

Clinical and Para clinical Findings in a Patient Confirming the Diagnosis of Glycogen Storage Disease Type II and Myotonic Dystrophy Type 1: Case Report

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Abbreviations

MD	Myotonic dystrophy
PD	Pompe disease
GAA	α -1, 4-glucosidase
OSAHS	Obstructive Sleep Apnea / Hypopnea Syndrome
CPK	Creatine phosphokinase
DBS	dry blood spotted
NCS	neuroconduction
EMG	electromyography

1. Case Report

We present the case of a 34-year-old woman from Bogotá, Colombia who presents frequent falls, distal muscle weakness, a feeling of “stiffness” predominantly in the upper limbs, and dyspnea. The disease impaired the different daily life activities, including the performance of her job. She was diagnosed with Obstructive Sleep Apnea / Hypopnea Syndrome (OSAHS), so management with Bi-Pap was initiated.

In the first physical evaluation, she mentioned that she had daytime sleepiness three years before the onset of weakness. Among her family history, she described that her paternal uncle and her brother presented similar clinical symptoms; however, they did not have studies to clarify the cause of their muscle weakness. The patient's mother did not report any symptoms, and the patient's father's history is unknown [1].



Image 1

Image 2

The initial physical examination (Image1) showed palpebral ptosis, posture with increased thoracic kyphosis, lumbar lordosis, protracted shoulders, generalized muscle weakness with severe distal involvement, myotonia, and Gowers sign, difficulty climbing steps, stoppage gait, she couldn't walk on tiptoe or heels.

She underwent spirometry, in which she had difficulty completing the study and was unable to perform forced expiratory maneuvers. In another study, the maximum inspiratory and expiratory pressures were moderately and severely lowered, respectively, suggesting diaphragmatic weakness. Creatine phosphokinase (CPK) (254 U / L) and transaminases (TGO 47.9 IU / L, TGP 62.6 IU / L) were increased.

A GAA activity assay was performed in dry blood spotted (DBS)

on filter paper, confirming a positive screening test. Then GAA gene sequencing was performed, identifying the pathogenic vari-

ant c.-32-13 T> G in a heterozygous state; no copy number variants were identified. (Table).

DBS on filter paper:	Neutral / Inhibited Ratio at 18.5% (RV: <16%)
	% alpha-glucosidase inhibition 86.7% (RV: <86%).
GAA activity assay in leukocytes using glycogen as substrate	Alpha glucosidase: 0.15 nmol/mg prot/h (Control: 0.4 - 1.43)
	% of residual activity 11.6%

Table 1: Enzyme tests for Pompe disease

PD is an autosomal recessive disease, so a heterozygous mutation doesn't confirm the diagnosis. A new GAA activity assay in leukocytes was performed using glycogen as substrate (Table) and identified a severe reduction of enzymatic activity, and PD was confirmed. Due to this diagnosis, enzyme replacement treatment with AL glucosidase Alfa was started, and the patient was adherent for approximately 18 months [2]. During treatment, she reported persistence of weakness, but fatigue improved.

(Image 2) but no weakness in the diaphragmatic muscles. Physical examination revealed alopecia, temporal muscle atrophy, weakness, and myotonia. A genetic study was carried out, and an allele with more than 100 CTG repeats of the DMPK gene was detected, confirming the diagnosis of DM1 [3]. The diagnosis of PD was discarded in this patient by evaluation of GAA enzyme activity and GAA gene sequencing.

A neurophysiological study with neuroconduction (NCS) and electromyography (EMG) was also carried out; NCS studies were normal, the EMG showed motor units of low amplitude and short duration in the evaluated muscles (first dorsal interosseous, Deltoids, Vastus Lateralis, Tibialis Anterior) with early recruitment and myotonic discharges, findings that are consistent with intrinsic muscle fiber disease.

Given the family history, the results in EMG studies, and the persistence of weakness despite treatment with AL glucosidase alfa, a genetic analysis of the DMPK gene was performed, detecting an allele with more than 100 CTG repeats in the analyzed region of the DMPK gene [4,5]. In addition, a new enzymatic GAA activity assay in leukocytes using glycogen as substrate (Table 2) confirmed the decrease in GAA activity and, therefore, the diagnosis of both muscular pathologies in the same patient: Pompe disease and Myotonic Dystrophy type 1.

After the diagnosis of PD in the patient, an assessment was made of her 38-year-old brother, who also had a similar clinical feature

GAA activity assay in leukocytes using glycogen as substrate	Alphaglucosidase: 0.16 nmol/mg prot/h (Control: 0.4 - 1.43)
	% of residual activity 19.8%

Table 2: Enzyme tests for Pompe disease

2. Discussion

The clinical findings, among the deficiency of the activity of the enzyme GAA, would confirm this diagnosis, as established in the consensus meetings of the European Pompe Consortium: "the diagnosis should be confirmed by enzyme analysis in leukocytes, fibroblasts or skeletal muscle and/or genetically by mutation analysis" however, the clinical findings could also correspond to DM1, which was genetically confirmed [6].

continue with studies and rejects the possibility of initiating enzyme replacement, which limits the case report.

A study showed that conventional diagnostic genetic studies could identify and diagnose most people with PD but consider the need to introduce new methods (generic-splicing assay, minigene analysis, SNP array analysis, and targeted Sanger sequencing) in cases in which conventional procedures are insufficient to be able to identify new variants in the GAA gene [7].

3. Conclusion

PD and DM1 are genetic diseases that compromise muscle-producing proximal and distal weakness. Due to the confirmatory family diagnosis, it was found that the patient, in addition to the PD confirmed with enzymatic studies that showed the decrease in GAA activity, also had type 1 Myotonic Dystrophy, a condition never reported before. We believe that, as it is a rare condition, with clinical findings that could correspond to both pathologies, additional studies such as Skin fibroblast assays and other genetic analyzes should be carried out to detect variants in the GAA gene and thus make the definitive confirmation of the PD.

We consider that the patient would benefit from an additional test such as quantifying the enzymatic activity in other tissues (Skin fibroblast assays) and specific genetic studies that clarify even better the activity of the enzyme. However, the patient does not agree to

4. Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

5. Disclosure of Conflicts of Interest

None of the authors has any conflict of interest to disclose

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