Left ventricle non-compaction with a dilative phenotype and novel genetic mutations

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We present a case of a 46-year-old man with decompensated heart failure, class III New York Heart Association (NYHA) classification. The patient had a history of severe pneumonia two months ago when left ventriclar (LV) systolic dysfunction was diagnosed. There was no medical or family history of cardiac diseases, no alcohol or narcotics use.

Electrocardiogram was performed (Figure 1A). The echocardiography revealed LV systolic dysfunction with a massively trabeculated LV apex (Figure 1B–C). The standard laboratory tests and cardiac enzymes were in the normal range, the level of B-type natriuretic peptide was 2335 pg/ml (reference range <125 pg/ml).

Given the initial clinical presentation, history of pneumonia, and echocardiographic findings at admission, we should differentiate between the most common types of dilative cardiomyopathy (DCM): post myocarditis, idiopathic cardiomyopathy, LV non-compaction (LVNC), or ischemic heart disease.

A positron emission tomography scan (PET) was performed to assess myocardial perfusion and viability. PET findings were very similar to those of ischemic cardiomyopathy (Figure S1). Coronary angiography revealed normal coronary anatomy. The left ventriculography confirmed the diagnosis of DCM. To clarify the etiology of cardiomyopathy endomyocardial biopsy was performed. Histology showed diffuse cardiac fibrosis, typical of DCM. Myocardial tissue samples were tested for the presence of enteroviral sequences by a polymerase chain reaction, yielding negative results. Cardiovascular magnetic resonance (Figure 1D–F) was done for further evaluation of cardiac function and volume.

Genetic and family screening is important for the correct diagnosis and prognosis. Genetic analysis was performed with a new generation sequencing techniques and showed two missense mutations in the titin gene c.54703C>T (p.Arg18235Cys), and c.47090G>C (p.Arg15697Pro) — a novel variant, not described in the literature, and a dominant missense mutation in the Filamin C gene 5071G>A (p.Asp1691Asn). Titin has been recently reported to be associated with LVNC. Titin truncating variants are prevalent, but there are data for pathogenic missense variants [1]. Mutations in these genes were associated with DCM and hypertrophic cardiomyopathy [2, 3]. This is the first reported clinical case with these variants of mutations and LVNC. Screening echocardiography of the patient's relatives was done, showing no signs of cardiomyopathy.

The patient was treated following the recommendations for heart failure management [4].

At the follow-up visit on the third month, he still had persistent LV systolic dysfunction yet without any signs of heart failure.

LVNC is an uncommon myocardial disorder. Clinical presentation with a classical triad (heart failure, arrhythmias, and thromboembolism) is very rare [5]. This case is an example of the heterogeneity and overlapping between the different types of cardiomyopathies. This was a patient with symptoms of decompensated heart failure, with a history of a recent severe inflammatory disease (differential diagnosis: DCM after myoraditis) and imaging tests specific for the DCM with LVNC. Even if an accurate diagnosis does not lead to improvement of patients prognosis currently, the detection of

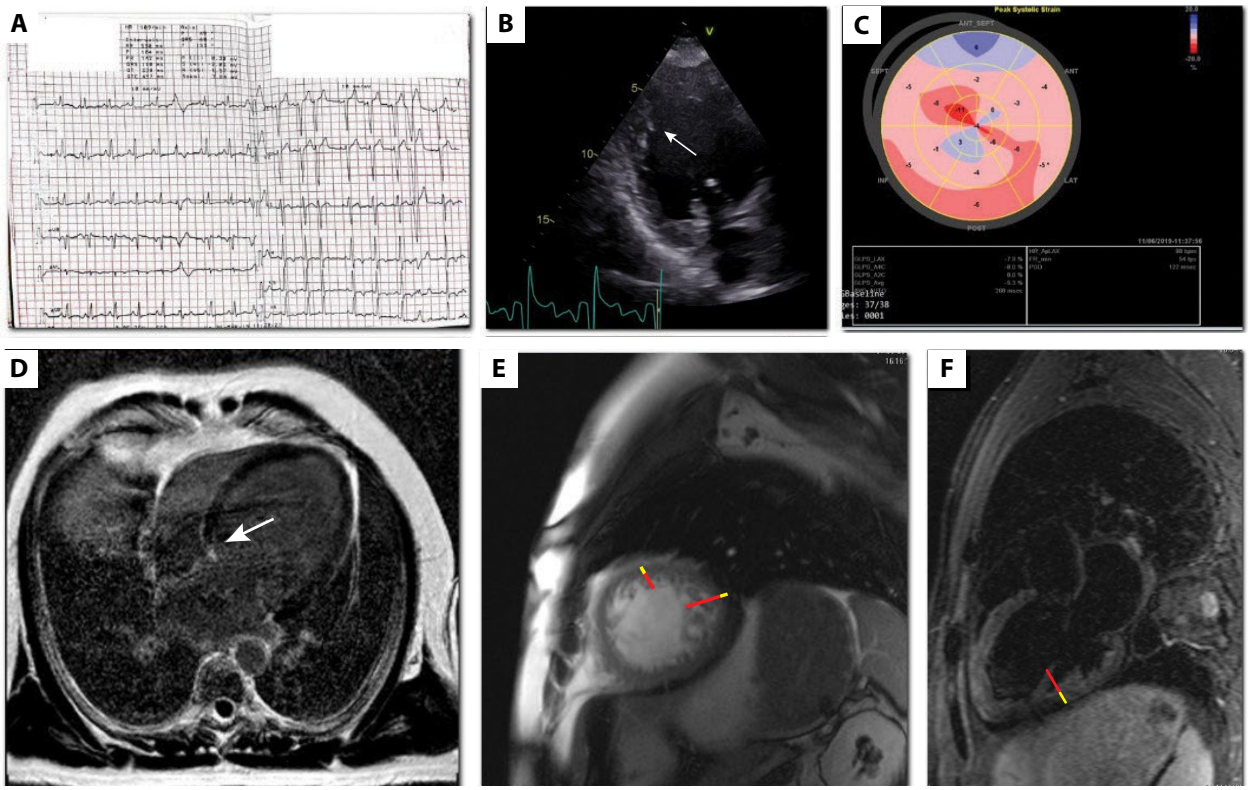

Figure 1. A. Electrocardiogram — sinus tachycardia, normal axis deviation, heart rate 109/min, poor R wave progression with nonspecific ST-T wave changes, and premature atrial and ventricular beats. **B.** Echocardiography — 2-chamber view. Massively trabeculated LV apex (white arrow). **C.** „Bull's-eye" representation of global left ventricle (LV) longitudinal strain measurements. Left ventriclar longitudinal function is reduced in all segments, average LV global longitudinal strain, GLS "–5.3%", typical for dilative cardiomyopathy. **D–F.** Cardiovascular magnetic resonance — late intramural gadolinium enhancement **(D)**; short-axis view **(E)**; and long-axis view **(F)** in end-diastole. End-diastolic volume 415 ml, end-systolic volume 318 ml, LV ejection fraction 23%. In addition, areas of non-compacted myocardium (red arrows), particularly in the free wall of the LV and most of the apex. The ratio of maximum thickness of non-compacted myocardium to compacted myocardium (yellow arrows) is 2.5/1. Late intramural gadolinium enhancement **(D)** in basal segments of the septum. The right ventricle was considered normal

a hereditary component of the disease and subsequent screening of relatives can help identify first-line relatives at risk.

Article information

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