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Case Report

Subendocardial perfusion deficits due to left ventricular non-compaction cardiomyopathy: a case report and literature review

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Abstract: Left ventricular non-compaction (LVNC) is a rare disease which is characterized by a two-layered myocardium with excessive trabeculation of the left ventricle. It can occur isolated or in association with other disorders, including congenital heart disease and musculoskeletal disorder. We herein report the case of a 61-year-old woman who presented with recurrent shortness of breath and chest discomfort for thirty years. A Doppler echocardiogram revealed global hypokinesis, with an ejection fraction (EF) of 41% and prominent trabeculations within the apical and lateral wall myocardial zones. LVNC were confirmed with cardiac magnetic resonance imaging (MRI), and suggested subendocardial perfusion deficits. A 64-slice multidetector computed tomography (MDCT) coronary angiograph revealed extensive abnormal interstitial markings and no severe atherosclerotic lesions. Single-photon emission computed tomography (SPECT) revealed a significant, almost irreversible degree of hypoperfusion in the inferior wall of the left ventricle, thus indicating that LVNC was associated with subendocardial myocardial necrosis.

Keywords: Left ventricular non-compaction cardiomyopathy, myocardial necrosis, computed tomography angiography, SPECT, magnetic resonance imaging

Left ventricular non-compaction (LVNC) is a recently recognized and rare cause of congestive heart failure (HF). It represents an arrest in the process of normal myocardial compaction that leads to the persistence of numerous and deep trabeculations communicating with the ventricular cavity. LVNC is associated with numerous mutations and genetically overlaps with different cardiomyopathic phenotypes, including hypertrophic cardiomyopathy [1]. LVNC is characterized by the following findings: 1) Changes in the myocardial wall due to the prominence of its trabeculations with deep intertrabecular recesses, which may be secondary to the intrauterine arrest of myocardial compaction that occurs in the early stages of fetal development. 2) A continuity between the ventricular cavity and the intertrabecular recesses, which are filled with blood from the ventricle and have no communication with the epicardial coronary system. 3) Decreases in the coronary flow reserve observed in most segments that show ventricular wall motion abnormalities [2]. LVNC can be genetically sporadic or familial. Echocardiography is used as the initial method to diagnose and monitor LVNC. However, other imaging tests, such as magnetic resonance imaging (MRI), which is the most commonly used method, computed tomography and left ventriculography, are also used to diagnose or confirm a clinical suspicion of LVNC.

We herein report a rare case of LVNC in a patient who had symptomatic HF for thirty-one years combined with subendocardial myocardium necrosis as determined by MRI and SPECT without severe atherosclerotic lesions confirmed by MDCT. Based on this case, we review the pathogenesis, clinical features, treatment and prognosis of LVNC according to the available literature.

Case report

A 61-year-old woman was admitted to our department for atypical chest discomfort and recurrent shortness of breath on exertion,

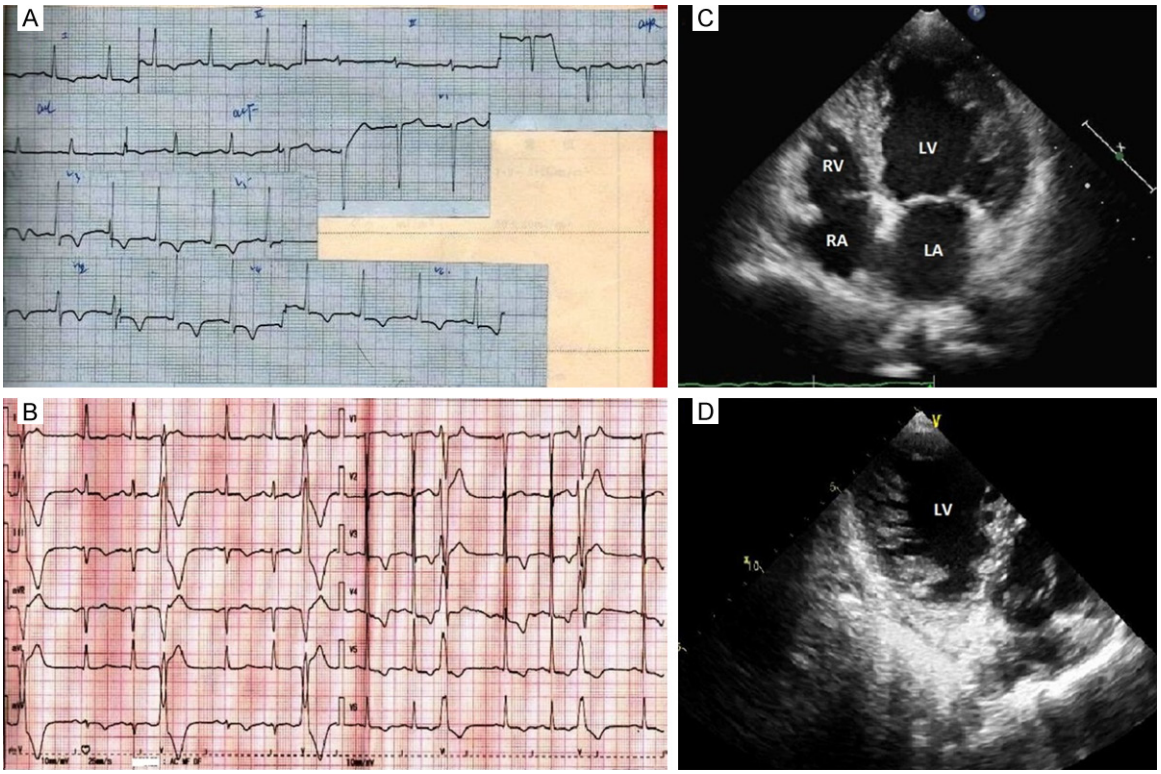

Figure 1. Electrocardiogram and echocardiogram: A. The electrocardiogram showed significant ST-segment changes in 1985, when the patient was thirty years old. B. The electrocardiogram showed frequent ventricular premature beats and significant ST-segment changes in 2016, which were similarly to those observed thirty years prior. C and D. The echocardiogram reveals prominent myocardial trabeculations and deep intertrabecular recesses communicating with the left ventricular cavity.

which she had complained of for the previous 31 years beginning in late pregnancy and which had been aggravated for the previous 4 years. A week prior to her admission, she presented with shortness of breath and chest discomfort again after catching a cold that appeared to be worsening. She also experienced paroxysmal nocturnal dyspnea and chest pressure-like symptoms. Her personal history included meningioma surgery 17 years prior and left breast carcinoma surgery 15 years prior. However, she had no hypertension, diabetes mellitus, smoking or family history of ischemic heart disease or other known cardiovascular risk factors.

On presentation, her blood pressure was 120/55 mmHg, and her heart rate was 81 bmp. A physical exam revealed cardiomegaly and a grade 2/6 systolic murmur at the apex on auscultation. Her level of NT-proBNP was 634 pg/ml, and her myocardial necrosis markers were within normal limits. A 12-lead electrocardiogram showed a normal sinus rhythm and a frequent ventricular premature beat with a significant ST-segment depression in the most of leads, which was similarly observed thirty years prior (**Figure 1A** and **1B**). An echocardiogram was performed, revealing a left ventricular end-diastolic diameter (LVEDD) of 6.25 cm, severe left ventricular systolic dysfunction, a marked trabeculation at the LV lateral-apical region that was more than 2-fold thicker than the compacted region and trabecular flow (**Figure 1C** and **1D**). The EF was decreased to 41%. Based on her medical history and a detailed examination, LVNC was the suspected diagnosis, and the patient was treated with metoprolol tartrate, fosinopril sodium, spironolactone, Lasix, digoxin and aspirin.

Three days later, to confirm the diagnosis and to assess the underlying cardiac structural changes, we performed a contrast-enhanced cardiac MRI, which confirmed left ventricular hypertrabeculation located on the LV lateral wall and apex with global systolic dysfunction. The exam also revealed a delayed enhance-

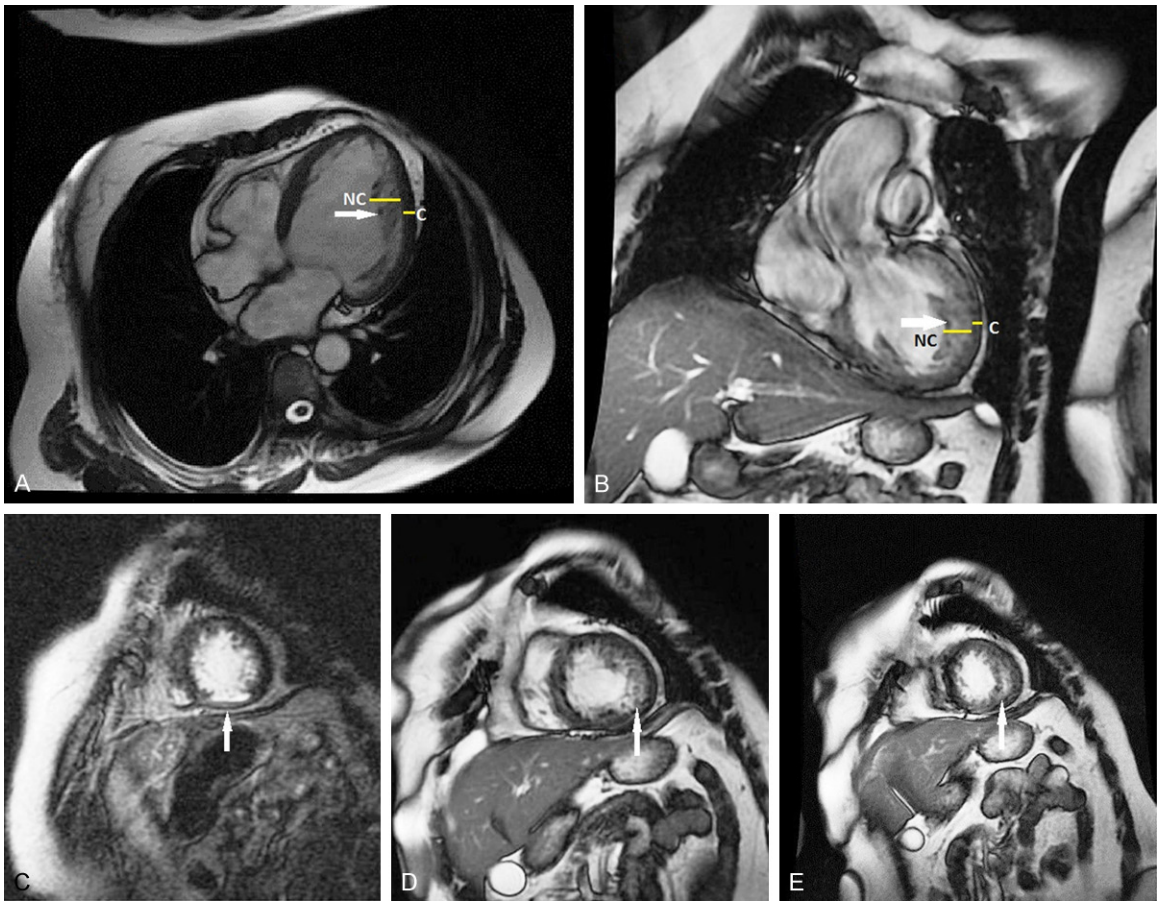

Figure 2. Cardiac MRI: A, B, D and E. The LV wall shows remarkable apex to basolateral trabecularization, and the lateral wall is also involved. The white arrow indicates the non-compacted myocardium. C. The apical subendocardial delayed enhancement suggestive of chronic infarction (white arrow). C, compacted myocardium; NC, non-compacted area.

ment suggestive of chronic infarction (**Figure 2**). To assess the presence of coronary artery disease (CAD) and to further confirm the suspected ventricular abnormality based on MRI and echocardiography, the patient was scheduled for MDCT and myocardial perfusion scintigraphy.

A 64-slice MDCT was performed, which showed 30-50% luminal stenosis in the proximal left anterior descending artery (LAD) (**Figure 3**). The stenotic artery had no correlation with the myocardial necrosis on the MRI. Functional cine reconstructions revealed a thickening of the left ventricular wall with prominent trabeculations and deep intertrabecular recesses, as well as wall motion abnormalities as seen by MRI. Short axis images revealed that the intertrabecular recesses were filled with blood and were "milked" during systole.

SPECT was performed with 20 mCi of technetium-99 m methoxyisobutylisonitrile after an exercise stress test and repeated with the patient at rest (**Figure 4**). An electrocardiogram after exercise did not indicate significant ST-segment changes. From the images taken after stress, hypoperfusion was seen in a part of the inferior wall near the apex of the heart. The perfusion of these segments at rest was nearly absent, as shown on the images taken with the patient at rest. This indicates that most of the myocardial ischemia was persistent and most of the subendocardial necrosis had already occurred. Together with no findings of significant coronary artery stenosis and no obvious dynamic electrocardiogram changes, these distributions and changes suggested that the LVNC was related to a previous anterior myocardial infarction.

Since the clinical and imaging evaluations supported the diagnosis of HF associated with LVNC without significant coronary artery stenosis or ischemic changes, the patient received

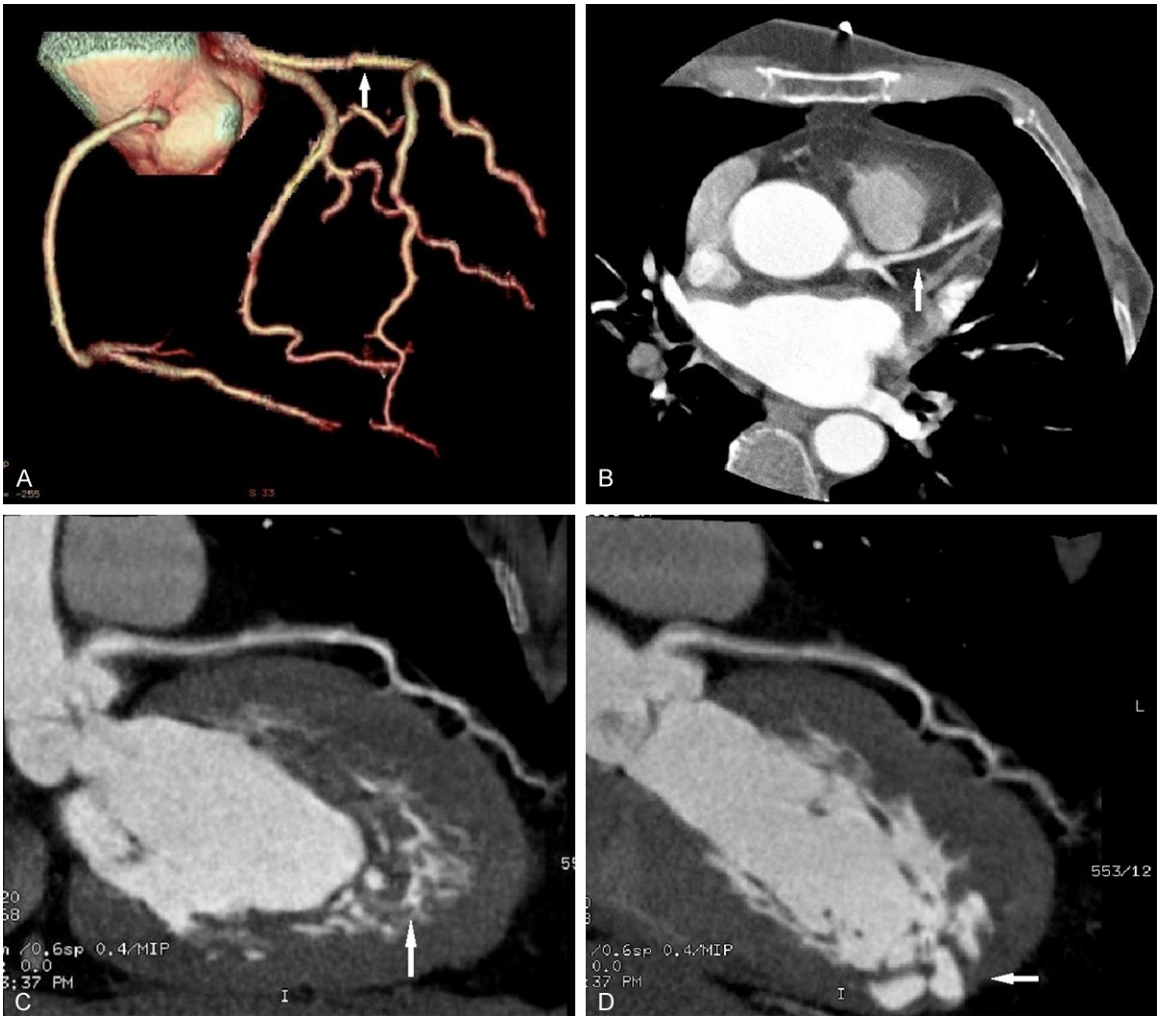

Figure 3. MDCT images of the coronary circulation and myocardium: A-C. MDCT showed 30-50% luminal stenosis in the proximal left anterior descending coronary artery, and the other coronary arteries were almost normal (white arrow). C and D. The LV wall showed remarkable trabecularization from the apex to the lateral wall (white arrow).

routine treatment for HF. The patient was discharged without complications on the ninth day after admission and has since experienced no further chest discomfort.

Discussion

LVNC is a disease that has been increasingly recognized in clinical practice over the past thirty years. LVNC is characterized by a non-compacted inner myocardial layer and a compacted outer myocardial layer with deep intratrabecular recesses that are communicated to the left ventricular chamber. Most cases of LVNC are discovered incidentally during echocardiographic analyses or in patients being treated for HF. In a study of children with all types of primary cardiomyopathy, LVNC was present in 9.2% of the cases [3]. The incidence of LVNC is reported to be approximately 0.014-1.3% in adult case series, and its expected prevalence is 3-4% greater in heart failure patients [4-6]. In the coming years, the prevalence of LVNC is likely to increase due to increasing awareness, more reports in the medical literature and improved diagnostic techniques, such as UCG and cardiac MRI. The sporadic form of LVNC affects both sexes equally.

The ontogenetic development of the myocardium is critical to the morphological appearance of LVNC. The emergence of trabeculations at the end of the fourth week of gestation and trabecular remodeling after the completion of ventricular septation at 8 weeks of gestation

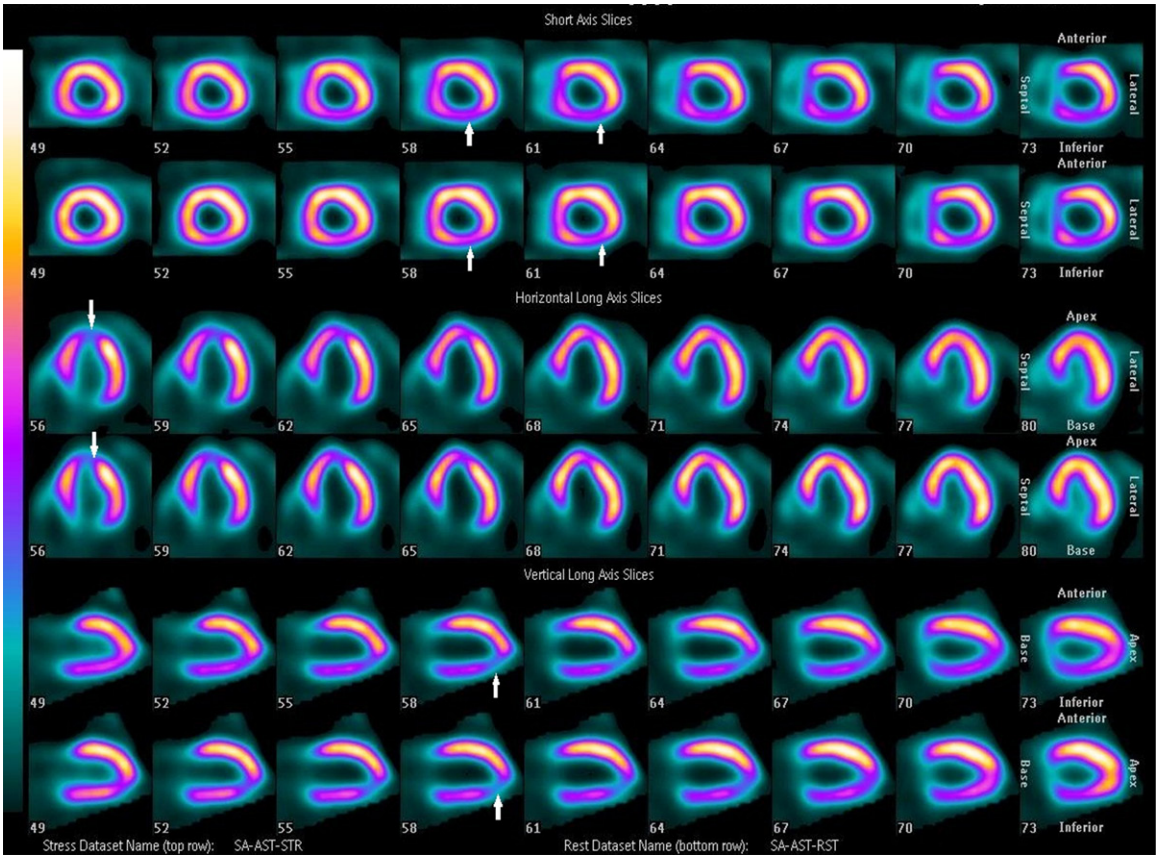

Figure 4. Single-photon emission-computed tomography (SPECT) in short axis, horizontal long axis, and vertical long axis standard views. Top row: Stress images clearly show the left ventricular myocardial imaging. Part of the left ventricular inferior wall near the apex can be seen with defects. Bottom row: The remaining images show that the above areas are not filled, compared with the stress images.

with the development of coronary circulation in humans are the key steps in understanding the development of LVNC [7]. The compaction process or trabecular remodeling gradually progresses from the epicardium to the endocardium, from the base to the apex and from the septum to the free wall in the LV and is more pronounced in the left ventricle than in the right ventricle.

LVNC may occur at any age, and most patients are asymptomatic at the time of diagnosis. However, the clinical manifestations related to this disorder may vary considerably between asymptomatic and symptoms of HF (50%), arrhythmias (41%, including atrial fibrillation, ventricular tachycardia, branch blocks or bradycardia and sudden cardiac death) or systemic embolizations (24%) [8, 9]. Ventricular dysfunction may be systolic or diastolic. Acute myocardial infarction (MI) has also been reported due to systemic embolizations.

A rare complications of LVNC have also been described, including subendocardial necrosis, which can be discerned in LVNC using MRI and positron emission tomography (PET) [6]. The patient described here is one of only a few MRI-documented cases reported with subendocardial perfusion deficits associated with LVNC. Our case also shows that SPECT can detect perfusion deficits. The identification of subendocardial perfusion deficits is very important for the prognosis of these patients, as subendocardial ischemia is thought to be the first indication of subendocardial fibrosis, as demonstrated by histologic examination of specimens from LVNC patients [10]. Although the cause of HF associated with LVNC is not well understood, it has been suggested that myocardial ischemia may play a crucial role [1]. Speculating on the reasons for this disorder, in patients with LVNC without severe atherosclerosis, endomyocardial compact transition fails to occur, leading to the development of a thick-

ened, non-compacted endomyocardial layer with prominent trabeculations that are continuous with the LV cavity and lack communication with the epicardial coronary system, together with deep recesses and a thin compacted epicardial layer [11].

For the present patient, it is interesting to note that the subendocardial perfusion deficits were detected at the apex subendocardial cells on delayed enhancement by MRI, the entire right coronary artery was free of apparent lesions, and the LAD had a slight lesion as visualized by MDCT. Considering the course and range of myocardial blood flow in the coronary tree, we speculate that LVNC caused myocardial ischemia or infarction. Furthermore, the persistent, significant and largely irreversible ischemia during exercise as determined by SPECT also supports a largely necrotic myocardium.

LVNC is subject to misdiagnosis due to the similarities of its nonspecific signs and is improperly treated when not recognized. Echocardiography is the most important modality for diagnosing LVNC; other imaging tests, such as cardiac MRI, can be used to diagnose this disease or to confirm clinical suspicion. The most widely used echocardiographic criteria are those proposed by Jenni et al. [12], which defined LVNC as a two-layer structure, with a thin, normally compacted layer (C) and a markedly thickened non-compacted layer (NC) (with a ratio of NC/C >2), excessively prominent trabeculations, and deep intertrabecular recesses measured at end-systole in the parasternal short-axis views. Cardiac MRI provides a more accurate and reliable evaluation of the extent of non-compacted myocardium than echocardiography images, especially in the LV apex, the most commonly non-compacted area [13]. According to the most accepted criteria using cardiac MRI, an NC/C >2.3 measured at end-diastole is a diagnostic indicator [14]. A recent study showed that a trabeculated LV myocardial volume above 35% of the total LV myocardial volume is diagnostic for LVNC with a high specificity of 89.7% (CI: 74.2-98.0%) and a sensitivity of 66.1% (CI: 52.6-77.9%) using MRI [15]. Dodd et al. reported that late gadolinium enhancement (LGE) could reflect myocardial damage and predict prognosis in LVNC patients. In our study, the diagnosis of LVNC was confirmed after an additional MRI was performed and showed delayed enhancement suggestive of subendocardial infarction [16].

MDCT findings of isolated LVNC have only rarely been reported in the literature; MDCT is a powerful tool, enabling quantitative and qualitative assessments of global and regional ventricular function in assessing CAD and general cardiac morphology. Accordingly, the integrative nature of cardiac MDCT suggests an advantage of this modality over other imaging tests, such as echocardiography and cardiac MRI, in this setting. Lee described a patient with new-onset HF in whom cardiac MDCT identified characteristic myocardial changes of isolated LVNC and associated global and regional functional abnormalities, as well as atherosclerotic CAD [17].

Although many cases of LVNC are asymptomatic and did not show any complications, a therapeutic approach must be adapted for each patient. There are no formal guidelines for the management of patients with LVNC. Chronic oral anticoagulation treatment is recommended in patients with decreased systolic function with an EF below 40%, history of thromboembolism or atrial fibrillation. The use of aspirin is recommended for asymptomatic patients with normal systolic function. The treatment of HF in patients with LVNC follows the general guidelines for HF treatment, including beta-blockers and ACE inhibitors, which are also recommended in LVNC [2]. In the case of symptomatic ventricular arrhythmia and in the context of impaired systolic function, antiarrhythmic agents or implantable cardiac defibrillators are indicated for the prevention of a sustained event and a potentially lethal arrhythmia. Despite other associated risks, early stage candidates may consider aggressive interventions, including implantable cardiac defibrillators, cardiac resynchronization therapy and an evaluation for transplant [2, 18].

The prognosis of LVNC is determined by its complications. There is no evidence that patients with LVNC have different outcomes and should be treated than HF patients without LVNC. Based on the limited published data, the adverse event rates are speculated to not be significantly different from patients with DCM of the same functional status, with a 3-year survival of 85% vs. 83%, respectively [19]. In our present report, the patient with symptoms of HF had a relatively stable course over thirty

years and was administered intensive beta-blockers and ACE inhibitors to treat HF and aspirin for anticoagulation treatment as she demonstrated a good, long therapeutic effect, there were no malignant arrhythmias, and she had an EF above 40%. After being optimally managed, she returned to her baseline functional status and was able to perform her daily living activities with only slight difficulty.

In conclusion, Cardiac MRI is currently considered to be the reference standard for morphological and functional assessments of the heart owing to its noninvasive nature, repeatability, and excellent temporal resolution; however, its use for coronary artery evaluation is limited. In these patients, cardiac CT may enable the noninvasive diagnosis of LVNC and compensate for the defects of MRI, thus highlighting the potential utility of this imaging test for elucidating rare and unexpected etiologies at the onset of HF as well as aiding in therapeutic planning. Furthermore, this case illustrates the integrative nature of cardiac MRI, MDCT and SPECT imaging, enabling the simultaneous evaluation of complex cardiac pathologies as well as coronary artery morphology. As LVNC can be complicated with subendocardial infarction, the diagnosis or treatment of specific aspects of this disorder can help to achieve better results.

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Disclosure of conflict of interest

None.

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