THE IMPORTANCE OF A NON-INVASIVE SCREENING IN PROXIMAL MYOPATHIES

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Background

Late-Onset Pompe Disease (LOPD) is caused by compound mutations of the acid alpha-glucosidase gene (*GAA*) which lead to deficiency of GAA enzyme activity and accumulation of glycogen within autophagic vacuoles. LOPD affects primarily proximal muscle, as in limb-girdle muscolar dystrophy and polymyositis.

Methods and Materials

We admitted to our Division three women aged between the fourth and fifth decade that received, at another Department, diagnosis of inflammatory myopathy. They underwent to steroid and immunosuppressor therapy that worsened clinical picture. At the time of our observation, they presented hyperCKemia, proximal muscle weakness, autoimmunity nonspecific indices slightly above the reference range. Therapeutic failure imposed clinical and instrumental revaluation.

Acid alpha- glucosidase GENE

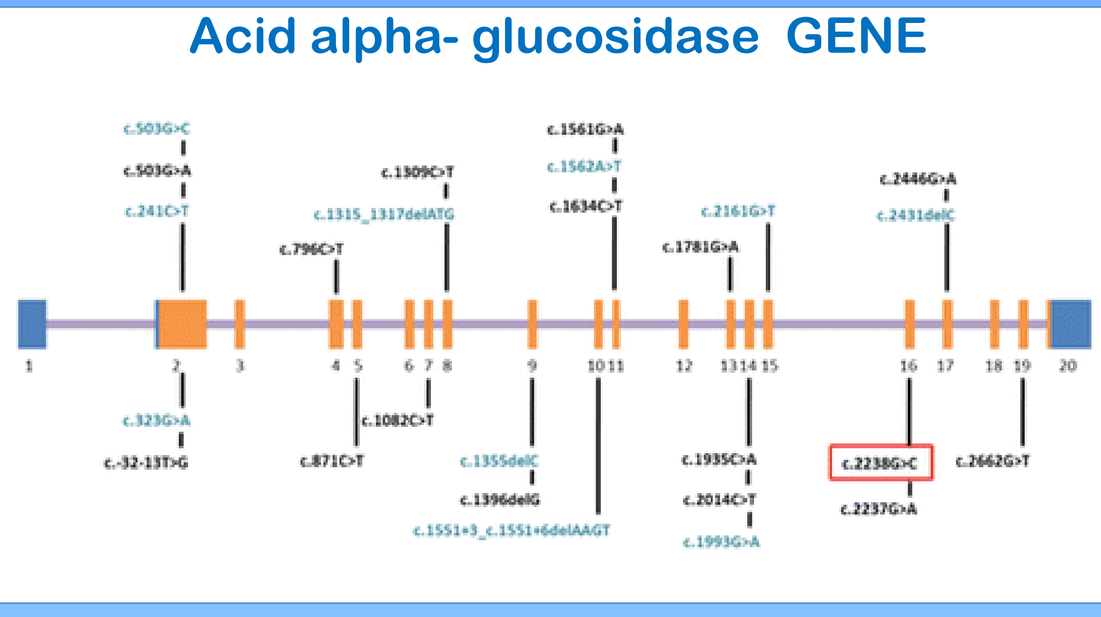

Fig. 1.
Lysosomal alpha-glucosidase, also called α-1,4-glucosidase and acid maltase, is an enzyme (EC 3.2.1.20) encoded by *GAA* gene. Errors in this gene cause Pompe disease.

Results

The first evaluation with lymphocytes on peripheral blood smear (PBS) disclosed PAS positive glycogen granula in their cytoplasm and Dried Blood Spot (DBS) revealed reduced GAA enzyme activity. Electromyography extended to paraspinal muscles showed a myopathic pattern with *complex repetitive discharges*. In suspect of LOPD we decided to repeat muscle biopsy. Histological examination confirmed a myopathic pattern characterized by consistent glycogen storage at intermyofibrillary and sub-sarcolemmal levels and numerous PAS and acid phosphatase positive vacuoles in many fibres. Moreover patients also performed an ANGIO-MRI that disclosed dolicho-ectasis of basilar trunk. Genetic investigations confirmed LOPD.

Discussion and Conclusions

Proximal muscle weakness and hyperCKemia should be screened, at first, with rapid and non-invasive methods like PBS and DBS to avoid, despite a rise in aspecific inflammatory markers, immunomodulatory therapies able to worse, potentially, the clinical features of a metabolic myopathy, and to start, in case of LOPD, enzyme replacement therapy (ERT) to improve life quality and to reduce muscular weakness.

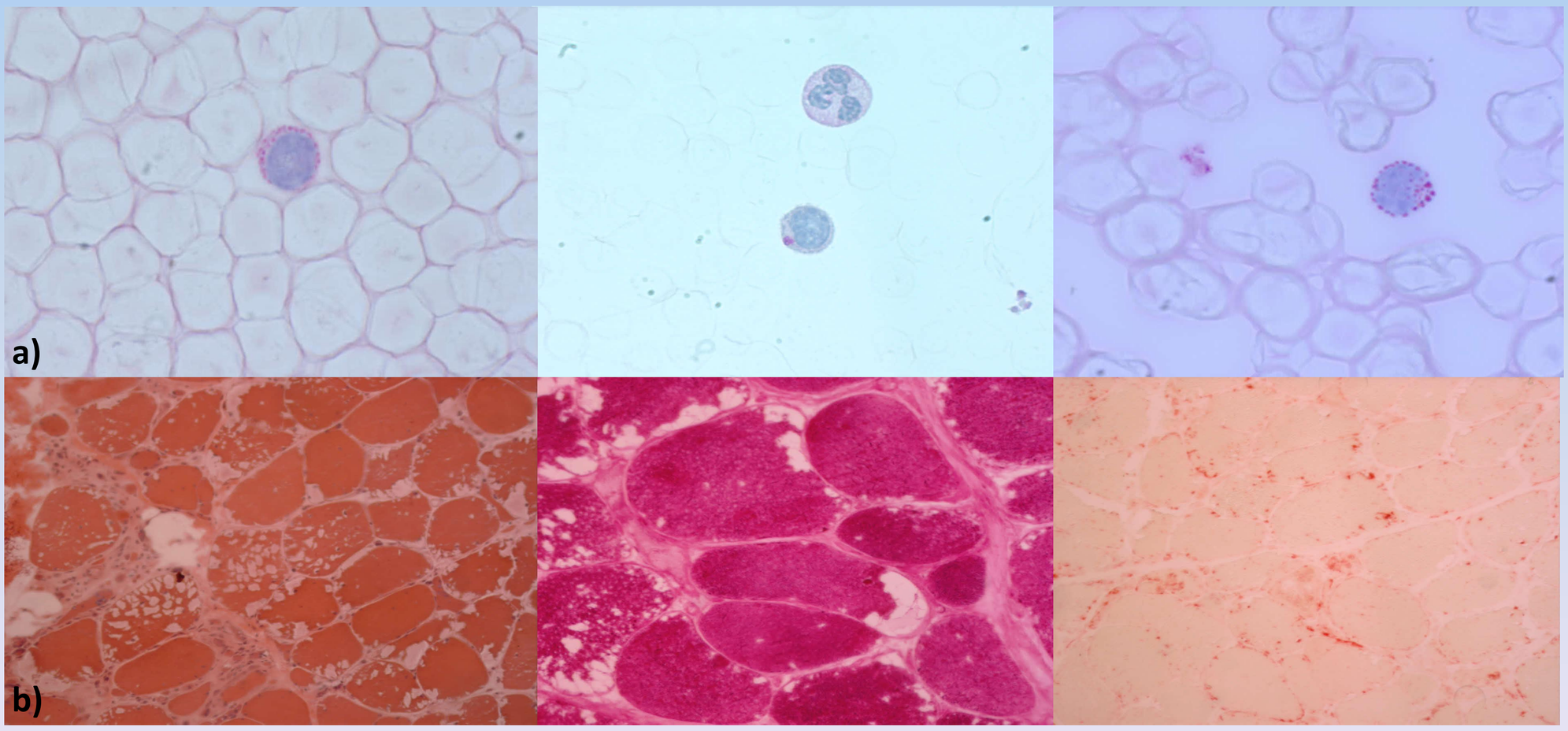

Fig. 2.
a) PAS positive glycogen granula in Lymphocytes cytoplasm on blood smears.
b) Histology and histochemistry of quadriceps muscle biopsy revealed a myopathic pattern characterized by presence of numerous vacuolary formations of variable shape, number and extension. These findings are suggestive of vacuolar myopathy, like LOPD.

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