Pseudomembranous necrotising bronchial aspergillosis complicating chronic airways limitation

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Abstract

Pseudomembranous necrotising bronchial aspergillosis is a variety of invasive aspergillosis found in immunosuppressed patients. A case is presented of a 66 year old woman whose only underlying disease was chronic airways limitation. The pathological findings and clinical implications are discussed.

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Keywords: aspergillosis, airways limitation, *Aspergillus*.

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Invasive aspergillosis usually complicates immunosuppressive processes such as leukaemia, AIDS, and cytotoxic therapy.¹⁻³ It has also been reported in a patient with fulminant viral pneumonia.⁴ Pseudomembranous necrotising bronchial aspergillosis is a variant of invasive aspergillosis and is also described in patients with impairment of the immune system.⁵ We present a case arising in a patient who was not on immunosuppressive therapy.

Case report

A 66 year old female smoker with a 20 year history of chronic obstructive airways disease

presented to the referring hospital with a severe exacerbation of her airways limitation. Her regular maintenance therapy included nebulised salbutamol and ipratropium bromide. She had been treated with short courses of oral corticosteroids but these had been withdrawn three years previously. She was not receiving inhaled steroids.

On admission widespread expiratory wheeze could be heard bilaterally. Arterial blood gas analysis revealed PaO_2 of 8.8 kPa, PaCO_2 of 10.9 kPa, and pH of 7.21 with an inspired oxygen concentration of 40%. A chest radiograph showed left lower lobe collapse and right basal shadowing. The blood count and electrolyte levels were normal. She failed to respond to intravenous bronchodilator and steroid therapy and, although her gas exchange did not deteriorate further, mechanical ventilation was indicated due to exhaustion. Cefuroxime and erythromycin were added to the intravenous bronchodilators and hydrocortisone. Mechanical ventilation resulted in an initial rapid improvement with falling PaCO_2 and a peak inspiratory pressure of less than 25 cm H_2O , but this progress was not maintained beyond 24 hours ventilation when airways pressures rose and gas exchange deteriorated again. There was little detectable wheeze and no response to increasing doses of bronchodilators. Bronchoscopy with bronchoalveolar lavage and biopsy was performed. Macroscopically no obstructing lesion was seen, but fungus was evident in both specimens and aspergillosis was considered likely. Fluconazole was commenced.

Persistent problems with pulmonary hyperinflation and gas trapping prompted referral to our unit after 10 days of mechanical ventilation. There was evidence of sepsis with deteriorating renal function and the white blood cell count had risen to $38 \times 10^9/\text{l}$. Antibiotic therapy was changed to include teicoplanin, piperacillin, and amphotericin. An IVOX (Cardiopulmonics, Utah, USA) intravascular device was inserted into the inferior vena cava to facilitate removal of carbon dioxide. Up to 80 ml CO_2 per minute was cleared, allowing a substantial reduction in the minute volume, the intensity of mechanical ventilation, and the pulmonary hyperinflation. Progressive sepsis could not be controlled, however, and the patient died 36 hours after IVOX implantation. The time between presentation and death was 11 days.

At necropsy both lungs were distended and contained palpable nodules. An attempt to instil formalin into the bronchi was unsuccessful. Slicing revealed numerous irregular firm cream nodules and plugging of airways of all sizes by soft cream material (fig 1). Microscopic examination showed that bronchi and bronchioles were plugged or lined by a pseudomembrane of necrotic debris and abundant hyphae of *Aspergillus* which infiltrated the bronchial walls and invaded adjacent blood vessels, causing a secondary arteritis (fig 2), thrombosis, and infarction. No fungus was identified elsewhere in the body.

Figure 1 Section of lung showing small nodular infarcts (curved arrows) and plugging of airways (straight arrows). Note that the intervening lung is not involved.

Figure 2 Fungal hyphae infiltrating a pulmonary artery causing vasculitis and thrombosis. Stain: haematoxylin and eosin, original magnification $\times 250$ reduced to 62% in origination.

Discussion

Three main forms of bronchopulmonary aspergillosis are described: allergic, saprophytic, and invasive.¹ Invasive aspergillosis is largely confined to immunosuppressed or pancytopenic individuals. It is characterised by necrotising pneumonia, haemorrhagic infarction, and at times fulminating septicaemia. The trachea is involved in up to 10% of cases.^{2,3}

Pseudomembranous necrotising bronchial aspergillosis is a variety of invasive aspergillosis where the fungus is centred on the airways and invasion is mainly limited to the peribronchial tissues.⁵ In our case there was also nodular pulmonary infarction, a feature not usually associated with this disease, evidently due to the

invasion of the adjacent pulmonary arteries by the fungus.

This case is notable because the patient was not receiving immunosuppressive therapy at the time of presentation. There was a history of intermittent treatment with oral steroids but this had been discontinued three years previously. There was also no evidence of malnourishment which might also have affected her immunocompetence. Invasive aspergillosis has previously been described in four patients with chronic airways limitation, three of whom died; none was of the pseudomembranous type. The fourth patient was diagnosed by transbronchial biopsy which revealed the presence of *Aspergillus* and necrotising pneumonia. This patient was successfully treated with amphotericin B.⁶

The possibility of invasive aspergillosis should therefore be considered in the differential diagnosis of patients with deteriorating chronic airways limitation, even if they are not immunosuppressed. Antifungal treatment should be commenced as early as possible to enhance the potential for successful treatment of a highly aggressive form of the disease.

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