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A young adult with Friedreich ataxia

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CLINICAL INTRODUCTION

A young adult with Friedreich ataxia complaining of exertional breathlessness underwent a cardiological evaluation. On physical examination, high blood pressure and a loud systolic murmur were noted. ECG showed sinus rhythm with voltage criteria for left ventricular hypertrophy (LVH) and T-wave changes in the inferolateral leads. Transthoracic echocardiography showed biventricular hypertrophy (maximum wall thickness of the interventricular septum 26 mm and 16 mm of the posterior wall), preserved systolic function, mild left ventricular intracavity gradient and an unremarkable mitral and aortic valve. A cardiovascular magnetic resonance (CMR) was requested for further assessment. CMR protocol, performed using a 1.5 Tesla scanner, included cine images (Fig.1a), native and post contrast T1 mapping (shMOLLI, Fig.1b and c), early and late gadolinium enhancement (LGE) images (Fig.1d,e and f). Native T1 values were mildly reduced ($\cong 911$ ms) in the septum and low-normal range (942-974 ms) in the lateral walls. Normal values 962 ± 25 ms at 1.5 Tesla. Post-contrast T1 values were diffusely reduced.

Which is the most likely diagnosis based on these findings?

- a) Anderson-Fabry's disease
- b) Hypertensive heart disease
- c) Hypertrophic cardiomyopathy
- d) Myocardial iron load
- e) Cardiac amyloidosis

ANSWER: D

In this case, reduced native T1 values may be explained by a mild cardiac iron accumulation, which has been described in autaptic Friedreich ataxia hearts⁽¹⁾.

Myocardial T1 mapping has been proposed as a method of detection of mild iron overload⁽²⁾. Friedreich ataxia is an inheritable mitochondrial disorder caused by the mutation of frataxine. Although the pathophysiology is not completely clear, it is commonly accepted that frataxine is involved in mitochondrial iron metabolism⁽³⁾. Cardiac involvement in Friedreich ataxia is a leading cause of heart failure and mortality and early tissue mapping changes can be detected by CMR⁽⁴⁾. Iron mediated cellular damage may represent an early stage of cardiomyopathy in these patients.

LVH phenotype can be observed in cardiac amyloidosis, hypertensive heart disease and hypertrophic cardiomyopathy. However, none of these conditions characteristically exhibit low native T1 values⁽⁵⁾, in fact native T1 mapping values are usually increased (options B, C and E excluded – Supplementary Figure). Moreover, early and LGE images do not show a typical amyloidosis pattern. Reduced native T1 values are also observed in lipid accumulation (Anderson-Fabry’s disease)⁽⁵⁾, but in a patient with a known diagnosis of Friedreich’s ataxia, the coexistence of these rare conditions is unlikely.

CMR is a useful tool to investigate cardiac involvement in Friedreich ataxia. Further larger studies are needed to confirm these findings.

Contributors CB-D and EM are responsible of the concept of the manuscript and wrote the manuscript, IH and CB-D reviewed the manuscript. IH obtained informed written consent.

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Competing interests None to declare

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a) Basal short axis cine; b) Native T1 mapping basal short axis; c) Post contrast T1 mapping basal short axis; d) Early gadolinium enhancement basal short axis; e) Basal short axis LGE; f) Three-chamber LGE.

200x134mm (72 x 72 DPI)

Supplementary Figure

a) Basal short axis cine showing septal hypertrophy (maximal wall thickness of the basal anterior septum 20 mm); b) Native T1 mapping values in the basal short axis; c) Post contrast T1 mapping values in the basal short axis; d) Early gadolinium enhancement basal short axis showing normal gadolinium kinetics and no hyperenhancement, thus excluding cardiac amyloidosis; e) Basal short axis showing LGE in the lateral wall (yellow arrow); f) Three-chamber showing LGE in the lateral wall (yellow arrow).