Case Report

Severe Right Heart Failure in a Patient with Chronic Obstructive Lung Disease: A Diagnostic Challenge

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ABSTRACT

A 55-year-old male was admitted for evaluation of severe dyspnoea and hypoxaemia. Physical examination upon admission showed elevated jugular venous pressure and an accentuated second heart sound. Chest radiograph showed cardiomegaly with increased bibasilar markings. Arterial blood gas analysis while breathing room air showed marked hypoxaemia. High resolution computed tomography angiography of the chest showed modestly enlarged mediastinal lymph nodes with discrete diffuse ground-glass attenuation especially at the lower lung zones. Positron emission tomography using ^{18}F labelled 2-deoxy-D-glucose (FDG) demonstrated the mediastinal lymph nodes were FDG-avid. Transthoracic echocardiography showed dilated hypokinetic right heart chambers with bulging of the interventricular septum to the left, compatible with acute cor-pulmonale. From the tricuspid regurgitation jet measurement a systolic pulmonary artery pressure (PAP) of 48mmHg was estimated. Patent foramen ovale was suspected on bubble test. Right heart catheterisation confirmed pulmonary arterial hypertension: mPAP 47mmHg, pulmonary artery occlusion pressure 5mmHg, cardiac index 1.1 L/min/m^2, pulmonary vascular resistance (PVR) 959 dyne.sec.cm^{-5}. Pulmonary function tests showed a marked diffusing capacity for carbon monoxide (DLCO) decrease of 32% predicted but no obstructive lung deficit. Before an open lung biopsy could be scheduled the patient developed acute cardiogenic shock. At autopsy pulmonary veno-occlusive disease with marked pulmonary hypertension was diagnosed. [Indian J Chest Dis Allied Sci 2013;55:159-162]

Key words: Diffusion capacity, COPD, Right heart failure.

INTRODUCTION

Pulmonary arterial hypertension should be suspected in patients presenting with breathlessness without overt signs of specific heart or lung disease. In patients with chronic obstructive pulmonary disease (COPD), pulmonary hypertension is more common. But even in severe COPD, pulmonary hypertension is usually mild, with an expected mean pulmonary artery pressure (mPAP) on right heart catheterisation of less than 35mmHg.[1] 'Out of proportion' pulmonary hypertension is suspected if dyspnoea is insufficiently explained by the degree of airway obstruction. 'Out of proportion' pulmonary hypertension in this setting is arbitrarily defined by a mPAP on right heart catheterisation of 40mmHg or more, at rest.[2] We report a patient with reduced single-breath diffusing capacity for carbon monoxide (DLCO) but normal forced expiratory volume in the first second (FEV$_1$) to forced vital capacity (FVC) ratio and minimal emphysematous changes on computed tomography (CT), illustrating that caution must be exercised before attributing pulmonary hypertension to an underlying lung disease.

CASE REPORT

A 55-year-old male was admitted for severe dyspnoea and hypoxaemia. Two years earlier, he was diagnosed to have mild pulmonary hypertension with a mPAP of 29mmHg (normal <25mmHg), cardiac index 2.12 L/min/m^2 (normal 2.5-4.2 L/min/m^2) and pulmonary vascular resistance (PVR) 489 dyne.sec.cm^{-5} (normal 150-250 dyne.sec.cm^{-5}) in another hospital. On echocardiography a patent foramen ovale without left-to-right shunt was also documented. This pulmonary hypertension was attributed to lung emphysema as he was a former smoker with a 10 pack-years smoking history but with only mild emphysematous changes in the lung apices. Autoimmune work-up was negative at that time. There was no mention of interstitial lung disease.

Physical examination at admission showed increased jugular venous pressure and an accentuated second heart sound. Blood pressure was 110/75 mmHg, pulse 90 beats/min. No peripheral oedema was noted. Pulmonary function tests showed

a normal FEV_1/FVC ratio of 71% but a marked DLCO decrease of 32% predicted with normal total lung capacity and no air trapping. The electrocardiogram showed sinus rhythm with right atrial enlargement and incomplete right bundle branch block.

Chest radiograph showed cardiomegaly with increased bibasilar markings. Arterial blood gas analysis while breathing room air showed marked hypoxaemia despite hyperventilation: pH 7.47, arterial carbon dioxide tension ($PaCO_2$) 28mmHg, arterial oxygen tension (PaO_2) 55mmHg. On administering oxygen with a mask and re-breathing bag at 10 L/min, PaO_2 rose to 73mmHg.

High resolution computed tomography angiography of the chest showed emphysematous changes in the lung apices and modestly enlarged mediastinal lymph nodes with discrete diffuse ground glass attenuation especially at the lower lung zones (Figures 1A and 1B).
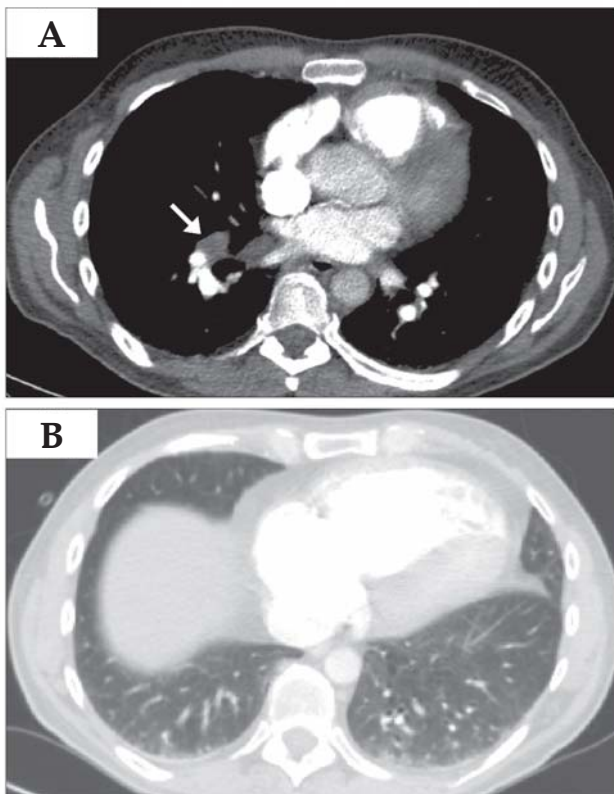

Figure 1. Computed tomography of chest (mediastinal window, taken at the level of the right inferior pulmonary artery) showing (A) mediastinal lymph node enlargement (arrow); (lung window, taken at the level of the right diaphragm) showing (B) ground-glass attenuation.

No pulmonary emboli were seen up to the subsegmental level. A subsequent positron emission tomography using ^{18}F labelled 2-deoxy-D-glucose (FDG) scan demonstrated intense right ventricular FDG uptake (Figure 2). The mediastinal lymph nodes were FDG-avid.

Figure 2. 18-FDG PET scanning showing a thickened right-ventricular wall (arrow) compared to the normal left-ventricular wall.

Transthoracic echocardiography showed dilated hypokinetic right heart chambers with bulging of the interventricular septum to the left, compatible with acute cor-pulmonale. From the tricuspid regurgitation jet measurement, a systolic PAP of 48mmHg was estimated. Patent foramen ovale was suspected on bubble test.

Right-sided heart catheterisation confirmed the pulmonary arterial hypertension: mPAP 47mmHg (normal <20mmHg), pulmonary artery occlusion pressure 5mmHg (normal 4-12 mmHg), cardiac index 1.1 L/min/m^2 (normal 2.5-4.2 L/min/m^2), PVR 959 dyne.sec.cm^{-5} (normal 150-250 dyne.sec.cm^{-5}).

No intracardiac left-to-right shunt was detected. Pulmonary vasodilatation testing with inhaled nitric oxide (NO) at 20 parts per million did not change pressures nor cardiac output. A slight improvement in general condition was noted with oxygen treatment and subcutaneous low molecular weight heparin administration.

Before an open lung biopsy could be scheduled the patient developed acute cardiogenic shock. After successful reanimation he was put on extracorporeal membrane oxygenation with temporary stabilisation, but he died 24 hours later.

At autopsy, the alveoli contained histiocytes with pigment that was Perl's stain positive (Figure 3A). The interalveolar septae were thickened and their capillaries congested. Though focal, this change was present in all the tissue samples. The lumen of the smallest intralobular pulmonary veins was obliterated by loose connective tissue; in some of them thin walled vessels could be identified (Figure 3B). The wall of several venules consisted of smooth muscle and resembled arteries (Figure 3C). The elastic lamina of some veins and the basement membranes of capillaries showed iron and calcium deposition resembling the Gamna-Gandy bodies described in the spleen. Focally, foreign body giant cells surrounded these structures; the latter changes were consistent with mineralising pulmonary elastosis (Figure 3D).
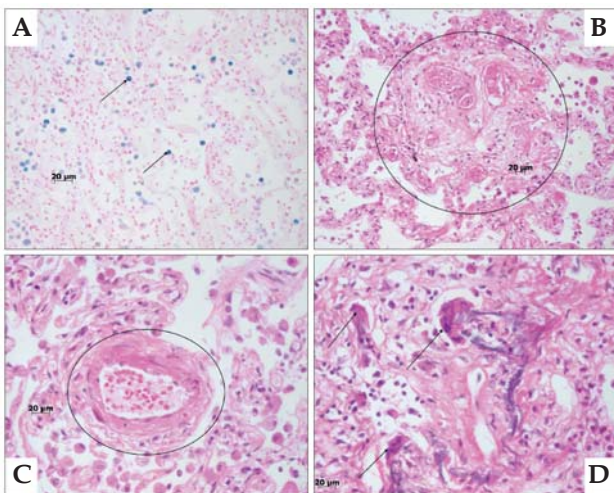
Figure 3. Photomicrograph showing (A) alveoli containing macrophages with iron pigment (arrows) (Perl's stain × 20μ); (B) obliterated intralobular vein, containing thin-walled vessels (circle) (Haematoxylin-eosin stain × 20μ); (C) arteriolisation of venules with the wall of some venules containing smooth muscle (circle) (Haematoxylin-eosin stain × 20μ); and mineralising pulmonary elastosis with deposition of iron and calcium in lamina elastica and basement membranes; (D) foreign body giant cells (arrows) surrounding the mineralised fibers can also be seen (Haematoxylin-eosin stain × 20μ).

Some of the muscular pulmonary arteries presented muscular and intima hypertrophy. The mediastinal lymph nodes showed reactive hyperplasia and some vascularisation of the sinuses. Thus, the patient was diagnosed to have pulmonary veno-occlusive disease (PVOD) with marked pulmonary hypertension.

DISCUSSION

Patients with distinctive degrees of lung emphysema may present with different degrees of pulmonary function abnormalities.[3] The physiologic hallmark of emphysema is loss of elastic recoil causing hyperinflation and airway obstruction and reduction in DLCO. Advanced emphysema, defined as low attenuation areas on high resolution CT of the chest, of greater than 23% of the lung, is always associated with airflow obstruction.[4] Mild radiographic evidence of emphysema, as in our patient, can be found without airflow obstruction.[5,6] The DLCO reduction correlates better with lower lobe emphysema than upper lobe emphysema.[7]

Most haemodynamic studies on pulmonary hypertension in COPD have been done in patients with very advanced disease. Retrospective data show that there exists a subset of COPD patients who manifest 'out of proportion' pulmonary hypertension. But even these patients had a reduced mean FEV_1 value of 50% predicted.[8] The rate of progression of the pulmonary hypertension in COPD is usually slow, although right ventricular diastolic dysfunction with

fluid retention and oedema can develop during COPD exacerbations. Right ventricular failure with low cardiac output is extremely rare in COPD.[9] The severe reduction in DLCO without obstructive or restrictive lung function changes in our patient should have served as a clue to the presence of a pulmonary vascular disease. Autopsy revealed PVOD.

The clinical presentation of PVOD is generally similar to that of idiopathic pulmonary arterial hypertension (IPAHT). That is why this disease was considered part of group 1 in the clinical Venice classification of pulmonary arterial hypertension.[10] In the new Dana point classification, PVOD is grouped together with pulmonary capillary haemangio-matosis (PCH) or pulmonary microvasculopathy in a group 1', as pathologic studies indicate that PVOD and PCH share similar changes in the pulmonary parenchyma and the development of pulmonary arterial intimal fibrosis and medial hypertrophy.[2]

Histolpathologically the disease is characterised by non-angiogenic occlusive lesions by fibrous tissue in veins in PVOD or pulmonary occlusive venopathy.[11,12] The involvement of pre-septal venules should be considered necessary for the histopatho-logical diagnosis of PVOD.[13] It can be difficult to distinguish from patch-like secondary obstructive capillary proliferation in veins and venular walls present in up to 80% of patients with PCH.[14] These findings suggest that PCH and PVOD may represent different presentations of a single disease.

The distribution of the lesions is usually panlobar and patchy.[15] Pulmonary haemosiderosis, characterised by haemosiderin-laden macrophages and type II pneumocytes, hallmark of local bleeding, is sometimes present. But the absence, as in our patient, does not rule out the disease.[16]

CT of the lungs may demonstrate widespread centrilobular ground-glass opacities. Other reported findings are septal thickening and lymph node enlargement.[17] When these changes are minimal, as has been the case with our patient, it is even more difficult to arrive at the final diagnosis.

Lymph node enlargement might be due to secondary lymphatic congestion, intra-sinusal haemorrhage with erythrophagocytosis and as in our patient, lymphoid follicular hyperplasia.[18] The presence of two or three of these radiographic abnormalities, in the right clinical context, had a sensitivity of 75% and a specificity of 84.6% for the detection of PVOD.[19] As the disease progresses the classic CT features of IPAHT with right heart enlargement and a dilated main pulmonary artery become evident.[20]

Ventilation-perfusion scintigraphy is not distinctive from other forms of pulmonary arterial hypertension. Normal scans as well as perfusion mismatch defects can be seen.[17] In patients with

concomitant COPD, ventilation-perfusion scintigraphy images are even more difficult to interpret. Lung function tests in a large series of PVOD patients reflect the decreasing working lung surface with a reduction in the single-breath diffusing capacity for carbon monoxide,[19] as present in our patient.

Although FDG-PET scanning is not necessary for the diagnosis, intense right-ventricular FDG uptake has been considered to be a hallmark of right-ventricular overload while the mediastinal lymph nodes are FDG avid.[21,22] There may be a role for bronchoalveolar lavage in patients with suspected PVOD to demonstrate an elevated level of haemosiderin-laden macrophages.[16]

Pulmonary-capillary wedge pressure, as measured with Swan-Ganz catheter, is usually normal in PVOD patients, as it measures the pressure distal to the site affected by the PVOD process. In PVOD patency in the large veins, communicating with the occluded cardiac balloon catheter, is usually well preserved.[13] Vasodilatation during catheterisation and especially treatment with epoprostenol have to be used with great caution because of the risk of pulmonary oedema.[19] Lung transplantation seems to be the definite treatment for this disease.[2] Recent work showed that, in selected cases epoprostenol treatment can be used as a bridge to lung transplantation.[23]

ACKNOWLEDGEMENT

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