Acquired Left Ventricular Hypertrabeculation/Noncompaction in Sarcoidosis—A Rare but Possible Preventable Cause of Myocardial Infarction

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ABSTRACT

Left ventricular hypertrabeculation/noncompaction (LVHT/NC) is a rare if not unique disorder of endomyocardial morphogenesis. Left ventricle in this condition consists of trabeculations that are both increased in prominence and excessive in number, was hypothesized to be caused by intrauterine arrest of compaction of the myocardial fibers and meshwork. LVHT/NC has been observed to have high prevalence in children as opposed to adults with genetic linkage. Acquired LVHT/NC has been recently reported to be associated with other autoimmune diseases like mitochondriopathy, myotonic dystrophy type 1, essential thrombocytopenia, Duchenne muscular dystrophy, and various neuromuscular disorders. We report here an interesting case displaying LVHT/NC in a patient with coexistent neuro-sarcoidosis at an age of 49 years with concomitant non-ST-Elevation Myocardial Infarction. Following diagnosis of LVHT/NC by means of transthoracic echocardiography, our patient was treated with a course of intravenous steroids with resultant improvement in his symptoms. This case is a unique presentation of the association of neuro-sarcoidosis with LVHT/NC with a presumptive complication in the form of non-ST-Elevation Myocardial Infarction due to synergistic interplay of pathophysiological mechanisms of these 2 individual conditions.

Left ventricular (LV) hypertrabeculation/noncompaction (LVHT/NC) is a rare if not unique disorder of endomyocardial morphogenesis, consists of trabeculations that are both increased in prominence and excessive in number, was hypothesized to be caused by intrauterine arrest of compaction of the myocardial fibers and meshwork.[1] LVHT/NC has been observed to have high prevalence in children[2,3] as opposed to adults.[4] Genetic abnormalities have been identified[5] in LVHT/NC patients displaying its heterozygous nature and presumptive spread either as an autosomal-dominant or X-linked recessive disorder. Based on highly variable presentations of LVHT/NC both in children and adults in the recent past, other pathogenetic processes are recently suggested to be responsible for noncompaction, which would then be acquired diseases.[6]

Acquired LVHT/NC has been recently reported to be associated with other autoimmune diseases like mitochondriopathy[7], myotonic dystrophy type 1,[8] essential thrombocytopenia,[9] Duchenne muscular dystrophy,[10] and various neuromuscular disorders.[11] We report here an interesting case displaying LVHT/NC in a patient with coexistent neuro-sarcoidosis at an age of 49 years with concomitant non-ST-Elevation Myocardial Infarction (NSTEMI). To our knowledge, this is the first ever case reporting association of LVHT/NC with sarcoidosis, which is an autoimmune disorder.

Case presentation

A 49-year-old African American female without any significant medical history presented with a complaint of sudden exacerbation of progressive dyspnea without any electrocardiogram changes or elevation of cardiac enzymes. The patient denied any previous history of hypertension or any other medical condition but mentioned exertional dyspnea for the last 6 months of intermittent course. Screening transthoracic echocardiogram (TTE) at this time was normal. Chest x-ray showed bilateral mediastinal and hilar lymphadenopathy without any cardiomegaly supported by chest computed tomographic scan, which was suspicious of pulmonary sarcoidosis. A lymph node biopsy at that time confirmed the presence of small noncaseating granulomas. The patient received a short course of intravenous steroids at that time with resolution of symptoms and sent home. One month later, the patient developed burning sensations in her feet, which over the next 3–4
weeks progressed into insidious left leg weakness, eventually making her completely nonambulatory. Magnetic resonance imaging on presentation in hospital showed diffuse involvement of the cervical spinal cord with multiple nodular enhancements consistent with neurosarcoïdosis. Based on the progressive course of her symptoms pointing to rapidly progressing nature of the spinal cord involvement, she was admitted for a course of intravenous steroids and close monitoring. On day 5 of admission, the patient suddenly became unresponsive, hypotensive, and tachycardic. Other laboratory findings included elevated calcium level of 11.6 mg/dl but normal lipid profile. Considering NSTEMI, the patient was taken for cardiac catheterization and found to have 50% mid left anterior descending artery atherosclerotic nonobstructive lesion. A precatheterization TTE showed an ejection fraction (EF) of 10% and mild-to-moderate LV hypertrophy with severe global LV systolic dysfunction along with spongiform and deep sinusoids in the anterior and inferior LV apical hypertrophied myocardium, typical appearance of LVHT/NC (Fig. 1). An endomyocardial biopsy was performed which showed no evidence of any virus persistence, myocarditis, or other specific cardiomyopathy. Repeat TTE confirmed the ratio of the compacted to noncompacted myocardial layers at end-systole > 2:1 — key diagnostic criteria in LVHT/NC. TTE with contrast 1 week later while on high dose steroids showed mild improvement in the EF up to 20% with no change in rest of the structural morphology. Diagnosis of LV noncompaction was confirmed by echocardiography using Jenni criteria. No family history of LVHT/NC or premature coronary artery disease was reported either by the patient or family members.

Discussion

Sarcoidosis is an enigmatic multisystem granulomatous disease of unknown etiology that primarily affects the lung, infrequently myocardium, and nervous system. Autopsy series suggest that up to 50% of patients with sarcoidosis have some degree of cardiac involvement, but only a fraction of these had previously recognized cardiac sarcoidosis (CS). CS most commonly affects the myocardium but may also affect the pericardium and endocardium. Myocardial infiltration may be associated with ventricular tachycardia, aneurysm formation, or global systolic dysfunction, but the most common clinical feature is conduction disease. Recently, an association of neurosarcoïdosis with CS has been reported, but the incidental finding of LVHT/NC in this patient with concomitant neurosarcoidosis is a striking novel presentation. The endomyocardial biopsy performed certainly ruled out the CS in this patient, and the echocardiographic findings confirmed the LVHT. The occurrence of sudden NSTEMI in this patient without known history of hypertension, coronary artery disease, or dyslipidemia is also an interesting concomitant presentation. Chronic hypercalcemia has long been shown to predispose patients to increased risk of myocardial ischemia either by atherosclerosis, coronary vasospasm, and/or mediasclerosis leading to reduced coronary vasodilator response. The coronary microcirculatory dysfunction in LVHT/NC resulting in subendocardial infarction associated with calcification has also been reported but only in pediatric population. The chronic hypercalcemia secondary to sarcoidosis in this patient superimposed on LVHT/NC induced microcirculatory dysfunction might have augmented the development of coronary artery disease with resultant NSTEMI. The coronary arterial circulation has been reported normal in patients with ventricular noncompaction by few studies (noncompacted LV perfused by a morphological left coronary artery), so extramural myocardial blood supply is not likely to be at fault. However, intramural perfusion, particularly subendocardial, may be adversely affected by the prominent trabeculations and deep intertrabecular recesses especially in the presence of chronic hypercalcemia in our case. The atherosclerotic nature of the lesion observed during cardiac catheterization in our patient certainly does not support that development of mural thrombi often seen in LVHT/NC within the deep intertrabecular recesses might have played any role in development of NSTEMI in this patient. This case report provides presumptive evidence in the favor of developing

Figure 1. Presence of multiple echocardiographic trabeculations, particularly in the apex and free wall of the left ventricle. Spongy appearance of the noncompacted layer is due to hypertrabeculation and recesses between the trabeculae.
consensus on uprising incidence of acquired form of LVHT/NC\textsuperscript{7,8} not only in conjunction with various hereditary diseases but also autoimmune disorders. This case demonstrates that LVHT/NC may also be associated with other autoimmune disorders as we observed in this case with neurosarcoaidosis. At the end, we conclude by emphasizing the need of prompt medical management of the patients presenting with sarcoidosis concomitantly with LVHT/NC to avoid complications as we experienced in our patient. Though this association between sarcoidosis and LVHT/NC is striking, we can not answer whether this association was causal or coincidental, requiring further research.

Conclusions
This case is a unique presentation of the association of neurosarcoaidosis with LVHT/NC with a presumptive complication in the form of NSTEMI due to synergistic interplay of pathophysiological mechanisms of these 2 individual conditions. Early and prompt diagnosis of this LVHT/NC in sarcoidosis patient population with medical optimization can certainly help to avoid cardiac complications in the form of NSTEMI.

Perspectives
LVHT/NC has been primarily linked to underlying genetic anomalies. However, recently new acquired cases of LVHT/NC have surfaced in the setting of mitochondriopathy, essential thrombocytemia, myotonic dystrophy, Duchenne muscular dystrophy, and other neuromuscular disorders. We report a patient with newly diagnosed neurosarcoaidosis with subsequently diagnosed LVHT/NC and concomitant NSTEMI. Early diagnosis of LVHT/NC should be sought with TTEs in patients diagnosed with sarcoidosis and clinicians should have low threshold for cardiac stress testing in symptomatic patients to diagnose underlying myocardial ischemia. In addition, this would justify medically optimizing this patient population with the use of antiplatelet agents, statins, and anti-anginal drugs to prevent clinically significant ischemic heart disease.

References