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Case Report

Granulomatous Mediastinitis: A Rare Cause of Pulmonary Hypertension

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Abstract

A rare case of a patient with chronic obstructive pulmonary disease who developed secondary anthracofibrosis to biomass exposure, fibrosing mediastinitis due to anthracotic enlarged lymph nodes in the mediastinum, and pulmonary hypertension because of compression of the lymph nodes on the pulmonary arteries is presented. This is a case report of a 71-year-old female patient who has been followed up with chronic obstructive pulmonary disease for 10 years, has no history of smoking, and has been exposed to biomass for many years. The patient, who had been hospitalized in various centers for the last 3 years due to progressive shortness of breath and dry cough, applied to us with dry cough and dyspnea complaints. On echocardiography, systolic pulmonary arterial pressure was found to be 59 mmHg. For the etiology of pulmonary hypertension, dual-energy thoracic computed tomography was performed with the suspicion of chronic thromboembolic pulmonary hypertension. No filling defect compatible with thromboembolism was detected. In right heart catheterization, mean pulmonary artery pressure was 27 mmHg, pulmonary capillary tip pressure was 7 mmHg, and pulmonary vascular resistance was 3.71 woods units. Endobronchial ultrasound was applied to the patient with the preliminary diagnoses of lymphoma, anthracosis, fibrosing mediastinitis, and infection. Widespread anthracosis was observed in all lobes and segments macroscopically. The lymph node in the subcarinal area was interpreted as anthracotic lymph node. Anthracosis is defined as black pigmentation involving the mucosal, and submucosal layers of the tracheobronchial tree and the lung parenchyma. If anthracosis is associated with luminal obliteration and/or mucosal proliferation causing obstruction, it is considered anthracofibrosis. In this case, we saw that secondary anthracofibrosis, fibrosing mediastinitis due to anthracotic enlarged lymph nodes in the mediastinum, and pulmonary hypertension may develop because of compression of the lymph nodes on the pulmonary arteries, and we wanted to draw attention to it was a rare case.

KEYWORDS: Anthracosis, anthracofibrosis, fibrosis mediastinitis, biomass exposure, pulmonary hypertension
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INTRODUCTION

Anthracosis is an accumulation of carbon particles in mucosal and submucosal layers of the tracheobronchial tree causing black pigmentation. The most common reason is recurrent inhalation of coal dust particles, smoke, or exposure to air pollution. Bronchial destruction and deformity caused by anthracosis are called anthracofibrosis. It is associated with luminal obliteration and/or mucosal proliferation that causes obstruction. Carbon particles can also accumulate in lymph nodes and it is one of the common causes of enlarged mediastinal lymph nodes in developing countries.

Fibrous mediastinitis is a rare benign pathology characterized by intense fibrous tissue proliferation in the visceral mediastinum. Although its etiology is unclear, anthracosis might be one of the reasons for fibrous mediastinitis. Moreover, in fibrous mediastinitis, pulmonary hypertension may develop secondary to pulmonary vein/artery involvement. Here, we present a rare case of pulmonary hypertension (PH) secondary to anthracofibrosis.

CASE REPORT

A 71-year-old female presented with progressive dyspnea and dry cough. She has been hospitalized in various centers for the last 3 years for her progressive symptoms and has been treated for chronic obstructive pulmonary disease (COPD). Although she was a non-smoker, she has been exposed to biomass for 60 years as a turd fire. Two years ago, she was diagnosed with pulmonary thromboembolism by perfusion scan only and had 6 months of anticoagulant treatment. She was admitted to our center for unresolving symptoms.

She was investigated for COPD and chronic thromboembolic pulmonary hypertension (CTEPH). She had mild hypoxemia (pO_2: 68.4 mmHg, SaO_2: 95%). Pulmonary function test revealed irreversible mild obstruction (FEV_1: 1600 cc, 100%,

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FVC: 2590 cc, 132%, FEV_1/FVC: 62%). Diffusing capacity of the lung for carbon monoxide (DLCO) was 56%. In her echocardiography, ejection fraction was 61 and maximum systolic pulmonary arterial pressure (PAP) was reported as 59 mmHg over tricuspid regurgitation. The bilateral lower extremity venous Doppler ultrasound was normal, and she had no signs of deep venous thrombosis.

Dual-energy thorax computed tomography angiography (CTA) was performed for the etiology of PH, due to the suspicion of chronic thromboembolic disease. No filling defect compatible with thromboembolism was detected in dual-energy CTA. However, lobar and segmental branches of the pulmonary artery were surrounded by the soft tissue in the hilar region and at this level, their calibration was decreased significantly (compression-fibrotic process?). In these regions, nonsegmental perfusion defects in iodine maps were noticed (Figure 1A and 1B). Soft tissue increment with millimetric calcifications and bilateral hilar conglomerated lymph nodes were reported. In addition, nodular soft tissue structures cohering with interlobar and lobar lymph nodes were reported in both lungs. These findings were not compatible with CTEPH.

The patient underwent right heart catheterization; the mean PAP, the pulmonary capillary end pressure (wedge pressure), and the pulmonary vascular resistance (PVR) were recorded as 27 mmHg, 7 mmHg, and 3.71 woods, respectively.

Because of the conglomerated lymph nodes and the presence of suspicion of malignancy, the patient underwent a positron emission tomography (PET) scan. A PET scan revealed pathological increased 18F-fluorodeoxyglucose (FDG) uptake in bilateral mediastinal and hilar lymph nodes, concerning malignancy (SUV_{max}: 11.0) (Figure 2A and 2B).

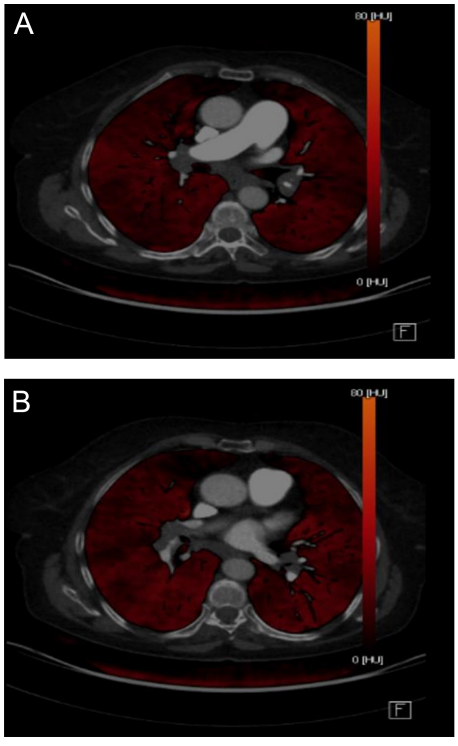

Figure 1. Nonsegmental perfusion defects in iodine maps.

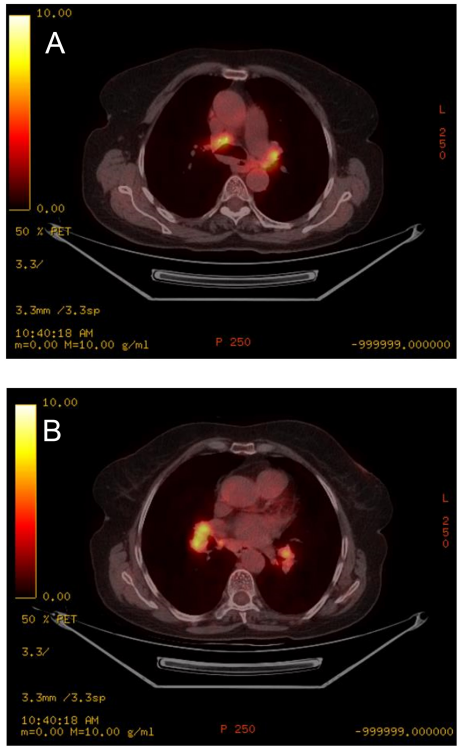

Figure 2. PET scan images.

The patient underwent endobronchial ultrasound (EBUS) which revealed mucosal anthracosis (Figure 3A). Endobronchial ultrasound-guided transbronchial needle aspiration of the paratracheal lymph node (Figure 3B) showed a large amount of anthracotic pigment on microscopic

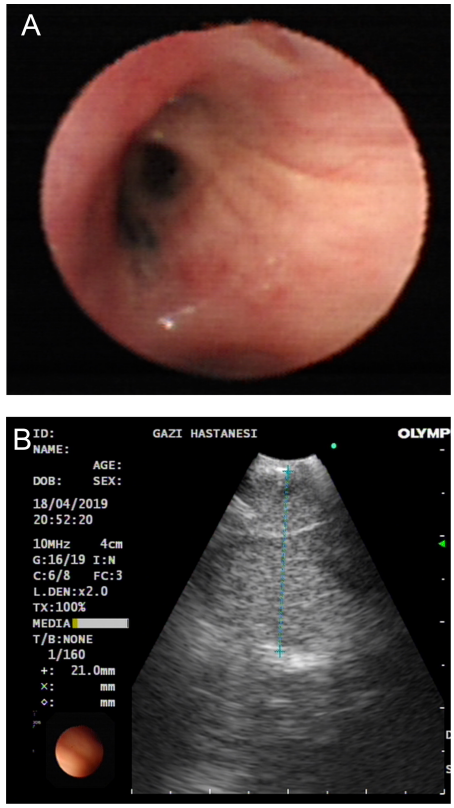

Figure 3. (A) Mucosal anthracosis. (B) EBUS-guided transbronchial needle aspiration of the paratracheal lymph node.

examination, there were no findings for specific granulomatous infection or lymphoprolipheratif disease, confirming the diagnosis of nodal anthracosis. She also had no signs of any granulomatous infection and acute phase parameters were normal.

The patient has been diagnosed as;

1. Anthracofibrosis secondary to biomass exposure
2. Fibrous mediastinitis due to anthracotic enlarged lymph nodes in the mediastinum
3. Pulmonary hypertension and perfusion defects as a result of lymph nodes pressing on the pulmonary arteries (fibrous mediastinitis).

Pulmonary arterial hypertension targeted therapies were not considered since there was no evidence that she would benefit from them. The patient was followed up with symptomatic treatment and inhaled a long-acting antimuscarinic agent for her mild COPD.

DISCUSSION

Here we presented a rare case of PH caused by fibrosing mediastinitis due to anthracofibrosis in whom all other causes of PH were excluded by detailed investigations. One might define anthracosis as infiltration of mucosal and submucosal layers of the tracheobronchial tree and black pigmentation, which includes the lung parenchyma. It is frequently found randomly in the bronchoscopic assessment of patients. If anthracosis is associated with luminal obliteration and/or mucosal proliferation that causes obstruction, it is identified as anthracofibrosis. Anthracofibrosis was first defined by Chung et al[1] in 1998. It should be considered in patients with COPD and asthma, usually middle-aged and old-aged women, who do not respond to the usual treatments, who have been living in a rural area, and who are non-non-smokers with a history of biomass exposure like turd fire as in our case.[2] Its pathogenesis includes indoor and outdoor air pollution, hereditary qualities, biomass history, chronic inflammatory conditions, or chronic infections. It was shown to be related to tuberculosis, COPD, pneumonia, asthma, sarcoidosis, and PH.

Anthracosis is also one of the common reasons for enlarged mediastinal lymph nodes in developing countries.[3] Anthracotic mediastinal lymph nodes often appear oval, with calcification. Sclerosing mediastinitis or mediastinal fibrosis terms are also used for "Fibrous mediastinitis." In addition, it has been defined an as "idiopathic fibro-inflammatory lesion." Even though the etiology has not been fully clarified, factors such as tuberculosis, aspergillosis, mucormycosis, blastomycosis, cryptococcosis, and anthracosis have been reported in the etiology of fibrous mediastinitis. In this case, all other causes were excluded, and athracosis was accepted as the etiology of fibrous mediastinitis. Furthermore, this chronic inflammatory process can cause compression in the vena cava superior, systemic veins, esophagus, tracheobronchial structures, pulmonary arteries, and veins. Besides, PH may develop secondary to pulmonary vein/artery involvement which is the situation in the case we presented.

Pulmonary hypertension is a progressive cardiopulmonary disease. Pulmonary hypertension is diagnosed with an increase in mean PAP ≥20 mmHg assessed by resting right heart catheterization.[4] Pulmonary artery pressure can increase due to precapillary or postcapillary diseases. Our patient had precapillary pulmonary arterial hypertension as she had increased PAP together with increased PVR, and normal wedge pressure. Pulmonary hypertension is classified into 5 main groups.[4] The PH in group V is also precapillary and is caused by unclear and/or multifactorial mechanisms. This group includes many conditions that may be complicated by complex and sometimes overlapping pulmonary vascular involvement.[4] Hematologic diseases such as chronic hemolytic anemia, myeloproliferative diseases, metabolic and systemic and diseases such as pulmonary Gaucher disease, sarcoidosis, Langerhans cell histiocytosis, neurofibromatosis, glycogen storage disease, chronic kidney failure, and complex congenital heart disease are among the diseases included in this group.[5] This group also lists tumor obstruction and fibrous mediastinitis.[4] Our patient's progressive dyspnea was thought to be caused by PH due to fibrous mediastinitis and mimicked pulmonary embolism before. Group IV PH (CTEPH) was ruled out in our case by dual-energy CTA which is mentioned as the new modality alternative perfusion imaging techniques in the current guideline.[4] No PH-directed therapy was initiated for the patient, as in group 5 PH, treating the underlying disorder remains the standard of care.[4]

Anthracotic enlarged mediastinal lymph nodes were investigated in other cases for malignancy and granulomatous infections.[3] Because of the pathological FDG uptake in PET scans, we wanted to rule out, especially malignancy or tuberculosis, no findings were noted for these possibilities in the histopathological investigation. Fluorodeoxyglucose can accumulate in inflammatory cells such as activated macrophages and neutrophils at the location of inflammation or infection. Fluorodeoxyglucose can also accumulate in granulomatous pathologies such as sarcoidosis and tuberculosis, which can cause false-positive PET scan results. Anthracotic particles can moreover act as an antigen and can stimulate macrophages. Some studies have reported increased FDG uptake in PET scans in anthracotic lymph nodes in the mediastinum.[5] In a study by Yilmaz Demirci et al[3], the mean SUVmax value was reported as 4.76 (1-16.8) in anthracosis sampled lymph nodes. As a result, if there is a history of exposure to hazards and noxious particles, the possibility of a benign condition ought to be considered when serious uptake in mediastinal and hilar lymph nodes is observed in a PET scan.[6]

EBUS–TBNA is considered a minimally invasive procedure that permits real-time assessment and biopsy of mediastinal lymph nodes.[5] Anthracosis is the most common source of endogenous particles in mediastinal lymph node samples and is mostly found within macrophages. Endobronchial ultrasound–TBNA is a useful procedure in the identification of anthracotic particles.[6] Kirchner et al[7] examined mediastinal lymph nodes with EBUS–TBNA. Then, the anatomical positions of these lymph nodes were analyzed by multislice computed thorax tomography, and they found that the foremost common location of anthracotic lymph nodes was the

subcarinal.[7] Yilmaz Demirci et al[3] evaluated 1138 mediastinal lymph nodes with EBUS–TBNA and reported that interlobar and subcarinal lymph nodes were the most frequently affected locations (34.3% and 36.8% respectively). It has been emphasized that anthracotic mediastinal lymph nodes most frequently have a well-defined oval shape with calcifications.

In conclusion, PH caused by fibrosing mediastinitis due to anthracofibrosis is a very rare condition. Anthracofibrosis may moreover be kept in mind within the handle of differential diagnosis of PH and granulomatous illnesses.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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