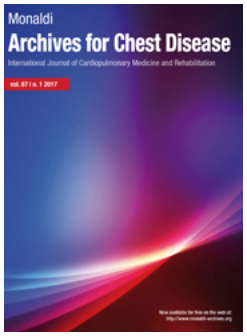

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The gatekeeper images in hypertrophic cardiomyopathy: the role of native T1 mapping in Anderson-Fabry disease

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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 an 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, reducing costs, and radiological exposure.

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

Case Report

This is the case of a young man of 49 years old, presenting with atypical chest pain and an hypertrophic phenotype cardiomyopathy without coronary artery disease at coroTC. The 12-lead ECG showed a sinus rhythm with an hypertrophy of the left ventricle. At cardiac magnetic resonance (CMR) the left ventricle was of normal volumes and preserved global ejection fraction (EF 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 has been calculated an average global value of 924 ms (clearly reduced) with lower values on the basal septum equal to 886 ms and an ECV of 19.4% (slightly reduces) (normal values in our Centre: T1 990 ± 42ms ; 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 gadoliunium 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 (Figure 1).

After cardiac MRI, in order to discriminate the doubt of an infiltrative cardiomyopathy in Anderson-Fabry disease, a genetic study with enzimatic assesment has been performed. The value of enzimatic activity of alpha-galactosidase A proved to be 1.3 nmoli/ml/h (normal value>3 nmoli/ml/h). In the exon 5 of the GLA gene it was revealed the mutation c.644 A>G determining the substitution from asparagine to serine aminoacid (p.N215S). The ferric profile of the patient as well as the ferritin resulted normal, than a diagnosis of Anderson-Fabry disease has been performed. A specific therapy with migalastat (123 mg once daily on alternate days) has been started after the diagnosis.

Discussion

Anderson-Fabry disease (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 predominat non-invasive e multiparametric imaging modality for the assessment of cardiac invelvement. Tissue characterisation with late gadolinium enhancement (LGE) has become the gold standard for highlihting focal myocardial fibrosis or scar, giving information about the underlying pathophysiology , prognosis and respose to treatment. However, the qualitative interprestation of LGE requires regional relative differences in the signal intensity between normal and abnormal myocardium and is unable to dectect diffuse myocarrdial disease. CMR parametric mapping have overcome this limitation, allowing absolute quantification myocardial of myocaardial changes both at intracellular/extracellular level. T1 and T2 mapping permit both visualization and quantification of the disease process, independently of wheter the myocardial disase is focla or diffuse and may help in the diagnosis of glycosphingolipids accumlation [4-6]. In paticular, 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: a) oedema (increase of tissue water in e.g. acute infarction of inflammation) or b) 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. Anderson-Fabry disease, 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 oncreased 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 cardiac MRI and the analysis of the T1 native mapping, compared with the normal values obtained in the Centre, may be

considered as a gatekeeper in the diagnostic assesment, avoiding redundant examinations , reducing costs and radiological exposure.

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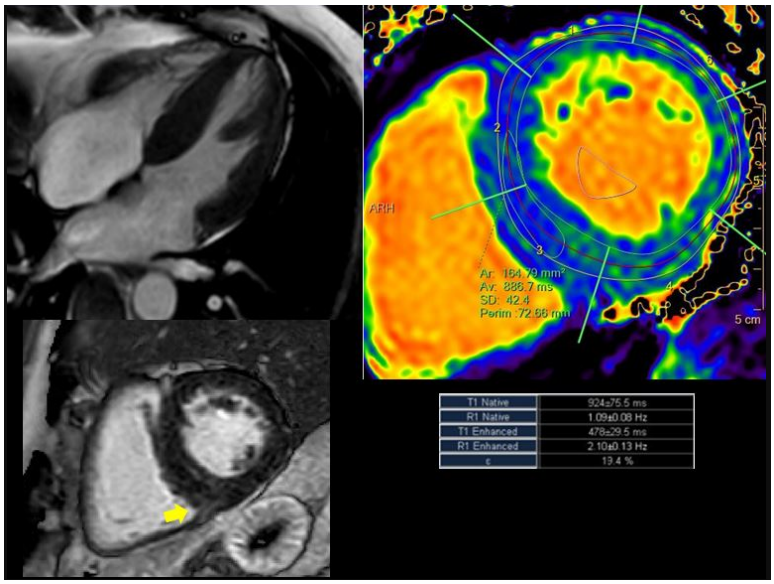

Figure 1. Cardiac magnetic resonance images with native T1 mapping. The yellow arrow indicates intramiocardial fibrosis.