Muscle Involvement in Lysosomal Diseases

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Abstract

Lysosomal storage diseases, LSDs, are rare, inherited diseases with accumulation of specific substrates. Specific therapies were already developed for selected LSDs, making the timely and correct diagnosis strategic for successful treatment. LSDs require Electron Microscopy, EM, for morphological diagnosis even if the biochemical techniques provide a reliable diagnosis. The identification of pathogenic mutations is recommended to provide final diagnosis, and for genetic counseling. LSDs-associated myopathies are characterized by the presence of autophagolysosomes leading to the accumulation of non-specific and/or specific content such as in glycogenosis, namely Pompe disease, or Danon disease and NCLs: granular osmiophilic deposits in CLN1,CLN10/CTSD; curvilinear profiles in CLN2, fingerprint profiles in CLN3, and mixed-type inclusions in CLN5, CLN6, MFSD8, CLN8. Muscle is one of the most responsive tissues to different physiological and pathological conditions by autophagy activation. Vacuolar myopathies are characterized by increased autophagic vacuoles containing myeloid structures, degraded organelles and other cytoplasmic contents detectable by muscle biopsy on both light microscopy (rimmed vacuoles) and EM evaluation. Altered autophagy is a common feature of many muscle diseases characterized by mutations in genes associated with vacuolar myopathies (GNE, LDB3/ZASP, MYOT, DES and GAA), but also in genes not regularly linked to altered autophagy (FKRP, DYSF, CAV3,COL6A2, GYG1 and TRIM32). For these reasons, ultrastructural analysis is essential for a differential diagnostics in the field of vacuolar/lysosomal diseases.