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【 CASE REPORT 】

Left Ventricular Noncompaction with Multiple Thrombi in Apical Aneurysm

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Abstract:

A 44-year-old man was admitted to our hospital due to heart failure. Transthoracic echocardiography demonstrated global hypokinesis with an ejection fraction of 25%, prominent trabeculation and deep intertrabecular recesses, and apical aneurysm with multiple thrombi (10×13 mm in the inferior wall, 15×8 mm in the anterior wall). Cardiac magnetic resonance imaging showed an increased ratio of noncompacted (NC) to compacted (C) myocardium (NC/C ratio >2.3) and apical aneurysm. Coronary angiography revealed no significant stenosis. He was therefore diagnosed with left ventricular noncompaction complicated by apical aneurysm. Four weeks after starting anticoagulation, the multiple apical thrombi disappeared without clinical signs of embolism.

Key words: left ventricular noncompaction, thrombus, aneurysm

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Introduction

Left ventricular noncompaction (LVNC) is a rare form of cardiomyopathy caused by the failure of myocardial compaction during embryogenesis (1). It is characterized by multiple prominent trabeculations with deep intertrabecular recesses (1). Its clinical features are variable, ranging from no symptoms to cardiac dysfunction, heart failure (HF), arrhythmias, and systemic thromboembolism (2). However, there have been only a few reports regarding its coexistence with LV aneurysm and thrombus (3).

We herein report a patient with LVNC showing severe LV dysfunction and multiple thrombi in LV apical aneurysm.

Case Report

A 44-year-old man who presented with shortness of breath on effort was admitted to our hospital. He had no history of hypertension, diabetes mellitus, or cardiovascular diseases. His blood pressure was 106/78 mmHg, pulse rate was 108 bpm, and blood oxygen saturation was 97% on room air. A Levine 3/6 holosystolic murmur and the third heart sound at the apex and bilateral rales were audible. Jugular venous distention and moderate pitting edema of the bilateral pretibials were noted.

Chest radiography revealed cardiac enlargement (cardiothoracic ratio 66%), pulmonary congestion, and mild pleural effusion (Fig. 1A). An electrocardiogram (ECG) showed sinus rhythm and complete left bundle branch block (QRS width: 132 ms) (Fig. 1B). Regarding laboratory data, serum aspartate transaminase, serum creatinine, and serum uric acid were mildly elevated. The brain natriuretic peptide level was 885 pg/mL, and the troponin T level was 0.057 ng/mL (Table). Transthoracic echocardiography demonstrated LV dilatation [LV end-diastolic diameter (LVDd): 70 mm] (Fig. 1C), global hypokinesis with an ejection fraction of 25%, prominent and deep intertrabecular recesses, increased noncompacted (NC) endomyocardial layer depth compared to the compacted (C) epicardial layer (NC 28.5

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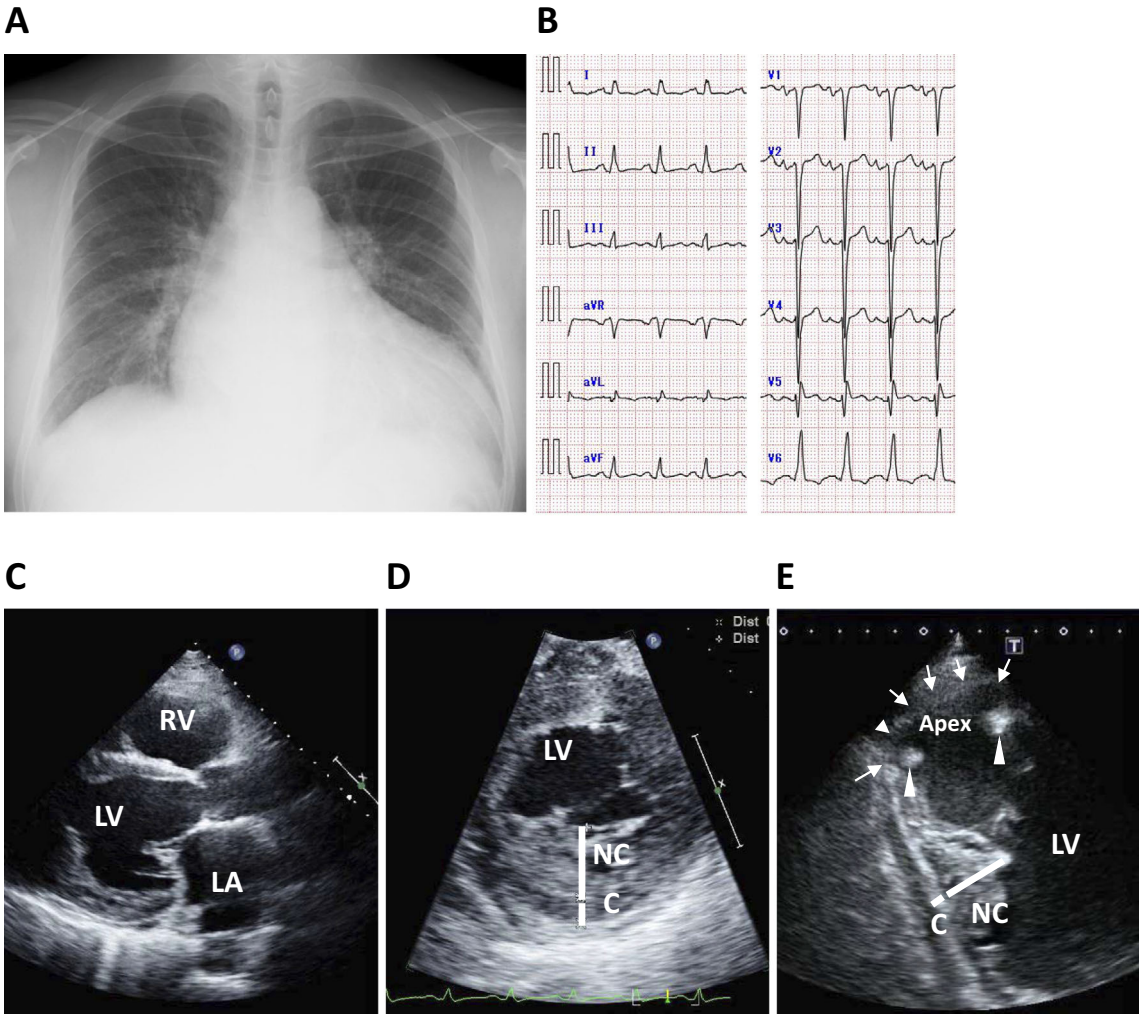

Figure 1. **Chest radiography exhibited cardiac enlargement, pulmonary congestion, and mild pleural effusion (A), and an electrocardiogram showed sinus rhythm and complete left bundle branch block (B). Transthoracic echocardiography demonstrated LV dilatation in the parasternal long-axis view (C), prominent trabeculation, deep intertrabecular recesses, and an increased NC/C ratio (>2) in the parasternal short-axis view (D) along with apical aneurysm (*white arrows*) with 2 thrombi (10×13 mm in the inferior wall, 15×8 mm in the anterior wall: *white arrowheads*) in the apical long-axis view (E). RV: right ventricle, LV: left ventricle, LA: left atrium, NC: noncompacted endomyocardial layer, C: compacted epicardial layer**

mm, C 8.3 mm, NC/C ratio >2.0) (Fig. 1D), and apical aneurysm with spontaneous echo contrast and 2 thrombi (10 ×13 mm in the inferior wall, 15×8 mm in the anterior wall) (Fig. 1E).

The NC region was localized at the mid-inferior and posterolateral LV and adjacent to the apical aneurysm. These thrombi were relatively highly echogenic and immobile and were detected in the apical aneurysm, not the NC region (Fig. 1E). Cardiac magnetic resonance imaging (cMRI) showed late gadolinium enhancement (LGE) in the endocardium in the apical anterolateral wall, an increased NC/C ratio (>2.3) (Fig. 2A), and 2 thrombi in the apical aneurysm (Fig. 2B). Coronary angiography revealed no significant obstructive stenosis (Fig. 2C), but a left ventriculogram showed an aneurysm in the apex (Fig. 2D). A pathological analysis demonstrated no evidence of secondary cardiomyopathy, such as myocarditis, sarcoidosis, amyloidosis or hemochromatosis. Based on these findings, he was diagnosed with LVNC complicated with apical aneurysm.

To determine the link between gene mutations and LV aneurysm in this case, we performed a genetic test to diagnose the LVNC. However, we detected no genetic mutations associated with LVNC or other cardiomyopathies. This patient did not have a family history of LVNC or a history of other congenital, acquired, significant valvular heart disease or neuro-muscular disease. This patient was therefore thought to be an isolated case of LVNC with LV dysfunction.

Carvedilol, enalapril, furosemide, and warfarin were started to manage HF and prevent stroke or systemic thromboembolism. Although the multiple apical thrombi disappeared without clinical signs of embolism after four weeks

Table. Laboratory Data on Admission.

Total protein (g/dL)	6.2	TC (mg/dL)	134
Albumin (g/dL)	3.8	TG (mg/dL)	60
AST (U/L)	30	LDL-C (mg/dL)	90
ALT (U/L)	54	WBC (/uL)	9,630
LDH (U/L)	240	RBC (/uL)	4.45×10^6
ALP (U/L)	357	Hb (g/dL)	13.0
CK (U/L)	66	Ht (%)	41.9
TB (mg/mL)	0.9	Platelt (/uL)	232×10^3
DB (mg/mL)	0.2	CRP (mg/dL)	0.25
BUN (mg/dL)	19.0		
Creatinine (mg/dL)	1.03	HbA1c (%)	6.5
Uric acid (mg/dL)	7.9	TSH (uIU/mL)	1.45
Sodium (mEq/L)	141	fT4 (ng/dL)	1.39
Potassium (mEq/L)	4.5	BNP (pg/mL)	885.4
Chloride (mEq/L)	107	TnT (ng/mL)	0.057
Calcium (mEq/L)	8.9		

AST: aspartate transaminase, ALT: alanine transaminase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase , CK: creatine kinase, TB: total bilirubin, DB: direct bilirubin, BUN: bloodurea nitrogen , TC: Total cholesterol, TG: triglyceride, LDL-C: low density lipoprotein cholesterol, WBC: white Blood Cell, RBC: red blood cell, Hb: hemoglobin, Ht: hematocrit, CRP: C-reactive protein, HbA1c: hemoglobin A1c, TSH: thyroid-stimulating Hormone, fT4: free total thyroxine, BNP: brain natriuretic peptide, TnT: troponin T

of anticoagulation, computed tomography (CT) revealed right cerebellar infarction (Fig. 3). Eight months after medical therapy, despite the improvement in the LV dimension (LVDd: 63 mm) and systolic function (LVEF: 34%), the thicknesses of the NC and C layers were not markedly changed (NC: 28.8 mm, C: 8.2 mm).

Discussion

We encountered a rare case of LVNC with multiple thrombi in LV aneurysm. This case indicates that coexisting of LVNC and LV aneurysm is accompanied by a high risk of thrombosis, and anticoagulation needs to be considered in patients with LVNC and LV aneurysm.

LVNC is a genetically heterogeneous congenital disease caused by the arrest of the compaction process during the second month of embryological development. LVNC was first described in a newborn case by Bellet and Gouley in 1932 (4). In 1990, Chin et al. proposed the existence of isolated LVNC in the absence of other cardiac anomalies (1). The prevalence of isolated LVNC ranges from 0.01% and 0.3% in the adult population (5-9). Unlike pediatric cases, adult LVNC occurs more sporadically with a less-frequent family history, and both sexes are equally affected in cases of sporadic LVNC (10). The American Heart Association classified LVNC as a primary genetic cardiomyopathy (11), and the European Society of Cardiology as well as the Japanese Circulation Society (JCS) consider LVNC an "unclassified cardiomyopathy".

The diagnosis of LVNC is mainly based on its anatomical characteristics on imaging. Although a universally established definition of LVNC is lacking, the following echocardiographic criteria are widely accepted: (i) two-layered myocardium with multiple, prominent trabeculations in end-systole; (ii) NC/C ratio >2; (iii) communication with the intertrabecular space demonstrated with color Doppler imaging; and (iv) absence of coexisting cardiac abnormalities (12). cMRI is superior to echocardiography for the evaluation of the extent of the two-layered structure, and an NC/C ratio >2.3 in end-diastole is used as the cut-off value for the diagnosis of LVNC (13). Of note, however, while Ross et al. reported the high diagnostic performance of cMRI, they also pointed out the possibility of overdiagnosis using this modality (14).

Patients with LVNC show a wide range of clinical features, such as congestive HF, arrhythmias, thromboembolic events, and sudden cardiac death. Generally, thromboembolic events in LVNC are thought to be secondary to the extensive trabeculated ventricle, atrial fibrillation, and decreased LV systolic function. Several cases of LVNC with LV aneurysm have been reported (15, 16). However, there are only few reports regarding LV aneurysm and thrombosis in LVNC (3). This is the first case report of LVNC coexisting with severe LV dysfunction and multiple thrombi in LV aneurysm. In our case, the NC region was localized at the basal level of the LV and adjacent to the apical aneurysm. Two thrombi were detected in the apical aneurysm but not in the NC region (Fig. 1E). Therefore, the formation of thrombi might be mainly due to blood stasis in the apical aneurysm. The mechanisms by which LV dysfunction and LV aneurysm develop are unclear. Abnormality of the microcirculation within the myocardium is speculated to be involved in this disease (12). In addition, gene mutations might be associated with cardiac trabeculation with LV aneurysm. Indeed, Shan et al. reported a mutation of LIM domain binding 3 (LDB3) in a patient who had LV aneurysm with LVNC (17). However, there were no genetic mutations in our case.

Medical treatment for LVNC depends on its clinical manifestations. Patients with a reduced LV function are treated with standard medical therapy, such as angiotensin-converting-enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and beta-blockers. The incident rate of thromboembolism in LVNC is controversial (1, 2, 18). Anticoagulation with warfarin is recommended in LVNC patients with history of thromboembolism, atrial fibrillation, and/or a reduced LV function (LV ejection fraction <40%) (19). In addition, anticoagulation is indicated for thrombus in the LV as first-line therapy according to the JCS guideline (20). Although surgical thrombectomy is a possible treatment option for LV thrombus, it often causes further deterioration of the LV function. In addition, Lee et al. reported that the rate of thromboembolism after surgical thrombectomy was not markedly different from that after anticoagulation therapy alone (21). If LV thrombi are not dissolved or thromboembolism recurs despite adequate anticoagulation, surgical

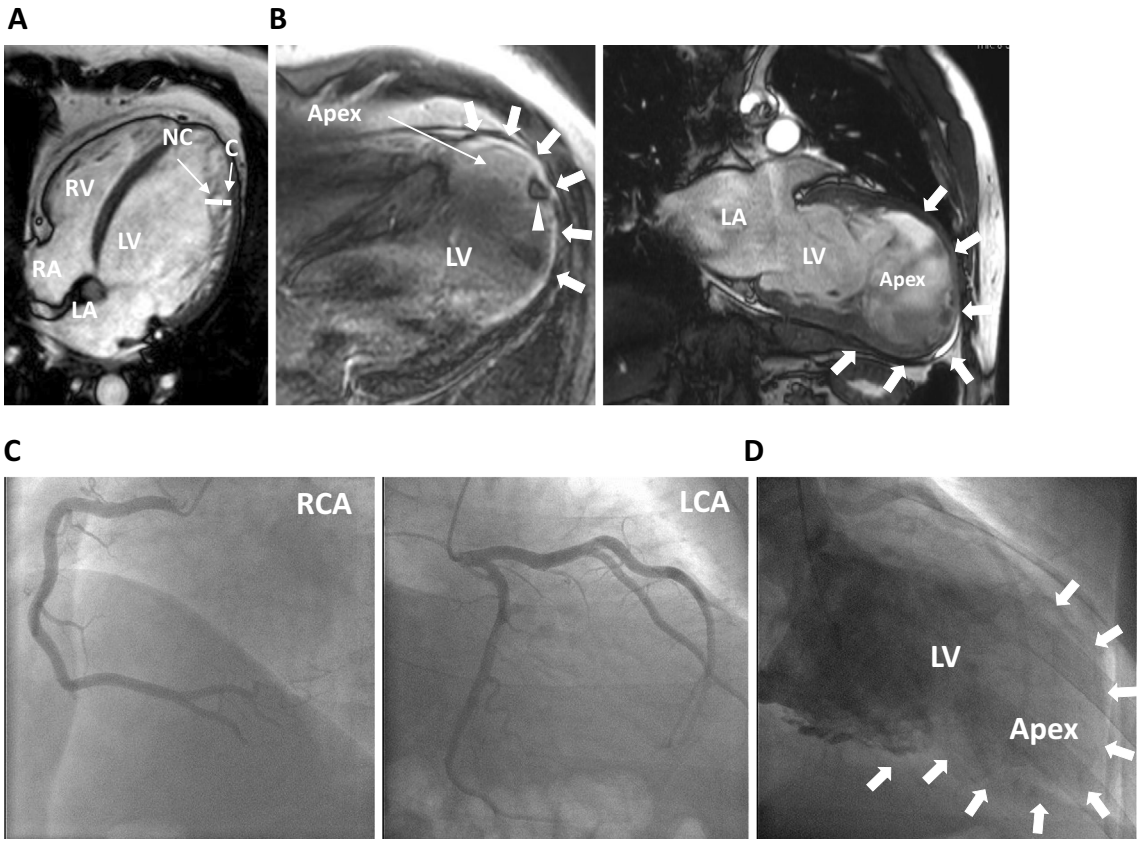

Figure 2. **Cardiac magnetic resonance imaging showed an increased NC/C ratio (>2.3) (A) and thrombus (*white arrowhead*) in the left ventricular apical aneurysm (*white arrows*) (B). Coronary angiography revealed no significant obstructive stenosis (C). A left ventriculogram in end-systole showed apical aneurysm in the left ventricular wall (*white arrows*) (D). RV: right ventricle, RA: right atrium, LV: left ventricle, LA: left atrium, NC: noncompacted endomyocardial layer, C: compacted epicardial layer, RCA: right coronary artery, LCA: left coronary artery**

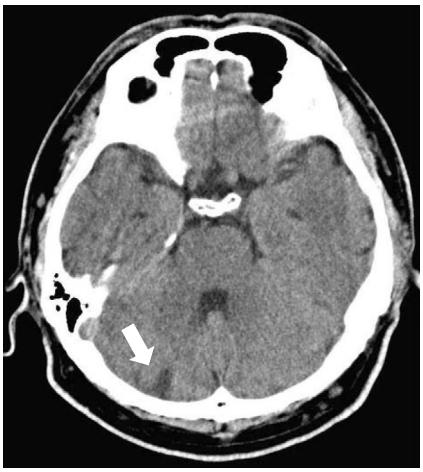

Figure 3. **Computed tomography imaging demonstrated right cerebellar infarction (white *arrow*).**

thrombectomy should be considered. In our case, the presence of asymptomatic cerebral infarction was considered to be a high-risk factor of further thromboembolism. Early anticoagulant treatment is needed in such high-risk cases.

In conclusion, we described a rare case of LVNC with multiple thrombi within LV aneurysm. The early detection of coexisting LV aneurysm is important for administering optimal therapy in LVNC. Anticoagulation therapy is definitely needed in LVNC patients complicated with LV aneurysm.

The authors state that they have no Conflict of Interest (COI).

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