

Poster Abstract: Clinical

Clinical and Treatment Management Decisions in Two Asymptomatic Late-Onset Pompe Disease Siblings – Further Evidence of Scoliosis as a Clinical Sentinel Sign for Juvenile Pompe Disease

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An asymptomatic 17-year-old long-term Pompe disease patient was identified by chance through his dermatologist due to partial alopecia. Through high CK (1,310 IU/L) and muscle/hepatic biomarkers (AST, 162 IU/L; ALT, 189 IU/L) a muscle biopsy was performed revealing vacuolated muscle pathology with H-E and PAS stains. A compound heterozygote pathogenic *GAA* genotype was detected (-32-13 T>G/c.2560C>T). A series of clinical and laboratory evaluations identified several abnormal clinical signs, despite the absence of clinical symptoms. As the patient had a positive DBS, diminished GAA activity in leukocytes (0.56 nml/h/mg protein – RV: 1.0–5.9), high urinary GLc₄ levels on HPLC, abnormal FVC drop during sitting–supine transition (>14%), and abnormalities on his tongue and edema of his thighs, seen on MRI, the decision was taken to initiate enzymatic replacement therapy (ERT) with 20 mg/kg rhGAA (Myozyme®), even though no subjective clinical symptoms were present. After 4 years on ERT treatment and motor/respiratory rehabilitation programs, all clinical parameters worsened, especially CK levels, muscle MRI with an overall muscle substitution for fat with muscle mass volume reduction; and a higher FVC drop during sitting–supine transition (>18%) were noted. Based on these clinical and labo-

ratory evaluations, Myozyme® dosing off-label increase (40 mg/kg) for ERT was considered.

The patient's asymptomatic 12-year-old sister revealed a similar *GAA* compound heterozygote genotype (-32-13 T>G/c.2560C>T), positive DBS and low *GAA* leukocyte activity (0.40 nmol/h/mg protein). Clinical follow-up with serial serum CK, urinary Glc₄ biomarker, pulmonary functional evaluations, motor and muscle functional and strength tests, muscle MRI and ENM were unremarkable. After 4 years of clinical follow-up, the physiotherapist observed an abnormal posture of the patient and an important scoliosis was diagnosed. An ENM of the paraspinal and sternocleidomastoid muscles revealed sporadic myotonic discharges. A new series of clinical and laboratory evaluations was performed and all evaluations were normal, including serum CK, muscle MRI, and pulmonary FVC sitting–supine evaluation. The decision to start Myozyme® ERT treatment was not a consensus among the clinical team. Scoliosis has been registered in few cases as a clinical complication in Pompe disease¹, and may serve as a clinical alert for screening for Pompe disease among the “idiopathic” juvenile scoliosis group.

REFERENCE

- [1] Roberts M., Kishnani P.S., van der Ploeg A.T., Müller-Felber W, Merlini L., Prasad S., Case L.E. The prevalence and impact of scoliosis in Pompe disease: lessons learned from the Pompe Registry. *Mol Genet Metab.* 2011;104(4):574–82.

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