Allergic bronchopulmonary stemphyliosis

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ABSTRACT A patient is described in whom a clinical picture resembling allergic bronchopulmonary aspergillosis was found to be caused by hypersensitivity to the fungus *Stemphylium lanuginosum*. Bronchopulmonary reactions to antigens other than *Aspergillus* may be more frequent than is currently believed.

Allergic bronchopulmonary aspergillosis was first described in Britain, and it is now a well-recognised condition in many parts of the world including Britain, America, Canada, and South Africa. The clinical picture is characterised by asthma, blood and sputum eosinophilia and chest radiograph shadows, while the immunological characteristics include high total IgE levels, specific IgE and IgG antibodies to *Aspergillus* in the serum and dual skin and bronchial reactions in response to prick tests and inhalation challenges with the *Aspergillus* antigen. Clinical, immunological, and histological data suggest that, in addition to the type 1 and type 3 reactions, cell-mediated hypersensitivity, antibody dependent cytotoxicity, and alternate pathway complement activation may play some role in the pathogenesis.

Other organisms which may on occasion produce a similar clinical picture include *Candida albicans*, *Pseudomonas aeruginosa*, and the mould *Helminthosporium spp.*

We report a patient in whom a bronchopulmonary reaction similar in many respects to that seen with *Aspergillus* resulted from inhalation of the fungus *Stemphylium lanuginosum*.

Case report

A 35-year-old man was referred in March 1977 for investigation of a persistently abnormal chest radiograph. In May 1975, he had developed right-sided pleuritic chest pain and a cough productive of mucopurulent bloodstained sputum. A chest radiograph showed two areas of consolidation, one in the right middle lobe and one in the lingula. His symptoms improved on antibiotics but the chest radiograph remained unchanged. Three-monthly radiographs over the next eight months showed slight increase in the size of both lesions and he had a further "bronchitic" episode during which time he coughed up some firm sputum plugs. When first seen in Cape Town in March 1977, he was completely asymptomatic. He gave a history of moderately severe asthma in childhood but had had only minimal symptoms requiring occasional bronchodilator therapy since the age of 13 years. He had never smoked, had no other chest disease, and had worked as a game ranger in the Transvaal for 10 years.

Physical examination was entirely normal. Investigations showed a haemoglobin of 15-2 g/dl, white cell count of 7200 x 10^9/l with 10% eosinophils. The erythrocyte sedimentation rate was 5 mm in the first hour. Skin prick tests produced 2 mm wheal reactions to house dust mite and *Aspergillus fumigatus*, and 3 mm wheals to several other antigens. His FEV₁/FVC was 4-3/4-9l, 88% (predicted vital capacity 5-4l). The plain chest radiograph was unchanged since the one taken in 1975 and the abnormalities were best seen on tomograms (fig 1).

Precipitins to *Aspergillus fumigatus*, *A niger*, and *A flavus*, were undetected by double diffusion in neat serum but were weakly positive when the serum was concentrated three times. At bronchoscopy, the only abnormality was of the right middle lobe orifice which was oedematous and occluded by mucopurulent secretions. Secretions aspirated directly from the right middle lobe bronchus were examined after gram staining and fungal elements were seen. The secretions were cultured on Sabouraud's and Littman's media at room temperature at 37°C. Growth as a pure culture first appeared on...
Littman’s medium at 37°C after two days, and then on the Sabouraud’s the next day. The growth was originally white and fluffy and later darkened to black, as the spores developed. The characteristic dark spores with irregular septa of *Stemphylium lanuginosum* were found on microscopic examination of the culture and confirmed by slide culture, from which a photograph was taken (fig 2). Several subsequent cultures of sputum and of mucus plugs yielded heavy growths of the same organism. All cultures were negative for *Aspergillus*, other fungi, and bacteria. An inoculum from the *Stemphylium* culture was incubated at 37°C on a sterile Hank’s lactalbumin 5% glucose medium until a firm growth was established in approximately 14 days. An antigen was prepared from this pure culture of *Stemphylium* by homogenisation, centrifuging, separation, filtration, dialysis, and finally concentration using standard methodology. Thiomersal 0.01% was added as a preservative to the final antigen. The patient’s unconcentrated serum was found to contain precipitating antibodies to the *Stemphylium* antigen when tested against the neat antigen (numerous dense lines) and a series of antigen solutions up to a dilution of 1:256. When the *Stemphylium* antigen was put up against a control serum known to contain *Aspergillus* antibodies, a very weak reaction was observed.

The patient was treated with prednisone and while on this he developed a cough productive of firm sputum plugs, from which *Stemphylium lanuginosum* was again cultured. The radiographic shadows cleared almost completely over several months. The dose of prednisone was tapered and stopped. Within weeks of stopping, the patient developed symptomatic recurrence of the right middle zone radiographic shadowing. Prednisone was restarted and he remained well on 10 mg on alternate days. On review, in July 1978, he was completely asymptomatic on this dose. Skin prick tests were repeated and these showed 3 mm wheal reactions to the same antigens as documented on the first occasion except that there was now no reaction to *Aspergillus*. On prick testing with the *Stemphylium* antigen, a 9 mm wheal resulted but there was no subsequent late reaction. An intradermal test was not done. There was no eosinophilia in the peripheral blood at this time but the patient was on steroids. FEV₁/FVC were much the same as in 1977 and single breath gas transfer for carbon monoxide was equal to the predicted value. Quantitative immunoglobulins and the plain chest radiographs were normal. No abnormality was seen at bronchoscopy.
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Discussion

Although our patient initially had positive skin and precipitin reactions to Aspergillus, the absence of Aspergillus from many spaya and the repeated heavy growths of Stemphylium lanuginosum in association with a strongly positive prick test and precipitins to the Stemphylium antigen strongly suggests that the bronchopulmonary reaction was the result of hypersensitivity to this latter fungus. Cross-reacting antigens could explain the positive Aspergillus reactions initially. The weak reaction between our Stemphylium antigen and serum known to contain Aspergillus antibody would support this. Had we not cultured the sputum and prepared a Stemphylium antigen for prick and precipitin testing, we would have failed to identify this causal organism and a diagnosis of allergic bronchopulmonary aspergillosis might have been made. Other unusual aspects of this case are the prolonged duration of the pulmonary shadowing with only mild asthmatic symptoms. The word Stemphylium comes from the Greek word stemphylon meaning a mass of pressed grapes, and the Stemphylium genus is characterised by clusters of muriform spores (dictyospores) which are not beaked and are not borne in chains. Stemphylium lanuginosum attacks cellulose and thus may be found on industrial fabrics such as coarse fabrics, paper, and strawboard.

Large numbers of fungal spores are found in the air throughout the year with the spores being derived from many different genera, each having its own distinct season. The fungi in highest concentrations in the ambient air in the UK include Cladosporium spp, Basidiospores, Asco spores, Sporobolomyces roseus, and Penicillium spp. Although Aspergillus fumigatus is present in very much lower concentrations, this fungus is found second in frequency only to Candida albicans in cultures of sputum and lung tissue, and can be implicated as the cause of pulmonary infiltrates and eosinophilia in about 80% of extrinsic asthmatics in the UK. The concentration of spores of Stemphylium in the atmosphere in the UK is less than one-fifth of that of Aspergillus and Stemphylium can be cultured from sputum and lung specimens very much less frequently than can Aspergillus. The discrepancy between the distribution of different fungi in the air and in the lung and in their propensity to produce allergic bronchopulmonary reactions needs to be considered, not only in relation to the concentration of spores inhaled but also to their antigenicity, their physical characteristics which determine penetration and site of deposition in the lung (aerodynamic behaviour and surface electrostatic charges), the temperature at which they grow best (most fungi are mesophilic and grow best at 28°C, whereas aspergilli are thermotolerant and grow well at 37°C), and the immunological status of the host.

This case draws attention to the need to consider the possibility that fungi other than Aspergillus may, on occasion, be the cause of allergic bronchopulmonary reactions. The only published reports of such reactions to other fungi include one relating to Candida albicans and another to Helminthosporium spp. A single, well-documented case of an allergic bronchopulmonary reaction to Pseudomonas aeruginosa indicates that such reactions may also occur in response to bacterial antigens.

Careful investigation of asthmatic patients with pulmonary infiltrates and eosinophilia in whom there is inadequate evidence to implicate Aspergillus as the cause may reveal more cases caused by other fungi or bacteria than have been reported to date.

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References

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