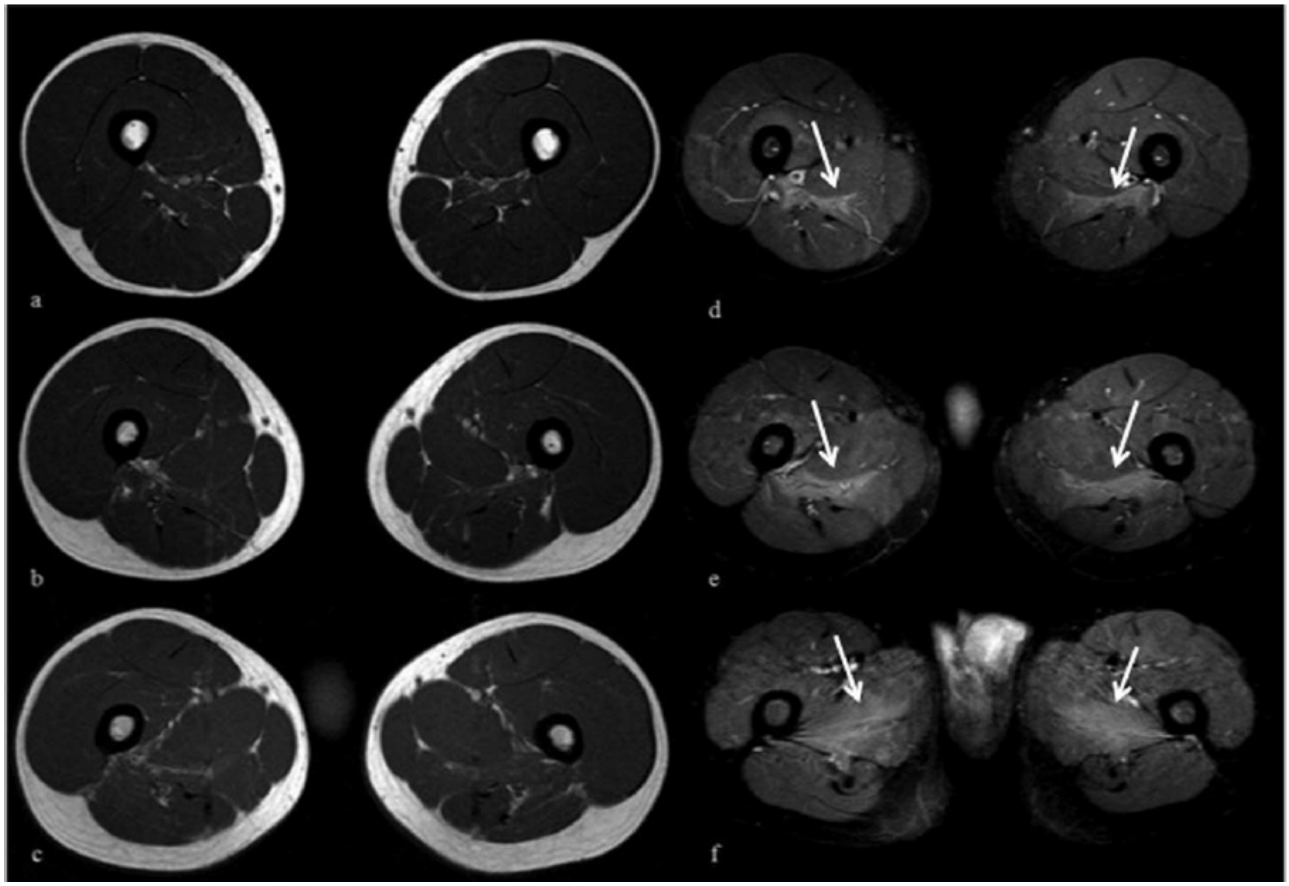
FIGURE 1. Axial T1 (a–c) and T2-STIR (d–f) weighted images at the thigh level. T1-w images are normal, with no selective pattern of adipose substitution. T2-STIR images show increased T2 times in both adductor magnus muscles, probably due to muscle edema and glycogen content. Slight hyperintensity of the vastus intermedius muscles is also evident.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