PO-006 - (23951) - ULTRASTRUCTURAL CHANGES IN FABRY DISEASE: A COMPARATIVE ANALYSIS ACROSS AFFECTED ORGANS

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Fabry disease (FD) is an X-linked lysosomal storage disorder caused by α-galactosidase A deficiency, leading to the accumulation of globotriaosylceramide (GB3) in multiple organs. This progressive intracellular deposition results in structural damage, particularly affecting the cardiovascular, gastrointestinal, and reproductive systems. The extent and pattern of ultrastructural alterations vary among tissues, influencing disease progression and clinical manifestations.

Ultrastructural evaluations were performed on myocardial, intestinal, and testicular biopsies of patients with FD using light microscopy (LM) and transmission electron microscopy (TEM). Morphometric assessments were accomplished to quantify GB3 accumulation and its impact on cellular and subcellular structures.

TEM revealed widespread GB3 accumulation in cardiomyocytes, smooth muscle cells, endothelial cells, and pericytes, forming characteristic myelin-like inclusion bodies. Cardiomyocytes exhibited extensive cytoplasmic accumulations of inclusion bodies with displacement of cellular organelles. Differently, enterocytes displayed GB3 deposits primarily in lysosomal structures, leading to altered cellular morphology. Testicular biopsies showed GB3 accumulation predominantly in vascular and interstitial cells, while Sertoli and Leydig cells remained largely unaffected. Furthermore, we observed the thickening of the basement membrane and degeneration of spermatogonia, suggesting an indirect impact of vascular damage on spermatogenesis.

The ultrastructural impact of FD differs across organs, with cardiomyocytes demonstrating significant cytoplasmic alterations, enterocytes exhibiting lysosomal inclusions, and testicular cells showing vascular-related alterations. These differences suggest that GB3 accumulation affects cellular integrity in a tissue-specific manner, contributing to the various clinical manifestations of FD. In conclusion, our results may offer key insights to guide therapeutic approaches aimed at restoring cellular function.

Palavras-chave : Fabry desease, Transmission Electron Microscopy, Globotriaosylceramide