Commentary: unusual manifestations of aspergillosis

David W Denning

Four cases of pulmonary aspergilloma in the context of cystic fibrosis are reported in this issue of *Thorax*. In one of the patients the development of an aspergilloma was preceded by allergic bronchopulmonary aspergillosis (ABPA), and in two others there was some evidence of an allergic response to *Aspergillus* but this was insufficient to establish the diagnosis of ABPA. A small number of aspergillomas in patients with cystic fibrosis have previously been reported, including two cases in children from Italy and an adolescent from California. Two cases have also been reported from St Vincent’s Hospital in Dublin, although one of these was probably the same as case 1 reported by Maguire et al on page 805.

Aspergilloma is an increasingly uncommon condition in the Western world with the decline in cavitary tuberculosis. Cases do, however, occur in patients with other conditions such as sarcoidosis, ankylosing spondylitis, and in patients who have previously had spontaneous pneumothoraces. Although the development of an aspergilloma has been a rare occurrence in patients with cystic fibrosis, it is likely to be seen with somewhat increasing frequency. Invasive aspergillosis is also likely to appear more often than previously, particularly in patients receiving steroids and/or those undergoing lung transplantation.

The treatment of aspergillomas is problematic. Surgical resection is useful for simple aspergillomas but there is a mortality rate of about 33% for patients with complex (multicavitary) aspergillomas. In addition, the site of the aspergilloma is critically important to surgical outcome. Pleural aspergillomas carry an extremely high complication rate (100%) following surgery, whereas simple pulmonary or bronchial aspergillomas do well. For this reason, bronchial or pulmonary aspergillomas without any pleural component should not be a contraindication to lung transplantation. However, in the context of cystic fibrosis, particularly late stage, surgical resection rather than transplantation is unlikely to be a viable option. The administration of oral itraconazole (in a dose of at least 400 mg/day for adult patients), with serial monitoring of serum concentrations or intracavitary amphotericin B, are viable treatment options. In patients who do not have cystic fibrosis repeated administration of amphotericin B into the aspergilloma cavity has shown some efficacy. New means of administering the amphotericin B in gelatin or glycerin may be beneficial. Ryan et al (pages 809–10) showed that this approach was feasible, despite fears of a pneumothorax.

Another case of pseudomembranous tracheobronchitis caused by colonisation by *Aspergillus* is reported by Nicholson et al (pages 807–8). This is a condition first described in 1890 in a non-immunocompromised child and, to date, over 60 cases have been reported in a variety of clinical settings. Recent reviews have emphasised the disease entity in the context of leukaemia, lung transplantation, and AIDS. My coworkers and I attempted to classify these diseases and to unify the terminology. We have suggested that the term “*Aspergillus* tracheobronchitis” should be applied to patients in whom there is evidence of bronchial and/or tracheal inflammation, excess mucus production, with *Aspergillus* as the only pathogen and without invasion of bronchial mucosa on biopsy. Focal, ulcerative, or plaque-like processes, which have been described in AIDS and in patients undergoing lung transplantation we termed “ulcerative *Aspergillus* tracheobronchitis” if histological invasion of the abnormal area of bronchial mucosa and/or cartilage showed hyphae consistent with *Aspergillus*. The term “pseudomembranous *Aspergillus* tracheobronchitis” is reserved for patients with very extensive involvement of the whole of the tracheobronchial tree, with a membranous slough overlying the mucosa containing *Aspergillus*. Separate from these conditions (in which the extensive inflammation and/or invasion of the tracheobronchial tree is absent) is a condition of obstructing bronchial aspergillosis described initially in patients with AIDS and now also in heart transplantation patients. In this condition thick mucous plugs full of *Aspergillus* are coughed up or found in the airways, with little or no inflammation and no evidence of invasion or allergic manifestations. This last group of patients is much more symptomatic than those with *Aspergillus* tracheobronchitis.

The case reported by Nicholson et al serves to emphasise that approximately 25% of patients with *Aspergillus* tracheobronchitis are non-immunocompromised or only mildly so. Symptoms are deceptively mild. Without bronchoscopy and antifungal treatment these patients are likely to succumb relatively rapidly as in the case presented. One possibly useful clinical clue to the diagnosis which otherwise is somewhat elusive is unilateral wheeze. It is disappointing that the authors of this case report chose to use fluorocarol for aspergillosis as it has no useful clinical activity; the only current therapeutic choices are amphotericin B or itraconazole.

Finally, Freixinet et al describe a case of *Aspergillus* colonisation of intralobar pulmonary sequestration, the second on record. It is likely
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that the cavities observed do not represent an aspergilloma but rather chronic necrotising pulmonary aspergillosis which is a very slowly progressive invasive form of aspergillosis.\(^{20-22}\) This sometimes leads to the radiological appearance of an aspergilloma but occurs in patients who have no pre-existing cavitory lesions in the lung. In the case presented we have the benefit of histological data which do not support the diagnosis of chronic necrotising pulmonary aspergillosis as no hyphae were seen within the lung tissue. This could represent a sampling error or a form of progressive disease mediated by extracellular toxins of *Aspergillus* without direct invasion of lung. Clearly much additional work is necessary to elucidate the pathogenesis of these unusual types of aspergillosis which defy accurate classification according to our present knowledge base.

These case reports all focus on relatively rare forms of *Aspergillus* disease. However, invasive aspergillosis is increasingly common. A recent necropsy survey of 11,000 unselected cases in two Frankfurt hospitals over 12 years has shown a 14-fold increase in invasive aspergillosis from 1978 to 1992.\(^{23}\) These hospitals have a 70% necropsy rate. In 1992 the pathologists found invasive mycoses at necropsy in 6% of all their patients, with invasive aspergillosis comprising over 60% of these cases. Increased awareness of infections caused by this common mould is clearly appropriate, as the case reports demonstrate.