Cardiovascular Pathology 42 (2019) 41–43

Contents lists available at ScienceDirect

Cardiovascular Pathology

Case Report

Left ventricular noncompaction with pulmonary capillary hemangiomatosis-like lesions: case report

Takafumi Ogawa [a], Sho Ogata [a,*], Kazuki Kagami [b], Susumu Tominaga [a], Kuniaki Nakanishi [a]

[a] Departments of Pathology and Laboratory Medicine, National Defense Medical College, Tokorozawa, Japan
[b] Department of Cardiology, National Defense Medical College, Tokorozawa, Japan

ARTICLE INFO

Article history:
Received 1 February 2019
Received in revised form 19 May 2019
Accepted 1 June 2019

Keywords:
Left ventricular noncompaction
Cardiomyopathy
Pulmonary capillary hemangiomatosis

ABSTRACT

Left ventricular noncompaction (LVNC) is a cardiomyopathy characterized by prominent left ventricular trabeculae and deep intertrabecular recesses. Pulmonary capillary hemangiomatosis (PCH) is a rare disease that causes uncontrollable proliferation of pulmonary capillaries. We experienced a 52-year-old man who was diagnosed with LVNC about 8 years previously who subsequently died of heart failure. The major autopsy findings were enlargement of the heart with prominent trabeculations and deep intertrabecular recesses in the apical and middle regions of the left ventricular wall. The mean ratio of noncompacted to compacted layers was 2.4. In the lung, thickened alveolar walls with numerous pulmonary capillaries were evident, findings very similar to PCH. PCH-like lesions and LVNC may have coexisted coincidentally, and both, or either of them, may have contributed to the development of his pulmonary hypertension.

1. Introduction

Left ventricular noncompaction (LVNC) is a cardiomyopathy that may be diagnosed at any age and which may not be as rare as once thought (see below). It is characterized by prominent trabeculations and deep intertrabecular recesses that communicate with the ventricular cavity [1–4]. It is generally thought that LVNC is caused by a failure of compaction of the myocardial fibers and meshwork, which is an important process in myocardial development. In a recent analysis, it was determined that 18% to 42% of LVNC cases were familial, and mutations in several genes have been found [1]. Although familial LVNC is usually detected in childhood [2], the incidence of the sporadic type found in adults is increasing due to improved imaging in echocardiography and the use of cardiac magnetic resonance imaging (MRI) [4]. In a 2003 study, echocardiography revealed 36 LVNCs among 344 childhood cardiomyopathy cases (9.5%) [5], while a 2016 study demonstrated LVNC in 4 adults out of 51 (7.8%) nonischemic cardiomyopathy patients among 105 patients with end-stage heart failure undergoing orthotopic heart transplantation [4].

Pulmonary capillary hemangiomatosis (PCH) is a rare disorder involving alveolar capillary proliferation and may be a cause of pulmonary arterial hypertension of unknown etiology [6]. PCH occurs most commonly in adults aged 20–40 years [6]. Recently, mutations in eukaryotic translation initiation factor-2 alpha kinase 4 have been reported to be one of the causes of autosomal recessive PCH [7]. In one study, as many as 11.5% of patients with left-sided cardiac failure were found to have PCH-like lesions featuring markedly widened alveolar walls containing numerous dilated capillaries [6]. In the present study, we examined an autopsy case with PCH-like lesions and LVNC, which may have coexisted coincidentally. We discuss the relationship between such lesions and the development of pulmonary hypertension.

2. Case report

A 52-year-old Japanese man was admitted to our hospital in August 2008 because of a history of cough. In cardiac MRI, the left ventricle displayed diffuse severe hypokinesis, and the left ventricular ejection fraction was 10.5%. Although the ratio of noncompacted to compacted myocardial layers in end-systole was 1.65 in the middle region of the lateral wall and 1.78 in the apical region of the lateral wall (diagnostic criterion, ≫2), the values obtained for the ratio of x (distance from the epicardial surface to the trabecular recess) over y (distance from the epicardial surface to the peak of trabeculation) at end-diastole for those two regions were 0.33 and 0.32, respectively (diagnostic criterion, ≪0.5) [3]. No fibrosis was found with late gadolinium enhancement. Moreover, no edema or myocarditis was found. The estimated systolic and diastolic pulmonary arterial pressures were 49 and 24 mmHg, respectively. These findings led to a diagnosis of cardiomyopathy due to suspected LVNC. Because of a major depressive disorder, he refused treatment for LVNC and did not attend clinic visits. At 2 months before death, he was admitted to our hospital because of severe limb edema

* Corresponding author at: Department of Pathology and Laboratory Medicine, National Defense Medical College, Tokorozawa 359-8513, Japan. Tel.: +81 4 2995 1511; fax: +81 4 2996 5192.
E-mail address: sogata@ndmc.ac.jp (S. Ogata).

https://doi.org/10.1016/j.carpath.2019.06.001
1054-8807/

due to congestive heart failure. The chest x-ray showed a dilated main pulmonary artery and bibasilar reticulonodular opacities. He was treated by diuretic and vasopressor therapy but died from a worsening of the disease. He had smoked 10 cigarettes/day for 32 years and had been treated for a major depressive disorder by another hospital for 10 years. The remainder of his medical history was unremarkable. A family history of cardiac or rheumatologic disorders was not found.

3. Materials and methods

At autopsy, heart and lung tissues were fixed in 10% formalin and paraffin -embedded. Sections 4 μm thick were stained by hematoxylin–eosin, elastica–van Gieson, and Masson's trichrome methods. The ratio of noncompacted to compacted layers in the left heart was measured in four measurement regions. The pathological criteria for LVNC were (a) macroscopically prominent left ventricular trabeculae (i.e., an absence of well-formed left ventricular papillary muscles) and (b) histological verification of more than 50% penetration of invaginated endocardial recesses toward the epicardial surface [2]. For immunohistochemistry, we employed the polymer-peroxidase method and used a commercially available monoclonal antibody against CD34 (QBEnd 10, prediluted; Beckman Coulter, Paris, France).

4. Results

Autopsy revealed an enlarged left ventricle (cardiac weight, 750 g; enlarged cavity, 88 by 64 mm; wall thickness of left ventricle, 15 mm) with prominent trabeculations and deep intertrabecular recesses in

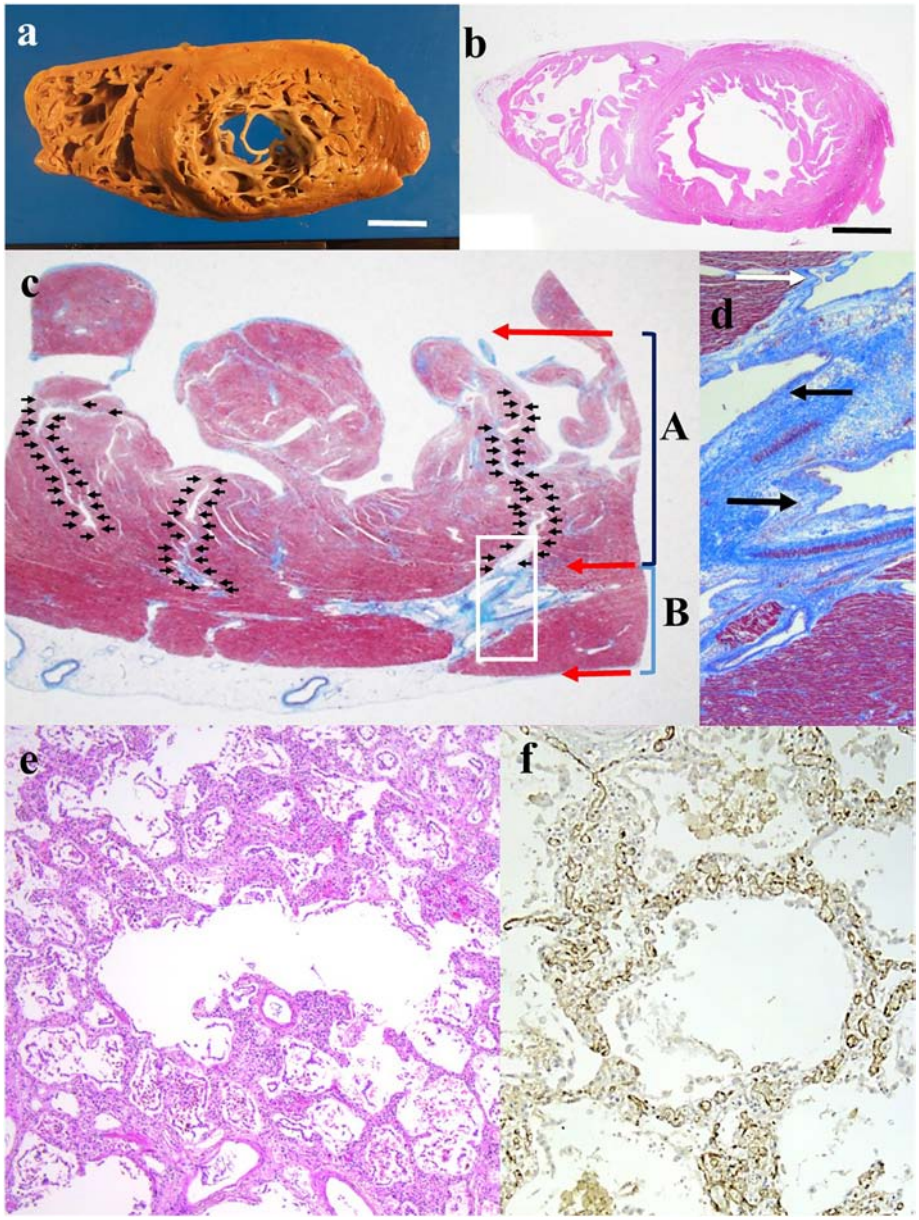

Fig. 1. Macroscopic and microscopic findings from apical regions of both ventricles and microscopic findings from the lungs. (a) Macroscopic findings. In noncompaction, broad trabeculae were seen anastomosing. Scale bar indicates 2 cm. (b) Microscopic findings, much the same as gross appearance. Hematoxylin–eosin staining. Scale bar indicates 2 cm. (c) Microscopic findings. Intertrabecular spaces (small black arrows) were evident. The ratio of noncompacted (A) to compacted (B) myocardial layers (long red arrows) in this view was 4.0. Area enclosed within white box is shown at higher power in figure d. Masson's trichrome staining. Scale bar indicates 5 mm. (d) Microscopic findings. High magnification of region with short arrows shown within white box in c. Intertrabecular space with fibrosis (deep endocardial recess: white arrow) is shown. Also shown are dilated veins with perivascular fibrosis (black arrows). Scale bar indicates 2 mm. (e) Microscopic findings from PCH-like lesions. In the alveolar septa, a prominent proliferation of capillaries was evident along both sides of the alveolar walls. Hematoxylin–eosin staining. Original magnification: ×10. (f) Immunohistochemistry against CD 34 antibody: proliferative capillaries exhibited a positive reaction. Original magnification: ×20.

the apical and middle regions of the left ventricular walls, and an absence of well-formed left ventricular papillary muscles (Fig. 1a and b). The right ventricle was also enlarged (cavity, 67 by 52 mm; wall thickness of ventricle, 3.5 mm). The myocardial wall was found to have a dual structure, with a thin compacted layer and a thick noncompacted layer (Fig. 1c and d). However, we found it difficult to differentiate endocardial fibrosis from perivascular fibrosis of dilated veins in the left cardiac wall. Therefore, we accepted as deep endocardial recesses only those recesses that were continuous from the endocardial surface. The mean ratio of noncompacted to compacted layers was 2.4. These findings fulfilled the pathological criteria for LVNC mentioned in Materials and Methods. Atherosclerosis in the coronary arteries was mild. Neither myocarditis nor myocardial infarction was found. In the lungs (weights, 950 g left and 1480 g right), pulmonary alveolar septa were thickened with multiple layers of proliferated capillaries, which immunoreacted against CD34 antibody (Fig. 1e and f). These findings are very similar to the lesions found in PCH. We could find no histological changes in pulmonary smaller arteries that might have been due to an increased pulmonary arterial pressure.

5. Discussion

Although LVNC is in some cases a genetic cardiomyopathy, many acquired types exist [3]. The most practical echocardiographic criteria proposed for LVNC diagnosis are (a) absence of coexisting cardiac abnormalities; (b) bilayered myocardium with multiple, prominent trabeculations in end-systole; and (c) a ratio of noncompacted to compacted layers ≫2:1. Although the present case did not meet all of the above criteria for diagnosis in clinical practice [1–3], our case was found to exhibit (a) macroscopically prominent left ventricular trabeculae, (b) histologically deep intertrabecular recesses, and (c) a thin compacted layer with a ≫2:1 ratio between the noncompacted and the compacted layer. That is, the present findings fulfilled the pathological criteria [2].

In a recent report, PCH-like lesions were found in severe pulmonary arterial hypertension causally associated with left-side cardiac failure [6]. The most reliable histological criteria are the presence of double capillaries along the two sides of the alveolar walls, and sheets or nodules with a back-to-back appearance [6]. In one study, the incidence of PCH-like lesions was 6 (11.5%) of 52 autopsy cases with left cardiac failure [6]. In the present case, therefore, PCH-like lesions and LVNC may have coexisted coincidentally, and it is possible that the PCH-like lesions were causally associated with the patient's heart failure. PCH may cause pulmonary hypertension, while LVNC may be associated with different stages of heart failure, which may lead to pulmonary hypertension. Therefore, both PCH-like lesions and LVNC, or either of them, may have contributed to the development of pulmonary hypertension in the present case.

Competing interests

The authors declare that they have no competing interests.

References

[1] Bhatia NL, Tajik AJ, Wilansky S, Steidley DE, Mookadam F. Isolated noncompaction of the left ventricular myocardium in adults: a systematic overview. J Card Fail 2011;17:771–8.
[2] Burke A, Mont E, Kutys R, Virmani R. Left ventricular noncompaction: a pathological study of 14 cases. Hum Pathol 2005;36:403–11.
[3] Ikeda U, Minamisawa M, Koyama J. Isolated left ventricular non-compaction cardiomyopathy in adults. J Cardiol 2015;65:91–7.
[4] Ottaviani G, Segura AM, Rajapreyar IN, Zhao B, Radovancevic R, Loyalka P, et al. Left ventricular noncompaction cardiomyopathy in end-stage heart failure patients undergoing orthotopic heart transplantation. Cardiovasc Pathol 2016;25:293–9.
[5] Pignatelli RH, McMahon CJ, Dreyer WJ, Denfield SW, Price J, Belmont JW, et al. Clinical characterization of left ventricular noncompaction in children: a relatively common form of cardiomyopathy. Circulation 2003;108:2672–8.
[6] Matsukuma S, Sato K. Pulmonary capillary haemangiomatosis-like lesions in severely congested lungs. Histopathology 2011;59:876–81.
[7] Best DH, Sumner KL, Austin ED, Chung WK, Brown LM, Borczuk AC, et al. EIF2AK4 mutations in pulmonary capillary hemangiomatosis. Chest 2014;145:231–6.