Bronchocentric granulomatosis and ankylosing spondylitis

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Development of pulmonary fibrocystic disease in the upper lobes is a well recognised extraskeletal manifestation of ankylosing spondylitis but its pathogenesis is obscure.1,2 Although pulmonary fibrosis may occur in association with other collagen vascular diseases, a predilection for the upper lobes is unique to ankylosing spondylitis. The fibrocystic disease is usually asymptomatic; if symptoms develop, they are usually due to superimposed colonisation or infection by fungi or mycobacteria.1-3 In this report we describe a patient with ankylosing spondylitis and apical fibrocystic disease, who developed a progressive left upper lobe cavitating infiltrate with haemoptysis and was found to have bronchocentric granulomatosis.

Case report

A 49 year old white male clerk with a 25 year history of ankylosing spondylitis was admitted to hospital four times from April 1981 to March 1982 for investigation of blood tinged purulent sputum and progressive radiographic changes in the left upper lobe. He denied fever, shortness of breath, and wheezing. Review of his chest radiographs showed that there had been minimal bilateral apical fibrosis since August 1980 and that a progressive left upper lobe infiltrate with cystic spaces had developed (fig 1A). The cystic spaces showed air-fluid levels during the last two admissions (fig 1B). Tomography failed to reveal a fungus ball within the cystic spaces. His work up showed a positive intermediate tuberculin test response. The result of the test for serum precipitins against Aspergillus was negative. During each admission bronchoscopy, cytological examination; bacterial, mycobacterial, and fungal cultures of bronchial secretions; and transbronchial lung biopsy failed to provide a specific diagnosis. During the final admission a left thoracotomy was performed because of persistent haemoptysis. The affected area was resected.

The cut surface of the gross specimen showed fibrotic lung with cystic cavities, which were lined by coarse granular tissue. The cut ends of bronchi were thickened. Microscopic examination (fig 2) showed inflammatory changes in bronchi and bronchioles ranging in severity from simple infiltration by plasma cells and lymphocytes to destruction of the epithelial lining and wall structures by palisaded epithelioid cells and multinucleated giant cells, which were organised into epithelioid granulomas with central zones of necrosis. Cystic spaces represented ectatic bronchi. Minimal inflammatory changes noted in blood vessels were considered to be secondary phenomena. The parenchymal changes consisted of interstitial and intra-alveolar fibrosis, plasma cell and lymphocytic infiltrations, and accumulation of eosin, plasma cells, and lymphocytes. The epithelium of airways was not involved.

Fig 1 Chest radiograph showing (A) local fibrocystic changes within the left apex and (B) the presence of an air fluid level within the cyst.

Fig 2 Microscopic appearances of surgical specimen. Infiltration and destruction of bronchi by epithelioid granulomas are shown. An adjacent pulmonary artery shows no inflammation. (Haemotoxylin and eosin, ×42.)
of foamy, pigmented macrophages consistent with bronchiolitis obliterans with organising pneumonia. Special stains for acid fast organisms and fungi showed nothing except a few septate branching hyphae consistent with Aspergillus on the surface of a small bronchiectatic cavity. Direct staining on fixed tissue with immunofluorescent antibody reagents against fungi was negative (courtesy of Dr W Kaplan, Center for Disease Control, Atlanta, Georgia). Cultures and serological tests for fungi gave negative results. Intradermal and skin prick tests with a mixture of Aspergillus antigens yielded negative immediate and delayed reactions. The final diagnosis was bronchocentric granulomatosis with localised fibrocystic change.

Discussion

In 1973 Liebow\(^4\) proposed a histopathological classification of focal granulomatous destructive lesions of the lung which were not associated with rheumatoid arthritis or invasive infectious agents. He distinguished angiocentric granulomatosis such as Wegener's granulomatosis, lymphomatoid granulomatosis, and necrotising "sarcoid" angiitis and granulomatosis from bronchocentric granulomatosis, because in the latter granulomatous and destructive lesions were confined primarily to bronchi with little evidence of angiitis or extrapulmonary lesions. The diagnosis of bronchocentric granulomatosis requires that pathogenic agents should not be present. In our case extensive search did not reveal any invasive pathogenic agent.

Since the original description by Liebow,\(^4\) Katzenstein et al\(^3\) and subsequently Koss et al\(^2\) have described the clinical and morphological features of idiopathic bronchocentric granulomatosis. They found two clinical forms despite similar histological and radiographic findings. The first form occurs at a younger age and is associated with asthma and eosinophilia. This form is probably a result of a hypersensitivity reaction to fungi, and is considered to be a variant of allergic bronchopulmonary aspergillosis.\(^7\) The second clinical form occurs in a relatively older population and is not associated with asthma or eosinophilia. The potential pathogens or antigens in this non-asthmatic form are not known. Despite colonisation by a few branching hyphae and the presence of bronchial symptoms of purulent sputum and haemoptysis, our patient never showed eosinophilia or features of bronchoconstriction and thus cannot be categorised as having the asthmatic clinical form of bronchocentric granulomatosis. We believe that it was closer to the non-asthmatic form because of his age, bronchial symptoms, negative skin test responses to Aspergillus antigens, and the absence of clinical features of asthmatic type.

We have described a case of bronchocentric granulomatosis in a patient with apical fibrocystic disease associated with ankylosing spondylitis. Although there is no proof of a direct relationship, the simultaneous occurrence of these two rare diseases in the same person and the association of both diseases with Aspergillus is compelling. Possibly fibrocystic disease impaired the local defences of the lung and permitted colonisation of the airways with Aspergillus. The diffusion of antigens from the Aspergillus organisms may have produced a granulomatous hypersensitivity reaction in the airways.

References