Case report

**Reduced coronary flow reserve in Anderson-Fabry disease measured by transthoracic Doppler echocardiography**

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**Abstract**

Coronary flow reserve was assessed in a patient with Anderson-Fabry disease complicated by symmetric left ventricular hypertrophy. Coronary flow reserve was measurable in all three major coronary arteries providing an opportunity to compare regional coronary flow reserve from different vascular beds. In this patient all the three vascular beds supplied diffusely hypertrophied myocardium. Coronary flow disturbances in small intramyocardial perforating arteries were visible. The coronary flow reserve was reduced to a similar level (around to 2.0) in all three major arteries. In our patient with Anderson-Fabry disease, the coronary vasodilation was blunted in a diffuse pattern corresponding to the myocardial hypertrophy distribution. In small intramyocardial arteries coronary flow was also disturbed. Accordingly, retrograde systolic flow and accelerated anterograde diastolic flow were documented.

**Background**

Anderson-Fabry disease is an X-linked, multisystem, lysosomal storage disease (deficiency of enzyme α-galactosidase A), characterized by the accumulation of glycosphingolipids in various tissues and organs [1,2], including skin, vascular endothelium, heart, kidneys, liver, lungs, pancreas and ganglion cells of the peripheral nervous system. The incidence is 1:177000. However, the rate may be underestimated because a common cardiac manifestation is myocardial hypertrophy that mimics hypertrophic cardiomyopathy. Abnormal storage in the cardiovascular system may also involve cardiac conduction system, valvular apparatus and endothelial cells in coronary vessels [1-3].

To assess coronary flow abnormalities in a patient with Anderson-Fabry disease, we performed transthoracic Doppler echocardiography. Using this method, coronary flow reserve is effectively measurable [4] and all three major coronary arteries are accessible in some patients [5,6]. In a large series of 658 patients [6], coronary flow reserve was contemporarily recorded in left anterior descending (LAD) coronary artery (98% of patients), right coronary artery (RCA) (66% of patients) and circumflex (Cx) coronary artery (43% of patients). Additionally, flow disturbances in small intramyocardial perforating arteries were assessed as blood flow abnormalities at this level of coronary circulation were previously reported in left ventricular (LV) hypertrophy [7].

**Case presentation**

This 49-year-old male patient with Anderson-Fabry disease was referred to our hospital. He did not complain of anginal symptoms or dyspnea. As a part of an overall clinical evaluation, transthoracic echocardiography was performed, revealing a diffusely distributed myocardial...
hypertrophy, i.e. involving both (LV) free walls and the septum (the myocardial thickness at diastole was measured in the short parasternal-axis: the anterior segment of the septum- 19.6 mm; the posterior segment of the septum – 20.8 mm; the LV posterior wall – 20.7 mm; and the anterolateral wall 16.8 mm). Left ventricular systolic function was preserved (LV ejection fraction 68%). A precise assessment of myocardial hypertrophy by magnetic resonance imaging confirmed increased LV mass to 386 grams.

**Methods**

Using noninvasive, inexpensive and widely accessible method, B-mode and color Doppler transthoracic echocardiography, the segments of three major coronary arteries: LAD, Cx and right posterior descending (RPD) coronary artery or RCA were visualized (Figure 1,2). High quality recordings of flow velocity in all these coronary arteries were obtained using spectral Doppler.

**Results**

The coronary flow reserve in response to intravenous adenosine (140 µg/kg/min) was homogeneously reduced to a similar value in the major coronary arteries (LAD – 2.07; Cx- 2.18; RPD/RCA- 1.91). Small, intramyocardial branches of epicardial coronary arteries were visualized [intramyocardial perforators originated from LAD (Figure 3) and branches from RPD (Figure 4)]. Increased resistance to flow (probably due to myocardial hypertrophy and increased extravascular compressive forces) was demonstrated by the detection of flow with high velocity in spectral Doppler (figure 5, 6, 7) and color Doppler (Figures 3, 4, 5) in these penetrating vessels. The peak diastolic flow velocity was higher in the LAD perforator (41 cm/s – figure 6) than in the distal portion of LAD (25 cm/s – figure 7). The systolic flow in the LAD perforator was abnormally retrograde (figure 6).
Discussion
Prevalence of Anderson-Fabry disease in patients with late-onset hypertrophic cardiomyopathy is about 6.3% in males [8] and 12% in females [9]. In contrast, among males with hypertrophic cardiomyopathy diagnosed at <40 years of age, the rate of appropriate verification of the diagnosis to Anderson-Fabry disease was lower i.e. 1.4% [8]. If properly recognized, Anderson-Fabry disease is treatable by enzyme replacement therapy and both cardiac and non-cardiac abnormalities may be reversed/reduced by substitution of α-galactosidase (especially in the early stage) [10]. Therefore, it is important to consider Anderson-Fabry disease in the differential diagnosis of hypertrophic cardiomyopathy. Anderson-Fabry disease is hardly indistinguishable from hypertrophic cardiomyopathy by echocardiography [9,11,12], however we made an attempt to identify potential differences (mainly...
quantitative) in table 1. Recently [13], the findings of magnetic resonance imaging have appeared useful in differential diagnosis (table 1). Clinical findings may be more helpful in differential diagnosis and we recommend to evaluate the presence or absence of all non-cardiac manifestations (dermatological, nephrological, neurological, ophthalmological) of Anderson-Fabry disease in patients diagnosed as having hypertrophic cardiomyopathy.

**Conclusion**

In our patient with Anderson-Fabry disease, the coronary vasodilatation was blunted in a diffuse pattern corresponding to the myocardial hypertrophy distribution. In small intramyocardial arteries coronary flow was disturbed. Accordingly, retrograde systolic flow and accelerated anterograde diastolic flow were documented. Transthoracic Doppler echocardiography is now the only method available to evaluate blood flow characteristics in small intramyocardial arteries.

**List of Abbreviations**

- LAD – left anterior descending coronary artery
- RCA – right coronary artery
- RPD – right posterior descending coronary artery
- Cx – circumflex coronary artery

**Competing Interests**

The author(s) declare that they have no competing interests.

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