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Myocardial Tissue Characterization With CMR for the Definitive Diagnosis of Infiltrative Cardiomyopathies

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TRANSTHORACIC ECHOCARDIOGRAPHY IS THE INITIAL IMAGING MODALITY USED FOR THE EVALUATION of cardiomyopathies but lacks the diagnostic specificity of cardiac magnetic resonance (CMR) myocardial tissue characterization. Although administration of gadolinium aids in CMR tissue characterization, native myocardial T1, T2, and T2* properties provide important diagnostic information. This group of 4 patients demonstrates the value of CMR toward making an accurate diagnosis and its impact on clinical decision making. The associated figures (Figures 1 to 5) for these cases highlight their clinical presentations and electrocardiographic and echocardiographic findings leading to an initial presumptive diagnosis. In all 4 cases, CMR with tissue characterization led to a modification of the diagnosis, changes in the treatment plan, and improved understanding of the underlying prognosis (Figure 6).

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FIGURE 1. Case A: Clinical and Multimodality Imaging Findings

Case A was a 62-year-old man with paroxysmal atrial fibrillation. The electrocardiogram depicted sinus rhythm, a short PR interval, and left ventricular hypertrophy (LVH) (A). Echocardiography demonstrated severe LVH and right ventricular (RV) hypertrophy (B,C) without outflow tract obstruction, normal systolic function, and grade III diastolic dysfunction (D). The presumptive diagnosis was hypertrophic cardiomyopathy (HCM). Cardiac magnetic resonance for risk stratification demonstrated severe concentric LVH (E). Pre- and post-contrast myocardial T1 maps depicted a low pre-contrast native T1 time with a normal extracellular volume (ECV) fraction (F,G). The long-axis (H to J) late gadolinium enhancement (LGE) images demonstrated no underlying replacement fibrosis. The differential diagnosis for a low native myocardial T1 time includes Anderson-Fabry disease and hemochromatosis. T2* decay time was normal, thereby excluding iron-overload cardiomyopathy (K). Patients with Fabry disease often have basal anterolateral and

inferolateral midwall LGE in contrast to RV insertion point and patchy LGE in the hypertrophied segments seen in HCM.

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FIGURE 2. Case A: Family Pedigree

Given these findings, there was a high suspicion for Anderson-Fabry disease, a lysosomal storage disease. Case A's alpha-galactosidase activity level was low at <0.2 (normal >1.2). Genetic testing revealed a hemizygous Anderson-Fabry cardiac-variant mutation (p.I232T), which is characterized by men presenting with cardiomyopathy in the fifth to eighth decade of life versus the classic phenotype that presents in childhood or adolescence. A detailed family pedigree was obtained. Case A is denoted by a **single asterisk**. His brother (******) was found to be affected, and his daughter, case A's niece, is a carrier (*******). It is assumed that their mother (********) was a carrier and passed the gene on to 2 of her 4 children. The patient was started on enzyme replacement therapy.

FIGURE 3. Case B: Clinical and Multimodality Imaging Findings

Case B was a 39-year-old man with palpitations. Echocardiography showed right ventricular (RV) dilation (A) and diastolic mitral regurgitation (B), commonly associated atrioventricular conduction disease as seen on initial electrocardiography (ECG) (C). Arrhythmogenic RV cardiomyopathy and other causes of RV dilation were in the differential diagnosis. Cardiac magnetic resonance showed patchy late gadolinium enhancement (LGE) (E,F). T2 black blood fat-saturated (G) and corresponding short-axis LGE slices (H) showed the matching pattern of increased T2 hyperintensity and LGE indicating active inflammation and edema, suggesting an inflammatory cardiomyopathy. Scout images showed hilar and peribronchial lymphadenopathy (I). Lymph node transbronchial biopsy revealed noncaseating granulomas consistent with cardiac sarcoidosis (J). Follow-up ECG showed progression of conduction disease with complete heart block (D). Despite normal systolic function, given the diagnosis of cardiac sarcoidosis, an internal cardioverter-defibrillator was

implanted. These patients are at high risk for ventricular tachyarrhythmias, and if there is an indication for permanent pacing, a defibrillator is recommended.

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FIGURE 4. Case C: Multimodality Imaging Findings

Case C was a 37-year-old man with sickle-cell disease admitted with decompensated heart failure. Echocardiography demonstrated a dilated left ventricle (A), mitral valve B bump indicative of elevated filling pressures (B), severe left atrial enlargement (C), and a grade III diastolic filling pattern (D) consistent with a restrictive cardiomyopathy. Patients with sickle-cell disease often receive blood transfusions, leading to excess iron stores. Cardiac magnetic resonance (CMR) demonstrated reduced T2* decay time (E,F). CMR detects iron indirectly using its paramagnetic effects that shorten relaxation times (T1, T2, and T2*). T2* time is inversely related to myocardial iron content (abnormal <20 ms). T2* mapping is a reliable and reproducible method of quantifying myocardial iron and is the only parametric mapping technique recommended for disease specific guidelines. T2* can identify patients at cardiovascular risk and can track progression and treatment response. The patient died prior to initiation of chelation therapy and follow-up imaging.

FIGURE 5. Case D: Clinical and Multimodality Imaging Findings

Case D was a 70-year-old man with a history of extracardiac sarcoidosis who was referred for evaluation of cardiac involvement. Electrocardiography showed low voltage in the limb leads and a septal infarct pattern (A). Echocardiography demonstrated moderate concentric left ventricular hypertrophy (B), a thickened interatrial septum (C), low tissue Doppler velocities (D,E), pseudonormal diastolic mitral inflow pattern (F), and reduced global longitudinal strain with apical sparing (G) leading to suspicion for an alternative diagnosis. Cardiac magnetic resonance (CMR) pre- and post-contrast myocardial T1 maps (H,I) demonstrated elevated native T1 time and extracellular volume fraction (J). There was extensive subendocardial and atrial wall late gadolinium enhancement (K to P). The CMR findings were highly suggestive of cardiac amyloidosis. Endomyocardial biopsy showed cardiac myocytes with patchy areas of interstitial expansion by amorphous-appearing extracellular material on hematoxylin-eosin stain (Q) and positive Congo red staining with apple green birefringence (R) indicating amyloid fibril deposition. Genetic testing was positive for 2 abnormal transthyretin variants.

FIGURE 6. Added Value of Myocardial Tissue Characterization With Cardiac Magnetic Resonance in the Diagnosis of Infiltrative Cardiomyopathies

In 4 patients, a presumptive diagnosis of a cardiomyopathy was obtained after assessing the clinical history and electrocardiographic and echocardiographic findings. In patient A, the initial diagnosis was a hypertrophic cardiomyopathy, and cardiac magnetic resonance (CMR) was performed for risk stratification. A markedly low T1 relaxation time suggested the presence of Anderson-Fabry disease, later confirmed with alpha-galactosidase and genetic testing. Patient B had palpitations, and because of an enlarged right ventricle, arrhythmogenic right ventricular cardiomyopathy was suspected. CMR showed patchy late gadolinium enhancement (LGE) consistent with sarcoidosis, leading to a confirmatory lymph node biopsy. Patient C had a dilated cardiomyopathy with a restrictive Doppler pattern. CMR was performed to evaluate the etiology. A severely reduced T2* decay time was consistent with myocardial iron overload. Patient D had presumed diagnosis of cardiac sarcoidosis. CMR revealed diffuse subendocardial LGE, prolonged native T1 time, and

markedly increased extracellular volume fraction suggesting cardiac amyloidosis, subsequently confirmed with histopathology.

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