Management of pulmonary disorders caused by the inhalation of aspergillus spores

Inhalation of the spores of *Aspergillus fumigatus* and other less common forms of aspergilli such as *A. nidulans*, *A. niger* and *A. flavus* can lead to the development of at least five separate pulmonary disorders: bronchial asthma, bronchopulmonary aspergillosis (BPA), mycetoma, invasive aspergillosis, and dial workers lung which is an extrinsic allergic alveolitis due to *A. flavus* and will not be further considered. Ninety per cent of aspergillus infections in man involve the respiratory tract and the most common form is mycetoma in a pre-existing tuberculous cavity. The disease entity which develops in a particular patient is influenced by his immunological reactivity and the condition of his lungs.

Aspergillus spores are ubiquitous and can be inhaled like other common antigens to produce bronchial asthma of the immediate type in atopic individuals. Positive immediate skin tests to extracts of *A. fumigatus* are found in about one fifth of such cases. Serum concentrations of reaginic antibody, IgE, are raised and IgE specific to *A. fumigatus* may be detected by the radio allergo-absorbent test.

Such bronchial asthma is treated along standard lines using inhaled bronchodilators for relief of bronchospasm and inhaled corticosteroids or disodium cromoglycate for prophylaxis. When *A. fumigatus* is repeatedly isolated from the sputum of an asthmatic patient, it is probable that bronchopulmonary aspergillosis has developed. This diagnosis should also be suspected when there are transient pulmonary infiltrates on the chest radiograph, eosinophilia in the blood or sputum and positive skin tests to various *Aspergillus* spp. (Malo, Hawkins & Pepys, 1977). The presence of precipitating antibody in the serum, culture of the fungus from the sputum, and a late type III skin or bronchial reaction to extracts of *Aspergillus* spp. (Leading article, 1977) help to confirm the diagnosis. Bronchograms may reveal bronchiectasis involving the proximal bronchi especially in the mid and upper lung fields.

It is thought, but not proven in man, that cell mediated precipitating antibody to aspergillus antigen produces local bronchial destruction, pulmonary consolidation and subsequently bronchiectasis.

The treatment of bronchopulmonary aspergillosis consists of inhaled bronchodilators to relieve bronchospasm and systemic corticosteroids for the pulmonary opacities. Daily maintenance steroid therapy using at least 10 mg of prednisolone is required to prevent recurrence of infiltrates which are much more likely with intermittent courses of steroids (Middleton et al., 1977). There is no proof yet, however, that corticosteroids will prevent the progression to irreversible airways obstruction and bronchiectasis. A recent trial by the British Thoracic Association (1979) has demonstrated that although inhaled corticosteroids control the asthmatic symptoms in BPA, they do not reduce, and may even increase the frequency of pulmonary opacities and hence they are not an alternative to systemic steroids.

In the past, inhalation of nystatin or natamycin and the endobronchial instillation of sodium iodide and amphotericin B have been used unsuccessfully to eliminate *Aspergillus* spp. from the sputum in BPA and mycetoma. A recent report offers some as yet unconfirmed promise. Horsfield et al. (1977) demonstrated clinical improvement in 7 of 13 patients treated with di-iodohydroxyquinoline, 1800 mg daily for 20 days. After treatment, sputum culture became negative in all of 10 patients and precipitins negative in 12 of 13. However, the microbiological aspects of these results are unexplained since the agent is only sparingly absorbed from the gastrointestinal tract. In Liverpool, using di-iodohydroxyquinoline at the above dosage, we have obtained sputum conversion in 4 asthmatics and cessation of haemoptysis in 4 subjects with mycetoma.

Mycetomas arise in lung cavities caused by tuberculosis, bronchiectasis, sarcoidosis, ankylosing spondylitis, bronchial neoplasm, pulmonary infarction, lung abscess and lung cysts.

The British Tuberculosis Association (1968) studied 544 patients with apical cavities previously successfully treated for pulmonary tuberculosis. 59 patients (11%) had definite mycetomas and there were a further 19 (4%) with highly suggestive appearances. In addition to the characteristic radiographic apical crescent of air above the dense fungal ball, patients with mycetoma produce large amounts of precipitating antibody giving numerous arcs on agar gel in over 90% of cases. The principal symptoms are chronic cough and haemoptysis which may simulate active tuberculosis. In nearly all instances this is not confirmed save for some notable exceptions (Katz, Weiss & Steinberg, 1977). In a follow-up study the British Thoracic and Tuberculosis Association (1970) showed that the death rate...
in patients with definite mycetoma (10 of 59) was 3½ times greater than expected and that haemoptysis had been fatal in 3 (5%) and required surgery in a further 4 (7%). In the U.S.A. surgical resection by lobectomy is recommended for mycetoma except in those patients whose general condition or respiratory reserve prohibit resection. The operative mortality is about 7% (Soltanzadeh et al., 1977) but persistent pneumothorax may require prolonged drainage or pneumonectomy so that Varkey & Rose (1976) have questioned the need to respect and recommend surgery only for frequent or massive haemoptysis. An additional argument for surgery in mycetoma is that the invasive form of aspergillosis might develop if a debilitating illness occurs. Invasive pulmonary aspergillosis is second only to candidiasis as a fungal complication in the compromised host. The diagnosis is frequently only made at necropsy (Williams, Krick & Remington, 1976) but should be suspected when an unexplained pulmonary infiltration develops after renal transplantation or during therapy for lymphoma or leukaemia. In these immunosuppressed patients, precipitin tests may not be of value (Young & Bennett, 1971). In patients without thrombocytopenia or coagulation defects, Aisner, Schimpff & Wiernek (1977) recommend aggressive methods to establish this diagnosis including trans-tracheal aspiration or bronchial brush biopsy.

These authors recommend treatment with amphotericin B when aspergillus is cultured or hyphae are seen histologically. This was successful in three of their six patients and partial in the other three when therapy was instituted within 96 h of the appearance of the infiltration. The 11 patients whose treatment commenced after a delay (usually two weeks) or to whom no treatment was given, all died with progressive aspergillosis. The toxic side effects of systemic amphotericin B on the marrow, kidney and liver discourage its use as empirical therapy in compromised hosts and the search for a less toxic systemic antifungal agent continues. Confirmation of the apparent clinical effectiveness of miconazole in this disorder is awaited with interest (Stille, Helm & Kilp, 1977).

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References