

A rare case of anthracofibrosis complicated with pulmonary embolism

Asterios T. Tzinis¹, Evangelia Panagiotidou¹, Evangelos Chatzopoulos¹, Athanasios Zacharias¹, Afroditi Boutou², Ioannis Stanopoulos¹, Georgia Pitsiou¹

ABSTRACT

We present a case of anthracofibrosis with a challenging diagnostic approach, complicated with pulmonary embolism (PE). A coal exposed 71-year-old woman presented with acute respiratory failure. Lung cancer was suspected, as computed tomography (CT) findings included a mass. Apart from mild stenosis of the RUL bronchus, bronchoscopy failed to reveal significant endobronchial findings, while biopsy and cytology were negative for malignancy. Fine needle aspiration (FNA) was performed, leading to the diagnosis of anthracosis, based on the new cytologic findings which included soot particles. Although bronchoscopy is the gold standard, pigmented lesions or bronchial stenosis were not detected. Moreover, during her hospitalization the patient also presented aggravating respiratory failure and CT pulmonary angiography (CTPA) showed PE. There have been reports that anthracofibrosis might generate a hypercoagulant state. The pathophysiological mechanisms that explain this occurrence are presented in this case report.

AFFILIATION

1 Respiratory Failure Unit, Medical School, Aristotle University of Thessaloniki, 'G. Papanikolaou' Hospital, Thessaloniki, Greece
2 Department of Respiratory Medicine, 'G. Papanikolaou' Hospital, Thessaloniki, Greece

CORRESPONDENCE TO

Asterios T. Tzinis. Respiratory Failure Unit, Medical School, Aristotle University of Thessaloniki, 'G. Papanikolaou' Hospital, Dimokritou 6, Epanomi 57500, Thessaloniki, Greece. E-mail: stergioztzinis@hotmail.com
ORCID ID: <https://orcid.org/0000-0003-3899-5624>

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INTRODUCTION

Anthracosis belongs to the greater group of environmental lung diseases, called pneumoconiosis¹. Although quite frequent in Asia^{2,3}, only few cases are reported in Greece annually. We present a case study in order to highlight the diagnostic challenges and clinical complications that we encountered.

CASE PRESENTATION

A 71-year-old refugee from Afghanistan presented with acute hypoxemic respiratory failure. She had recently been hospitalized due to fever, dyspnea and intense wheezing, that were treated with intravenous methylprednisolone. She was not a smoker; however, she was exposed to biomass fuels in a poorly ventilated household for at least 50 years and reported having chronic cough and dyspnea the last 5 years. She was also hospitalized 3 years ago for a lower respiratory tract infection.

Her vital signs included a pulse rate of 84 beats per minute, body temperature of 37°C, and respiratory rate of 22 breaths per minute. Blood saturation was approximately 90% with a nasal cannula oxygen supply of 4 L/min, while blood pressure was normal. Physical examination of the chest revealed wheezing sounds during respiration in both lungs.

Complete blood count showed elevated leukocytes (19400/μL) and neutrophils (93.8%), possibly due to

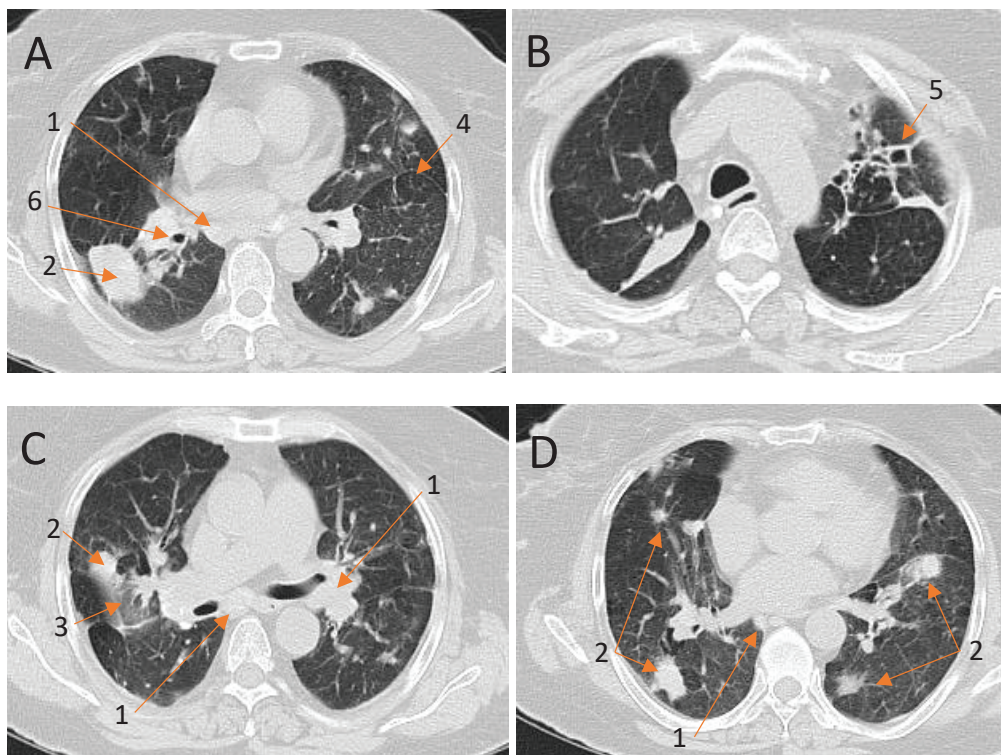
recent corticosteroid treatment. C-reactive protein was slightly elevated at 4.03 mg/dL (normal range <0.8 mg/dL). B-natriuretic peptide, angiotensin converting enzyme and procalcitonin values were normal. Auto-antibodies screen was also negative.

Pulmonary function tests showed restrictive ventilatory defects combined with small-airway obstruction with forced vital capacity (FVC) of 1.17 L (50% of predicted value), forced expiratory volume in 1 second (FEV1) of 0.85 L (44% of predicted value), FEV1/FVC ratio of 75.5%, and forced expiratory flow between 25% and 75% of vital capacity (FEF25–75%) of 0.76 L (30% of predicted values).

Chest X-ray revealed masses in both hilar areas. Chest computed tomography (CT) (Figure 1) revealed:

1. Multiple enlarged mediastinal lymph nodes; many of them presented peripheral calcification.
2. A large disparate, calcified consolidation in the posterior part of the right upper lobe (RUL), which attracted the side pleura and caused stenosis of the bronchus for the right upper and the middle lobe.
3. Bilateral lung nodules of various sizes, with the largest presenting dimensions of 4×2.4 cm.
4. Ground glass infiltration in the RUL.
5. Bronchiectasis in the apical part of the left upper lobe (LUL) with fibrotic features and attraction of the mediastinal pleura.

Figure 1. Chest computed tomography scan (CT) (A) – (D). These images reveal several enlarged mediastinal lymph nodes (1), bilateral lung nodules (2), ground glass infiltration (3), mosaic attenuation pattern (4), and bronchiectasis in the apical part of the left upper lobe (LUL) with fibrotic features and attraction of the mediastinal pleura (5), stenosis of RUL bronchus (6)



6. Mosaic attenuation pattern.

The possibility of malignancy was thoroughly investigated. Sputum cytology was negative for neoplastic cells. Bronchoscopy was performed revealing highly inflammatory and hemorrhagic mucous membrane and mild stenosis of the RUL bronchus. Bronchial biopsy was taken from the stenotic region of the RUL and revealed inflammation of the mucosa and hyperplastic lesions, without evidence of dysplasia. Cytology revealed abundance of inflammatory cells, mainly alveolar macrophages, as well as squamous and bronchial epithelium cells. Bronchoalveolar lavage (BAL) cultures for common bacteria, *Mycobacterium tuberculosis*, *Histoplasma capsulatum*, *Nocardia* and *Pneumocystis jiroveci* were negative. Serum galactomannan values were also negative.

The next step of the diagnostic approach was to order a positron emission tomography scan CT (PET/CT) that revealed bilateral, hypermetabolic, nodule lesions. The largest nodule was sited in the RUL and presented an intake of 4.8 maximum standard unit value (SUVMAX), making the diagnosis of an inflammatory, rather than a malignant disease, more likely (Figure 2).

CT guided fine needle aspiration (FNA) from the largest hypermetabolic nodule was then performed. The FNA cytologic examination was conclusive, as macrophage cells

containing particles of soot were evident.

Subsequently, during her hospitalization, the patient developed tachycardia (about 120 bpm), accompanied with elevated oxygen needs, pain on lower limb palpation and T-wave inversion in the V1, V2, V3 chest leads. The patient's Well's and Geneva scores were 6 and 10 points respectively, determining a moderate risk for PE. D-dimmers levels were also elevated and a CT pulmonary angiography (CTPA) was performed with the upcoming findings (Figure 3):

1. Filling defects in multiple vessels of the LUL and the left lower lobe (LLL).
2. Complete defect of perfusion for multiple vessels of the posterior part of the RUL, the middle lobe (ML) and the right lower lobe (RLL).

The patient was already on prophylaxis with enoxaparin, as she was bedridden, with oxygen needs, throughout a long hospitalization and subsequently begun treatment with therapeutic dose of enoxaparin for 5 days, that was switched to rivaroxaban, as clinical stability was ensured.

Pro-coagulant factors, other than immobilization during her hospitalization, were not detected. Protein C, protein S, antithrombin III and homocysteine levels were normal, and she was negative for Factor V Leiden mutation.

The patient was treated with inhaled corticosteroid

Figure 2. PET computed tomography scan (PET/CT) (A) – (D). These images reveal bilateral, hypermetabolic, nodulus lesions, indicative of inflammatory/infectious disease

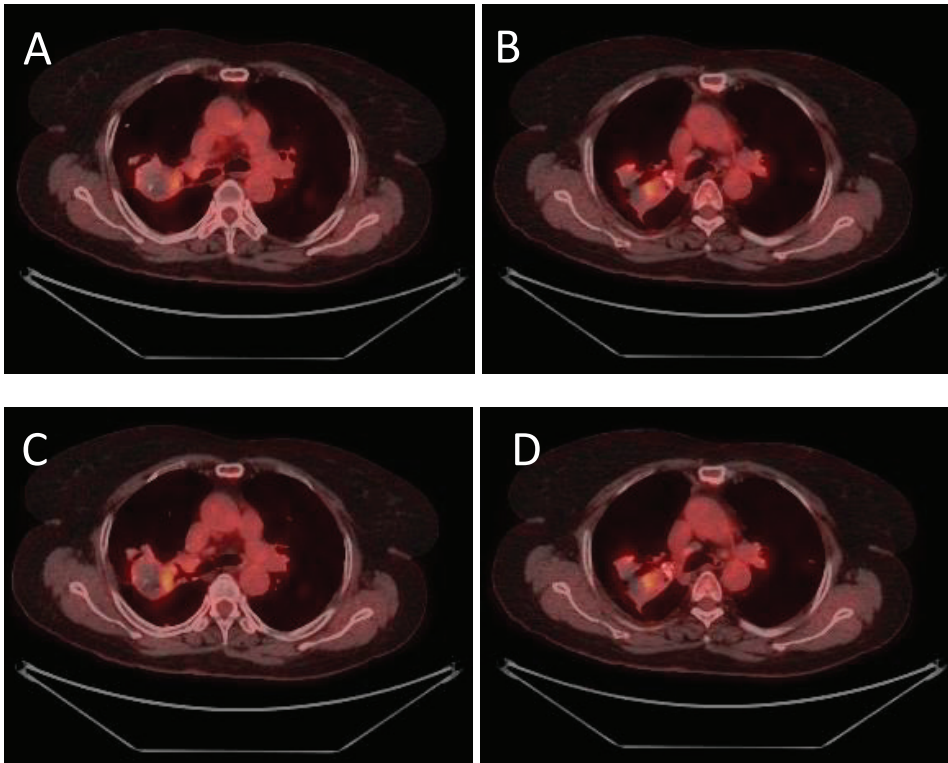
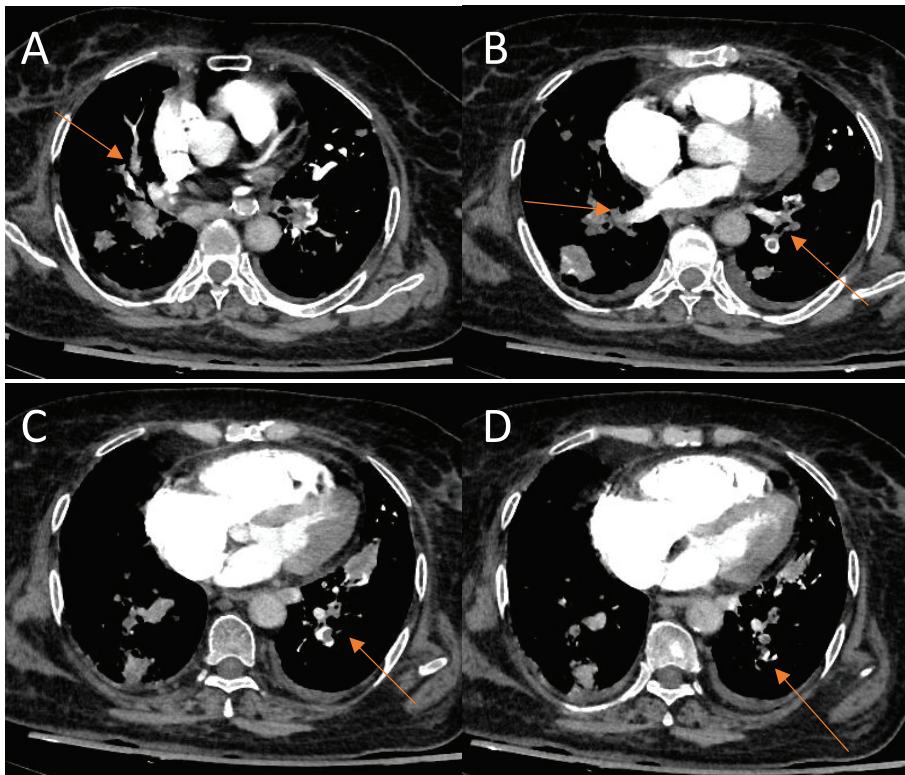


Figure 3: CT pulmonary angiography (CTPA) (A) – (D) These images reveal filling defects in multiple vessels of each lobe in both lungs.



plus long-acting beta-agonist (ICS/LABA) and oral methylprednisolone, given the fact that severe wheezing episodes were very frequent. Instructions for gradual withdrawal of corticosteroids were given to the patient.

DISCUSSION

Anthracosis seems to occur following accumulation of carbon in the lungs due to exposure to coal dust particles⁴. It may also be complicated with mucosal proliferation, luminal obliteration and/or obstruction, resulting in the condition called anthracofibrosis⁵.

Small size inhaled particles (0.5–5 µm), which are either engulfed by macrophages in the submucosa or remain in the bronchial tree due to deficient mucociliary clearance, lead to bronchial epithelial cells deposition⁶. Black macules are formed that gradually progress to the nodules of the surrounding lung parenchyma, causing progressive massive fibrosis (PMF)⁷, thus leading to bronchial wall hypertrophy, lumina narrowing and pulmonary dysfunction⁶. Coexistence of Tuberculosis (TB) and anthracofibrosis might also be relevant as lymph nodes accumulated by carbon and silica might rupture into the adjoining tracheobronchial tree as soon as they get infected by *M. tuberculosis*, leading to black pigmentation and subsequent inflammation⁸.

Given the pathogenic importance of coal exposure, anthracosis appears with increasing incidence in industrialized countries, especially in Asia, with most cases of anthracofibrosis induced by indoor pollution recorded in Korea⁶ and Iran². In Europe, anthracosis was common in coal workers between the 1960s and 1980s, but recent reports show that it is currently prevalent in farmers and rural dwellers⁹. Due to low physical strength, and the progressive nature of the disease, older individuals seem to be more vulnerable¹⁰. Meanwhile, a female preponderance has been reported by most researchers².

Diagnosis of anthracofibrosis is a complex procedure as it is a rare condition with limited literature in Europe. Clinical symptoms are barely specific. Most patients present with dyspnea (90–100% of cases), cough (29.8–83.6% of cases)² and wheezing⁶. Hemoptysis or non-specific chest pain, constitutional symptoms, and sputum production, both black and watery, are also occasionally observed. There are also reports of new onset weight loss or fever, enlarged mediastinal lymph nodes, and subsequent complications such as vocal cord paralysis or broncholithiasis as initial symptoms⁶. Normal physical examination is also noted in some cases⁶.

The usual chest CT findings, according to Kahkouseh et al.¹, include enlarged lymph nodes, hyperattenuation of the lung parenchyma, and multisegmental atelectasis. Bronchial narrowing, peribronchial cuffing, consolidation, mosaic lung attenuation and pulmonary nodules are also common¹.

Moreover, bronchoscopy is considered to be the gold standard diagnostic tool, with multiple pigmented anthracotic

lesions and bronchial stenosis as principal findings⁶.

However, anthracosis is not always localized in bronchi and may spread to the parenchyma¹. Histopathological findings in biopsy samples of anthracofibrosis patients revealed infiltration of non-specific mononuclear inflammatory cells with typical intracellular and extracellular black particles observed in the epithelium and stroma⁶.

In our case, the cytological finding of macrophages containing soot particles, along with a suitable radiologic image was sufficient to set the final diagnosis, since bronchoscopy did not reveal the typical findings and other possible diagnoses were excluded.

Anthracosis is known to be associated with a number of pulmonary diseases. Among them, tuberculosis (TB) seems to be the most dominant⁸ in 15.8% of the anthracotic patients¹¹. Chronic obstructive pulmonary disease (COPD)⁶, respiratory infections¹² and sarcoidosis¹³ have also been reported as related conditions, while the association between anthracofibrosis and asthma is under investigation².

Pulmonary function tests¹⁴ show controversial findings with approximately two-thirds of patients manifesting obstruction, and one-third restriction⁶. Specific association between lung cancer and anthracofibrosis has not been found yet, although adenocarcinoma seems to be the most prevalent histopathological type in patients with anthracosis¹⁵.

Moreover, pulmonary embolism is a condition which seems to be prevalent in chronic respiratory disease (CRD) patients³. Anthracofibrosis seems to be the second most common (25%) chronic lung disease among patients with pulmonary embolism³ after COPD (32%), according to a recent study in Korea. Immobility, chronic inflammation, recurrent infections and other comorbidities seem to create pro-coagulant conditions, responsible for this clinical complication.

In particular, anthracofibrotic lungs contain granulation tissue and fibrotic lesions⁶, indicative of hyperactivity of the tissue factor which is a key element in the coagulation pathway¹⁶. In addition, squamous metaplasia, dysplasia and hyper vascularization have also been occasionally reported⁶, pointing to a pre-neoplastic condition which is also characterized by hypercoagulant activity. Moreover, there have been reports of elevated factor VIII levels, associated with endothelial injury in respiratory failure patients¹⁷, while BAL fluids of fibrotic patients have shown increased levels of plasminogen activator inhibitor¹⁸. Increased platelet activation, mediating inflammatory and thrombotic responses, have also been demonstrated in a number of respiratory diseases¹⁹. The aforementioned factors introduce a hypercoagulant activity in any severe lung disease, including anthracofibrosis.

Lastly, specific treatment for anthracofibrosis has not been established yet. The symptomatic relief includes antibiotics for concomitant respiratory infections, bronchodilators, mucolytic agents and inhaled corticosteroids⁶. Anti-tuberculosis treatment in TB endemic regions and

combination of corticosteroids with tamoxifen as anti-fibrotic agents have shown promising results, while endobronchial stent placement, for patients with severe bronchial stenosis is also under investigation⁶. Anticoagulants in prophylaxis dose are occasionally administered in hospitalized patients, due to their deteriorated general condition and their increased oxygen needs, which keep them bedridden and physically restricted. However, in the context of outpatient thrombosis prevention, preemptive initiation of anticoagulants remains controversial.

CONCLUSION

Extensive imaging and laboratory examinations might be required to establish the diagnosis of anthracofibrosis. Although bronchoscopy is the gold standard, in our case it was non diagnostic and it was the cytologic examination of the aspirate that set the diagnosis. In this direction, anthracosis should always be considered as a potential diagnosis in patients with coal exposure history, particularly when other profound causes are excluded and the differential diagnosis remains confusing. In the meantime, the risk of pulmonary embolism remains increased in the context of chronic inflammation and should always be considered as a possible complication.

CONFLICTS OF INTEREST

The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

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ETHICAL APPROVAL AND INFORMED CONSENT

Ethical approval was not required for this study. Informed consent was given by the patient.

DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created.

AUTHORS' CONTRIBUTIONS

Research concept and design: ATT, EP, EC, AZ, AB, GP; collection and/or assembly of data: ATT, EC, AZ; data analysis and interpretation: ATT, EP, AB; writing the article: ATT, EP, EC, AZ, GP; critical revision of the article: ATT, EP, AB, IS, GP; final approval of the article: EP, IS and GP.

PROVENANCE AND PEER REVIEW

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