CASE REPORT

**Left Ventricular Noncompaction with Multiple Thrombi in Apical Aneurysm**

Daisuke Yakabe, Shouji Matsushima, Saori Uchino, Kisho Ohtani, Tomomi Ide, Taiki Higo and Hiroyuki Tsutsui

**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

(Intern Med Advance Publication) (DOI: 10.2169/internalmedicine.3489-19)

**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
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 the HF and prevent stroke or systemic thromboembolism. Although the multiple apical thrombi disappeared without clinical signs of embolism after four
weeks 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 both 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 LVNC patients with history of thromboembolism and atrial fibrillation, and/or a reduced LV function (LV ejection fraction <40%) (19). 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

### Table. Laboratory Data on Admission.

| Parameter          | Value       |
|--------------------|-------------|
| Total protein (g/dL)| 6.2         |
| Albumin (g/dL)     | 3.8         |
| AST (U/L)          | 30          |
| ALT (U/L)          | 54          |
| LDH (U/L)          | 240         |
| ALP (U/L)          | 357         |
| CK (U/L)           | 66          |
| TB (mg/dL)         | 0.9         |
| DB (mg/dL)         | 0.2         |
| BUN (mg/dL)        | 19.0        |
| Creatinine (mg/dL) | 1.03        |
| Uric acid (mg/dL)  | 7.9         |
| Sodium (mEq/L)     | 141         |
| Potassium (mEq/L)  | 4.5         |
| Chloride (mEq/L)   | 107         |
| 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: blood urea 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, tT4: free total thyroxine, BNP: brain natriuretic peptide, TnT: troponin T.
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).

References

1. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. Circulation 82: 507-513, 1990.
2. Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: A distinct cardiomyopathy with poor prognosis. J Am Coll Cardiol 36: 493-500, 2000.
3. Ahn JH, Koh JS, Park JR, et al. Isolated left ventricular noncompaction with a congenital aneurysm presenting with recurrent embolism. J Cardiovasc Ultrasound 20: 103-107, 2012.
4. Engberding R, Bender F. Identification of a rare congenital anomaly of the myocardium by two-dimensional echocardiography: Persistence of isolated myocardial sinusoids. Am J Cardiol 53: 1733-1734, 1984.
5. Ritter M, Oechslin E, Sutsch G, Attenhofer C, Schneider J, Jenni...
R. Isolated noncompaction of the myocardium in adults. Mayo Clin Proc 72: 26-31, 1997.
6. Benjamin MM, Khetan RA, Kowal RC, Schussler JM. Diagnosis of left ventricular noncompaction by computed tomography. Proc (Bayl Univ Med Cent) 25: 354-356, 2012.
7. Ozkutlu S, Ayabakan C, Celiker A, Elshershari H. Noncompaction of ventricular myocardium: A study of twelve patients. J Am Soc Echocardiogr 15: 1523-1528, 2002.
8. Stollberger C, Finsterer J. Left ventricular hypertrabeculation/non-compaction. J Am Soc Echocardiogr 17: 91-100, 2004.
9. Weiford BC, Subbarao VD, Mulhern KM. Noncompaction of the ventricular myocardium. Circulation 109: 2965-2971, 2004.
10. Zambrano E, Marshalko SJ, Jaffe CC, Hui P. Isolated noncompaction of the ventricular myocardium: Clinical and molecular aspects of a rare cardiomyopathy. Lab Invest 82: 117-122, 2002.
11. 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 113: 1807-1816, 2006.
12. Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: A step towards classification as a distinct cardiomyopathy. Heart 86: 666-671, 2001.
13. Petersen SE, Selvanyagam JB, Wiesmann F, et al. Left ventricular non-compaction: Insights from cardiovascular magnetic resonance imaging. J Am Coll Cardiol 46: 101-105, 2005.
14. Ross SB, Jones K, Blanch B, Puranik R, et al. A systematic review and meta-analysis of the prevalence of left ventricular noncompaction in adults. Eur Heart J 12019.
15. Sato Y, Matsumoto N, Yoda S, et al. Left ventricular aneurysm associated with isolated noncompaction of the ventricular myocardium. Heart Vessel 21: 192-194, 2006.
16. Sun JP, Ni X, Yang XS, Yu CM. Noncompaction cardiomyopathy with apical aneurysm. Int J Cardiol 186: 48-49, 2015.
17. Shan S, He X, He L, Wang M, Liu C. Coexistence of congenital left ventricular aneurysm and prominent left ventricular trabeculation in a patient with IDB3 mutation: A case report. J Med Case Rep 11: 229, 2017.
18. Fazio G, Corrado G, Zachara E, et al. Anticoagulant drugs in non-compaction: A mandatory therapy? J Cardiovasc Med (Hagerstown) 9: 1095-1097, 2008.
19. Kido K, Guglin M. Anticoagulation therapy in specific cardiomyopathies: Isolated left ventricular noncompaction and peripartum cardiomyopathy. J Cardiovasc Pharmacol Ther 24: 31-36, 2019.
20. Murasaki K. Guidelines for management of anticoagulant and antiplatelet therapy in cardiovascular disease (JCS 2009). Nihon Rinsho 69 Suppl 9: 567-571, 2011.
21. Lee JM, Park JJ, Jung HW, et al. Left ventricular thrombus and subsequent thromboembolism, comparison of anticoagulation, surgical removal, and antiplatelet agents. J Atheroscler Thromb 20: 73-93, 2013.

© The Japanese Society of Internal Medicine
Intern Med Advance Publication