Mammoth Ventricular Hypertrophy

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A 23-year-old man was referred to the cardiology clinic because of an abnormal ECG and a murmur. He was asymptomatic from the cardiac perspective, and there was no significant family history of cardiac disease or sudden death. He was physically active but was not an athlete and did not exercise regularly. On physical examination, he had a blood pressure of 140/70 mm Hg in both arms with a normal jugular venous pressure of 8 cm water. Cardiac auscultation revealed a soft crescendo-decrescendo systolic murmur heard loudest over the lower left sternal edge. The rest of the physical examination was normal.

His ECG showed sinus rhythm with markedly increased voltages suggestive of left ventricular hypertrophy (Figure 1). His echocardiogram was of very limited quality as a result of poor acoustic windows but was suggestive of left ventricular hypertrophy. Cardiac magnetic resonance cine imaging showed striking mammoth asymmetrical left ventricular hypertrophy with preserved systolic function (Figures 2–4 and Movies I and II in the online-only Data Supplement). The basal septum measured 5.8 cm at its maximum dimension compared with 2.0 cm at the basal inferolateral wall. There was also severe right ventricular hypertrophy with a basal free wall dimension of 1.3 cm. Late-gadolinium-enhancement imaging demonstrated extensive patchy hyperenhancement throughout the myocardium (Figures 5–7 and Movie III in the online-only Data Supplement). A 24-hour Holter monitor showed sinus rhythm throughout.

The differential diagnosis of mammoth left ventricular hypertrophy in adults includes Danon disease, mutations in the gene for the PRKAG2 subunit of adenosine monophosphate–activated protein, and sarcomeric hypertrophic cardiomyopathy. However, the extensive late-gadolinium-enhancement pattern seen in this patient is not typical of sarcomeric hypertrophic cardiomyopathy, which usually shows a patchy midwall distribution with predilection for the anterior and posterior right ventricular insertion sites.

Danon disease is a glycogen storage disease caused by mutations in the X-linked lysosome-associated membrane protein (LAMP2) gene.1 Although noncardiac features such as intellectual impairment and myopathy may be seen in some patients, it can present with an isolated cardiac phenotype of symmetrical or asymmetrical ventricular hypertrophy with pre-excitation. Moreover, it has been associated with particularly massive left ventricular hypertrophy, including the most substantial hypertrophy reported in humans (60–65 mm).1 Early diagnosis is vital because Danon disease leads to a lethal cardiomyopathy, with few patients surviving beyond the third decade of life. Cardiac transplantation offers the best chance for long-term survival.2

PRKAG2 mutations also lead to a glycogen storage disease, which may present with mammoth symmetrical or asymmetrical ventricular hypertrophy and pre-excitation with conduction system disease.3 The prognosis of these patients is significantly better than the prognosis for those with Danon disease.

Given the striking appearances and differential diagnoses in this patient, genetic testing with a commercially available panel (Familion) was performed. Direct sequencing of all coding exons and flanking introns for the following genes associated with ventricular hypertrophy was performed: LAMP2, PRKAG2, α-actin (ACTC), α-galactosidase A (GLA), myosin-binding protein (MYBPC3), β-myosin heavy chain (MYH7), regulatory myosin light chain (MYL2), essential myosin light chain (MYL3), cardiac troponin T (TNNT2), cardiac troponin I (TNNI3), cardiac troponin C (TNNC1), and α-tropomyosin (TPM1).

Interestingly, no mutations were seen in the LAMP2 and PRKAG2 genes. However, he was found to have a sarcomeric mutation in exon 3 of the α-actin (ACTC) gene (His90Tyr). This mutation has previously been described in a pediatric patient with ventricular hypertrophy.4 However, it is important to emphasize that this does not necessarily prove that this is the disease-causing mutation in this case because the presence of novel mutations in other genes cannot be excluded.5 Our patient declined further testing, including endomyocardial biopsy, as well as defibrillator placement. He remains asymptomatic at the 2-year follow-up. This case illustrates the importance of considering the differential diagnosis of mammoth ventricular hypertrophy and the potential utility of cardiac magnetic resonance and genetic testing in this setting.
Disclosures

None.

References


Figure 1. A 12-lead ECG showing sinus rhythm with markedly increased voltages suggestive of left ventricular hypertrophy.

Figure 2. Cardiac magnetic resonance cine imaging in the basal short-axis view showing striking mammoth asymmetrical left ventricular hypertrophy with preserved systolic function. The basal septum measures 5.8 cm at its maximum dimension compared with 2.0 cm at the basal inferolateral wall. There is also severe right ventricular hypertrophy with a basal free wall dimension of 1.3 cm.

Figure 3. Cardiac magnetic resonance cine imaging in the 3-chamber view showing striking mammoth asymmetrical left ventricular hypertrophy with preserved systolic function.
Figure 4. Cardiac magnetic resonance cine imaging in the 4-chamber view showing striking mammoth asymmetrical left ventricular hypertrophy with preserved systolic function.

Figure 5. Late-gadolinium-enhancement imaging in the basal short-axis view showing extensive patchy hyperenhancement throughout the myocardium.

Figure 6. Late-gadolinium-enhancement imaging in the mid short-axis view showing extensive patchy hyperenhancement throughout the myocardium.

Figure 7. Late-gadolinium-enhancement imaging in the apical short-axis view showing extensive patchy hyperenhancement throughout the myocardium.
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