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Whole-body muscle MRI in 20 patients suffering from late onset Pompe disease: Involvement patterns

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Abstract

To describe muscle involvement on whole-body MRI scans in adult patients at different stages of late-onset Pompe disease. Twenty patients aged 37 to 75 were examined. Five were bedridden and required ventilatory support. Axial and coronal T1 turbo-spin-echo sequences were performed on 1.5 T or 3 T systems. MRI was scored for 47 muscles using Mercuri's classification. Whole-body scans were obtained with a mean in-room time of 29 min. Muscle changes consisted of internal bright signals of fatty replacement without severe retraction of the muscles' corpus. Findings were consistent with previous descriptions of spine extensors and pelvic girdle, but also provided new information on recurrent muscle changes particularly in the tongue and subscapularis muscle. Moreover thigh involvement was more heterogeneous than previously described, in terms of distribution across muscles as well as with respect to the overall clinical presentation. Whole-body MRI provides a very evocative description of muscle involvement in Pompe disease in adults.

Keywords: Pompe disease; Muscle; MRI; Whole-body; Muscle mapping

1. Introduction

To the best of our knowledge, whole-body muscle involvement has never been described in late onset Pompe's disease. We have been able to assemble a group of twenty adult Pompe's patients in order to provide a comprehensive assessment of disease burden at different stages of this rare condition.

Pompe's disease, also named acid maltase deficiency (AMD) or glycogen storage disease type II, is an autosomal recessive disorder characterized by a deficiency in the lysosomal enzyme acid alpha-glucosidase (GAA). Several phenotypes are described, ranging from rapidly progressive infantile forms, in which death usually occurs within the first year of life unless specific enzyme replacement therapy (ERT) is started [1], to slowly progressive adult-onset forms, with progressive respiratory insufficiency [1,2] and sleep-disordered breathing [3]. Affected adults typically

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develop a progressive myopathy [4] often resembling limb-girdle muscular dystrophy [5]. Even within the adult form, both symptoms at onset and natural disease course vary widely [6]. This heterogeneity in disease expression together with the possibility that ERT might be effective in mitigating symptoms in adults [7], justifies careful and reiterated disease assessment, which should include clinical, functional and respiratory evaluations and muscle testing.

Recent studies have shown that, in patients with inherited muscular disorders, extensive evaluation of muscle alterations by magnetic resonance imaging (MRI) can significantly contribute to a specific diagnosis [8]. In chronic diseases, muscle involvement detected by MRI is based principally on signal intensity changes resulting from fat infiltration into muscle for one part, and decreased muscle volume for the other. These abnormalities can vary from one muscle group to another, and also across individual muscles within the same muscle group, with patterns that can be indicative or even in some instances highly suggestive of the underlying genetic defect. In addition, precise identification and grading of individual muscle alterations also provides most useful information in assessing disease severity.

To this end, medical imaging might prove more accurate than standard clinical evaluation of the different muscle territories. As imaging tools, computed tomography (CT), and ultrasounds (US) are possible options. However, these techniques either expose the patient to ionizing radiations, or are not sensitive enough and too time consuming to ensure extended muscle examinations (US). Because it is exempt of side effects, especially ionizing radiation exposure, and has good soft-tissue contrast with a higher sensitivity for identifying fatty replacement in muscles and spatial resolution, MRI has become the method of choice for muscle imaging [9–11]. MRI also provides muscle scanning, not only in transverse, but also in coronal planes [12]. Muscle screening using sequential scanning techniques (conventional MR) allows the study of contiguous anatomical regions, but coil rearrangement and repositioning of the patient are necessary to explore non-contiguous regions (for example arms and legs), making this procedure too lengthy to assess multiple regions. This is particularly important for severely affected patients requiring ventilatory support [12,13].

We have defined a protocol using new commercially available MR software which performs whole-body scanning in a relatively short time, making it possible to examine patterns of muscle involvement including in patients with more severe forms of late onset Pompe's disease.

2. Materials and methods

2.1. Patients

Patients were classified into three groups according to disease severity:

Group A. Mild: able to walk without assistance and not requiring ventilatory support.
Group B. Moderate: able to walk without assistance and requiring ventilatory support.
Group C. Severe: unable to walk or only 10 meters or less if assisted and requiring ventilatory support.

All patients had a low GAA activity measured in either peripheral blood leukocytes or skin fibroblasts [14]. Genetic analyses have been performed in all patients.

The study was approved by the research ethics committee at our institution, and informed consent was obtained from all patients prior to inclusion.

2.2. Motor function

Functional activity was assessed using the Brooke score (from one: normal to six: no function for upper extremity) [15] and the Vignos score (one: able to climb stairs without help to 10: bedridden for lower limb function) [16]. Time to walk 10 meters and use of ambulation assistance devices (e.g. wheelchair, walking stick) were also recorded.

Muscle strength of neck flexors, shoulder abductors, elbow extensors and flexors, wrist extensors, hip flexors, quadriceps femoris, and foot extensors on both sides were graded using the Modified Medical Research Council (MMRC) scale. This scale has been used in muscle diseases such as Duchenne muscular dystrophy [17]. The MMRC scale has six grades (0–5: normal) followed by ± for some values (1+, 2−, 2+, 3−, 3+, 4−, 4+, 5−). In order to have a fully numerical scale we allocated +0.33 to " + " and −0.33 to "−". With this transformation a numeric value was attributed to each muscle.

2.3. Lung and respiratory muscle function

Both sitting and supine slow vital capacity (SVC), along with maximal inspiratory and expiratory pressures (PI_{max} and PE_{max}) were measured according to the standardization guideline [18]. The SVC values were reported as percent of theorical values.

Pressures PI_{max} and PE_{max} were measured using a flanged mouthpiece with the maneuvers repeated at least three times or until two identical readings were obtained [19].

2.4. Muscle imaging

In 15 patients, whole-body imaging was performed on a 1.5-tesla (1.5T) Philips MRI system (Achieva Release 11, Philips Medical Systems, Eindhoven, The Netherlands), with built-in volume transmitter/quadrature detection receiver coil (Q body coil). The five other patients were scanned with a 3-tesla (3T) imager (Siemens, Magnetom Trio TIM, Erlangen, Germany) which employs multiple phased-array surface receiver elements. In the whole-body configuration, the patient was wrapped in 88 of these