

An uncommon left ventricular hypertrophy: A misdiagnosed etiology!

Une cardiomyopathie hypertrophique inhabituelle: Une étiologie méconnue.

Omar Guerhazi, Leila Abid, Rania Hammami, Salma Charfeddine, Faten Triki, Dorra Abid, Samir Kammoun

Service De Cardiologie, Hôpital Hédi Chaker, Sfax

Résumé

L'approche diagnostique devant l'hypertrophie ventriculaire gauche reste problématique compte tenu de la longue liste des étiologies et la contribution de plusieurs outils pour élucider le diagnostic approprié. Nous décrivons un cas rare d'une hypertrophie ventriculaire gauche rare ainsi que notre approche pour atteindre le diagnostic de la maladie de Fabry qui présente plusieurs particularités cliniques et d'imagerie.

Mots-clés

Fabry, cardiomyopathie hypertrophique, IRM cardiaque

Summary

Diagnostic approach in front of left ventricular hypertrophy remains problematic considering the long list of etiologies and the contribution of several tools to elucidate the appropriate diagnosis. We describe a rare case of an uncommon left ventricular hypertrophy as well as our approach to achieve the appropriate diagnosis of Fabry disease which presents several clinical and imaging particularities.

Keywords

Fabry, hypertrophic cardiomyopathy, cardiac MRI

Correspondance

Omar Guerhazi

Service de cardiologie, hôpital Hédi Chaker, Sfax

mail: omar.guer.med@gmail.com

INTRODUCTION

Left ventricular hypertrophy (LVH) is a challenging situation in daily cardiology practice. Several etiologies could be involved, among which Fabry disease. This latter consists on a rare and hereditary storage disease that affects many cell types causing several organ dysfunctions. The cardiomyocyte may be concerned by this systemic damage. We report an unusual case of left ventricular hypertrophy consisting in a Fabry disease, from which we present our approach in front of LVH finding on transthoracic echocardiography (TTE).

CASE REPORT

An 18 years old man was admitted in our cardiology department for chest pain with lipothymia. He was a smoker and his uncle suddenly died at the age of six. At presentation, neither physical examination nor biological testing concluded to particular abnormalities. An electrocardiogram (ECG) was first performed. It showed regular sinus rhythm at 50 beats per minute, limit PR interval at 110 to 120 milliseconds without preexcited QRS complexes and biventricular hypertrophy with negative T waves in the anterior leads (**Figure 1**).



Figure 1 : Electrocardiographic findings : limit PR interval at 120 ms and biventricular hypertrophy.

In front of such pathological findings on ECG, a TTE was indicated. This exam revealed a concentric and symmetrical left ventricular hypertrophy (LVH) with a maximal wall thickness of 38 mm, a systolic anterior motion of the mitral valve without significant regurgitation but with an intraventricular obstruction with a maximal gradient of 190 mm Hg. This LVH was associated with a right ventricular hypertrophy (**Figure 2**). Otherwise, there were no increased afterload

conditions such as arterial hypertension or aortic stenosis. In front of this unexplained ventricular hypertrophy with uncommon features against the diagnosis of a classical hypertrophic cardiomyopathy, we completed by more advanced imaging investigations. A speckle tracking study was performed. It showed an alteration of the global longitudinal strain of -5.2% with the deeper alteration concerning the posterolateral wall of the left ventricle (**Figure 3**). Likewise, a cardiac magnetic resonance imaging (MRI) concluded to a concentric and symmetrical biventricular hypertrophy with intramural late gadolinium enhancement (LGE) in the posterolateral wall of the left ventricle which indicates the presence of fibrosis in this zone (**Figure 4**). These features, namely a concentric and symmetrical biventricular hypertrophy affecting a young male with sinus bradycardia, limit to short PR interval and high voltage QRS on ECG, signs of fibrosis involving particularly the posterolateral wall of the left ventricle as revealed by the speckle tracking and cardiac MRI are consistent with the diagnosis of Fabry disease. In order to confirm this diagnosis we carried out a dosing of α -galactosidase in leukocytes which concluded to a low activity of this enzyme, confirming the diagnosis of Fabry disease.

Our patient was lost to follow up and did not benefit from the enzyme replacement therapy, a specific treatment of Fabry disease.

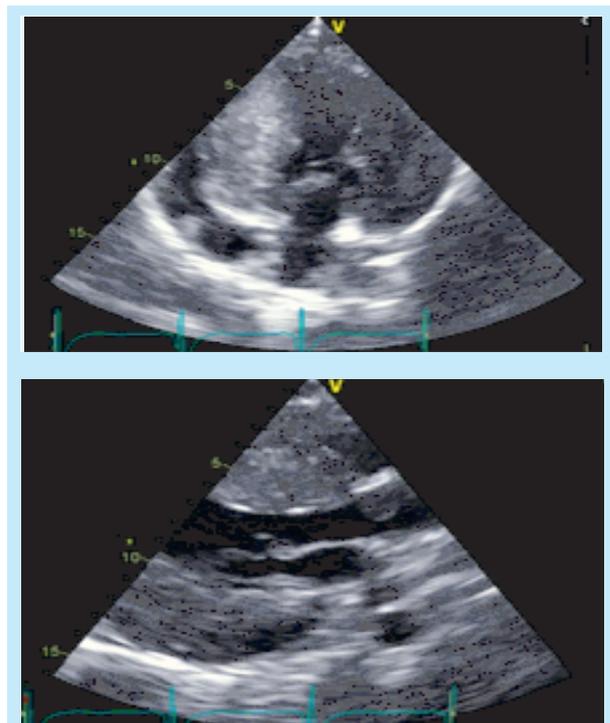


Figure 2: Echocardiographic findings: concentric and symmetrical left ventricular hypertrophy associated to right ventricular hypertrophy.

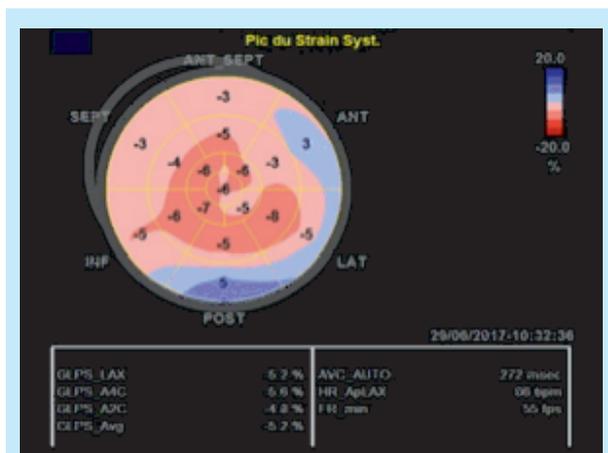


Figure 3: Speckle tracking findings: alteration of global longitudinal strain, which is deeply marked in the posterolateral left ventricular wall.

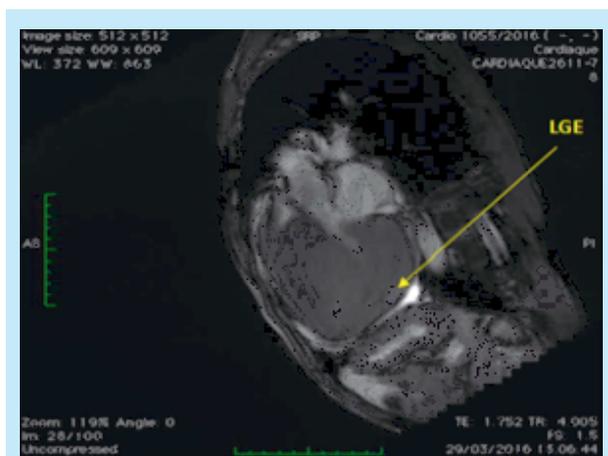


Figure 4: cardiac MRI findings: biventricular concentric hypertrophy with late gadolinium enhancement (LGE) in the posterolateral left ventricular wall.

DISCUSSION

We described a rare case of LVH caused by a Fabry disease. According to 2014 ESC guidelines about hypertrophic cardiomyopathy (HCM), 5 to 10% of LVH cases are due to genetic or non-genetic causes other than sarcomeric HCM. Fabry disease is a principal etiology among the group of storage diseases (1). It presents 0.5 to 1% of etiologies of LVH among typically 35 to 40 years old patients (2). It is a chromosome X-linked disease characterized by a deficiency of the α -galactosidase A enzyme (GLA) leading to the accumulation of glycosphingolipids in different cell types: kidney, nervous system, eye, skin and heart causing multiple systemic organ damage with a vital

and/or functional poor prognosis from a young age unless early screened and well managed (3).

We consider this Fabry disease report particular for many reasons:

First, it stresses the importance of thinking to differential diagnosis of sarcomeric HCM in front of uncommon features of LVH. In fact, on the background of our young age patient with family history of sudden cardiac death, the first suspected diagnosis of LVH detected by TTE is HCM. However, signs as symmetrical LVH, association to right ventricular hypertrophy may suspect other etiologies of LVH, among which, Fabry disease (4). Binary appearance of the endocardium is a particular sign, absent in our case, but which was studied in several reports with a sensibility and specificity of 15% and 73% respectively (5).

Second, the contribution of ECG to suggest specific diagnoses of LVH is particularly useful in Fabry disease. In our case, the association of limit to short PR interval, high QRS voltage and sinus bradycardia highly suggested the disease. This association is widely described in literature to be associated to Fabry disease (6).

Third, this case highlights the particular value of tissue characterization to differentiate potential causes of LVH by studying the distribution of fibrosis. The first indispensable tool is cardiac MRI that reveals posterolateral involvement of fibrosis by showing LGE in this myocardial region (7). A second more rapid and accessible tool is speckle tracking, a developing technique largely used in this challenging situation. Despite a normal ejection fraction in Fabry disease patients, global longitudinal strain is reduced, and the key feature is the earlier and deeper alteration of strain in posterolateral wall of the left ventricle in the same way of cardiac MRI, exactly as shown in our case (4). A recent study validated two-dimensional speckle tracking as a non-invasive tool for identification of myocardial fibrosis in Fabry disease by comparing systolic strain alteration of basal posterolateral segments to LGE. Authors concluded that this particular regional strain alteration is the most powerful predictor to distinguish between patients with and without LGE with a sensibility of 90% and specificity of 97% and a significant $p=0.001$ (8). In our case we combined these two key tools to study the distribution of fibrosis in order to achieve the appropriate diagnosis of Fabry disease.

In men, as in our case, definite confirmation of Fabry disease is based on detecting low activity of α -galactosidase enzyme in leukocytes. In women this may show a lack of sensibility and a DNA analysis to detect the GLA gene mutation is sometimes mandatory (9). However, Given the unavailability of enzyme activity testing and genetic assay in our center, the approach of combining cardiac MRI to speckle tracking remain reasonable to specify the appropriate diagnosis of Fabry disease considering their specific signs.

The interest of this particular diagnosis is that it could be a reversible etiology of LVH in the light of the specific enzyme replacement therapy (ERT). This treatment was largely studied and reports concluded to a certain effect on kidney involvement but a variable impact on LVH. This latter depends on the existence of fibrosis. ERT is more efficacious in case of absent or moderate fibrosis ($p=0.045$), but it showed no anatomic or outcome improvement in case of extensive fibrosis ($p>0.3$) as demonstrated by Weidmann in a Speckle tracking based trial evaluating ERT (10). The second limitation of this therapy is that it is a very expensive and inaccessible treatment in our center.

CONCLUSION

Fabry disease is a rare but potentially reversible etiology of LVH. This diagnosis is suggested in front of uncommon features of HCM on TTE, particular signs on ECG, and detection of fibrosis in the posterolateral wall of left ventricle by speckle tracking and cardiac MRI. Searching for extracardiac manifestations is important because of their prognostic impact. And finally selected patients with absent or moderate fibrosis could benefit from enzyme replacement therapy, which efficacy should be more elucidated and accessibility have to be improved.

REFERENCES

- 1- 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy. EHJ, 2014
- 2- Pantazis, FIRST IN A SERIES ON FABRY DISEASE: WHAT IS THE PROBLEM AND HOW DOES THIS TRANSLATE INTO CLINICAL SIGNS?. EJCP, 2016
- 3- Christine M. Eng, Fabry disease: Guidelines for the evaluation and management of multi-organ system involvement. Genetics in medicine, 2006
- 4- Niemann M, Echocardiography in Fabry disease. Cardiogenetics, 2013.
- 5- Juha W, Echocardiography in Fabry disease: diagnostic value of endocardial border binary appearance. Clin Physiol Funct Imaging, 2009.
- 6- Namdar M, Electrocardiographic changes in early recognition of Fabry disease. Heart, 2011.
- 7- Moon JC, Gadolinium enhanced cardiovascular magnetic resonance in Anderson-Fabry disease. Evidence for a disease specific abnormality of the myocardial interstitium. Eur Heart J, 2013.
- 8- Joahannes Krämer, Two-dimensional speckle tracking as a non-invasive tool for identification of myocardial fibrosis in Fabry disease. Eur Heart J, 2013.
- 9- Dawn A, Fabry Disease Practice Guidelines: Recommendations of the National Society of Genetic Counselors, J Genet Council, 2013
- 10- Weidmann, Long-term effects of enzyme replacement therapy on fabry cardiomyopathy: evidence for a better outcome with early treatment. Circulation, 2009