Glycogen storage disease may affect the heart, particularly as a result of a mutation of the \textit{LAMP2} and \textit{PRKAG2} genes encoding for structural proteins of cardiomyocytes.\textsuperscript{1} Its recognition and differentiation from hypertrophic cardiomyopathy and other infiltrative and storage diseases may influence treatment and prognosis but are difficult to obtain by conventional noninvasive imaging.

A 26-year-old man with family history of sudden cardiac death at a young age (an aunt and grandfather died before 40 years of age) was referred for cardiac magnetic resonance examination because of unexplained increased left ventricular wall thickness at echocardiography (maximal wall thickness, 17 mm) associated with reduced left ventricular function. The ECG (the Figure, A) showed sinus rhythm with increased QRS voltages and abnormalities of ST segment and T wave.

Cardiac magnetic resonance was performed with a 1.5-T system (Magnetom, Avanto, Siemens Medical Systems, Erlangen, Germany) with an 8-element torso coil. The acquisition protocol included first-pass perfusion imaging at rest and cine steady-state free precession and inversion recovery after contrast injection (gadopentetate dimeglumine, Multihance, Bracco, Milan, Italy).

The right ventricle (RV) had increased wall thickness with severely compromised function resulting in an ejection fraction of 28\% by cine imaging (see the Figure, B, and Movie I in the online-only Data Supplement). Likewise, the left ventricle had increased wall thickness and was diffusely hypokinetic (ejection fraction, 40\%). After gadolinium administration, an extensive hyperenhancement of the RV was depicted (the Figure, C and D).

The patient underwent coronary angiography and targeted RV biopsy of late-enhancement areas. Coronary arteries were normal. Histology showed large metachromatic cardiomyocyte vacuoles (the Figure, E) that at electronic microscopy were due to extensive cytoplasmic accumulation of glycogen, often incorporated into autophagosomes (the Figure, F), consistent with glycogen cardiomyopathy. No interstitial edema and fibrosis or replacement fibrosis was observed after Masson trichrome and Miller elastic van Gieson stain. Gene analysis confirmed a mutation of the \textit{LAMP2} gene. The patient had a cardioverter-defibrillator implanted in accordance with his family history and elevated risk of developing life-threatening ventricular arrhythmias.

The \textit{LAMP2} gene encodes for an X-linked lysosome-associated membrane protein. Its mutation causes Danon disease, a multisystem disorder with neurological, liver, skeletal, and heart muscle involvement. The heart may be predominantly affected with mild or minimal systemic disease. Cardiac involvement results in myocardial glycogenosis with progressive thickening of cardiac walls clinically characterized by manifestation at young age, rapid deterioration of cardiac function, and electric instability.\textsuperscript{2} Implantation of a cardioverter-defibrillator may be crucial to prevent sudden death as a bridge to cardiac transplantation.

The observed pattern of RV late enhancement has not been previously reported in patients with storage or infiltrative myocardial diseases.\textsuperscript{3} A possible explanation for the late enhancement observed in this patient could be related to sarcolemmal damage resulting from the advanced storage disease and subsequent diffusion and retention of the gadolinium within the intracellular space, similar to what was described in acute myocardial infarction.\textsuperscript{4} RV late enhancement at cardiac magnetic resonance can be a precious hint for the diagnosis of glycogen cardiomyopathy, orienting gene analysis and/or cardiac biopsy.


disclosures

None.

References

Figure. A, A 12-lead ECG showing increased QRS voltages associated with abnormalities of ST segment and T wave. B, Cine steady-state free-precession image acquired on the end-diastolic horizontal long-axis view showing thickening of biventricular walls. C and D, T1-weighted inversion-recovery short-axis and 4-chamber views after intravenous injection of gadolinium showing a diffuse and homogeneous enhancement of the RV myocardium (black arrowheads) involving the free wall, apex, and right portion of the interventricular septum. The late-enhancement pattern of the left ventricle is predominantly subepicardial (white arrows), with patchy involvement of the midwall (black arrows). E and F, RV endomyocardial biopsy showing normal interstitium and large, metachromatic (light blue, arrows), cardiomyocyte vacuoles (semithin sections, Azan II, ×400) that at electron microscopy consist of extensive areas of glycogen focally included in an autophagosome (white star). N indicates nucleus; G, glycogen.
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