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Electron microscopy reveals evidence of perinuclear clustering of mitochondria in cardiac biopsy proven allograft rejection

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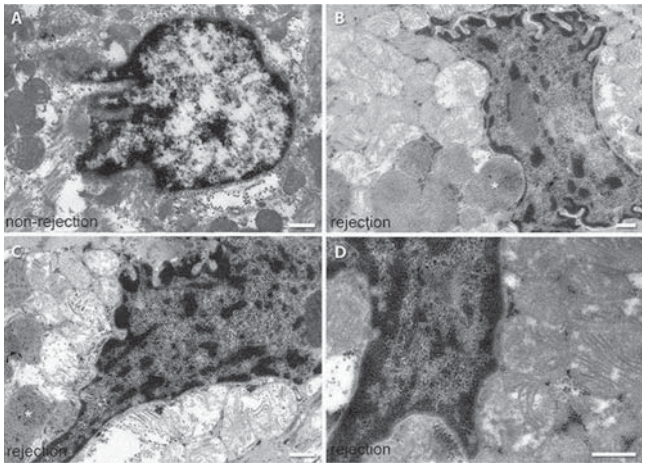
Background: Despite improved efficacy of immunosuppression therapy, allograft rejection continues to be a significant risk, especially early after transplantation. Endomyocardial biopsy (EMB) is the standard tool with a recognized role in the surveillance of posttransplant cardiac rejection and is based on optical microscopy analysis. However, this method presents technical limitations.

Purpose: In this work we focus on the analysis of new ultrastructural findings in cardiac biopsy specimens.

Methods: This study include heart transplanted patients from a single center who were referred for EMB as a scheduled routine screening. Participants were divided into 2 groups: patients transplanted without allograft rejection (n=5), and patients with biopsy-proven allograft rejection (n=5). Rejection episodes were assessed according to the International Society for Heart and Lung Transplantation (ISHLT) consensus report.

Results: We detected by electronic microscopy a significative increase in the number of mitochondria ($p<0.0001$) and dense bodies in the rejection group ($p<0.05$). But the most significative finding was the presence of local accumulations of mitochondria close to the nuclear envelope, pressing and shaping the morphology of this membrane in all rejection samples. We found these perinuclear clustering of mitochondria in a 68±27% of the total cardiac nucleus observed from rejection samples. We not observed this phenomenon in non-rejection samples, thus reflecting an excellent sensitivity and specificity.

Conclusion: We observed by electron microscopy a specific phenomenon, perinuclear clustering of mitochondria, in endomyocardial biopsies from patients with cardiac rejection that affects to the architecture of the nuclear membrane. This ultrastructural approach might complement and improve the diagnosis of rejection.



Perinuclear clustering of mitochondria