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Chronic pulmonary aspergillosis following pulmonary embolism

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ABSTRACT

Chronic pulmonary aspergillosis (CPA) is predominantly found alongside cavitating or bullous lung diseases. Although pulmonary embolism may cause cavitation, an association with CPA has not been well described. We describe a case of CPA in a 79-year-old female following bilateral pulmonary emboli. The clinical implications are numerous, including the dilemma of anticoagulation. This link suggests that a lower threshold for suspecting CPA following pulmonary embolus is required, even in the absence of other respiratory disease.

1. Introduction

Chronic pulmonary aspergillosis (CPA) is an uncommon but increasingly recognized cause of lung disease believed to affect approximately 240 000 people in Europe alone [1]. Symptoms are usually indolent, and include malaise, weight loss, anorexia, productive cough, breathlessness and haemoptysis [2]. Treatment comprises oral or intravenous azoles or amphotericin B, often for prolonged courses, with urgent treatment of massive haemoptysis sometimes being necessary.

We report a case of CPA as a complication of pulmonary embolism. This association is not well-documented and appears to be very unusual. In a previous report, Terzano et al. described a patient with a thin-walled cavity and *Aspergillus* growing from respiratory secretions four months after an episode of pulmonary embolism. However, no information is provided on the clinical presentation at the time of *Aspergillus* isolation, and on follow up after treatment [3]. A review of patients referred to the National Aspergillosis Centre over the last five years revealed no additional patients with pulmonary embolism as the predisposing condition for CPA.

2. Case

A 79-year-old woman was referred to the National Aspergillosis Centre with weight loss and haemoptysis. Nineteen months before presentation to our centre, she had an elective total knee replacement in another hospital. Six weeks later, she presented with dyspnoea and was diagnosed with bilateral pulmonary emboli following a CT pulmonary angiogram. The emboli were seen affecting all lobar branches on the right, and the left upper lobe/lingular branch on the left. There was no evidence of right heart strain. Patchy ground glass changes were seen in the right middle lobe. An indeterminate lung nodule was seen peripherally in the left upper lobe. She was started on rivaroxaban, remained stable and was discharged.

Sixteen months before presentation, she was readmitted with weight loss and a cough productive of green sputum. A CT thorax demonstrated areas of cavitating consolidation peripherally in the right upper lobe and anteriorly in the left upper lobe which were presumed to reflect areas of pulmonary infarction and secondary infection [Fig. 1a and b].

Aspergillus fumigatus was isolated from a sputum culture. *Aspergillus fumigatus* specific IgG antibody was in excess of 200 mg/L and *Aspergillus*-specific IgE was 0.5 kUA/L (ImmunoCap). Eosinophil count was 2.54×10^9/L. She was ANCA negative. She was prescribed broad spectrum antibiotics but, due to lack of response and suspicion of chronic pulmonary aspergillosis (CPA), a two-week course of voriconazole was given.

Ten months prior to presentation to our centre, a sputum culture again grew *Aspergillus fumigatus*. A CT thorax showed reduction in size of the right upper lobe irregular-walled cavity with intracavitary material suggestive of aspergilloma [Fig. 2].

The left-sided cavity had almost resolved, with a small thin-walled cavity remaining. She was started on itraconazole nine months prior to presentation, which was stopped three months later due to significant gastrointestinal side-effects. Following cessation of itraconazole, she

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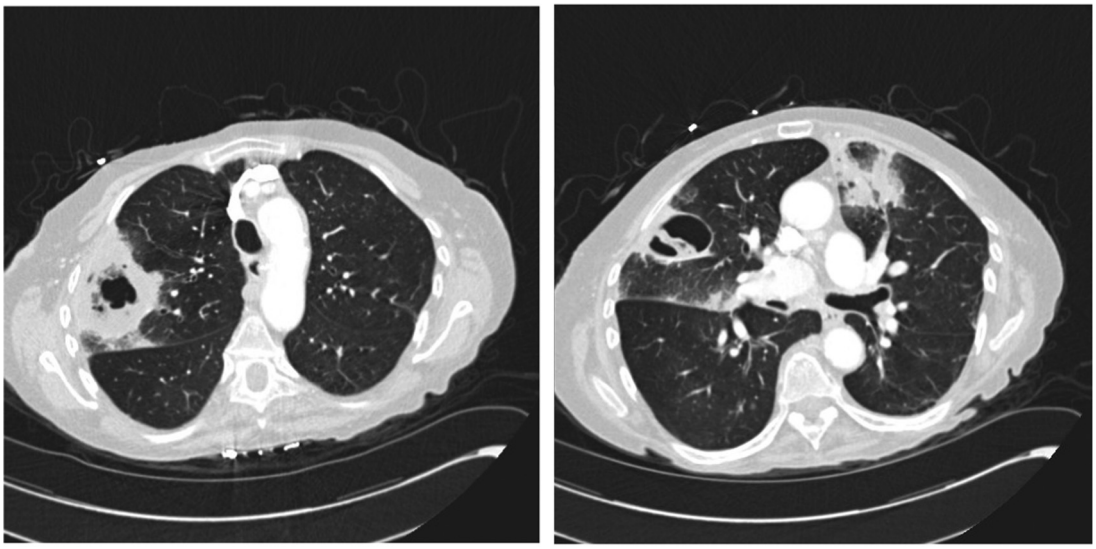

a *b*

Fig. 1. a and b. CT thorax performed on presentation with weight loss and productive cough following the episode of pulmonary embolism. 1a and 1b represent different slices of the same study. Figure a shows an empty thick-walled cavity adjacent to the pleura in the right upper lobe with some interior wall irregularity, consistent with fungal growth. Figure b shows the possible presence of fungal material in the inferior portion of the same right upper lobe cavity, which is much more thin-walled in this cut. There is also an irregular area of inflammation and consolidation with some peripheral ground glass appearance in the left upper lobe anteriorly.

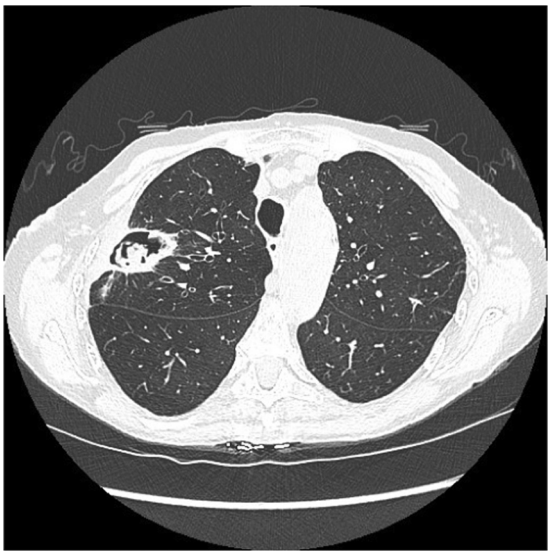

Fig. 2. CT thorax of the patient performed 6 months after the scan in Fig. 1. The cavity thickness is reduced; however there is now a developing aspergilloma and more obvious interior wall irregularity.

had an episode of significant haemoptysis necessitating bronchial artery embolisation. Concomitant diagnosis of deep vein thrombosis led to placement of an inferior vena cava filter. A repeat CT thorax showed no new lesions.

When seen at the National Aspergillosis Centre, she reported one recent episode of low-volume haemoptysis, weight loss of 4kg over two months, fatigue, dyspnoea (Medical Research Council dyspnoea score of 4) and a non-productive cough. Physical examination was unremarkable. Her past medical history included osteoarthritis and chronic obstructive pulmonary disease (COPD). Her medications included inhaled tiotropium, inhaled budesonide/formoterol and oral co-codamol as needed. There was no family history of note. She was a retired nurse and had never smoked, used alcohol or illicit substances. She reported no recent travels.

Laboratory tests showed haemoglobin 109 g/l, C-Reactive protein of 49 mg/L, albumin of 34 g/L and *Aspergillus* IgG antibody titre of 397 mg/L. The diagnosis of CPA was made and oral posaconazole 200 mg once daily was commenced. Posaconazole level was 2.4 mg/l four weeks later.

Four months later, she had had no further haemoptysis and had gained 3kg, yet reported persistent fatigue. Posaconazole was stopped after six months. Over the subsequent six months, she had two episodes of haemoptysis which were self-limited. A repeat CT thorax four months after stopping posaconazole was unchanged. She remains under follow up.

3. Discussion

CPA almost universally occurs in the context of one or more pre-existing lung diseases which alter the lung structure and function and predispose to cavities or bullae, and it is not uncommon for symptoms of CPA to be attributed to other respiratory diagnoses. Mycobacterial infection, both tuberculous and non-tuberculous, has been identified as the most common primary underlying condition. COPD, previous treated lung cancer, pneumonia and pneumothorax are also implicated in the development of CPA [4]. This case adds pulmonary embolism to this list; pulmonary infarction is relatively common in the setting of pulmonary embolism, occurring in up to one third of cases, with cavitation developing in 7% of cases of pulmonary infarction [5–7]. Our patient had COPD, a predisposing condition for CPA, but there was no evidence of CPA prior to the presentation with pulmonary embolism.

Timely diagnosis of CPA is crucial to avoid progressive lung destruction and improve symptoms. Criteria for diagnosis are persistent pulmonary and/or constitutional symptoms, cavitation on thoracic imaging (with or without nodules or a fungal ball), plus objective evidence of *Aspergillus* infection in the form of microscopy, culture, histology or specific immunological response [2].

Oral triazole therapy is first-line treatment in CPA, and intravenous azoles or amphotericin B may be required in cases of progressive disease or intolerance or resistance to oral treatment [2]. Prolonged treatment is often required, and the disease can relapse following cessation of antifungals. Our patient demonstrated almost complete resolution of the left-sided cavity following voriconazole treatment,

remained stable on itraconazole and then off treatment until her symptoms recurred prior to posaconazole being started. An episode of haemoptysis was controlled with bronchial artery embolization.

Haemoptysis, sometimes massive, is an uncommon but potentially fatal complication which may require surgical management or bronchial artery embolization. A causal link between CPA and pulmonary embolism could prove clinically problematic in patients who require therapeutic anticoagulation due to the risks of haemoptysis and drug interactions.

The presence of progressive pulmonary and/or constitutional symptoms in a patient with cavitation following pulmonary infarction should warrant consideration of concomitant CPA as a potential cause. A low threshold for investigation will permit earlier diagnosis of CPA, prompt anti-fungal therapy and minimize complications such as haemoptysis and disease progression.

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Not applicable.

Conflict of interest

There is no conflict of interest.

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