Unusual scarring patterns on cardiac magnetic resonance imaging: A potentially treatable etiology not to be missed

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A case of cardiomyopathy and ventricular tachycardia previously assumed to be idiopathic in origin is described. Investigation with cardiac magnetic resonance imaging prompted the diagnosis and successful treatment of an underlying disorder based on typical scarring patterns seen with late gadolinium enhancement. The present report suggests that clinicians should have a low threshold for actively excluding this condition in patients presenting with cardiomyopathy, even in the absence of other disease features, particularly if typical scarring patterns are found on cardiac magnetic resonance imaging because disease-specific therapy appears to significantly improve both symptoms and prognosis.

Key Words: *Cardiomyopathy; CMR; Fabry; Ventricular tachycardias*

A 47-year-old man presented with a history of symptomatic aortic regurgitation with left ventricular cavity dilation necessitating valve replacement. Despite a well-functioning prosthesis, he developed deteriorating exercise capacity over the following three years, culminating in shortness of breath on minimal exertion and episodic exertional syncope. He had no significant extracardiac symptoms, previous medical diagnoses or family history. Plasma brain natriuretic peptide was found to be elevated at 50 ng/L, while both urea and creatinine were within normal limits. Transthoracic echocardiography showed global left ventricular systolic dysfunction with an akinetic basal posterior segment and severe functional mitral regurgitation. Coronary angiography demonstrated unobstructed arteries. Invasive electrophysiological testing identified an easily inducible hemodynamically unstable monomorphic ventricular tachycardia (Figure 1). Subsequent cardiac magnetic resonance imaging revealed a mildly dilated left ventricle, concentric hypertrophy (Table 1) and diffuse mesocardial late gadolinium enhancement in the basal inferolateral wall with relative endocardial sparing, consistent with nonischemic cardiomyopathy (Figure 2). Owing to this unusual scarring pattern, serum and leukocyte alpha-galactosidase levels were measured and found to be low, consistent with Fabry disease. The diagnosis was confirmed on genetic testing. Accordingly, the patient was started on enzyme replacement therapy (ERT), with an excellent symptomatic response to treatment.

DISCUSSION

Fabry disease is an X-linked (Xq22) lysosomal storage disease caused by a deficiency of alpha-galactosidase A, leading to accumulation of globotriaosylceramide and other glycosphingolipids in the lysosomes of many cells and organs. Its incidence, reported to be one in 55,000 live male births, is almost certainly underestimated as a result

Des motifs de cicatrisation inhabituels à l'imagerie par résonance magnétique cardiaque : Une étiologie au potentiel traitable à ne pas négliger

Les auteurs décrivent un cas de cardiomyopathie et de tachycardie ventriculaire qu'on croyait auparavant être d'origine idiopathique. Les explorations par imagerie par résonance magnétique (IRM) cardiaque ont suscité le diagnostic et le traitement réussi d'une maladie sous-jacente fondée sur des motifs de cicatrisation caractéristiques observés grâce à un contraste tardif au gadolinium. Selon le présent rapport, les cliniciens devraient avoir un faible seuil avant d'exclure activement ce trouble chez des patients qui consultent à cause d'une cardiomyopathie, même en l'absence d'autres particularités pathologiques, surtout s'ils observent des motifs de cicatrisation caractéristiques à l'IRM cardiaque, car une thérapie axée sur la maladie semble améliorer considérablement à la fois les symptômes et le pronostic.

Figure 1) Electrophysiological testing. Monomorphic ventricular tachycardia of a morphology consistent with a location at the midventricular level of the posterior wall

TABLE 1
Ventricular wall dimensions obtained from cardiac magnetic resonance imaging

	EDV, mL	ESV, mL	SV, mL	EF, %	Maximum wall thickness, mm	Mass, g (g/m ²)
LV	291	148	143	49	17	332 (138)
RV	238	87	151	64	—	—

EDV End-diastolic volume; EF Ejection fraction; ESV End-systolic volume; LV Left ventricle; RV Right ventricle; SV Stroke volume

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Figure 2) Cardiac magnetic resonance imaging without (A) and with (B) late gadolinium enhancement, demonstrating an area of mesocardial fibrosis or infiltration with endocardial sparing within the basal and midventricular myocardium

of misdiagnoses, particularly of milder variants (1). While traditionally described in men, approximately 70% of heterozygous women also show clinical disease phenotypes, although these are usually milder and of later onset than their male counterparts. In men, symptoms typically start in the second or third decade of life. Common presenting features include neuropathic pain, gastrointestinal disturbance, angiokeratomas, stroke and chronic renal failure. Cardiac involvement, including phenotypic hypertrophic or dilated cardiomyopathy, conduction abnormalities or ventricular tachycardia, occurs in

approximately two-thirds of patients and may be the only clinical manifestation. The posterolateral left ventricular wall seems to be particularly prone to focal involvement (2); this feature on cardiac imaging should prompt further investigation.

Cardiac Fabry disease appears to account for a significant proportion of cardiomyopathy of unknown etiology, with systematic testing of men presenting with late-onset hypertrophic cardiomyopathy finding that 6% had Fabry disease (3). However, owing to its perceived rarity and heterogeneous clinical features, the average delay from symptom onset to diagnosis of Fabry disease is 13.7 years for men and 16.3 years for women (4). The initial investigation is with measurement of alpha-galactosidase A levels in plasma or leukocytes, which are markedly reduced in Fabry disease. Diagnostic confirmation is obtained through analysis of the *GLA* gene, in which more than 300 different mutations have been shown to cause clinically significant enzyme deficiency. Once diagnosed, routine measures include symptomatic relief, and aggressive management of complications and comorbid conditions. In addition to this, ERT has been shown to confer an improvement in symptoms, left ventricular dimensions (5) and renal function.

In the present case, a diagnosis of Fabry disease was primarily considered in a patient with dilated cardiomyopathy and ventricular tachycardia following demonstration of typical scarring patterns affecting the posterolateral wall of the left ventricle on cardiac magnetic resonance imaging. However, it could be argued that measurement of serum alpha-galactosidase A levels should have been considered earlier, in particular with the finding of an akinetic basal posterior segment of the left ventricle on echocardiography in the absence of coronary artery disease, or even in the initial assessment of late-onset cardiomyopathy in a male patient. Therefore, we suggest that clinicians need to maintain a low threshold for testing for Fabry disease in patients with heart failure or monomorphic ventricular tachycardia, even in the absence of extracardiac disease features. As illustrated in the present case, the measurement of serum alpha-galactosidase A levels should certainly be performed if scarring or systolic dysfunction predominantly affecting the posterolateral left ventricular wall is seen on cardiac imaging. Early diagnosis is particularly important because ERT is known to reduce symptoms and may improve prognosis in Fabry disease.

REFERENCES

1. Spada M, Pagliardini S, Yasuda M, et al. High incidence of later-onset Fabry disease revealed by newborn screening. *Am J Hum Genet* 2006;79:31-40.
2. Sechtem U, Mahrholdt H, Vogelsberg H. Cardiac magnetic resonance in myocardial disease. *Heart* 2007;93:1520-7.
3. Sachev B, Takenaka T, Teraguchi H et al. Prevalence of Anderson-Fabry disease in male patients with late onset hypertrophic cardiomyopathy. *Circulation* 2002;105:1407-11.
4. Mehta A, Ricci R, Widmer U, et al. Fabry disease defined: Baseline clinical manifestations of 366 patients in the Fabry Outcome Survey. *Eur J Clin Invest* 2004;34:236-42.
5. Hughes DA, Elliott PM, Shah J, et al. Effects of enzyme replacement therapy on the cardiomyopathy of Anderson-Fabry disease: A randomized, double-blind, placebo-controlled clinical trial of agalsidase alfa. *Heart* 2008;94:153-8.