Danon disease presenting as severe myocardial hypertrophy

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A 15-year-old boy presented with abnormal electrocardiogram on regular examination, which showed left ventricular hypertrophy and a Wolff–Parkinson–White pre-excitation pattern. Clinical examination displayed mild limb muscle weakness and atrophy and slight mental retardation. Laboratory testing revealed increased plasma creatine kinase concentration. Transthoracic echocardiography showed massive left ventricular hypertrophy (interventricular septum 25 mm and left ventricular lateral wall 24 mm) (Panel A). Cardiac magnetic resonance found late gadolinium enhancement in the left ventricular wall (Panel B, arrows). Endomyocardial biopsy was performed and light microscopy showed diffuse myocyte hypertrophy and intracytoplasmic vacuoles (Panel C, arrow). Electron microscopy showed sparse glycogen particles, myelin-like lamellar material, granular debris, and the autophagic vacuoles (Panel D). Genetic analysis identified a mutation in the exon 6 of lysosome-associated membrane protein-2 (LAMP2) gene.

The final diagnosis was Danon’s disease, an X-linked lysosomal disease due to a primary deficiency of LAMP2. The absence of LAMP2 leads to an accumulation of autophagic vacuoles, mainly in the heart and skeletal muscle cells. The characteristics of Danon’s disease include childhood onset, male predominance, hypertrophic cardiomyopathy, mild myopathy, and mental retardation. Unfortunately, there is no causal therapy for Danon’s disease. As the disease progresses, the only remaining therapeutic option is cardiac transplantation.