COPD patients in general, but in particular COPD patients with comorbidities and exacerbations of respiratory symptoms, should be carefully monitored through a control panel for their complexity [10].

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Tracheal oxalosis associated with *Aspergillus niger* tracheobronchitis

To the Editor:

Aspergillus is a widespread mould that can cause a variety of human diseases, usually in the setting of immunosuppression. Invasive pulmonary aspergillosis is the most aggressive form of *Aspergillus* infection and it is associated with morbidity and mortality. Invasive *Aspergillus* tracheobronchitis is a rare entity, primarily affecting lung transplant recipients, and patients with AIDS or chronic obstructive pulmonary disease (COPD). *Aspergillus niger*, and to a lesser extent *A. fumigatus*, can cause calcium oxalate crystals to accumulate in the lung, a condition termed pulmonary oxalosis. Tracheal oxalosis due to invasive *Aspergillus* tracheobronchitis has, to our knowledge, not been described before. Here, we report the case of a patient with probable invasive *Aspergillus* tracheobronchitis who developed tracheal oxalosis. Clinical, radiological and pathological correlation is given.

Invasive pulmonary aspergillosis is the most aggressive form of *Aspergillus* infection and it is related with a high morbidity and mortality [1]. The majority of patients with invasive aspergillosis are critically ill, requiring intensive care unit (ICU) admission. The presence of *Aspergillus* in the airways of critically ill patients carries higher mortality risk [2], and should prompt further diagnostic evaluation, including fibreoptic bronchoscopy [3].

Invasive *Aspergillus* tracheobronchitis is thought to be a rare entity, primarily affecting lung transplant recipients [4], patients with AIDS [5] and those with COPD [6]. Oxalosis is a condition in which calcium oxalate crystals accumulate in different organs. Oxalosis has been documented in patients with pulmonary aspergillosis [7] or mucormycosis [8] infections. However, there is no previous report in the medical literature of tracheal oxalosis associated with *Aspergillus* infection.

Here we present an immunosuppressed patient who developed probable invasive *Aspergillus* tracheobronchitis and the formation of calcium oxalate monohydrate crystals in the tracheal wall.

A 67-year-old female was assessed for fever and generalised myalgia. She had a medical history of splenectomy due to idiopathic thrombocytopenia. She was diagnosed with septic shock due to *Streptoccocus pneumoniae* infection and was admitted to the ICU. Chest radiograph on admission showed no infiltrates in the lung parenchyma. She rapidly developed multiple organ dysfunction syndrome with acute respiratory distress syndrome

(ARDS), and acute kidney injury requiring mechanical ventilation and continuous veno-venous haemofiltration. Antibiotic therapy, vasopressors and a 7-day course of hydrocortisone (200 mg per day) were initiated to treat the septic shock.

Due to persistent respiratory failure, a chest computed tomography (CT) was performed on day 14 which showed bilateral pleural effusions, lower lobes consolidation and a high-density lesion on the tracheal wall (fig. 1a). The pleural effusions were transudates and sterile. Bronchial aspirates grew *A. niger* on day 16 and anidulafungin was started the same day. ARDS persisted, as well as positive respiratory cultures for *A. niger*. Anidulafungin was switched to vorizonazol and amphotericin B on day 20. Bronchoscopy was performed 2 weeks after antifungal therapy was started which showed grey exophytic endotracheal lesions of hard consistency and cream-coloured ulcers (fig. 1b).

Endotracheal biopsies taken from the plaques showed areas of necrosis with melanocytic pigment. Crystals were seen under polarised light (fig. 1e). Hyphae were not seen with periodic acid-Schiff or Grocott stains. Under electron microscopy, the lesion revealed crystallised plaques. Spectroscopic analysis identified the crystals as calcium oxalate monohydrate. Bronchoalveolar lavage and bronchial aspirates only grew *A. niger*, and no crystals where observed.

The patient died of respiratory failure on hospital day 45. Autopsy was not consented by the family.

In the present article, we describe a patient who developed tracheal oxalosis in the context of tracheobronchial *A. niger* infection. Clinical, radiological, and pathological correlation is given.

For proven invasive *Aspergillus* tracheobronchitis, the demonstration of fungal elements in the diseased tissue is required [9]. Probable invasive *Aspergillus* tracheobronchitis is defined by the presence of a host factor (individual predisposition to invasive fungal disease), clinical criteria (tracheobronchial ulcerations, nodules, pseudomembranes, plaques or eschars on bronchoscopic examination) and mycological criteria (detection of the mould in the respiratory tract by direct or indirect tests). In the present case, the diagnosis was probable invasive *Aspergillus* tracheobronchitis since pathological analysis of the tracheal lesions did not show *Aspergillus* hyphae. However, two other features of *A. niger* infection were present on the biopsy: melanocytic pigment and oxalic acid crystals. Since antifungal therapy was given before biopsies, it is probable that the *Aspergillus* was eradicated from the tracheal mucosa. Neither the presence of melanin pigment nor oxalic acid crystals in the pathologic specimen is included in the definition of proven invasive fungal disease [9]; however, we believe that they represent evidence of fungal invasion, and could have a role in the diagnosis of invasive *Aspergillus* tracheobronchitis.

To our knowledge, this is the first documented case in the medical literature of tracheal oxalosis associated with *A. niger* infection. We only have found two cases of tracheobronchial oxalosis in the literature; a tracheal involvement in a patient who probably aspirated a piece of rhubarb [10], and bronchial oxalosis in a patient with pulmonary mucormycosis [8].

Based on our findings, we suggest that: 1) early bronchoscopic evaluation should be performed in critically ill patients with *Aspergillus* spp. isolated from the respiratory tract; 2)

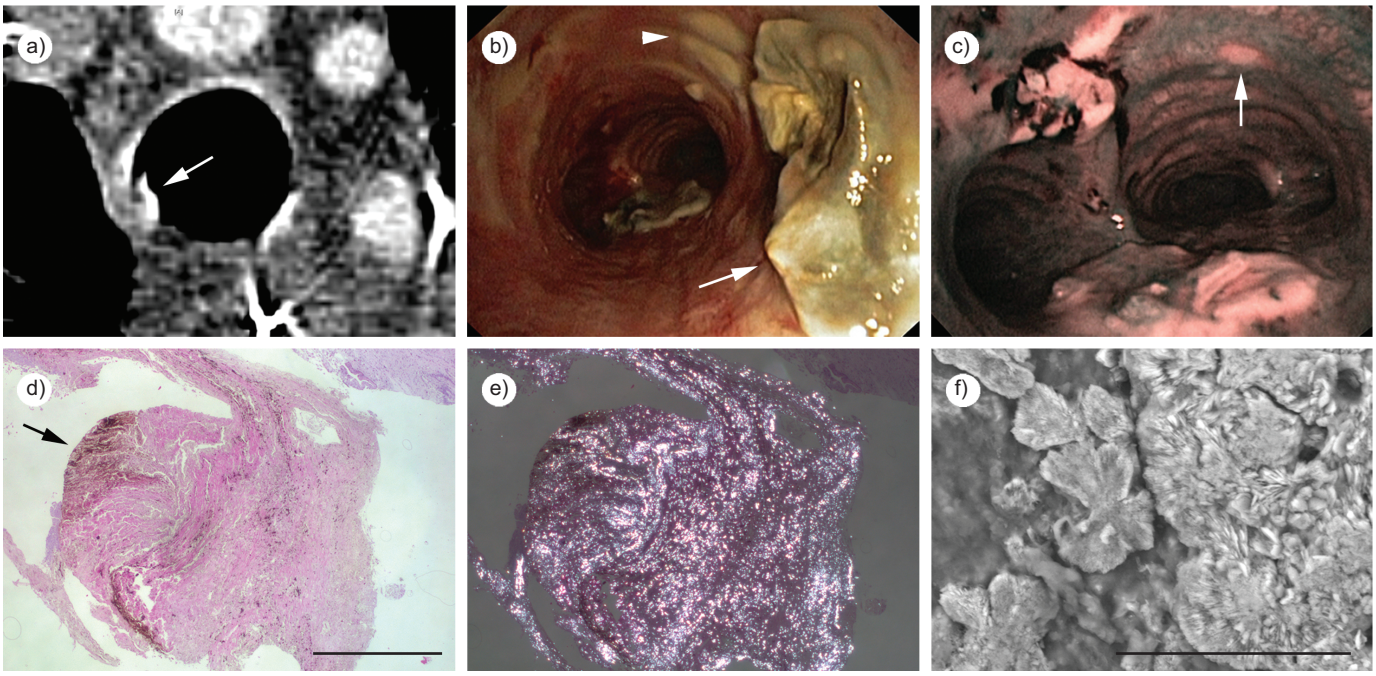

FIGURE 1. a) Chest computed tomography (CT) of the tracheal wall lesion (arrow). b) Tracheal ulcers (arrow head) and pseudomembranous lesion corresponding to the one seen on the CT image (arrow). c) Bronchoscopic blue light inspection after biopsies were taken showing areas of poor vascularisation (brighter areas, arrow) and an ulcer. d) Pseudomembranous lesion. Fragment of necrotic acellular tissue tinged with melanocytic pigment (arrow). Haematoxylin and eosin stain. Scale bar=1 cm. e) Same section as d under polarised light. Abundant birefringent crystals are seen. f) Calcium oxalate monohydrate crystals from necrotic tracheal plaque. Scale bar=40 nm.

microscopic evaluation under polarised light should be done to exclude oxalosis in pulmonary specimens, where fungal infection is suspected; 3) oxalosis should be included in the differential diagnosis of high-density endotracheal lesions on chest CT; and 4) the presence of melanocytic pigment or crystals in tissue biopsies from the respiratory tract could be considered in the diagnostic criteria of invasive fungal disease.

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