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Isolated pulmonary vasculitis: Case report and literature review

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ABSTRACT

Background and objectives: Single-organ vasculitis has been reported to affect the skin, kidneys, central nervous system, peripheral nerves, genitourinary tract, calf muscles, aorta, coronary arteries, retina, or gastrointestinal tract. However, isolated pulmonary vasculitis is a very rare entity. Our aims were to describe a case of localized pulmonary vasculitis affecting medium-sized vessels and review the literature.

Methods: A patient with localized pulmonary vasculitis affecting medium-sized vessels that presented as pulmonary arterial hypertension is described. A MEDLINE database search of cases with localized pulmonary vasculitis was also conducted.

Results: A 30-year-old man presented with pulmonary hypertension due to isolated pulmonary medium-sized vessel vasculitis that was confirmed histologically. Initially he responded to corticosteroids and vasodilator treatment, but therapy eventually lost efficacy. Treatment with rituximab was not effective, and as the clinical situation worsened, lung transplant was performed. Isolated large pulmonary vessel disease, often related to Takayasu disease or giant cell arteritis, may present as pulmonary artery hypertension, thus mimicking chronic thromboembolic disease. Medium- and small-vessel pulmonary vasculitis usually develops in the context of a systemic disease. Some cases of isolated small-vessel vasculitis have been reported presenting as diffuse alveolar hemorrhage. In contrast, our case developed pulmonary artery hypertension secondary to medium-sized vessels vasculitis. To our knowledge, this is the first case of lung transplantation in isolated pulmonary vasculitis.

Conclusions: Pulmonary isolated vasculitis is a rare cause of pulmonary hypertension but it must be taken into consideration after more common disorders are excluded.

Introduction

The vasculitides constitute a group of heterogeneous conditions characterized by blood vessel inflammation and necrosis, leading to subsequent tissue or organ injury [1,2]. They are usually systemic diseases affecting multiple territories or organs with overlapping clinical and pathologic manifestations. However, there are cases in which inflammation is restricted to a single organ [3,4], where lesions may be focal or diffuse. In these cases the isolated nature of the disease needs to be confirmed after at least 6 months of follow-up [5].

Single-organ vasculitis (SOV) has been reported to affect the skin, kidneys, central nervous system, peripheral nerves, genitourinary tract, calf muscles [6], aorta, coronary arteries, retina, or gastrointestinal tract [7]. Isolated pulmonary vasculitis is a very rare entity. In this regard, only a few cases, mostly affecting large pulmonary vessels, have been described [8,9].

In this report, we describe a patient with localized pulmonary vasculitis affecting medium-sized vessels that presented as pulmonary arterial hypertension. A literature review of cases of localized pulmonary vasculitis was also conducted.

Case report

A 30-year-old man, former smoker of 10 cigarettes/day with otherwise unremarkable past medical and family history, who had

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been diagnosed with idiopathic pulmonary hypertension, was sent to our hospital for further treatment. Four months before admission he began to experience fatigue, shortness of breath, and weight loss. He denied environmental exposure (our patient was an engineer working at an office), and there was not a previous history of drug-induced phenomenon. Physical examination showed blood pressure of 100/60 mmHg, pulse oximetry 95% (while breathing through a high-flow oxygen mask), a mild systolic mitral murmur, and normal pulmonary auscultation. He had hepatomegaly and significant edema affecting the lower limbs. No other clinical findings were found. The erythrocyte sedimentation rate was 11 mm/1st hour (normal value <20). C reactive protein was <0.1 mg/dl (normal up to 0.5 mg/dl). Blood cell count showed 12,300 leukocytes/mm^3 (normal value 4800–10,800/mm^3) and hemoglobin 11.2 g/dl (normal value 13.5–18). Routine blood chemistry profile, including renal and liver function tests, was normal, except for a mild hypoproteinemia and hypoalbuminemia. Antinuclear antibodies, rheumatoid factor, complement levels, and antiphospholipid antibodies were either negative or normal. Hepatitis B and C as well as HIV testing were negative. Antineutrophil cytoplasmic antibody testing and glomerular basement membrane antibodies were negative. Urinalysis did not show microscopic hematuria or proteinuria. A chest radiograph disclosed enlarged pulmonary arteries. Computed tomography (CT) scan revealed right ventricle enlargement and dilation of the pulmonary artery branches with ground-glass opacities that were attributed to congestive heart failure. Echocardiography confirmed a right ventricle enlargement with moderate dysfunction, moderate to severe tricuspid insufficiency, and an estimated systolic pulmonary artery pressure of 100 mmHg. Respiratory function test results were FVC 94%, FEV1 94%, FEV1/FVC 78.5%, and DLCO 31.6%. He walked 248 m in the 6-min walking test, stopping at 4 min due to a fall in pulse oximetry (90%) and reflex tachycardia (150 bpm). Right heart catheterization demonstrated a pulmonary artery pressure of 81/40/53 mmHg with a markedly decreased cardiac index in the absence of shunts. All these findings were in keeping with the diagnosis of pulmonary arterial hypertension.

When admitted to our hospital, he was in functional class III according to the NYHA scale. At that time, he experienced a marked worsening and had to be transferred to the intensive care unit. Treatment with dobutamine and continuous epoprostenol infusion was started. Right heart catheterization was performed with the following results: pulmonary artery pressure of 116/50 mmHg, pulmonary capillary pressure of 12 mmHg, and cardiac output of 2.4 l/min. Chest CT was repeated, confirming the previous findings and showing mediastinal and hilar lymphadenopathy that formed a soft tissue mass in the subcarinal region (Fig. 1), which later showed no high fluorodeoxyglucose uptake on positron emission tomography (PET). With a suspicion of an underlying malignancy, mediastinoscopy and an open lung biopsy were performed. The sample obtained from the mediastinal mass showed lymph nodes with lymphoid cell depletion and fibrosis. It turned out to be an adenopathy conglomerate. Lung biopsy demonstrated an interstitial lung disease where bronchovascular bundles were predominantly affected with enlarged arterial diameter and wall thickening. An inflammatory component formed by mature lymphocytes and polymorphonuclear leukocytes with fibrinoid necrosis and thrombotic arterial disease without evidence of plexogenic changes was found. No immunoglobulin deposits were seen.

Taking into account the histopathologic findings, a diagnosis of isolated pulmonary vasculitis was made. The patient was started on treatment with high-dose intravenous corticosteroids (1 g of methylprednisolone every 24 hours for 3 consecutive days) followed by prednisone 50 mg/day. Vasodilator therapy with sildenafil (60 mg/day), bosentan (250 mg/day), and continuous epoprostenol infusion (20 ng/kg/min) was also commenced. He experienced a marked clinical improvement manifested by the improvement of the walking test from 248 to 438 m as well as a significant decrease in the pulmonary artery pressure estimated by echocardiography (from 100 to 64 plus central venous pressure). Three months later, right heart catheterization confirmed the great decline in pulmonary artery pressure (77/52/35 mmHg), as well as in pulmonary capillary pressure (12 mmHg), an important increase of cardiac output, from 2.4 to 7.28 l/min, and a significant decrease of the pulmonary vascular resistance, from 16.6 to 7.1 Wood units. Once treatment with corticosteroids was started, the mediastinal mass was reduced and disappeared at follow-up chest CT scan. This fact confirmed the benign reactive nature of the adenopathy conglomerate.

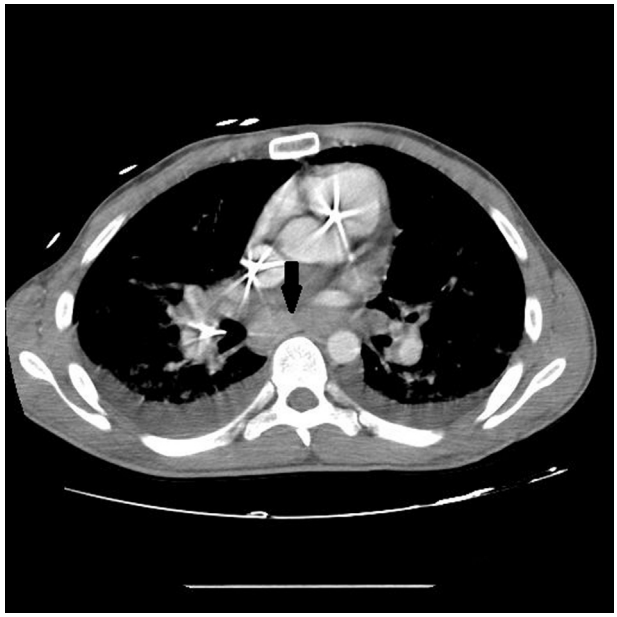

Fig. 1. Axial CT scan of the lungs and mediastinal region showing mediastinal and hilar lymph node enlargement forming a mass of 3 cm in the subcarinal region (arrow).

During the follow-up, prednisone dose was gradually tapered and 3 months later, when on 30 mg/day, treatment with azathioprine was started (100 mg/day). The patient remained stable in functional class II according to the NYHA scale for the following 2 years. At that time, while he was on prednisone 10 mg/day, he experienced acute clinical worsening with a change to functional class III–IV and severe right heart failure, with pulmonary artery pressure of 135 plus central venous pressure as estimated by echocardiography. A thromboembolic disease was excluded by imaging techniques. In addition, no signs of thromboembolic disease were seen on the histopathology. Also, infections were also excluded. Therefore, as soon as secondary causes of exacerbation were excluded, treatment with high-dose intravenous corticosteroid therapy (0.5 g of methylprednisolone every 24 hours for 3 consecutive days) followed by prednisone 60 mg/day and an increase in epoprostenol infusion (25 ng/kg/min) was started. Rituximab was also given at this time, 575 mg/week for 4 consecutive weeks, and azathioprine was discontinued. Regrettably, despite therapy with rituximab, high-dose corticosteroids, and higher dose of epoprostenol infusion (42 ng/kg/min), the patient remained on functional class III–IV with severe right heart failure. Given the lack of response to drug therapy and the progressive clinical deterioration, lung transplantation was considered in this patient. Bilateral lung transplantation was performed 2 weeks later. Interestingly, the histology of explanted lungs confirmed the former diagnosis, pulmonary hypertension related lesions with