

Electron microscopic (EM) morphometric analysis of hydroxychloroquine-induced lysosomal accumulation in a patient with progressive cardiomyopathy and dysrhythmia

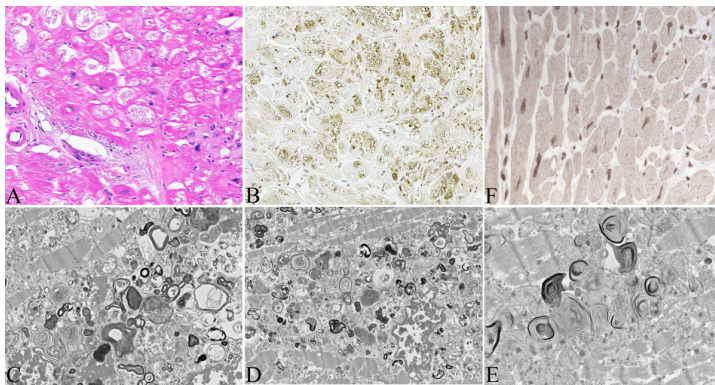
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Abstract

A 69-year-old woman with a history of undifferentiated connective tissue disorder controlled on more than 20 years of hydroxychloroquine (HCQ), presented with syncope and subsequently developed complete heart block necessitating pacemaker implantation and heart transplant 20 months after symptom onset. Light microscopy of the heart showed cytoplasmic PAS(+) vacuoles staining with abs to poly-ubiquitin (Fig 1B). EM showed lysosomal expansion by lamellar myeloid dense body inclusions (Fig 1C-E) consistent with HCQ-induced cardiomyopathy. Morphometric analysis performed by point counting method showed $56\pm 11\%$ replacement of cytoplasm of cardiomyocytes by the storage material. Staining with abs to transcription factor EB (TFEB) showed increased nuclear signal (Fig 1F) suggesting an activation of lysosomal stress response.

Discussion: This case highlights the rare but serious risk associated with long-term HCQ use, emphasizing the need for strong vigilance by both clinicians and pathologists in evaluating potential cardiotoxicity.



H&E (A), poly-ubiquitin (B), TFEB (F) stained and TEM preparations of the explanted heart in hydroxychloroquine-induced heart failure. Expanded lysosomes show myeloid dense bodies-like (C, D) and lamellar bodies (E) appearance. Increased nuclear staining with abs to transcriptional factor EB suggests activation of lysosomal stress response (F).