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Case report

An autopsy case of refractory pulmonary hypertension with sarcoidosis

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ABSTRACT

A 63-year-old man with sarcoidosis-associated pulmonary hypertension (SAPH) died suddenly of decompensated right heart failure. At autopsy, microscopy showed subpleural and interlobular fibrosis in both upper lobes, with marked broncho-bronchiolectasis, as well as bronchovascular bundle fibrosis and fibrotic organization in alveolar lumens, which are consistent with pulmonary sarcoidosis. Intimal fibrosis and medial hypertrophy were noted in the proximal elastic to distal muscular pulmonary arteries (Heath-Edwards, grades II–III) within intensive fibrotic lesions. Additionally, diffuse alveolar capillary multiplication (DACM) was present in macroscopically normal lung parenchymal lesions, associated with wall muscularization. In this case, muscularization of capillaries may have been induced by hypoxemia and hypoxic pulmonary vasoconstriction, resulting in pulmonary hypertension.

1. Introduction

Most patients with SAPH have stage IV disease, with corresponding impairment in pulmonary function. However, PH severity is not always correlated with the severity of parenchymal lung fibrosis and hypoxemia, suggesting that other mechanisms may be involved in pulmonary hypertension (PH). Here, we report key pathological findings from an autopsy case of SAPH.

2. Case report

A 63-year-old man with SAPH was admitted to our hospital complaining of worsening dyspnea on exertion, and edema in both legs. His body weight had increased by 8 kg during the previous month. He had a smoking history of 20 pack-years and no history of dust exposure. At age 26, histologic analysis of a biopsy specimen from the right cervical lymph node revealed several non-caseous epithelioid cell granulomas

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(Fig. 1a). Pulmonary sarcoidosis (stage III) was diagnosed, and treatment with prednisolone (40 mg/day) was initiated, which maintained to prednisolone (5 mg). He had been receiving home oxygen therapy for the previous 5 years, but his condition gradually worsened to World Health Organization functional class IV.

On admission, the patient's plasma brain-type natriuretic peptide concentration was 1443 pg/mL (0–18.4) and angiotensin-converting enzyme level was 5.7 U/L (8.3–21.4).

The results of arterial blood gas analysis were pH 7.305, $PaCO_2$ 63.9 Torr, and PaO_2 79.1 Torr on a 7 L/min oxygen-conserving nasal cannula. The pulmonary function test indicated mixed ventilatory impairment (%VC, 46.8%; FEV1/FVC, 36.9%) and decreased diffusion capacity for carbon monoxide (18.9%). A chest radiograph at the time of admission showed that both upper lung fields were affected, with loss of lung volume (Fig. 2a). Chest computed tomography (CT) images showed conglomerate masses associated with traction bronchiectasis, predominantly in both upper lobes (Fig. 2b,c). Echocardiography showed high estimated pulmonary arterial pressure (77 mm Hg), flattening of the interventricular septum, right ventricular dilatation, and moderate tricuspid regurgitation. The results of CT pulmonary angiography and venous Doppler ultrasound were negative for thromboembolism. Combination therapy with prostacyclin, bosentan, and sildenafil was administered, but his clinical condition remained unchanged, and he died suddenly of decompensated right heart failure.

At autopsy, macroscopic examination of both upper lobes revealed subpleural grayish-white zonal lesions with contraction, distortion of the lung architecture, and prominent pleural thickening (Fig. 3a). The right ventricular wall was severely hypertrophied (Fig. 3b). Microscopic examination showed subpleural and interlobular fibrosis in both upper lobes, with marked broncho-bronchiolectasis and fibrotic organization in alveolar lumens (Fig. 3c). Bronchovascular bundle fibrosis is consistent with fibrotic changes associated with pulmonary sarcoidosis (Fig. 3d). Furthermore, intimal fibrosis and medial hypertrophy with partial destruction of elastic fibers were observed from proximal elastic to distal muscular pulmonary arteries (Heath-Edwards classification; grades II–III) with intensive fibrosis (Fig. 3e–g). Additionally, diffuse alveolar capillary multiplication (DACM) was present in relatively normal lung parenchyma (Fig. 3h). Swollen endothelial cells were observed in the preseptal vein (Fig. 3i). Hyperplasia was present in capillary blood vessels in the preseptal and septal veins (Fig. 3j), and in smooth muscle (arterialization) in the septal vein (Fig. 3k). There was no evidence of plexiform lesions, veno-occlusive disease, or myocardial sarcoidosis. Some aspects of DACM stained positively with α-smooth muscle actin antibody (Fig. 4). Moreover, biopsy specimens obtained from the right cervical lymph

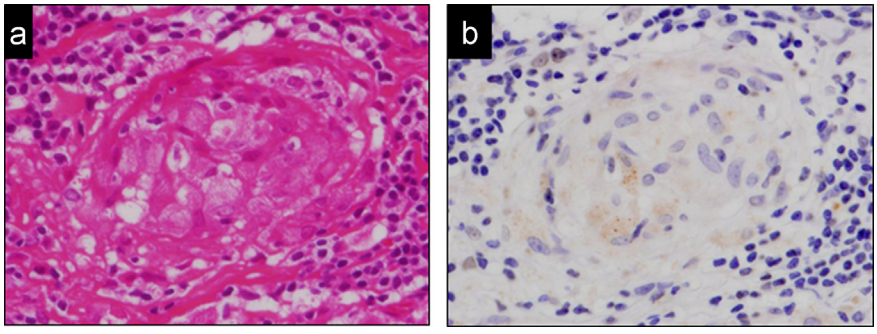

Fig. 1 – (a–c) Histologic analysis of a biopsy specimen from the right cervical lymph node reveals several non-caseous epithelioid cell granulomas (a, Hematoxylin eosin stain, 100 ×) that stained positive for *Propionibacterium acnes* antibody (b, 100 ×).

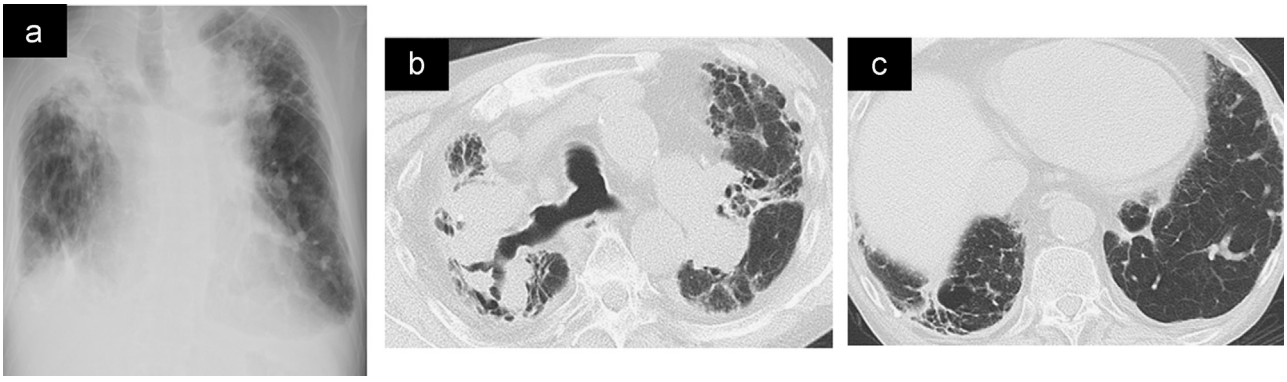

Fig. 2 – (a) Chest radiograph on admission shows predominant involvement of both upper lung fields and loss of lung volume. (b,c) Chest computed tomography images show conglomerate masses associated with traction bronchiectasis, predominantly in both bilateral upper lobes.

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