In 2005, a 55-year-old man received the diagnosis of Fabry disease attributable to a Y216C (c647A>G) mutation. Heart, kidney, skin, and ocular involvement were documented, and enzyme replacement therapy (ERT) with agalsidase alfa (0.2 mg/kg every other week) was started and regularly administered for 6 years. Baseline cardiac evaluation included electrocardiography, 2-dimensional echocardiography, and cardiac magnetic resonance. During follow-up, acroparesthesias disappeared, and renal function maintained stable with mild proteinuria and normal plasma creatinine values, whereas cardiac involvement significantly worsened with a progressive increase of cardiac maximal wall thickness and mass (interventricular septum from 18 to 25 mm) and myocardial fibrosis as documented by electrocardiography and cardiac magnetic resonance (Figures 1 and 2). Blood pressure always remained within the normal range. In addition, after 2 years of treatment, the patient started to experience chest pain and dyspnea on effort in the presence of ST-segment depression and negative T waves in anterolateral precordial leads (Figure 1, bottom). Despite the evidence of myocardial perfusion defects at myocardial scintigraphy, coronary angiography documented normal coronary arteries. Angiotensin-converting enzyme inhibitors and low-dose diuretics and carvedilol were introduced with a mild improvement of symptoms.

In Fabry disease, ERT has been proved effective in removing glycosphingolipids from affected tissues. However, there is growing evidence that the beneficial effects may be variable in different tissues and patients. Recent studies have demonstrated that the presence of late enhancement before treatment start is associated with the lack of a significant regression of hypertrophy and worsening of segmental myocardial function during ERT. Moreover, the occurrence, while on treatment, of chest pain in the absence of coronary artery disease confirms that ERT has no effect on the functional and structural abnormalities of myocardial microcirculation that play an important role in the physiopathology of the cardiomyopathy.

The effects of ERT on Fabry cardiomyopathy critically depend on the stage of the disease at baseline, because patients with evidence of fibrosis at cardiac magnetic resonance may have limited or no benefits from ERT. Treatment is best started before myocardial fibrosis has developed to achieve at least a stabilization of cardiac involvement.

Progression of cardiomyopathy in our patient is emblematic and reinforces the need for early diagnosis and treatment but also the need for new therapeutic strategies for this increasingly recognized cardiomyopathy.

Disclosures

None.

References


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Figure 1. Electrocardiographic progression of cardiac involvement in Fabry disease. Baseline electrocardiography in 2005 (top) shows sinus rhythm with short PR interval (118 ms), prolonged QRS duration (118 ms), and nonspecific ST-segment T-wave abnormalities, whereas sinus rhythm with a normal PR interval (132 ms) and significant left ventricular hypertrophy with ST-segment depression and giant negative T waves can be observed in the 2011 electrocardiograph (bottom).

Figure 2. Cardiac magnetic resonance progression of cardiac involvement in Fabry disease. A through C, Baseline evaluation before enzyme replacement therapy (2005). D through F, Follow-up evaluation after 6 years of treatment (2011). Horizontal long-axis views using cine steady-state free precession (SSFP) sequences demonstrate a significant increase of both left and right ventricular wall thickness from 2006 (A) to 2011 (D). The increase of ventricular walls mainly involves the basal septum, but a significant enlargement of papillary muscles is also present. Short-axis views of basal segments using cine SSFP sequences show an increase of ventricular wall thickness at the upper septum level from 18 mm (B) to 25 mm (E).
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