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The gatekeeper images in hypertrophic cardiomyopathy: the role of native T1 mapping in Anderson-Fabry disease

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Abstract

We presented a case of a 49-year-old presenting with atypical chest pain and hypertrophic phenotype cardiomyopathy without coronary artery disease. At cardiac magnetic resonance (CMR), the left ventricle was of normal volumes and preserved global ejection fraction with asymmetric wall hypertrophy. The evaluation of native myocardial T1 has been calculated at an average global value of 924 ms, compatible with hypertrophic phenotype cardiomyopathy with reduced native T1 values as observed in Anderson-Fabry disease. The genetic analysis confirmed the Anderson-Fabry disease with a mutation in the exon 5 of the *GLA* gene, revealing the mutation c.644 A>G. This case report demonstrated that the images obtained in CMR and the analysis of the T1 native mapping, compared with the normal values obtained in the Center, may be considered a gatekeeper in the diagnostic assessment, avoiding redundant examinations, and reducing costs, and radiological exposure.

Key words: Anderson-Fabry disease, cardiac MRI, cardiac imaging, differential diagnosis.

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Case Report

This is the case of a 49-year-old man, presenting with atypical chest pain and hypertrophic phenotype cardiomyopathy without coronary artery disease at coronary computed tomography. The 12-lead electrocardiogram showed a sinus rhythm with hypertrophy of the left ventricle. At cardiac magnetic resonance (CMR), the left ventricle was of normal volumes and preserved global ejection fraction (64%). Asymmetric wall hypertrophy located in the septum, with a maximum thickness of 18 mm in the basal inferior septum, and 16 mm in the basal anterior septum, emerged. The parametric acquisitions for the evaluation of native myocardial T1 have been calculated an average global value of 924 ms (clearly reduced), with lower values on the basal septum equal to 886 ms and an extracellular volume (ECV) of 19.4% (slightly reduced) (normal values in our Center: T1 990±42 ms ; ECV 26±3%). The parametric acquisitions for the evaluation of native myocardial T2 (not shown) showed a value equal to 46-47 ms (normal). Late acquisitions after administration of gadolinium contrast revealed minimal and very low intensity intramyocardial fibrosis in the basal inferior septum and mid-basal posterior junctional area. The MR picture is compatible with hypertrophic phenotype cardiomyopathy with reduced native T1 and ECV values as observed in Anderson-Fabry disease (AFD) (Figure 1).

After cardiac magnetic resonance imaging, in order to discriminate the doubt of an infiltrative cardiomyopathy in AFD, a genetic study with enzymatic assessment has been performed. The value of enzymatic activity of α-galactosidase A proved to be 1.3 nmoli/mL/h (normal value >3 nmoli/mL/h). In the exon 5 of the *GLA* gene, the mutation c.644 A>G was revealed, determining the substitution from asparagine to serine aminoacid (p.N215S). The ferric profile of the patient as well as the ferritin resulted normal, so a diagnosis of AFD was performed. A specific therapy with migalastat (123 mg once daily on alternate days) has been started after the diagnosis.

Discussion

AFD is classified as an X-linked storage disorder caused by the abnormal activity of a lysosomal enzyme called α-galactosidase A. The accumulation of glycosphingolipids in several tissues is the pathological characteristic that generates different disease phenotypes according to the extent and severity of the involved organ [1,2]. In fact, renal failure, cardiomyopathy, as well as peripheral and central nervous system involvement are the main causes of morbidity in these patients [3]. Cardiomyopathy is the leading cause of death in AFD, accounting for 38% of all-cause mortality [1].

CMR represents the predominant non-invasive and multipara-

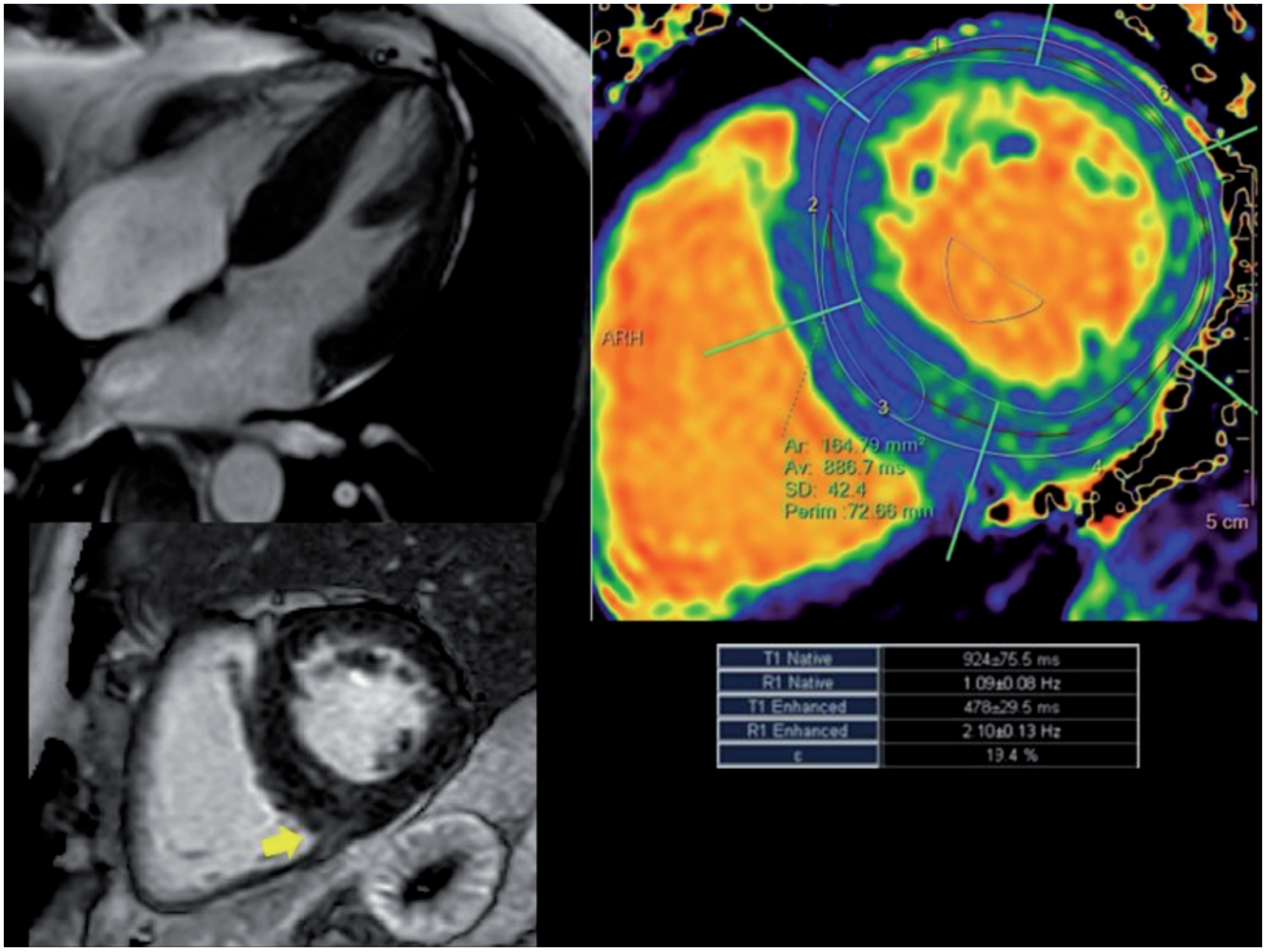

Figure 1. Cardiac magnetic resonance images with native T1 mapping. The yellow arrow indicates intramiocardial fibrosis.

metric imaging modality for the assessment of cardiac involvement. Tissue characterization with late gadolinium enhancement (LGE) has become the gold standard for highlighting focal myocardial fibrosis or scar, giving information about the underlying pathophysiology, prognosis, and response to treatment. However, the qualitative interpretation of LGE requires regional relative differences in the signal intensity between normal and abnormal myocardium and is unable to detect diffuse myocardial disease. CMR parametric mapping has overcome this limitation, allowing absolute quantification of myocardial changes at both the intracellular/extracellular levels. T1 and T2 mapping permit both visualization and quantification of the disease process, independently of whether the myocardial disease is focal or diffuse, and may help in the diagnosis of glycosphingolipid accumulation [4-6]. In particular, T1 mapping measures the longitudinal or spin-lattice relaxation time of the myocardium without administration of a contrast agent, which is determined by how rapidly protons re-equilibrate their spins after being excited by a radiofrequency pulse. Currently used T1 mapping methods acquire a set of non-segmented raw images within separate cardiac cycles of a single breath-hold. As a result, the acquisition duration for each raw image is limited to approximately 200 ms within the cardiac cycle, which limits the spatial resolution that can be achieved. The are two most important biological causes to explain an increase in native T1: i) edema (increase of tissue water in *e.g.*, acute infarction or inflammation) or ii) increase of interstitial space (*e.g.*, fibrosis of infarction (scar) or cardiomyopathy, and in amyloid deposition). If a reduction of native T1 values occurs, the two possible explanations are: lipid overload (*e.g.*, AFD, lipomatous metaplasia in chronic myocardial infarction) or iron overload.

We report a case in which the prominent septal hypertrophy is not associated with marked fibrosis and/or localized in the basal inferolateral wall, typical of Anderson-Fabry cardiomyopathy [7]. Just the reduced native T1, in the absence of areas of pseudonormalized or increased T1 indicative of possible focal fibrosis, guided the diagnostic suspicion, directing the subsequent genetic research.

Conclusions

This case report demonstrated that the images obtained in CMR and the analysis of the T1 native mapping, compared with the normal values obtained in the Center, may be considered as a

gatekeeper in the diagnostic assessment, avoiding redundant examinations, reducing costs, and radiological exposure.

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