Left Ventricular Hypertrophy in a Runner
Things Are Not Always What They Seem

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Case Presentation
A 63-year-old male runner presented for outpatient cardiology evaluation of decreased exercise tolerance and increased left ventricular (LV) wall thickness noted on an echocardiogram obtained by his primary care provider. The patient had been an avid runner since a young age; however, over the previous months he had noted decreased exercise tolerance prompting evaluation by his primary physician. His medical history was only significant for hypertension that had been well controlled with a single medication. ECG revealed sinus bradycardia with markedly elevated voltage in the anterolateral precordial leads (Figure 1). Echocardiography with strain imaging demonstrated increased LV wall thickness measuring 1.8 cm at the basal septum and 1.7 cm at the basal inferolateral wall (Figure 2A). Ejection fraction was noted to be normal; however, longitudinal strain imaging was markedly abnormal throughout the septum, extending into adjacent regions of the anterior and inferior walls and normalizing in the lateral wall and apex (Figure 2B and 2C).

Differential diagnosis at this time included hypertrophic cardiomyopathy, cardiac amyloidosis, Fabry disease, LV hypertrophy attributed to longstanding hypertension, and athlete’s heart, as he was an avid runner. Athlete’s heart generally does not reach wall thicknesses >15 mm, and his hypertension had been well controlled; thus, hypertrophic cardiomyopathy was thought to be the most likely diagnosis. A cardiac magnetic resonance imaging subsequently demonstrated LV thickening most prominent throughout the septum that spared the middle and apical lateral walls (Figure 2D). Late gadolinium enhancement (LGE) was seen throughout the thickened segments (Figure 2E and 2F, black arrows) corresponding with areas of abnormal longitudinal strain seen on echocardiography. Precontrast and postcontrast T1 mapping demonstrated abnormal precontrast (1207 ms) and postcontrast (345 ms) T1 times, resulting in an extracellular volume percentage of 42% (Figure 2G and 2H). The pattern of LGE and T1 mapping was most consistent with an infiltrative process prompting endomyocardial biopsy. The biopsy specimen stained positive for Thioflavin S under UV microscopy (Figure 3A, white arrows), indicating amyloid deposits and that immunohistochemical staining for transthyretin was positive (Figure 3B, black arrows). Genetic testing failed to identify a heritable mutation on the transthyretin (TTR) gene; thus diagnosis of wild-type TTR cardiac amyloidosis was made.

Discussion
This case demonstrates an atypical presentation of TTR cardiac amyloidosis with many findings that, although described, are not typical in cardiac amyloidosis, as well as the additive diagnostic support that multimodality imaging can provide. Classically, patients with cardiac amyloidosis have low voltage on ECG, although our patient had normal limb lead voltages with increased voltage in V4/V5. Interestingly, 1 series of patients with TTR amyloidosis found that 25% actually had electrocardiograms that met LV hypertrophy criteria. Echocardiography generally demonstrates increased LV wall thickness with preserved ejection fraction, biatrial enlargement, valvular thickening, intraatrial septum thickening, and abnormal longitudinal strain sparing the apex. This relative apical sparing seen on longitudinal strain imaging has been shown to be both sensitive and specific in differentiating cardiac amyloidosis from other causes of increased LV wall thickness. Although our patient did have preservation of longitudinal strain at the apex, he was also noted to have normal strain in his lateral wall, likely explained by a lack of LGE of the lateral wall, indicating a relative absence of amyloid infiltration of this region. In cardiac amyloidosis, cardiac magnetic resonance imaging typically demonstrates diffuse transmural or diffuse subendocardial LGE, although focal LGE is seen in a small percentage of cases. Cardiac magnetic resonance imaging may also demonstrate LGE in the atria, abnormal gadolinium kinetics, and general findings including increased LV and right ventricular thickness. As demonstrated in this case, noncontrast T1 mapping and quantification of extracellular volume are elevated in both TTR and light-chain cardiac amyloidosis when compared with patients with hypertrophic cardiomyopathy and normal subjects. Noncontrast T1 times >1090 ms and extracellular volume fraction >40% have been shown to be highly specific for cardiac amyloidosis. In our patient, the noncontrast T1 time was 1207 ms, and the extracellular volume fraction was 42%.

Disclosures
None.

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References


Figure 1. ECG demonstrating sinus bradycardia with increased voltage throughout the anterolateral precordial leads.
Figure 2. A, Two-dimensional echocardiogram in the parasternal long-axis view showing significant thickening of the anteroseptal (1.8 cm) and inferolateral (1.7 cm) walls. B and C, Longitudinal strain imaging demonstrating abnormal strain throughout the septum extending into the adjacent walls that normalized in the lateral wall and apex seen here on the apical 4-chamber view and the polar map. D, Cardiac magnetic resonance imaging 4-chamber view showing increased wall thickness of the septum and basal lateral wall that normalizes in the distal lateral wall. E and F, Late gadolinium enhancement of the thickened segments seen on the 4-chamber view and throughout the septum seen on the short-axis view (black arrows) that largely spared the lateral and inferolateral walls (white arrows). Precontrast (G) and postcontrast (H) T1 mapping demonstrated abnormal septal precontrast (1207 ms) and postcontrast (345 ms) T1 times, as well as an extracellular volume fraction of 42%, consistent with infiltrative disease.

Figure 3. A, Endomyocardial biopsy specimen stained positive for Thioflavin S under UV microscopy (white arrows) indicating amyloid deposits. B, Immunohistochemical stained positive for transthyretin (black arrows).
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