

CASE REPORT

## Presyncope – not always an orthostatic problem

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A 41-year-old female was brought to the ER after a presyncope and absence episode while riding a bike. She recalled no prodromi. Her physical and neurological examinations were unremarkable; past medical, family, substance, and travel history bland. She reported a constant tiredness, sporadic slight cephalgia, responsive to acetaminophen, and a recent syncope while jogging, resulting in a fall, circumstances of which she could not recall. Non-compaction cardiomyopathy is a type of cardiomyopathy that was first described 25 years ago. Its molecular genetic basis is not yet fully clear, and the same is true of its diagnosis, treatment, and prognosis. Further study of these matters is needed.

Keywords: *non-compaction cardiomyopathy; orthostase; presyncope; syncope; trabeculations; cardiac MRI*

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Received: 23 February 2015; Revised: 21 March 2015; Accepted: 2 April 2015; Published: 15 June 2015

A 41-year-old in-house mother of two was brought to the ER after a presyncope and an absence episode while riding a bike. She recalled no prodromi before she felt lightheaded, experiencing muscle weakness, and feeling faint. No loss of consciousness occurred. Past medical, family, substance, and travel history were bland. However, she reported a constant tiredness have been present for the last 6 months, accompanied by a slight, sporadic cephalgia (responsive to acetaminophen). Until recently, the patient had tolerated regular, light exercise (jogging and bike riding) without limitations. On further, detailed interview, the patient mentioned a syncope (with loss of consciousness for an unclear period of time), which she experienced 8 days before, while jogging. Her physical and neurological examinations were unremarkable, vital signs stable (BP 125/87, HR 56 bpm while resting in bed, T 36.8°C, SpO<sub>2</sub> 100%). Schellong test was normal.

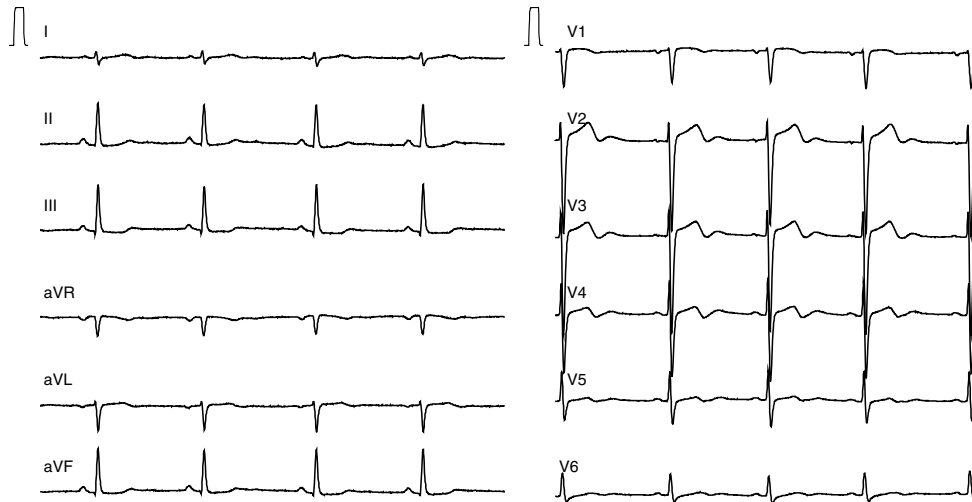
Routine laboratory results (including ABGA, cardiac enzymes, and D-dimers) were normal except for an elevated creatine kinase (177 U/L), which we attributed to the recent fall. Head MRI was unremarkable and excluded emergent cerebral condition (e.g., sinus vein thrombosis, tumor, or epileptogenic foci). ECG showed a normal sinus rhythm, QTc 422 ms, but a slight T-wave inversion in leads V1–V5 (see Fig. 1). To investigate a cardiac genesis, we performed transthoracic echocardiography. The overall left ventricular ejection fraction (LVEF) was 56%, with no resting regional wall motion abnormality. However, the LV sphericity was striking, accompanied by an inferoapikal double myocardial layer with prominent trabeculae. The

direct blood flow was from the ventricular cavity into the deep intertrabecular recesses, as assessed by color Doppler echocardiography. The endsystolic ratio of not compacted to compacted myocardium was >2. The remaining echocardiographic report was regular (Figs. 2 and 3).

These findings fulfilled the criteria of isolated left ventricular non-compaction cardiomyopathy (NCCM). Further investigation with cardiac MRI confirmed the diagnosis (Figs. 4 and 5). Ergometry test showed excellent physical performance, but it had to be ceased prematurely because of dyspnea. Telemetric monitoring over 48 h was normal. The patient was advised to forgo excessive sports and to be followed up with a loop recorder and transthoracic echocardiography in 6 months. An indication for a permanent pacemaker was not given.

### Discussion

Isolated NCCM was first described in 1984, but it only regained recognition in the last decade. Now, it increasingly attracts scientific attention, especially because the condition has not been fully understood so far and is thus a subject of ongoing investigations on its pathology, development, clinical course, and therapy (1). NCCM is a primary genetic cardiomyopathy, caused by a defect in endomyocardial morphogenesis. As a result, the muscle of the ventricle is built out of trabeculae with intratrabecular recesses, giving a typical appearance of muscular bands in a ‘spongy mashwork’. This specific morphology is reminiscent of the myocardium during early embryogenesis. Between the 4th and 18th week of cardiogenesis,



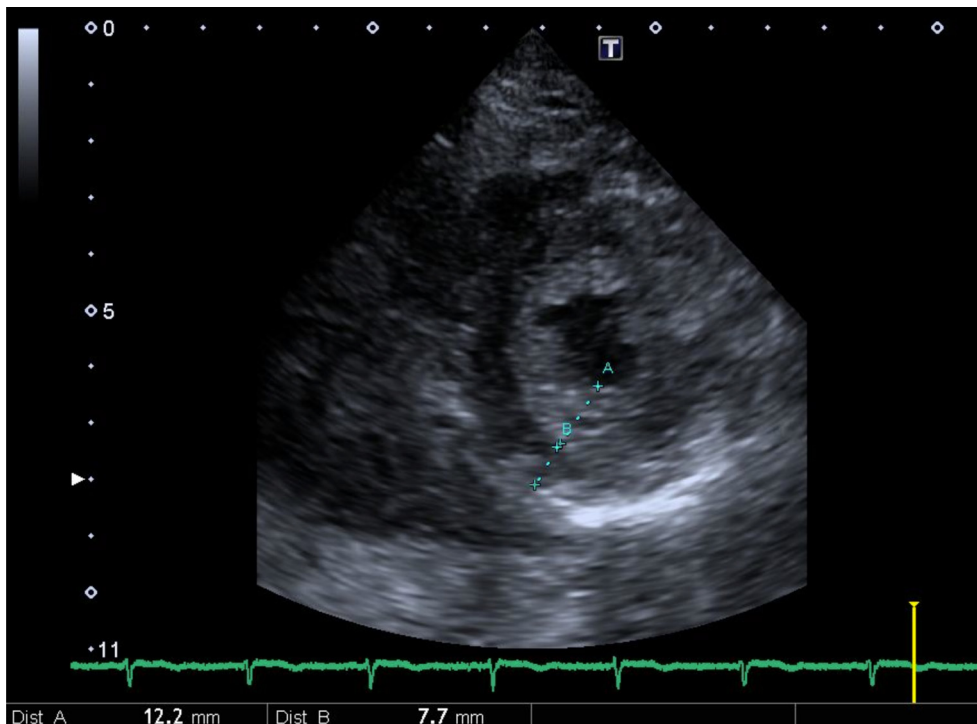
*Fig. 1.* Admission ECG. Regular sinus rhythm, regular QTc, negative T wave in V1–V5.

a non-compacted structure is essential for the nutrition of the cells, since the muscle is being supplied primarily by diffusion of blood that flows in the intratrabecular spaces. When the angiogenesis of coronary arteries is not accompanied by a simultaneous regression of trabeculae, NCCM is occurring (2).

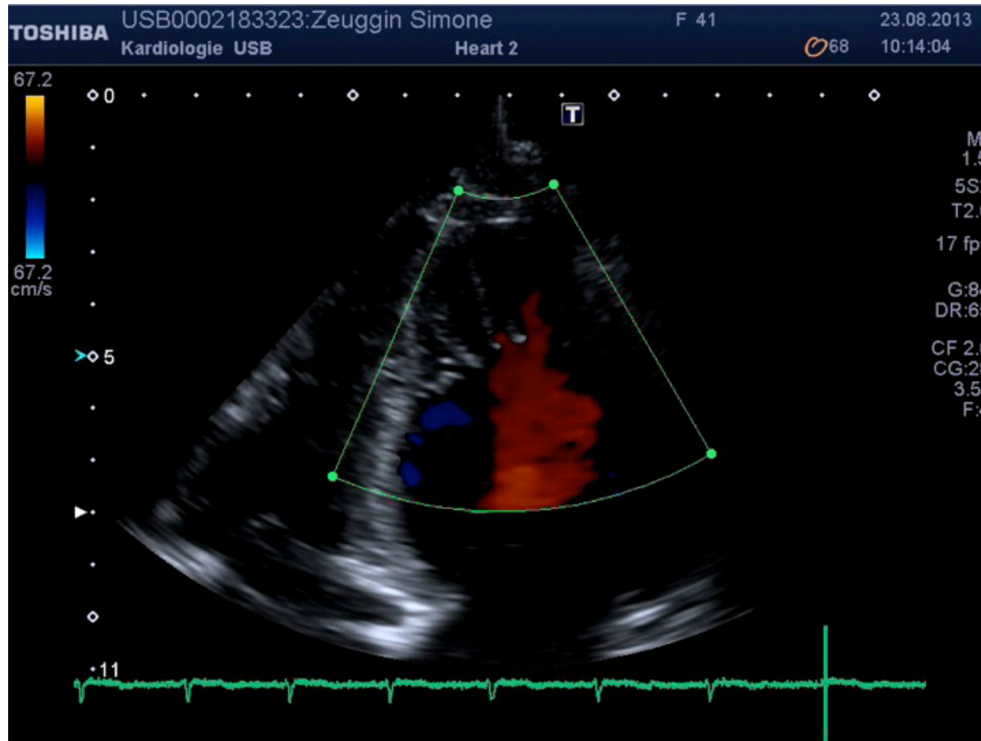
A number of genes have been suggested to be associated with NCCM. Mostly, they encode for sarcomere and cytoskeleton proteins, such as tafazzin (TAZ), LIM

domain binding protein 3 (LDB3),  $\alpha$ -dystrobrevin (DTNA), lamin A/C (LMNA), etc. The transmission is frequently autosomal dominant and X-linked.

The exact prevalence is not known and it is assumed to bear a significant number of undiagnosed cases. In echocardiography, it is found in 1 of 2,000 studies. Since the diagnosis is defined by structural features, which can only be evaluated by cardiac imaging, mostly transthoracic echocardiography. A diagnosis can be made in the



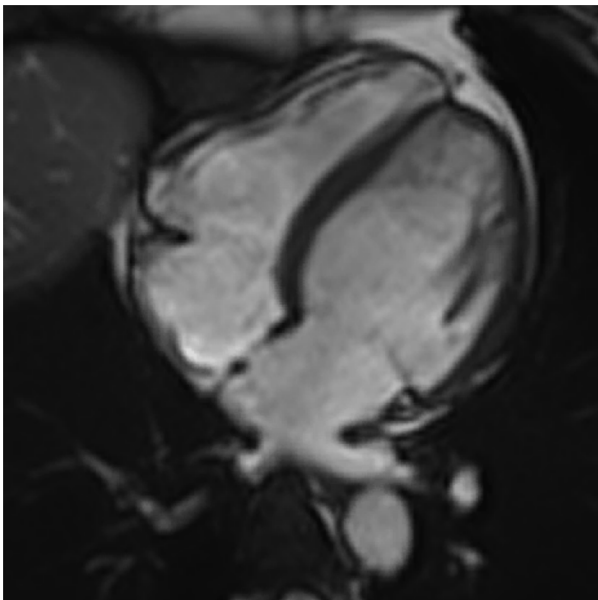
*Fig. 2.* Transthoracic echocardiography (TTE) in apical short axis view (PAX). Parasternal short axis images at the level of the ventricles shows multiple trabeculae and intertrabecular recesses in inferior, lateral, walls, middle and apical portions of the septum, and apex of the left ventricle.



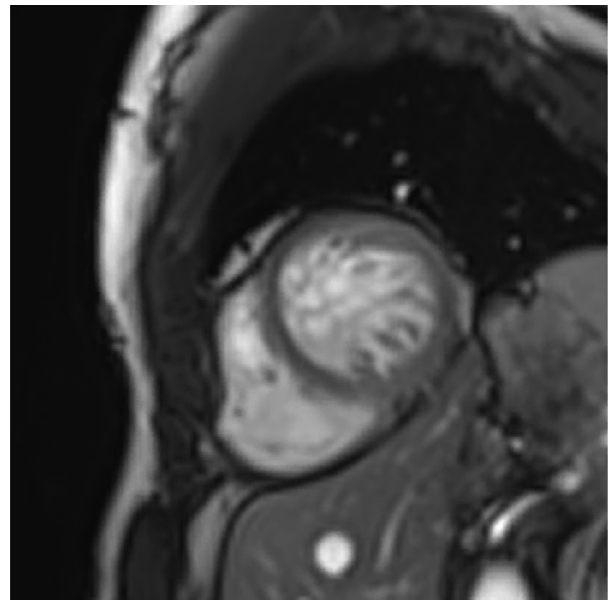
*Fig. 3.* Doppler echocardiography. Transthoracic two-dimensional study with color shows flow within the deep intertrabecular recesses.

presence of three factors: 1) a thickened left ventricular wall consisting of two layers with a maximum ratio of non-compacted to compacted myocardium  $>2:1$  at end-systole in PAX, 2) color Doppler evidence of flow within the deep intertrabecular recesses, 3) prominent trabecular

meshwork in the LV apex or midventricular segments of the inferior and lateral wall (3). Various criteria systems have been described; however, they all disembody in the structural features and quantifications. The ECG mostly reveals none or unspecific abnormalities. Cardiac MRI is



*Fig. 4.* Cardiac MRI. Four-chamber image showing dilated left and right ventricles with trabeculation in the LV apex.



*Fig. 5.* Cardiac MRI. Ventricular short axis at the lower mid to apical regions showing heavy trabeculation in both ventricles.

an advanced option for gaining a closer motion insight of the myocardium.

It is especially useful if the morphology is overlapped with other cardiopathies (4), due to its enhanced spatial resolution, improved tissue characterization, and lack of ionizing radiation (5).

The disease may remain silent along the entire life or appear unspecifically, depending to what extent the heart function is affected: dyspnea, fatigue, limbs edema, limited physical capacity, and exercise intolerance. Furthermore, tachycardia has recently been found associated with NCCM, leading to hypotension. Syncopies have not been mentioned so far in possible signs of the disease but are plausible since it is a result of cerebral hypoperfusion.

In advanced stages, the disease presents with heart failure, systemic embolic events, and ventricular arrhythmias. The prognosis is difficult to predict and has to be individualized, but it can be geared to the resulting cardiac impairment grade. Patients with symptomatic NCCM have a poor prognosis. Since there is no specific treatment so far, the essential approach is the early recognition of any cardiac dysfunction, prevention of complications and symptom-based therapy, including ACE inhibitors, beta-blockers, and aspirin. Installation of a pacemaker is being considered in patients with arrhythmia. More aggressive treatments such as surgical interventions have been reported in severe NCCM cases (6). In our case, the symptoms were still limited to situations where our patient is physically challenged. Thus, she was advised to forego intensive sports and advised to have regular check-ups with a cardiologist (including loop recording and TTE). Patient's children have been advised to undergo a cardiologic check-up as well.

## Conclusion

NCCM is a type of cardiomyopathy that was first described 25 years ago. Its molecular genetic basis is not yet fully clear, and the same is true of its diagnosis, treatment, and prognosis. Further study of these matters is needed.

## Conflict of interest and funding

The author has not received any funding or benefits from industry or elsewhere to conduct this study.

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