THE FIRST EVIDENCE OF LIVER MICRO ANATOMICAL, MOLECULAR AND METABOLIC CHANGES IN PATIENTS WITH MITOCHONDRIAL NEUROGASTROINTESTINAL ENCEPHALOMYOPATHY

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Comprehensive analysis of liver tissue from MNGIE patients reveals that the liver is a target organ characterized by steatosis, fibrosis, mtDNA depletion, metabolic rearrangement, and immune system involvement.

KEY POINTS

- MNGIE liver tissue from 9 patients showed intense steatosis and fibrosis with collagen septa formation, altered vascular and biliary branches, and increased hypoxia indicated by HIF-1α positive staining.
- Microdissection revealed mtDNA depletion in hepatocytes and portal spaces, while cytochrome-c-oxidase negative hepatocytes were observed.
- NMR metabolomic assessment demonstrated abnormal triglyceride production and intracellular accumulation along with a significant decline in aerobic metabolism.
- RNA-seq identified modulation of genes involved in lipid metabolism, vascular architecture, oxidative stress and immune system activation, with immune infiltrates including mast cells, lymphocytes and macrophages confirmed by immunohistochemistry.
- The findings establish liver as a target organ in MNGIE with immune system involvement implicating an inflammatory component in disease progression.

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