HONEYCOMB LUNG AND CHRONIC RHEUMATOID ARTHRITIS

A CASE REPORT

BY

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The following case showed unusual features and is published in the hope that similar cases may be brought to our notice.

Case Report

A medical practitioner, aged 34, first developed episodic swellings diagnosed as angioneurotic oedema in 1948. These cleared up, but in March, 1950, he developed a polyarthritis. Attacks of joint swelling were at first intermittent, but after 9 months his symptoms were severe and continuous and subcutaneous nodules appeared on the elbows. In 1951 he treated himself with 100 mg. cortisone acetate daily, with partial remission of his disease. For a few months in 1952 he took 600 mg. daily of phenylbutazone instead, but stopped this because of unfavourable reports. Swelling of the right leg and of the right inguinal lymph nodes developed late in 1952. One of these nodes was removed for histological examination, and Professor R. A. Willis reported that it showed a non-specific reactive hyperplasia.

The patient resumed taking cortisone acetate (75 mg. daily) and improved. He first came under supervision at this hospital in November, 1953, when he already showed gross symmetrical swelling and inflammation of the small peripheral as well as of the major limb joints. Large subcutaneous nodules were present in both elbow regions. There was moon face and ankle oedema. Despite these changes he was able to carry on his work as an assistant in a busy general practice. In July, 1954, he developed diarrhoea which persisted for 8 months before clearing up spontaneously. No certain cause for this was found although *Giardia lamblia* was isolated on one occasion.

In May, 1955, the patient developed a productive cough and first noticed dyspnoea on exertion. In August, 1955, his treatment was changed from 125 mg. cortisone to 25 mg. dexamethasone daily. There was an initial "lift" in symptoms, and a transient increase in strength of grip, but no lasting improvement in his arthritis. He began to put on weight. Increasing breathlessness on effort, at first attributed to his increasing weight, soon became his chief disability, and eventually he was unable to continue at work. He was admitted to hospital for further

investigation, and within a week had deteriorated so much that he was cyanosed despite continuous oxygen therapy. Antituberculous chemotherapy, given in the hope that the lung shadows seen on x-ray examination might represent an unusual form of tuberculosis, was without effect. Increased amounts of dexamethasone in no way helped him. He died of asphyxia.

The only significant previous illness was bilateral lobar pneumonia at the age of 3 years. There was no history of rheumatism in the family, but his mother suffered from various allergic complaints.

Laboratory Investigations.—The differential agglutination titre (Ball, 1950) was positive at 1 : 128 at 18 hrs in June, 1955. The patient reported that his Mantoux reaction had been positive when he was a student, but no record of this has been kept. In one phase of his disease, the haemoglobin levels fell to 60 per cent., but in the last 6 months of life these levels were normal. The total white cell count was always somewhat elevated at about 13,000 per c.mm. with a normal differential in the last 3 years. The albumin/globulin ratio was reversed at 2 : 4. The erythrocyte sedimentation rate was always elevated.

Multiple cultures of the sputum yielded only normal flora.

Numerous other examinations of blood and urine were consistently normal.

Radiological Findings

(A) Chest

Before 1950: Routine chest films when the patient was a medical student were normal.

1951: A film taken before starting cortisone was reported as normal, but one 9 months later showed a generalized increase in lung markings.

February, 1953: Increased lung markings were again noted, particularly in the left lower zone. In addition the hilar markings were prominent.

December, 1953, to January, 1955: Five films showed no change.

May, 1955: The lung markings and hilar shadows had further increased.

October, 1955: The abnormal lung pattern was reported as being much more accentuated and the hilar shadows still more prominent (Fig. 1a and b).

November, 1955: A few days before death the abnormal pattern had shown an even greater increase and presented as reticular and confluent shadowing.

(B) Joints

X rays of the hands (Fig. 2), feet, and other joints showed progressive osteoporosis and articular destructive changes entirely consistent with rheumatoid arthritis.

Autopsy

Macroscopic Findings

Lungs.—Both were voluminous; the right weighed 1,340 g., the left 1,300 g. There were old pleural adhesions posteriorly on the right side; the left pleural cavity was normal. On section there were dark red consolidated areas (up to 5 cm. in diameter) in the left upper and right lower zones. Both lungs presented a striking honeycomb appearance, the air sacs of which measured up to 20 mm. in diameter, though most were less than 5 mm. (Fig. 3). The bronchi down to branches about 2 mm. were normal apart from the presence of frothy mucus. The hilar lymph nodes were slightly enlarged.

Remaining Viscera.—Not remarkable.

Microscopic Findings

Metacarpo-Phalangeal Joint.—There was a chronic erosive arthropathy typical of rheumatoid arthritis (Fig. 4).

Lungs.—In the consolidated zones there was a recent bronchiolitis, and a pneumonic process involving alveoli of normal proportions; in addition there were scattered foci of interstitial fibrosis and more solid fibrotic areas showing fragmentation and destruction of elastic tissue, and sometimes scantily infiltrated with lymphocytes and plasma cells (Fig. 5, overleaf).

A similar but more diffuse fibrosing granulomatous process was present in the honeycomb areas between groups of small cysts. The cystic air sacs themselves were mostly empty and without a well-defined epithelial lining, though occasionally flat, cuboidal, or columnar epithelium could be seen (Fig. 6, overleaf).

Fig. 1(a).—Postero-anterior chest radiograph, October, 1955.

Fig. 1(b).—Enlargement of left hilar region.

Fig. 2.—Subluxation and articular bone erosion at 2nd and 3rd right metacarpophalangeal joints.

In both the cystic and non-cystic zones, dust particles were inconspicuous and the fibrosis and associated inflammatory infiltration were histologically non-specific; lesions resembling those usually regarded as characteristic of rheumatic fever or rheumatoid arthritis could not be found. There was no increase in smooth muscle.

These findings are essentially the same as those described by Heppleston (1956) in cases in which honeycombing was considered to be due to a patchy non-specific interstitial fibrosis or granuloma involving the bronchioles and their subdivisions.

Fig. 3.—Lung, showing extensive cystic change areas of consolidation in non-cystic Actual size, areas.

Fig. 4.—Typical rheumatoid process in a metacarpophalangeal joint. $\times 85$.

Discussion

We have encountered a wide variety of pulmonary and pleural complications of rheumatoid arthritis. Most of these do not differ from the pleuritis, pneumonias, fibroses, pneumoconioses, and segmental collapses that can be seen in the ordinary run

Fig. 5.—Lung, showing non-cystic area with old interstitial fibrosis. Alveoli contain mainly macrophages with some lymphocytes and rare polymorphs. $\times 105$.

Fig. 6.—Cystic area of lung showing fibrosis and chronic inflammatory infiltration. $\times 120$.

of hospital admissions, as Aronoff, Bywaters, and Fearnley (1955) have pointed out. Other observers of rheumatic diseases have been impressed with the possibility that a specifically "rheumatoid" lung lesion may occur. A number of different lung pathologies have been tendered as meriting this description. Many have been described in considerable detail, and they range from a diffuse chronic fibrosing interstitial pneumonitis (Ellman and Ball, 1948; Price and Skelton, 1956), to necrobiosis of large circumscribed areas of lung tissue (Christie, 1954). A sterile empyema in which only amorphous debris could be made out on microscopical examination of the pus-like fluid, was illustrated by Case 8 of Ellman and Cudkowicz (1954). Very similar pathological changes in the lungs are known to occur in the absence of evidence of polyarthritis. Moreover, and in contrast to the lung lesions, the accompanying arthritis has usually not been described in any detail. In our opinion a reproducible diagnosis of fully-developed rheumatoid arthritis requires the presence of subcutaneous nodules, of erosions of articular

bone on radiological examination, and of a positive titre in the sheep cell agglutination test, in addition to chronic polyarthritis. In the absence of this detail, and especially in the presence of atypical features, *e.g.* severe nephrosis with "wire-loop" changes in the kidney (Christie, 1954; Case 1), and chronic rash (Rubin, 1955; Case 1), there is room for doubt whether the reported lung changes were not visceral manifestations of connective tissue diseases other than rheumatoid arthritis. For example, fibrosis of the lungs, with or without honeycombing, may complicate generalized scleroderma. Getzowa (1945) and Evans and Parker (1954) are amongst those who have observed cases. To date, only one pulmonary condition, that which has been called "Caplan's syndrome", has been shown to have a greater prevalence in the rheumatoid as compared with the non-rheumatoid members of a sample population (Caplan, 1953; Miall, 1955), in this case a mainly coal-mining population. Studies based on patients attending hospital for treatment of rheumatoid arthritis can give only limited evidence as to the

reason for an observed association of lung and joint disease, because of the selection factor. We recognize this limitation and can make no claim that this case represents "rheumatoid lung disease". It is of interest that Aronoff and others (1955) found honeycomb lung as one of the few pulmonary conditions in otherwise uncomplicated rheumatoid arthritis—four cases out of 130 x-rayed—which was not found in their x ray control series.

The complete lack of response of the lung lesion in the present case to large doses of corticosteroids is worth noting. Indeed, the lesion originally developed whilst the patient was taking cortisone acetate, and deterioration followed an increase in dose and change to the clinically more effective deltacortisone. Corticosteroids have been used in the treatment of the clinically-related chronic, diffuse, interstitial fibrosis of the lungs with poor results. A fatal outcome could not be prevented in the three cases of Peabody, Buechner, and Anderson (1953), although one did show an initial temporary improvement. Similar results have been noted by Price and Skelton (1956) and by Scadding (1956).

Summary

The development of honeycomb lung in a patient with rheumatoid arthritis treated with cortisone is reported.

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Le "poumon en nid d'abeille" et l'arthrite rhumatismale chronique

RÉSUMÉ

On décrit la formation d'un "poumon en nid d'abeille" chez un malade atteint d'arthrite rhumatismale et traité à la cortisone.

El pulmón "apanalado" y la artritis reumatoide crónica

SUMARIO

Se describe la formación de un pulmón "apanalado" en un enfermo con artritis reumatoide tratado con la cortisona.