Molecular Genetics and Metabolism Reports 38 (2024) 101046

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Correspondence

New mutations identified in a case of Glycogenin-1 deficiency

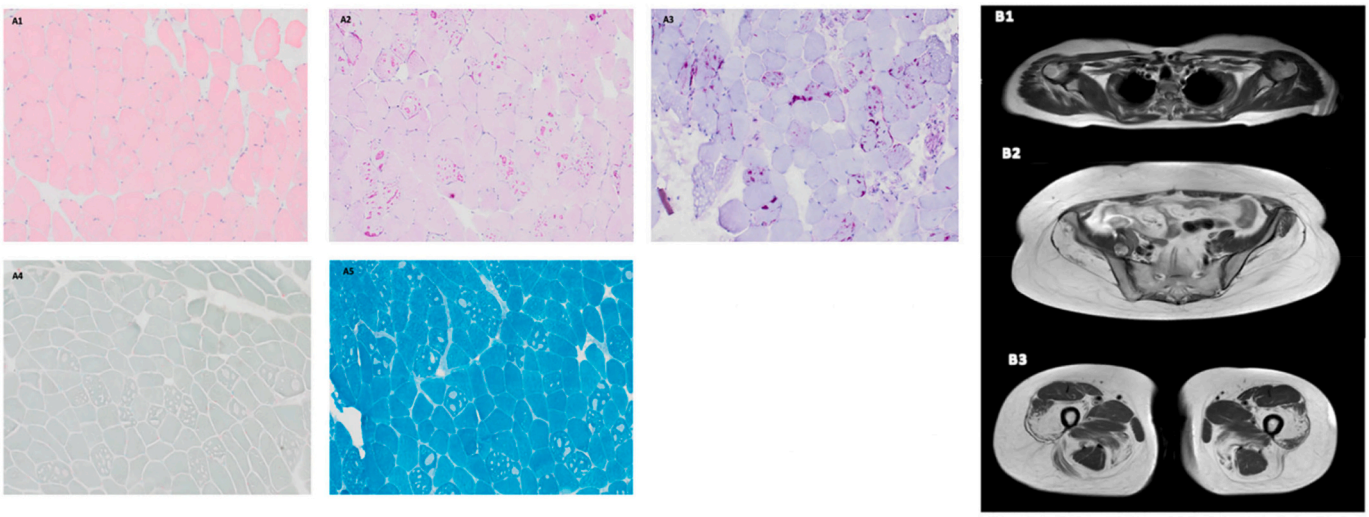
We read with great interest Lefeuvre et al.'s [1] report on a case of glycogenin-1 deficiency mimicking limb-girdle muscular dystrophy [2–6]. Here, we report another description of a 64-year-old woman, born to non-consanguineous French parents, with normal acquisition during childhood and without any family history of muscle disease, who presented gait disorders from a decade. First, a rhumatismal origin wih coxopathy was suspected, a right hip replacement was done, which didn't solve the problem. Physical examination emphasises a waddling gate with hyperlordosis, a slight facial asymmetry, right scapular winging, right trapezius amyotrophy, a mild asymetric, predominant in proximal, limb weakness, no sensory or cognitive symptoms. Serum creatinine kinase was at first normal at 100 UI/L, then slighty elevated at 204 UI/L. Electrophysiological examination found myopathic features in the right vastus medialis, peripheral neurogenic signs on the tibialis anterior muscle and spinal nerve root right L5. A pelvic girdle and limb-girdle MRI (Fig. 1B) shows fat replacement of several muscles as gluteal and deltoid muscles. The study of a panel of 234 genes of myopathy revealed two not previously described compound heterozygous variations in *GYG1* gene (NM_004130.4: c.7G > A and c.319G > T) which are predicted both to lead to missense changes, p.(Asp3Asn) and p.(Val107Phe) respectively, and possibly effect on splicing with a strong predicted effect on donor splice site of exon 1 and a moderate predicted effect on acceptor splice site of exon 4 respectively. A left deltoid muscle biopsy showed the presence of PAS positive inclusions (Fig. 1A).

The expression of glycogenin-1 in skeletal-muscle tissues of the patient was also studied by Western blot analysis [Fig. 1C] a profound reduction of glycogenin-1 was found for our patient.

CRediT authorship contribution statement

R. Pruvost: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **M. Csanyi:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing. **G. Lefebvre:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing. **V. Biancalana:** Formal analysis, Supervision, Validation, Writing – original draft, Writing – review & editing. **E. Malfatti:** Data curation, Formal analysis, Writing – review & editing. **F. Cassim:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing. **C. Oldfors:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing. **L. Defebvre:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing. **A. Oldfors:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing. **C. Tard:** Conceptualization, Data curation, Formal analysis, Resources, Writing – original draft, Writing – review & editing.

https://doi.org/10.1016/j.ymgmr.2023.101046
Received 26 August 2023; Received in revised form 22 December 2023; Accepted 24 December 2023



C

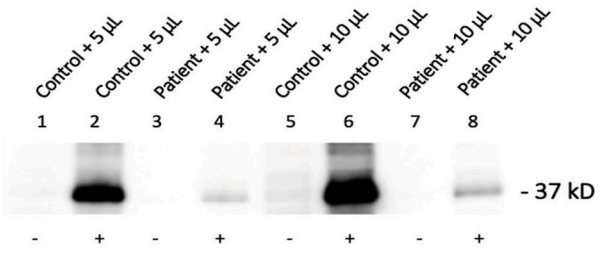


Fig. 1. A. Muscle morphology: deltoid muscle biopsy.
HES staining 100× (A1) revealing vacuolar appearance of some muscle fibers.
PAS staining, 100× (A2) showing round PAS positive inclusions inside some muscle fibers.
PAS after alpha-amylase digestion, 100× (A3) showing alpha-amylase resistant polysaccharide corresponding to polyglucosan bodies.
Acid phosphatase 100× (A4) and Gomori 100× (A5) indicating the absence of vacuole staining.
B. Muscular MRI: limb-girdle and thights examination.
In phase T1-weigheted MR axial slices (DIXON technique).
In scapular girdle: (B1) mild involvement with partial fatty infiltration in the right deltoid muscle only,
In pelvic girdle: (B2) severe involvement: glutei muscles are completely fat-replaced.
In thigh: (B3) severe involvement: gluteus maximus, gluteus medius, vastus intermedius and biceps of the thight are totally fat replaced. Adductor magnus, semi-membranous, vastus medialis, vastus lateralis are mostly fat replaced too but better preserved, symmetricaly.
C. Protein analysis.
Western-blot analysis of glycogenin-1 in skeletal muscles from a normal control and the patient, performed with (+) or without (−) alpha-amylase treatment, and with 5 µL or 10 µL of monoclonal antibodies against human glycogenin-1 (Abnova, M07/3B5, 1:500). Without alpha-amylase treatment of the sample (−), glyocogenin-1 was undetectable for the patient, but detectable for the control. With alpha-amylase treatment (+), glycogenin-1 was detectable for the patient, but reduced compared to the control, but the small amount of residual glycogenin-1 is functional, since it is only seen after digestion with alpha amylase, which removes the sugar residues from the glycogen molecules and hydrolyze the internal α-1,4-glycosidic linkages between the autoglucosylated residues.

Declaration of competing interest

None.

Data availability

No data was used for the research described in the article.

References

[1] C. Lefeuvre, S. Schaeffer, R.Y. Carlier, et al., Glycogenin-1 deficiency mimicking limb-girdle muscular dystrophy, Mol Genet Metab Rep. 24 (2020) 100597. . Published 2020 May 24, https://doi.org/10.1016/j.ymgmr.2020.100597.
[2] E. Malfatti, J. Nilsson, C. Hedberg-Oldfors, et al., A new muscle glycogen storage disease associated with glycogenin-1 deficiency, Ann. Neurol. 76 (6) (2014) 891–898, https://doi.org/10.1002/ana.24284.
[3] C. Hedberg-Oldfors, A. Mensch, K. Visuttijai, et al., Polyglucosan myopathy and functional characterization of a novel GYG1 mutation, Acta Neurol. Scand. 137 (3) (2018) 308–315, https://doi.org/10.1111/ane.12865.
[4] C. Hedberg-Oldfors, W. De Ridder, O. Kalev, et al., Functional characterization of GYG1 variants in two patients with myopathy and glycogenin-1 deficiency, Neuromuscul. Disord. 29 (12) (2019) 951–960, https://doi.org/10.1016/j.nmd.2019.10.002.
[5] K. Visuttijai, C. Hedberg-Oldfors, C. Thomsen, et al., Glycogenin is dispensable for glycogen synthesis in human muscle, and Glycogenin deficiency causes Polyglucosan storage, J. Clin. Endocrinol. Metab. 105 (2) (2020) 557–566, https://doi.org/10.1210/clinem/dgz075.
[6] C. Prats, T.E. Graham, J. Shearer, The dynamic life of the glycogen granule, J. Biol. Chem. 293 (19) (2018) 7089–7098, https://doi.org/10.1074/jbc.R117.802843.

R. Pruvost[a,*], M. Csanyi[b], G. Lefebvre[c], V. Biancalana[d], E. Malfatti[e], F. Cassim[a], C. Oldfors[f], L. Defebvre[a], A. Oldfors[f], C. Tard[a]
[a] *Department of Movement Disorder and NS-PARK/centre de référence des maladies neuromusculaires Nord/Est/Ile-de-France, Inserm 1172 University of Lille, Lille, France*

[b] Department of Pathology, Lille Universitary Hospital Center, Lille, France
[c] Musculoskeletal Imaging Department, Centre de Consultation et d'Imagerie de l'Appareil Locomoteur, CHU Lille, University of Lille Nord de France, F-59000, Lille, France
[d] Laboratory of Diagnostic Genetics, Faculty of Medicine, University of Strasbourg, France
[e] Biology of the Neuromuscular System, University Paris-Est Créteil, INSERM, U955 IMRB, F-94010 Créteil, France
[f] Department of Pathology, Sahlgrenska University Hospital, Goteborg, Sweden

[*] Corresponding author.
E-mail address: roxane.pruvost.etu@univ-lille.fr (R. Pruvost).