Case report

Hypertrophic-phenotype cardiopathy: the great simulator

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A 41-year-old Caucasian man was sent to our center after discharge, a few days earlier, from the emergency department (ED) where he was hospitalized due to a car accident. During hospitalization, high blood pressure (190/120 mmHg), ECG and echo-cardiography signs of left ventricular hypertrophy were found.

The medical history did not report any previous pathology worthy of note.

Among the risk factors, he presented an active smoking habit and mixed dyslipidemia. The family history was positive for arterial hypertension (AH) and ischemic heart disease, but not for sudden cardiac death.

The patient reported no history of angor, dyspnea, or palpitation and experienced a single syncopal episode after administration of antihistamine in 2018. He had practiced competitive sports until 14 years earlier, regularly achieving the required medical certification as stated by Italian law.

The patient was taking calcium channel blocker, sartan, and diuretics as recommended at discharge from the ED.

On physical examination: weight 80 kg, height 175 cm, blood pressure 160/85 mmHg, heart rate 105 bpm. On thoracic and abdominal auscultation, no significant findings were found. Cardiovascular compensation was satisfactory.

Blood chemistry tests performed at the ED were negative for relevant alterations (particularly high sensitivity troponin, NTproBNP, renal function were within normal range).

The ECG (Fig. 1a) showed sinus tachycardia with regular atrio-ventricular and intraventricular conduction, and negative T-wave in the infero-lateral leads as from severe left ventricular hypertrophy/overload, not evident in a previous ECG performed 1 year earlier.

An echocardiogram was then done (Fig. 2a), documenting severe hypertrophy, suggestive for hypertrophic cardiomyopathy (ISV 18 mm, PP 17 mm, mass 189 g/m^2, RWT 0.72) with no evidence of left ventricular outflow obstruction. Systolic function was at lower normal limits (ejection fraction 50%). Grade I diastolic dysfunction was observed.

Calcium channel blocker therapy was titrated and Nebivolol was introduced. In addition, a 24-h Holter-ECG was programmed to assess the possible arrhythmic burden and a cardiac-MR was prescribed to better define the anatomic and functional status.

Cardiac-MR (Fig. 3) confirmed marked concentric symmetric left ventricular hypertrophy (maximal thickness 19 mm in the lower mid-septal ventricular wall) with global left ventricular hypokinesis (EF 50%) in the absence of segmental contractility defects and wall hypertrophy of the right ventricle. Inhomogeneous T2 signal intensity of the left ventricle was identified with short tau inversion recovery (STIR) sequences, predominantly antero-septal and inferior-lateral at the basal-middle ventricular plane, without perfusion defects at rest. Moreover, late gadolinium enhancement (LGE) was described, with mesocardial distribution, diffuse appearance, with predominant involvement of the lateral wall of the left ventricle, inferior septal junction and basal antero-septal area. No evidence of significant alterations in native T1 values was identified.

Holter-ECG recording showed sinus rhythm with an average heart rate of 76 bpm, isolated supraventricular and ventricular extrasystole, a 4-beats run.

The patient was re-evaluated after 6 months. At follow-up, optimal control of the blood pressure (BP 130/80 mmHg) was achieved, no symptoms were reported and a hemodynamic compensation was observed. ECG (Fig. 1b) showed a regular sinus rhythm (80 bpm) and ventricular repolarization was within limits. Echocardiography (Fig. 2b) showed a partial reduction of wall hypertrophy (SIV 14 mm) and a contractile function within normal limits (EF 55%). Cardiac-MR also showed

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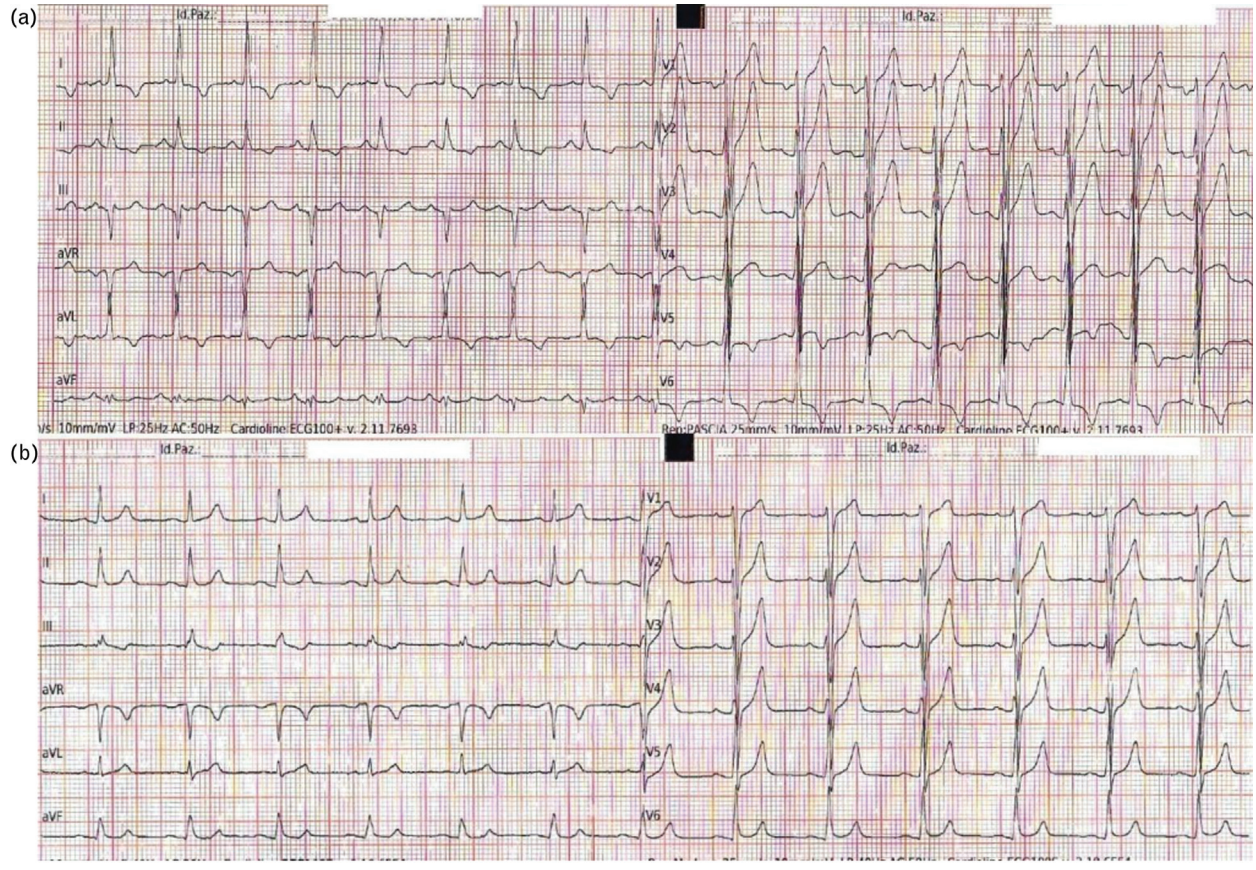
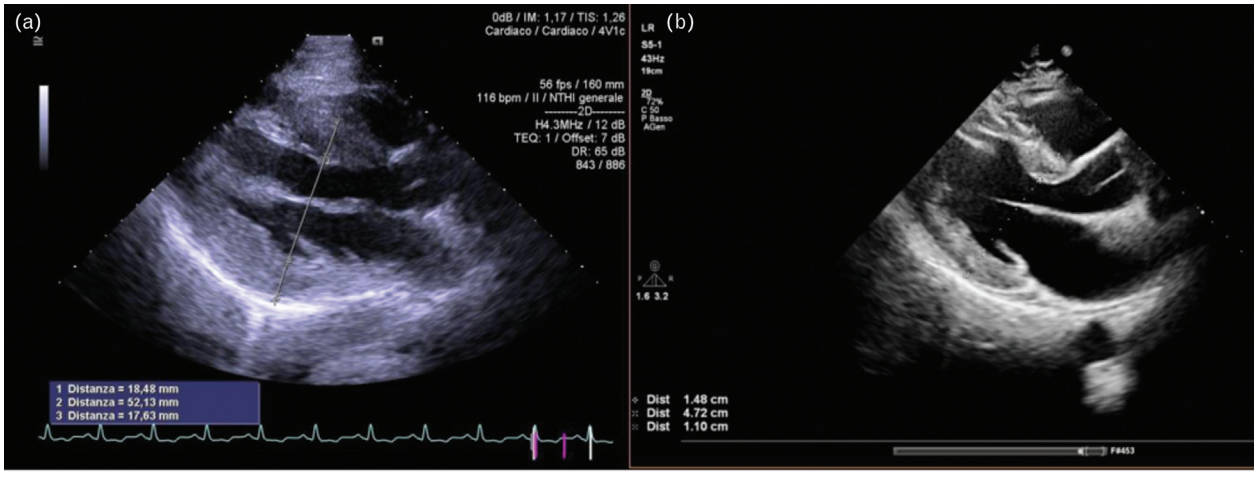
Fig. 1



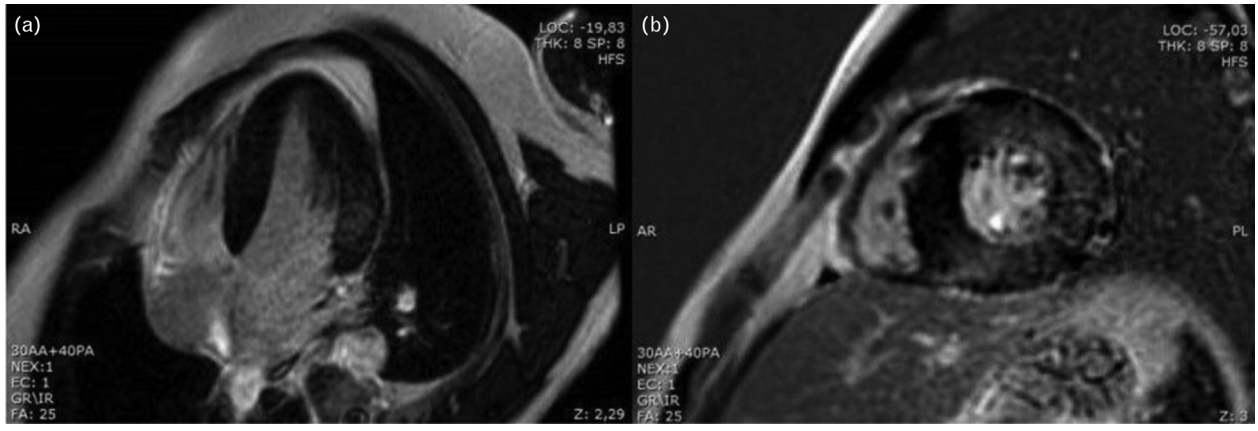
(a, top) ECG at first visit: negative T-wave in infero-lateral location as from severe left ventricular hypertrophy/overload. (b, below) Follow-up ECG with normal ventricular repolarization.

Fig. 2



(a) Echocardiogram at first visit: severe concentric hypertrophic phenotype. (b) Follow-up echocardiogram: considerable reduction of wall hypertrophy.

Fig. 3



Cardiac-MR: marked symmetric concentric left ventricular hypertrophy with LGE with diffuse mesocardial distribution. LGE, late gadolinium enhancement.

inverse remodeling with reduction in wall thickness and good contractile performance; LGE was unchanged.

Ventricular hypertrophy is a not infrequent ECG and echocardiographic finding in clinical practice that requires recognition and differentiation of the underlying etiological substrates, as they are responsible for different diagnostic, therapeutic and prognostic scenarios.

The term 'ventricular hypertrophy' refers to an increase in wall thickness and myocardial mass. This condition may be primary, often caused by mutation of genes encoding for sarcomere proteins (Hypertrophic Cardio-Myopathy, HCM)[1,2] or less frequently caused by infiltrative (e.g. amyloidosis) or metabolic (e.g. Fabry) diseases, or by syndromes (e.g. Noonan). It may also represent the secondary expression of myocardial adaptation to conditions involving increased afterload (e.g. AH, aortic valve stenosis) or to para-physiological conditions such as intense physical training. All of the above conditions present a pattern that is often overlapping and sometimes difficult to distinguish phenotypically.

Given the significant prevalence of AH in the adult population, the coexistence of AH with HCM is not so remote an association and this eventuality has been considered in the present clinical case. Isolated AH typically results in a uniform and symmetric compensatory hypertrophy of the left ventricle,[3] as observed by imaging of the clinical case, where, however, a significantly greater thickness has been documented than that normally observed in hypertensive patients. In support of a possible hypertensive origin in the present case is the, albeit partial, subsequent regression of the electrocardiographic and echocardiographic aspect after the setting of an adequate and effective antihypertensive therapy.

Another possible etiology to be excluded was the athlete's heart. The differential diagnosis between this and HCM is of paramount importance because the latter represents the main cause of sudden cardiac death in young athletes in contexts where preventive sports medicine screening is not mandatory. In the present case, the excessive wall thickness (>16 mm) and the anamnestic history of cessation of competitive sports activity for a long time allowed this etiology to be set aside. However, it is important to emphasize that the mere wall thickness (> or <15 mm) is absolutely arbitrary in orienting towards or rouling out the diagnosis of the athlete's heart, since in clinical reality this parameter is extremely changeable according to multiple variables, including sex, race, body surface area, type of sport practiced, training load and the assumption of doping substances.

An abrupt reduction in wall thicknesses may be observed in inflammatory forms with a significant edemigenous impact on the myocardial. At the MRI, an inhomogeneous T2 signal could suggest the presence of an inflammatory substrate. However, the lack of compatible symptoms and of a significant infectious history, together with the negativity of the inflammatory indices (white blood cells, PCR, VES) in the blood tests performed in the ED after the car accident, made this hypothesis implausible. Said MRI pattern is indicative of nonspecific myocardial inflammation, which can be a consequence of various conditions, including AH, and whose reduction can explain the partial regression of the wall thickness observed in our clinical case, where a long-lasting degenerative process was present too, as documented by LGE at both the first visit and follow-up.

An ischemic substrate could be suspected given the ECG pattern and the cardiovascular risk profile of the patient (familiar history, AH, smoking habit, dyslipidemia). However, the finding of a Troponines level within

the normal range in the blood test performed in the ED, the absence of perfusion defects at the MRI and the negative result of an exercise stress test performed after 6 months (after ECG normalization) ruled out that ischemic burden could be contributing to the originally depicted ECG alterations.

Among the various etiological hypotheses, an amyloidotic substrate was considered, then ruled out for lack of the known 'red flags' in the patient's clinical history, as indicated by the recent ESC position paper on diagnosis and treatment of cardiac amyloidosis.

Anderson-Fabry disease and PRKAG2 gene mutation cardiomyopathy were excluded because of the absence of suggestive conduction abnormalities on ECG tracing and because of imaging findings at cardioRM that were not typical for these conditions.

The use and the correct interpretation of specific clinical-diagnostic procedures allow the framing of the individual case within the broad spectrum of differential diagnosis imposed by the finding of left ventricular hypertrophy. A careful, multidisciplinary and multi-instrumental evaluation of the patient, and the identification of any 'red flags' are therefore essential elements in order to formulate a correct differential diagnosis and set the most appropriate therapeutic management, as well as to identify conditions worthy of screening in family members at risk.

Conflicts of interest

There are no conflicts of interest.

References

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