CASE REPORT

Isolated left ventricular non-compaction (LVNC) and recurrent strokes: to anticoagulate or not to anticoagulate, that is the question

Ahmed Subahi,¹ Abubaker A I Hassan,¹ Hossam Abubakar,¹ Walid Ibrahim²

¹Department of Internal Medicine, Wayne State University, Detroit, Michigan, USA

²Department of Internal medicine, Detroit Medical Center, Detroit, Michigan, USA

Correspondence to
Dr Ahmed Subahi,
asubahi@med.wayne.edu

Accepted 9 August 2017

SUMMARY

Isolated left ventricular non-compaction (LVNC) is an uncommon primary cardiomyopathy associated with significant risk of thromboembolic stroke. We report a case of a 69-year-old man with a medical history of ischaemic stroke who presented with a stroke for the second time, and during stroke workup transthoracic echo was suggestive of increased apical trabeculation. He underwent cardiac MRI study to evaluate the left ventricular structure, which revealed LVNC cardiomyopathy, which we believe is the main culprit of his recurrent strokes. Given the high risk of stroke recurrence, antiplatelets followed by anticoagulation for secondary prevention were initiated. This case demonstrates the association between LVNC and recurrent stroke, with a literature review trying to address the dilemma facing the clinician to decide on anticoagulation in such patients.

BACKGROUND

Left ventricular non-compaction (LVNC) is a rare cardiomyopathy, frequently complicated by heart failure, arrhythmia or systemic thromboembolism. Furthermore, the echocardiographic diagnosis of this cardiomyopathy is often challenging and could easily be missed during the stroke workup. Therefore, the inclusion of LVNC in the differential diagnosis of cryptogenic or recurrent stroke is crucial. The aim of this report is to expand the awareness and understanding of the probable association between LVNC and recurrent strokes, highlighting the relevant literature about the role of anticoagulation and its indications in the syndrome.

CASE PRESENTATION

A 69-year-old right-handed African-American male presented to the hospital with a 4-day history of difficulty of walking. Medical history was significant for ischaemic stroke a year before his current presentation, type 2 diabetes mellitus, systemic hypertension and dyslipidaemia. At baseline, he had mild right-sided residual weakness and flattening of the nasolabial fold as a sequel of the previous stroke. He reported feeling dizzy and unable to walk due to postural and gait instability. He described his dizziness as everything swirls around him. However, he reported no vomiting, loss of vision, headache, convulsion, syncope, ear pain, diplopia, dysarthria, dysphagia, numbness, urinary or bowel incontinence.

He used to smoke; no family history of cardiomyopathy or sudden cardiac death was reported. On examination, he was afebrile, heart rate was regular at 81 bpm, and blood pressure was 146/92 mm Hg, respiratory rate of 18 breaths/min, temperature of 36.8°C and pulse oximetry 99% on room air. He was alert and oriented to time, place and person with minimal cerebellar dysarthria, Glasgow Coma Scale 15/15; he could interact and follow instructions without difficulty. Pupil size was 3 mm bilaterally, reactive with intact visual fields bilaterally. Tongue protrudes slightly to the right; the right nasolabial fold was blunted, an asymmetric grin on the lower right face but eyebrows raise symmetrically, uvula at midline, ocular motor nerves intact, hearing acuity equal and intact bilaterally, cranial nerves otherwise grossly intact. There were right-sided dysidiadochokinaesia, intention tremor and positive heel-shin test. Upper and lower limbs deep tendon reflexes were mildly exaggerated, and plantar reflex was up towards the right side. Gait was ataxic (broad based). The rest of neurological and general examinations were unremarkable.

INVESTIGATIONS

Initial laboratory studies revealed normal complete blood count, basic metabolic panel, bleeding profile and random blood glucose with negative urine drugs screen including cocaine. Cardiac workup was insignificant with normal ECG and absence of atrial fibrillation or arrhythmia in both inpatient telemetry and 48 hours Holter monitoring. Non-contrast CT of the brain showed no haemorrhage, midline shift or mass effect with a large hypodense focus in the right cerebellar hemisphere, most likely represents an ischaemic change. MRI and MR angiography (MRA) of the head and neck showed subacute right cerebellar and pontine stroke with no significant narrowing or atherosclerotic defect in his common carotids, internal carotids or cerebral arteries. Carotids Doppler ultrasound was also normal. Three-dimensional contrast-enhanced transthoracic echocardiogram (TTE) showed increased apical trabeculation and normal left ventricular systolic function (ejection fraction was 55%). Cardiac MRI (CMR) demonstrated the two-layered appearance of the left ventricular apical chamber, with an extensive trabecular network and thinned overlying apical myocardium associated with apical hypokinesis and late gadolinium contrast endocardial

CrossMark

To cite: Subahi A, Hassan AAI, Abubakar H, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220954

Figure 1 Apical two-chamber cardiovascular MRIs (T1 sequence) showing the marked hypertrabeculation. The thickness of non-compacted myocardium (yellow line) is greater than 2.3 times the thickness of compacted myocardium (red line).

enhancement. The ratio of this apical trabeculation to the overlying compact apical myocardium was 3.7 (figure 1).

DIFFERENTIAL DIAGNOSIS

- ▶ Posterior circulation brainstem or cerebellar stroke;
- ▶ Benign paroxysmal positional vertigo;
- ▶ Vestibular neuritis;
- ▶ Meniere disease.

TREATMENT

Neurology and cardiology teams were involved in the patient care, recommended aggressive risk factors modification. Aspirin 81 mg and Plavix 75 mg daily were initiated for 2 weeks aiming to switch him to rivaroxaban 20 mg daily after.

OUTCOME AND FOLLOW-UP

The patient was seen several times over the next year in the cardiology and neurology outpatient clinics. He was counselled about the risks of anticoagulation.

DISCUSSION

Isolated LVNC is an uncommon primary cardiomyopathy characterised by hypertrabeculation of the myocardium which leads to the creation of wide intertrabecular spaces in the absence of any other structural cardiac defects.¹ These wide intertrabecular spaces are filled directly with blood from the ventricular cavity without communication with the coronary arteries. As result of this hypertrabeculation, the myocardium is divided into two layers; a thick non-compacted epicardial layer and thin compacted endocardial layer. These morphological features are thought to be secondary to the arrest of the myocardial compaction which occurs between the 10 and 16 weeks of embryogenesis.² Our understanding of the genetic pathophysiology behind the LVNC myocardial morphology is currently expanding thanks to the large number of linked

mutations, and chromosomal defects discovered including but not limited to the taffazin, nicotinamide nucleotide transhydrogenase, beta-myosin heavy chain and the PRDM16 gene.³ Most of the involved genes are encoding transcription factors, sarcomeric and mitochondrial proteins.⁴ The diagnostic criteria of The LVNC are evolving. Furthermore, about 11% of the patients are asymptomatic,⁵ as result of these facts, the actual prevalence of the LVNC is unknown; however, the prevalence of LVNC among patients undergoing echocardiography is 0.05%–0.27%.^{6–8} The most common presenting symptom is dyspnoea.⁵ Furthermore, isolated patients with LVNC can present with heart failure,⁵ serious arrhythmia⁵ or systemic thromboembolism.⁹ TTE is usually the initial modality of choice for diagnosis¹⁰ followed by CMR for confirmation if TTE is equivocal. Several diagnostic criteria were proposed with no gold standard criteria or imaging modality agreed on yet. Jenni criteria are the most popular TTE criteria¹¹ with three components, all are needed for diagnosis and all are measured in the end systolic short axis parasternal view:

- ▶ The presence of two myocardial layers, a thin compacted and a thick non-compacted layer;
- ▶ The ratio of the non-compacted layer to the compacted layer is more than 2:1;
- ▶ Positive Doppler flow within the intertrabecular spaces which indicates communication with the ventricular cavity;
- ▶ The absence of other congenital cardiac anomalies.

On the other hand, there are also several CMR criteria, the most popular one of them is Jacquire criteria¹² which diagnose LVNC with a sensitivity and specificity of 94% when the ratio of the trabeculated LV mass to the global LV mass is more than 20%. To improve the diagnostic efficiency, specificity and to reduce interobserver discrepancy, a recent editorial by Garcia-Pavia *et al*¹³ suggested that definitive diagnosis will be achieved by the presence of both TTE–Jenni and CMR–Jacquire criteria, plus one of the following:

- ▶ LVNC-related heart failure, arrhythmia or thromboembolism;
- ▶ Presence of a pathogenic mutation known to be associated with LVNC;
- ▶ Regional wall motion abnormalities;
- ▶ LVNC in another family member.

Due to our limited knowledge about the pathophysiology of the LVNC, no specific management is recommended, instead symptoms targeted therapy is the current management approach. Patient with heart failure or arrhythmia should be treated according to the current guidelines.¹⁰ Thromboembolism occurs in 13%–24% of patients with LVNC^{14 15} and presents as transient ischaemic attack/stroke, renal infarction, mesenteric ischaemia, cardiac ischaemia and peripheral vascular occlusion.¹⁰ The central question we encountered in this patient was whether to start anticoagulation or not and what agent shall we recommend. There is scarce data in the literature about the appropriate indications, risk stratification and efficacy of anticoagulation therapy in LVNC with no randomised trials done yet. Our literature reviews showed that oral anticoagulation in LVNC is advised in the presence of the following indications¹⁰:

- ▶ Atrial fibrillation despite insufficient CHADS2 and CHA2DS2-Visual Analogue Scale risk scores as these patients might carry high risk and cheat the score like some of the other cardiomyopathy patients¹⁶ furthermore, LVNC patient with atrial fibrillation tend to have a higher incidence of thromboembolism¹⁵;
- ▶ Thromboembolic events to the pulmonary or systemic circulation¹⁷;

- ▶ Reduced LV ejection fraction as patient with LVNC reduced ejection fraction tends to have a higher incidence of thromboembolism¹⁵;
- ▶ Intracardiac thrombi¹⁸;
- ▶ Elevated CHADS2 and CHA2DS2-VASc risk scores more than or equal 2 in the absence of the above indications is also associated with significant risk of thromboemboli.⁹

The patient has multiple risk factors for atherosclerosis including hypertension, diabetes and hyperlipidaemia which increases his risk of in situ cerebrovascular disease. Nevertheless, he presented 1 year before his recent stroke with acute infarction in the left insular area, had CT angiogram of head and neck showed no narrowing or defect in common carotids, internal carotids, basilar, vertebral or cerebral arteries. Over the next 12 months, he was on regular follow-up with neurology clinic for risk factors optimisation. He was on aspirin/dipyridamole 25/200 mg twice a day, atorvastatin 40 mg daily and amlodipine 10 mg. Low-density lipoprotein was between 75 and 30 mg/dL, haemoglobin A1c range 6.4%–6.8% and blood pressure was consistently less than 150/90 mm Hg. Furthermore, MRA of head and neck after his second stroke showed no significant narrowing or defect in common carotids, internal carotids or cerebral arteries. Due to all these factors, cardioembolism is the most plausible cause of recurrent strokes which involves multiple cerebrovascular territories.

Our patient had LVNC with recurrent ischaemic stroke, which puts him at higher risk of recurrent cardioembolic insults in the future. Due to high risk of stroke recurrence, he was started on oral rivaroxaban for secondary prevention. The absence of randomised trials due to low disease incidence and the challenging diagnosis retrospective case series are the best available guides on anticoagulation in LVNC. Nevertheless, large controlled trials are needed to provide stronger evidence-based guidance derived from larger patient populations.

Learning points

- ▶ Left ventricular non-compaction (LVNC) is a challenging to diagnose cardiomyopathy that should be considered in differential diagnosis of recurrent thromboembolic strokes.
- ▶ The case emphasises the importance of multimodality cardiac imaging including transthoracic echocardiogram and cardiac MRI in the recurrent stroke workup to diagnose LVNC.
- ▶ Our case also demonstrates the indications of anticoagulation in patients with LVNC and thromboembolic stroke.

Contributors AS, conducted the discussion and learning points. AAIH and HA conducted the summary, background and differential diagnosis. HA conducted the case presentation. WI conducted the literature review and investigations.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Maron BJ, Towbin JA, Thiene G, *et al.* Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. *Circulation* 2006;113:1807–16.
- 2 Sedmera D, McQuinn T. Embryogenesis of the heart muscle. *Heart Fail Clin* 2008;4:235–45.
- 3 Klaassen S. Malformations of the left ventricle: what comes first: form or function? *Circ Cardiovasc Genet* 2015;8:537–40.
- 4 Arbustini E, Favalli V, Narula N, *et al.* Left ventricular noncompaction: a distinct genetic cardiomyopathy? *J Am Coll Cardiol* 2016;68:949–66.
- 5 Bhatia NL, Tajik AJ, Wilansky S, *et al.* Isolated noncompaction of the left ventricular myocardium in adults: a systematic overview. *J Card Fail* 2011;17:771–8.
- 6 Ritter M, Oechslin E, Sütsch G, *et al.* Isolated noncompaction of the myocardium in adults. *Mayo Clin Proc* 1997;72:26–31.
- 7 Ronderos R, Avegliano G, Borelli E, *et al.* Estimation of prevalence of the left ventricular noncompaction among adults. *Am J Cardiol* 2016;118:901–5.
- 8 Stöllberger C, Blazek G, Winkler-Dworak M, *et al.* Sex differences in left ventricular noncompaction in patients with and without neuromuscular disorders. *Rev Esp Cardiol* 2008;61:130–6.
- 9 Stöllberger C, Wegner C, Finsterer J. CHADS2- and CHA2DS2VASc scores and embolic risk in left ventricular hypertrabeculation/noncompaction. *J Stroke Cerebrovasc Dis* 2013;22:709–12.
- 10 Finsterer J, Stöllberger C, Towbin JA. Left ventricular noncompaction cardiomyopathy: cardiac, neuromuscular, and genetic factors. *Nat Rev Cardiol* 2017;14:224–37.
- 11 Jenni R, Oechslin E, Schneider J, *et al.* Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. *Heart* 2001;86:666–71.
- 12 Jacquier A, Thuny F, Jop B, *et al.* Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction. *Eur Heart J* 2010;31:1098–104.
- 13 Garcia-Pavia P, de la Pompa JL. Left ventricular noncompaction: a genetic cardiomyopathy looking for diagnostic criteria. *J Am Coll Cardiol* 2014;64:1981–3.
- 14 Oechslin EN, Attenhofer Jost CH, Rojas JR, *et al.* Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. *J Am Coll Cardiol* 2000;36:493–500.
- 15 Stöllberger C, Blazek G, Dobias C, *et al.* Frequency of stroke and embolism in left ventricular hypertrabeculation/noncompaction. *Am J Cardiol* 2011;108:1021–3.
- 16 Weir RA, MacKenzie N, Petrie CJ. Cheating the CHA2DS2-VASc score: thromboembolism in apical hypertrophic cardiomyopathy. *Case Rep Cardiol* 2014;2014:1–3.
- 17 Lindenfeld J, Albert NM, Boehmer JP, *et al.* HFSA 2010 comprehensive heart failure practice guideline. *J Card Fail* 2010;16:e1–194.
- 18 Vandvik PO, Lincoff AM, Gore JM, *et al.* Primary and secondary prevention of cardiovascular disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141:e637S–e668S.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow