Abstract: P1284

An atypical case of Fabry disease with obstructive hypertrophic cardiomyopathy: a multimodality imaging based diagnosis

Authors:
IS Visoiu1, RC Rimbas2, AO Ciobanu2, AI Nicula1, M Iascone3, R Jurcut4, M Cinteza2, D Vinereanu2,
1University Emergency Hospital - Bucharest - Romania, 2Carol Davila University of Medicine and Pharmacy, University and Emergency Hospital Bucharest, Cardiology Department - Bucharest - Romania, 3ASST Papa Giovanni XXIII, Molecular Genetics Laboratory - USSD LGM - Bergamo - Italy, 4“Prof. Dr. C.C. Iliescu” Institute of Emergency for Cardiovascular Diseases, Cardiology - Bucharest - Romania.

Topic(s):
Imaging: Myocardial Disease

Citation:
European Heart Journal - Cardiovascular Imaging (2019) 20 (Supplement 1), i862

Funding Acknowledgements:
supported by grant no. 49/02.05.2018/UEFISCDI/PN-III-P1-1.1-TE-2016-0669

Introduction: Fabry disease (FD) is a rare disorder, caused by X-linked inherited mutations in the GLA gene, encoding a lysosomal hydrolase, alpha galactosidase A (AGAL-A). The non-classical forms are usually underdiagnosed, having a higher residual activity, with a late onset.

Purpose: To report an atypical case of late onset FD with obstructive hypertrophic cardiomyopathy (HCM) and advanced fibrosis, evolving with complete atrioventricular block (CAVB), identified by transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR) and confirmed by genetic analyses.

Methods and Results: A 65-year-old man presented with exertional angina pectoris, dyspnea and recurrent syncope. Clinical examination revealed a crescendo-decrescendo mid-systolic heart murmur between the apex and left sternal border. The ECG showed sinus bradycardia and left ventricular hypertrophy (LVH), with strain pattern. Blood tests detected an increased NTproBNP (7047 pg/ml) and a normal troponin I. TTE confirmed LVH, with an asymmetrical pattern (septum-21 mm) and preserved left ventricular ejection fraction (LVEF). We noted papillary muscles hypertrophy (PMH) and an unusual left ventricle outflow tract (LVOT) obstruction, due to a systolic anterior motion of mitral chordae tendineae, with a dynamic pressure gradient of 37 mmHg, increased after Valsalva maneuver to 57 mmHg (Figure 1-A,B, C). LV global longitudinal strain was decreased (-16 %), with the lowest values in the inferior and infero-lateral, basal and mid-basal segments (Figure 1-D). The CMR certified HCM, with a LV mass of 139 g/m2, LVEF of 73%, adding diffuse late gadolinium enhancement with a prominent focus within the mid basal infero-lateral mid-wall segment (Figure 1-E). We decided in favor of surgery, the medical treatment being limited by persistent bradycardia. However, the patient developed CAVB, being cardiostimulated (DDD). After pacing the LVOT gradient normalized, with complete resolution of symptoms. High QRS voltage with marked repolarization abnormalities, CAVB, associated with PMH, infero-lateral impairment of myocardial deformation, with corresponding intramural fibrosis at CMR raised the suspicion of FD. Genetic analysis consisting of a next generation sequencing cardio-panel was performed, identifying a pathogenic hemizygous mutation in exon 3 of GLA gene, c.416A>G (p.N139S). In dried blood spot, AGAL-A activity was decreased by 46% (1.8 µmol/l/h), with increased lyso-Gb3 (1.5 ng/ml). He has no other significant organ involvement.

Conclusions: TTE and CMR give us important "red flags" for FD in patients with hypertrophic cardiomyopathy, combined with ECG and clinical criteria. Early screening for FD in high risk patients, with HCM and highly suggestive imagistic criteria is very important, in order to start the enzyme replacement therapy before
An atypical case of Fabry disease with obstructive hypertrophic cardiomyopathy: a multimodality imaging based diagnosis

Introduction: Fabry disease (FD) is a rare disorder, caused by X-linked inherited mutations in the GLA gene, encoding a lysosomal hydrolase, alpha galactosidase A (AGAL-A). The non-classical forms are usually underdiagnosed, having a higher residual activity, with a late onset.

Purpose: To report an atypical case of late onset FD with obstructive hypertrophic cardiomyopathy (HCM) and advanced fibrosis, evolving with complete atrioventricular block (CAVB), identified by transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR) and confirmed by genetic analyses.

Methods and Results: A 65-year-old man presented with exertional angina pectoris, dyspnea and recurrent syncope. Clinical examination revealed a crescendo–decrescendo mid-systolic heart murmur between the apex and left sternal border. The ECG showed sinus bradycardia and left ventricular hypertrophy (LVH), with strain pattern. Blood tests detected an increased NTproBNP (7047 pg/ml) and a normal troponin I. TTE confirmed LVH, with an asymmetrical pattern (septum-21 mm) and preserved left ventricular ejection fraction (LVEF). We noted papillary muscles hypertrophy (PMH) and an unusual left ventricle outflow tract (LVOT) obstruction, due to a systolic anterior motion of mitral chordae tendineae, with a dynamic pressure gradient of 37 mmHg, increased after Valsalva manoeuver to 57 mmHg (Figure 1-A, B, C). LV global longitudinal strain was decreased (-16 %), with the lowest values in the inferior and infero-lateral, basal and mid-basal segments (Figure 1-D). The CMR certified HCM, with a LV mass of 139 g/m², LVEF of 73%, adding diffuse late gadolinium enhancement with a prominent focus within the mid basal infero-lateral mid-wall segment (Figure 1-E). We decided in favor of surgery, the medical treatment being limited by persistent bradycardia. However, the patient developed CAVB, being cardiostimulated (DDD). After pacing the LVOT gradient normalized, with complete resolution of symptoms. High QRS voltage with marked repolarization abnormalities, CAVB, associated with PMH, infero-lateral impairment of myocardial deformation, with corresponding intramural fibrosis at CMR raised the suspicion of FD.

Genetic analysis consisting of a next generation sequencing cardio-panel was performed, identifying a pathogenic hemizygous mutation in exon 3 of GLA gene, c.416A>G (p.N139S). In dried blood spot, AGAL-A activity was decreased by 46% (1.8 µmol/l/h), with increased lyso-Gb3 (1.5 ng/ml). He has no other significant organ involvement.

Conclusions: TTE and CMR give us important “red flags” for FD in patients with hypertrophic cardiomyopathy, combined with ECG and clinical criteria. Early screening for FD in high risk patients, with HCM and highly suggestive imagistic criteria is very important, in order to start the enzyme replacement therapy before development of irreversible organ damages.

development of irreversible organ damages.