Utility of Cardiovascular Magnetic Resonance in the Diagnosis of Anderson-Fabry Disease

Christopher A. Gange, MD; Mark S. Link, MD; Martin S. Maron, MD

A 54-year-old man was evaluated for a 6-month history of intermittent palpitations with associated shortness of breath, fatigue, and lightheadedness. The episodes would last several hours and were triggered by exertion, although he never experienced syncope. He had no prior medical problems, and he had no family history of heart disease or unexplained sudden death.

He was normotensive and had no abnormalities on physical examination. A 12-lead electrocardiogram showed sinus arrhythmia, left bundle-branch block, and left ventricular (LV) hypertrophy with associated ST- and T-wave strain abnormalities (Figure A). A 2-dimensional echocardiogram demonstrated hyperdynamic LV systolic function with an ejection fraction of 65% (online-only Data Supplement Movie I). There was concentric LV hypertrophy, with the ventricular septum and free wall measuring 17 mm at end diastole. Biatral enlargement was noted, but no valvular disease or LV outflow tract obstruction was present.

A 1-month loop monitor recorded bursts of rapid atrial fibrillation and atrial tachycardia, which corresponded to his

Figure. A 54-year-old man with Anderson-Fabry disease and cardiac involvement. A, Twelve-lead electrocardiogram showing sinus arrhythmia, left bundle branch block, and LV hypertrophy with strain ST- and T-wave abnormalities. B and C, Cine CMR at end diastole in the long-axis 4-chamber view (B) and the basal LV short-axis view (C) demonstrating concentric LV hypertrophy (17 mm maximal wall thickness in ventricular septum and LV free wall) with biatrial enlargement. D, Contrast-enhanced CMR image of the basal LV short axis with an area of late gadolinium enhancement confined to the midmyocardium of the inferolateral wall (arrows). LA indicates left atrium; RA, right atrium; and RV, right ventricle.

From Division of Cardiology, Tufts Medical Center, Boston, Mass.

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Correspondence to Dr Martin S. Maron, Assistant Professor of Medicine, Tufts Medical Center, 800 Washington St, Boston, MA 02111. E-mail mmaron@tuftsmedicalcenter.org

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symptoms. He was initiated on low-dose β-blockade and referred to our institution for further management of cardiac arrhythmias and assessment of risk for sudden death with a presumed diagnosis of hypertrophic cardiomyopathy.

To further characterize cardiac morphology, the patient underwent cardiovascular magnetic resonance (CMR) imaging (online-only Data Supplement Movies II and III). Cine CMR confirmed concentric LV hypertrophy in both the septum and free wall (Figures B and C). After intravenous injection of gadolinium, contrast-enhanced images demonstrated late gadolinium enhancement localized to the midmyocardium of the basal inferolateral wall (Figure D). Late gadolinium enhancement confined to this segment of the LV myocardium is not typical for hypertrophic cardiomyopathy but has been reported in patients with Anderson-Fabry disease (AFD). As a result, the contrast-enhanced CMR finding prompted further testing, and a diagnosis of AFD was ultimately confirmed with a serum α-galactosidase A level of 3 nmol · h⁻¹ · mg⁻¹ (normal range of 50 to 150 nmol · h⁻¹ · mg⁻¹).

AFD is an X-linked lysosomal storage disease caused by deficient activity of the enzyme α-galactosidase A. This inborn error in metabolism can result in the accumulation of glycosphingolipid in multiple organs, including the peripheral nervous system (neuropathic pain), kidneys (hypertension, proteinuria, and renal failure), skin (telangiectasias and angiokeratomas), and central nervous system (blindness and cerebrovascular stroke). Cardiac manifestations include conduction defects, supraventricular and ventricular arrhythmias, and heart failure symptoms associated with progressive LV dysfunction. In addition, concentric LV hypertrophy is common in patients with AFD, producing a cardiac phenotype that can appear similar to other causes of LV hypertrophy, such as hypertrophic cardiomyopathy.

The most common causes of death in AFD are stroke, heart failure, and progressive renal failure. Intravenous enzyme replacement therapy is the current treatment for patients with AFD. Several recent studies have shown a reduction in LV hypertrophy and improvement in systolic function after treatment. Because of the novel treatment strategies currently available to patients with AFD, differentiating this disease from other causes of LV hypertrophy is critical. Contrast-enhanced CMR provides unique information with regard to myocardial tissue characterization, which may influence diagnosis and can therefore serve an important role in the evaluation of patients with unexplained LV hypertrophy.

Disclosures

None.

References

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