Case report

Progressive cavitating pulmonary changes in rheumatoid arthritis: a case report

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SUMMARY Progressive cavitating changes in the lung apices were found in a middle-aged man with seropositive rheumatoid arthritis. These findings were attributed at autopsy to a combination of nodule-type formation, necrosis, and mild fibrosis.

Pleuropulmonary complications in rheumatoid arthritis (RA) include an increased incidence of infections, pleuritis, sterile empyemas, nodules, and fibrosis.^{1,2} Cavitation, particularly of pulmonary rheumatoid nodules, has been described,^{3–10} but we report here a patient exhibiting an unusual progressive and extensive bilateral cavitary process.

Case report

The patient was 39 years old in 1972 when he first developed joint pains and early morning stiffness. After an initial improvement attributed to salicylate therapy his joint condition worsened, and in 1973 he had definite, seropositive, erosive RA. His sedimentation rate was low; an antinuclear test was positive, but LE cells could not be demonstrated. Chloroquine was added and indomethacin later substituted for the salicylate therapy. Radiological examinations in 1974 and 1975 showed progressive erosive changes. He smoked 10 cigarettes daily, and except for some white sputum in the morning he had no pulmonary complaints. Recurrent bronchitis was known in the family, and his mother had RA.

In 1976 he was admitted to a nearby hospital with a lung abscess and empyema from which a haemolytic streptococcus was cultured. Despite initial therapy with Ampiclox (ampicillin 250 mg and cloxacillin 250 mg) and closed pleural drainage the empyema persisted, and subsequently right lower lobectomy and decortication were necessary. There followed an

exacerbation of his polyarthritis, and in view of further erosive changes chloroquine was replaced by gold in November 1977. Subcutaneous nodules were identified for the first time. His disease remained clinically active, and, even though there was a mild proteinuria and a frequent excess of red and/or white cells in the urinary sediment, gold therapy was continued. In early 1978 complaints of prickling in the hand led to a neurological consultation and electromyographic support for a diagnosis of polyneuropathy. In the same period an occasional vasculitis-like lesion was seen, usually on the hands. Biopsies of skin or other tissues were not performed.

In August 1978 a routine chest radiograph revealed extensive inhomogeneous densities with probable cavity formation in the right upper lobe (Fig. 1). Increased shift of the mediastinum to the right suggested a further loss of volume in the remaining lobes of the right lung. Bronchography disclosed bronchiectasis in the apical region. In addition there was an exudative process with pleural thickening in the apex of the left lung. Extensive investigations failed to find an infective cause of these appearances. Lung spirometry was within normal limits but there was a reduced carbon monoxide transfer (5.7 mmol/min/kPa, normal 11.1) and a low compliance (0.16 l/cm H₂O, normal 0.4–0.9). Serum alpha-1-antitrypsin was 4 g/l, the Pi phenotype M. Percutaneous biopsies of the right lung revealed interstitial fibrotic and chronic inflammatory changes. A focus of fibrinoid necrosis with surrounding granuloma formation was found in the pleura biopsy and considered to be compatible with a rheumatoid nodule. Re-examination of the right lower lobe disclosed similar findings. No changes in therapy were made

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Fig. 1 Tomogram of right upper lobe showing extensive inhomogeneous densities and cavity formation.

except that gold was discontinued largely on account of ineffectiveness and continuing proteinuria.

In January 1979 he was readmitted because of fever (39°C), fatigue, and purulent sputum. Mild clubbing of the fingers and toes was noted. The chest radiograph revealed a destroyed right lung with thick walled cavities. *Aspergillus fumigatus* was cultured from the sputum. In the Ouchterlony test 5 precipitin lines against *A. fumigatus* antigen were seen. The skin test showed an early reaction which was strongly positive. Miconazole intravenously and later econazole by mouth were given. Econazole was also administered to the right upper lobe for 2 weeks by an indwelling bronchial catheter (introduced through the cricothyroid membrane) and thereafter by a fibroscope 3 times a week for 6 weeks, after which a clearance pneumonectomy was performed. No aspergillus species could be cultured from the resected material. Histologically fibrotic changes, mononuclear cell infiltration, and rheumatoid nodules were found. Two weeks after pneumonectomy a massive sterile pleuritis on the left side required drainage.

Several months later a pseudomonas infection of the right thoracic cavity was successfully treated with tobramycin, ticarcillin, and closed drainage.

His joint disease continued to deteriorate both clinically and radiologically. In addition skin vasculitis was variably present, mainly in the form of superficial ulcers on the buttocks and lower legs, with an occasional erythematous papule elsewhere. Circulating immune complexes were strongly positive by a Clq binding test, but complement fractions were not depressed. A trace of protein persisted in the urine, and an excess of erythrocytes was found on several occasions without any other sediment abnormalities.

In January 1980 progressive cavitary changes were seen in the left apex (Fig. 2). These developed in the absence of any respiratory complaints, and physical examination of the left lung was normal. A search for infective causes was fruitless. In particular sputum cultures and bronchial washings were all negative for tuberculosis and fungi. Furthermore the Ouchterlony test for *Aspergillus fumigatus* now showed only one precipitin line. An arterial blood gas analysis was normal.

During a holiday in the Canary Islands in April 1980 he developed a cough productive of yellow sputum. Increasing dyspnoea prompted a premature return to Holland and his admission for treatment of a pneumothorax and a pseudomonas empyema, both on the left side. During insertion of a drain he collapsed. A toxic infectious shock developed and despite various resuscitatory measures the

Fig. 2 Tomogram of left apex showing multiple densities and cavity formation.

patient succumbed 2 days later from respiratory insufficiency.

The post-mortem examination revealed a small left pneumothorax, extensive thickening of the pleura, and numerous small cavities (maximum 2.5 cm diameter), mainly in the upper lobe. The whole left lung appeared to be fibrotic, and this was confirmed by microscopic examination. In addition there were numerous areas of necrotic granuloma formation, many with palisading histiocytes, mononuclear cell infiltrate, and giant cells (Figs. 3, 4). Cavities were

Fig. 3 Microscopic section of lung showing distorted alveoli, cavity formation, fibrosis, and extensive mononuclear cell infiltration. (Haematoxylin and eosin, $\times 45$).

Fig. 4 Detail view of central part of Fig. 3 showing fibroblasts, mononuclear cell infiltration, and giant cells. (Haematoxylin and eosin, $\times 110$).

associated with several of these necrotic areas and in some bleeding into the cavity had taken place. No evidence was found of vasculitic lesions in the lung. There was a slight bronchopneumonia. Further studies, including cultures, were negative for tuberculosis, bacterial and fungal infections, and amyloid. Apart from some intimal association of the pericardium with the thickened pleura, examination of the heart was unremarkable. The liver contained a small hamartoma but was otherwise normal, as were the kidneys and spleen.

Discussion

In the course of a few years this patient had pleuritis, pneumothorax, and empyema, all well recognised complications of RA.^{1,2} In addition he developed a progressive, destructive, cavitary process, most obvious in the upper lobes, which is not typical of RA but has been described in association with the upper lobe fibrosis in both ankylosing spondylitis¹¹ and recently RA.¹² Our patient had no sacroiliitis or limitation of spinal movement and fulfilled the preliminary ARA criteria for RA.¹³

Secondary colonisation of cavities by aspergillus species is not unusual,^{11,13,14} but eradication of infection is difficult. The intensive antifungal therapy, including bronchial instillations, was successful in our patient as judged by the subsequent negative cultures and the improvement in the Ouchterlony test. The aspergillus infection in the right lung was a serious clinical complication in an already damaged lung. We consider that the aspergillus played no role in the development of the cavitating process in either lung. Unfortunately the right lung was so destroyed that pneumonectomy was considered inevitable. With the appearance of cavity lesions in the left apex it was surprising, especially in view of the later autopsy findings, to record a normal arterial gas analysis. However, more sensitive indicators of impaired pulmonary function—for example, carbon monoxide transfer test, desaturation on exercise plotted against oxygen consumption¹—were not tested.

The mild fibrosis found at autopsy was attributed to the rheumatoid disease. The absence of vasculitis in the lung was not surprising, as it is rarely found in RA lung, even when granulomata are present. The histological evidence of widespread rheumatoid nodule type formation in the lung associated with areas of necrosis and cavity formation in the absence of infection suggests that the rheumatoid disease process is responsible for the histological and radiological picture. In this respect we are in agreement with Petrie *et al.*¹² that cavitation in the upper lobe should be regarded as yet another intrathoracic manifestation of rheumatoid disease.

It is a pleasure to record the secretarial expertise of Ms H. Houdijk.

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