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RHEUMATOID PNEUMOCONIOSIS (CAPLAN'S SYNDROME) IN AN ASBESTOS WORKER

BY

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The association of certain features in chest radiographs of patients with rheumatoid arthritis and pneumoconiosis is now well known. The original observations, by Caplan (1953), were made on coalworkers of South Wales, but later reports have described the occurrence of the syndrome in workers following a variety of occupations and exposed to dusts other than coal. In Great Britain, potteries, sand-blasting, and brass and iron foundries have been implicated (Caplan, Cowen, and Gough, 1958). Silica is the factor common to these, and also to a series of European cases, quoted by the same authors.

After coal dust and silica, asbestos is a major cause of pneumoconiosis, and Rickards and Barrett (1958) have published what appears to be the first description of this condition in an asbestos worker. This patient had severe and widespread rheumatoid joint lesions. However, as Caplan (*loc. cit.*) pointed out, the development of the typical lung lesions, at least in coalworkers, may precede the onset of arthritis. Under these circumstances, diagnostic difficulties may arise.

The following report is of an otherwise healthy man, exposed to an asbestos hazard, who presented with a singular chest radiograph and whose pulmonary lesions conform histologically to the pattern of rheumatoid pneumoconiosis.

Case Report

A 39-year-old man had been in good health until early March, 1959, when he developed fever, shortness of breath, and left-sided chest pain of a pleuritic nature. Pneumonia was diagnosed and treatment begun with tetracycline-oleandomycin. A few days later, signs of fluid were noted, and chest radiographs at this time showed a moderate-sized left pleural effusion together with a small cavity in the posterior basal segment of the left lower lobe. With continued treatment, the patient recovered apparently completely, and further films one week later showed that the fluid had been absorbed and the left base was quite clear. However, several unusual opacities on the right side, noted in the first films, were still present unaltered, and accordingly the patient was referred by his family doctor for further investigation.

When seen on April 16 the patient stated that he had experienced a slight morning cough, without sputum, for many years, which had remained unchanged until his recent illness. At this time he had ceased smoking, having previously smoked 25–30 cigarettes daily, and the cough had not recurred. The chest pain and dyspnoea had disappeared within two weeks of the onset of the illness, and he had had no haemoptysis and no loss of weight. He now felt completely well, and had resumed work at the beginning of April.

There was no family history of chest disease. Apart from diabetes mellitus diagnosed five years earlier, and well controlled by insulin and diet, he had always enjoyed good health. He had not been recalled after routine chest radiographs six and four years ago. On examination, the patient appeared to be a fit and healthy man, and no significant abnormality was discovered.

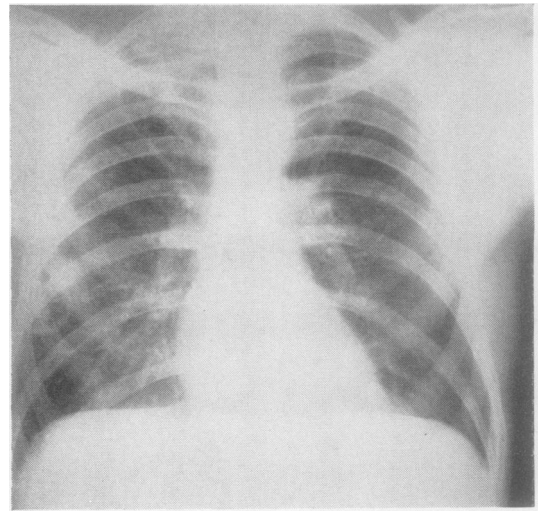

FIG. 1.—Chest radiograph of April, 1959, showing unusual cavitated lesions in the right lung. No features typical of asbestosis are present.

A repeat film (Fig. 1) showed no apparent lesion on the left side. The appearances on the right side were identical with those noted on the two previous occasions. A ring shadow, 4.0 × 2.5 cm. in diameter, its wall not exceeding 0.5 cm. in thickness, with a second smaller opacity lying within its central translucency, was present at the level of the fourth costal cartilage at the periphery. Another opacity at the right apex appeared in the lordotic projection (Fig. 2) to comprise a larger, thick-walled shadow measuring 5.0 × 3.0 cm. with central cavitation and a probable fluid level, and a smaller uniform round lesion just below and lateral to the other. It was presumed that the febrile episode was due to staphylococcal pneumonia, with acute cavity formation and effusion, and that the lesions in the right lung antedated this illness and were unrelated to it.

The erythrocyte sedimentation rate (Wintrobe) was 18 mm. in one hour, and the haemoglobin 13.8 g. per 100 ml. There were 8,600 leucocytes per c.mm. (neutrophils 59%, lymphocytes 30%, monocytes 6%, and eosinophils 5%), and the erythrocytes showed slight anisocytosis and occasional punctate basophilia. The Heaf tuberculin test was negative, so also was the Wassermann reaction. A trace of sputum was produced which on culture yielded a mixed growth

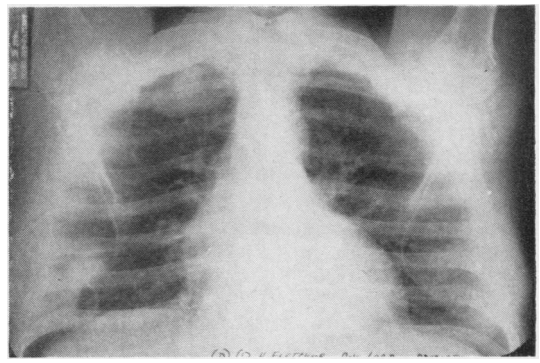

FIG. 2.—Anterior lordotic projection showing apical lesions more clearly.

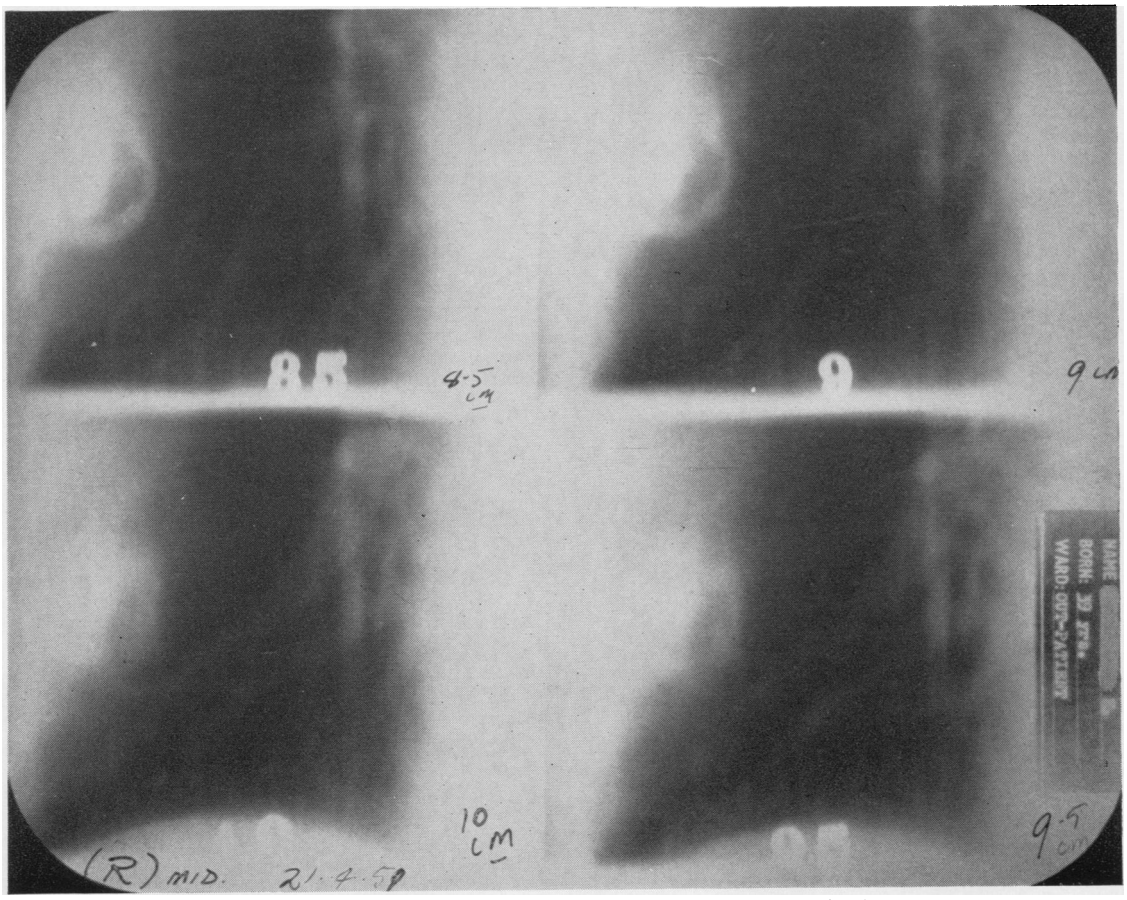

FIG. 3.—Antero-posterior tomograph cuts, demonstrating the dual lesions in the right lower zone.

of non-pathogens. The patient had worked for three years, from the age of 16, on a dairy farm; however, a Casoni test was negative, and likewise the complement-fixation test for hydatid.

Tomography added no further information, except the impression that in the lower lesion the more solid opacity lay slightly anterior to the ring shadow (Fig. 3). No calcification was noted in either upper or lower lesions. At this stage the diagnosis was quite uncertain. The patient was known to have worked with asbestos, but in the absence of any of the characteristic features, e.g., "ground-glass" appearance, progressing to more definite fibrosis, particularly in the lower half, with pleural adhesions, and a "shaggy" heart outline, and in the absence of physical signs, or of demonstrable disability, this possibility was not entertained. It was decided, therefore, to proceed to exploratory thoracotomy.

The operation was performed on June 29, 1959, by Mr. P. J. Heery, visiting thoracic surgeon, and Mr. F. W. Ross. The fissures were quite free and likewise the pleural cavity, except for some easily divisible adhesions over the extreme apex. There was a mass the size of a large hen's egg in the apical segment of the right upper lobe, and a similar mass in the apical and lateral portion of the lower lobe. In the middle lobe abutting on the major fissure was a firm nodule, some ½ in. (1.5 cm.) in diameter. The larger lesions felt cavitated, while the smaller was solid.

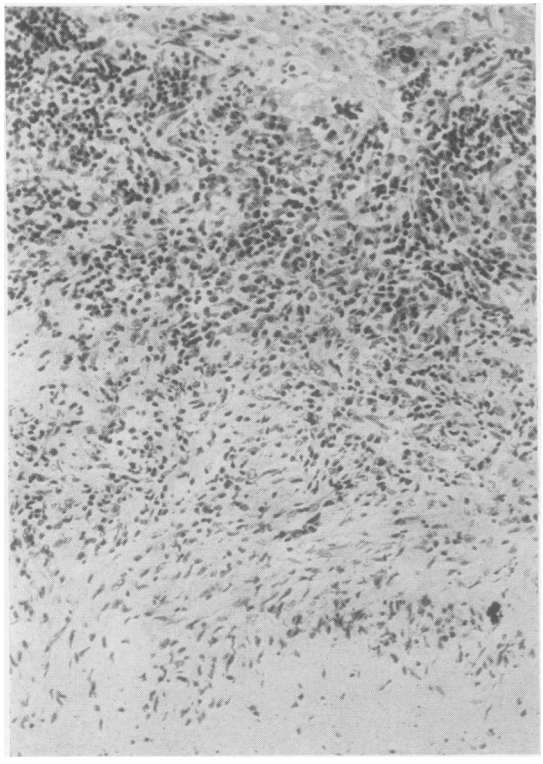

FIG. 4.—The necrotic collagen, palisading of fibroblasts, and cellular infiltrate of the typical lesion. Haematoxylin and eosin, × 100.

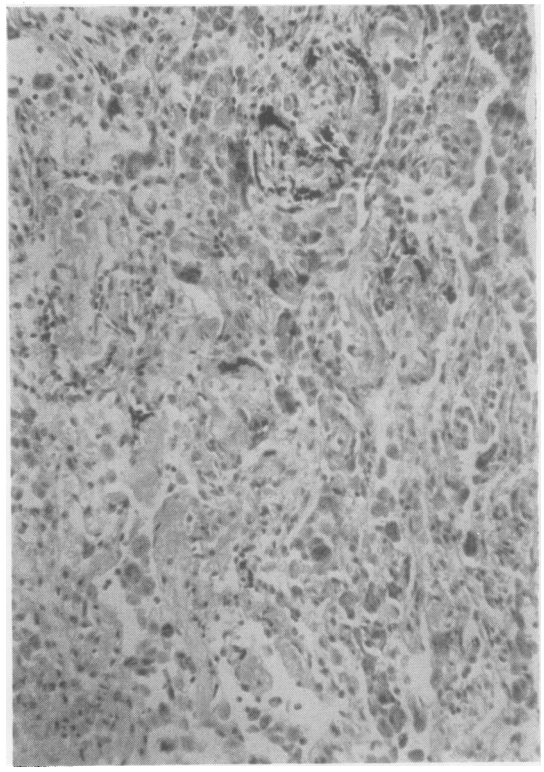

FIG. 5.—Well-marked fibrosis in the excised apical segment of the right upper lobe. Haematoxylin and eosin, × 200.

A portion of the upper lobe lesion was excised and the frozen section was reported upon by Dr. J. M. Garvan, of St. Vincent's Hospital, as non-malignant. Accordingly, all masses were excised, by wedge resection from the middle and lower lobes and by apical segmentectomy in the case of the upper lobe. The post-operative course was uneventful, and the patient was discharged, quite well, two weeks later.

Each mass was bisected, and a portion of each cultured on blood agar and on Löwenstein–Jensen medium. Contents of the lower-lobe cavity were more fluid, resembling pus; examination by Gram staining and by Ziehl–Neelsen staining of the concentrated deposit, and cultures on Sabouraud's medium were also undertaken. In all instances no organisms were detected.

Dr. V. St. E. D'Abrera, of the Institute of Clinical Pathology and Medical Research, Lidcombe, reported that the lung parenchyma showed diffuse dense fibrosis (Figs. 5 and 6). In places nodular lesions were present (Fig. 4) which showed intense peripheral cellular reaction, with numerous macrophages, and proliferating endothelial cells. Many of the macro-

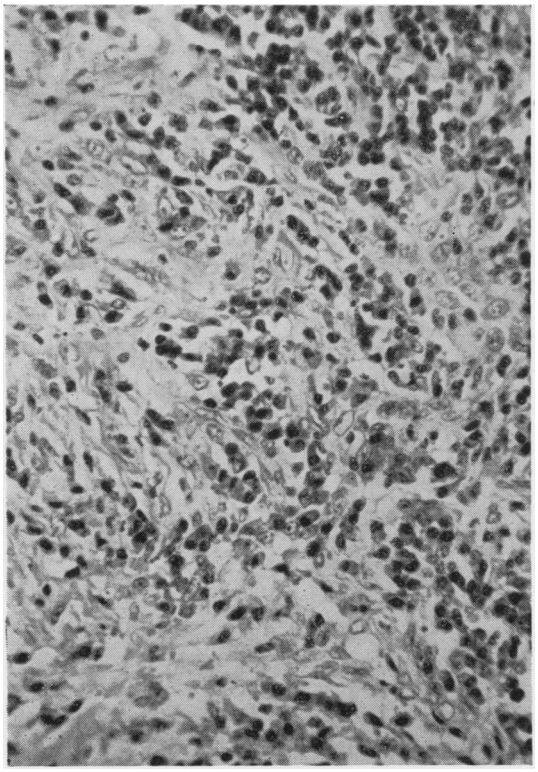

FIG. 6.—Similar appearances of extensive fibrosis. Haematoxylin and eosin, × 200.

phages were aggregating into masses, and some foreign-body giant cells were present. Among these clumps of macrophages well-marked asbestosis bodies were present (Fig. 7).

DISCUSSION

Caplan (*loc. cit.*) described the radiological appearances of this condition as seen in coal-miners in the following terms: "The characteristic feature is the presence of multiple well-defined round opacities, 0.5 to 5 cm. in diameter, distributed throughout both lung fields but particularly at the periphery. An important finding is that the background of simple pneumoconiosis is often slight or absent." The opacities may appear and develop to their maximum size with startling rapidity, often in crops, but then tend on the whole to remain stationary. Cavitation is not uncommon in the lesions of coal-miners, and contraction, leaving an area of stellate fibrosis, or calcification, may be seen as end-results.

The specific histological appearance which so sharply differentiates these lesions from those of progressive massive fibrosis is that of a rheumatoid process. Typically, the nodule has a centre of necrotic collagen, surrounded by a zone in which active destruction of collagen is taking place, marked by infiltration of macrophages and of polymorphonuclear leucocytes. Beyond the inflammatory zone lies an accumulation of fibroblasts orientated radially to resemble a palisade. Sometimes multinuclear giant cells are seen in this layer. Outside this, dense and apparently normal collagen may be found, distributed circumferentially and demarcating the nodules from the adjacent tissues. Liquefaction may occur in some cases, progressing to cleft formation, and, carried further, perhaps accounts for the development of cavitation.

The findings in the present instance correspond closely with the foregoing. The photomicrograph (Fig. 4) shows the characteristic lesion comprising collagen, inflammatory cellular zone, and palisading of fibroblasts. The background of pulmonary fibrosis is well seen in Figs. 5 and 6 and the causative agent indicated by the asbestosis body shown in Fig. 7.

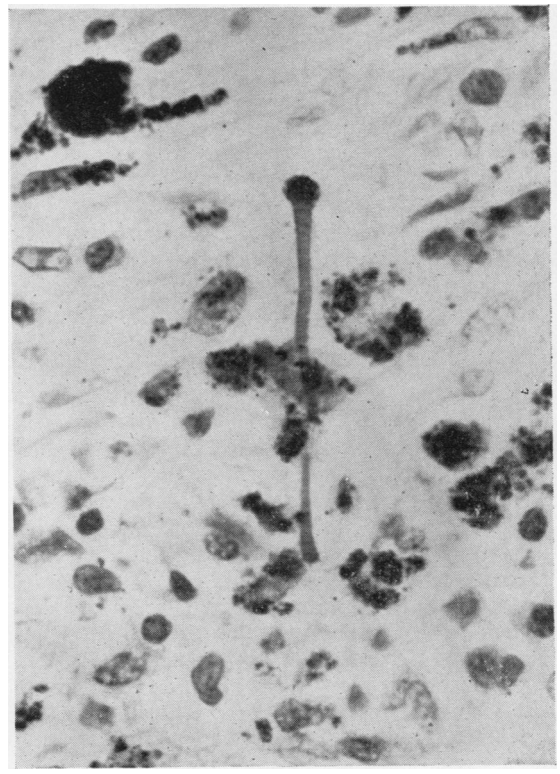

FIG. 7.—Asbestosis body with macrophages. Haematoxylin and eosin, × 840.

This, then, is another example of rheumatoid pneumoconiosis, and the second associated with asbestosis. However, certain features deserve emphasis, particularly those which differ from the observations in the case reported by Rickards and Barrett.

Their patient came under notice with active rheumatoid arthritis, and the chest radiographs at that time showed fibrotic changes and a loss of radiolucency in the middle and lower zones of both sides. At necropsy, six months after this film had been taken, and some 11 months after the onset of joint pains, multiple breaking-down nodules were found distributed in the middle and lower lobes and varying in size from a pin-head to a maximum of 1.5 cm. in diameter.

By contrast, the present patient was referred after what appears to have been an unrelated pulmonary infection with a chest radiograph already showing large cavitated lesions. There was no evidence, and this has been confirmed since by a number of observers aware of the final diagnosis, of any of the radiographic changes associated with asbestosis or other interstitial process. As already mentioned, this finding is the rule in coalworkers with the syndrome. Furthermore, the patient had none of the symptoms or stigmata of rheumatoid arthritis.

Such variability in the time of origin of the features of this condition agrees with the studies of Miall, Caplan, Cochrane, Kilpatrick, and Oldham (1953) relating to coalworkers. They found that the lung lesions might be detected for as long as 11 years before the onset of arthritis, or might not appear for six years or more after the joints have been affected.

It is interesting to speculate on how long the pulmonary lesions had been present. Their size might suggest a rather lengthy period, though in coalworkers such development has been observed in a period of months. No direct evidence is available on this point, but it is known that they were not present in June, 1953, six years earlier, when a survey of asbestos workers was made by the Division of Occupational Health of the N.S.W. Department of Public Health. The radiograph taken on that occasion has been seen and confirmed as within normal limits (Fig. 8). The patient had attended a mobile mass miniature *x*-ray survey held in his district in 1955 and had not been recalled. It may be presumed, therefore, that the lesions had been present for less than four years.

He had been exposed to an asbestos hazard for 15 years, from 1942 to 1957, in a Sydney factory making asbestos-cement sheets and mouldings for the building industry. Three types of asbestos were used—amosite, chrysotile, and crocidolite—and the sources of supply were Western Australia, Canada, and South Africa. The raw asbestos was emptied from bags and mixed by hand shovels, then shovelled or hand-fed into pulverizers. The contents were blown into storage hoppers, and as required raked into barrows, weighed, and finally tipped into water to which cement was added, for the moulding process. In the case of sheets, the wet mixing and moulding was performed by machine, but pipes and guttering, etc., were moulded by hand. The patient had worked on moulding for seven years, and spent the remaining years in the store, working with the bagged dry fibre. All the processes took place in a single large shed, and there was a fairly high dust content throughout, in his opinion.

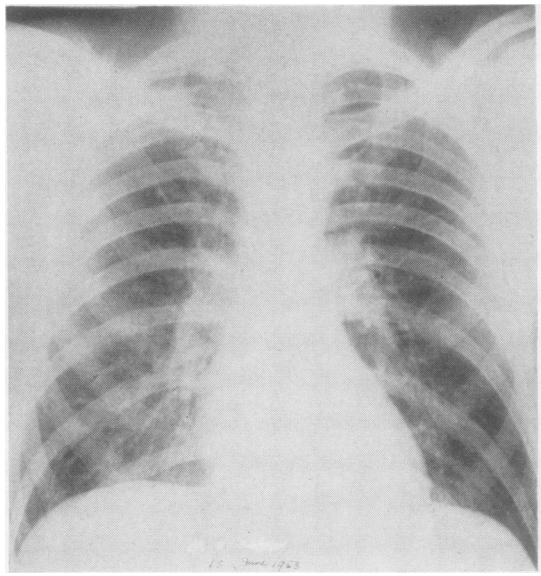

FIG. 8.—Chest radiograph taken during factory survey of June, 1953. Regarded as within normal limits.

During the survey mentioned above (Roberts and Whaite, 1953) dust counts in this factory showed extreme variation from place to place. The lowest average figure obtained was 0.3 million particles per cubic foot, while the highest average figure was 15.7 million particles per cubic foot, recorded in the areas devoted to the bagging, blending, and feeding processes.

This patient had been exposed, it was estimated, to an average density of 0.3 million particles per cubic foot, and his cumulative exposure at the time

of the survey was thought not to exceed 4 million particle-years per cubic foot.

American experience, quoted by Roberts and Whaite, suggests that clinical asbestosis is unlikely to develop unless the cumulative exposure exceeds 25 million particle-years per cubic foot, and that advanced cases are seldom found amongst those with a cumulative exposure under 100 million particle-years per cubic foot. This was borne out by the findings in their survey. The well-marked interstitial fibrosis in the present patient, therefore, is of interest. His employment in the years following the survey had been in areas of lower average dust counts than in the years preceding, and his cumulative exposure would not have exceeded 5 million particle-years per cubic foot. Moreover, his chest radiograph in 1959 did not reveal any features typical of asbestosis.

It is suggested, therefore, that just as the nodular lesions are the product of a rheumatoid process in a lung altered by exposure to specific dust, the extensive and unexpected fibrosis may similarly be due to an abnormal response to asbestos of tissues whose subtle chemistry has been altered by, or perhaps is predisposed to, the rheumatoid state.

Why the lesions, or, to be accurate, the radiographically visible ones, should be confined to the one lung cannot be answered. Certainly in coal-workers, and in the asbestos worker first reported, bilateral changes have been the rule.

Subsequent Events

The patient made a good recovery and returned to work. He has been seen regularly, and has remained in normal health, though since April, 1960, a nodule has been visible in the lower zone of the right lung, adjacent to the right heart border, and in seven weeks has increased in size and now measures 1.5 × 2.5 cm. This nodule was not palpable at the time of operation.

From June, 1960, he complained of pains in both shoulders, though his activities were not limited. In December, 1960, however, he reported pain and swelling in the right index finger, present for a few weeks only, and was found to have a typical fusiform swelling of the proximal interphalangeal joint. The Rose–Waaler test was now positive, the differential agglutination titre being 1 in 64. The serum proteins showed a slight increase in α_1 and α_2 globulins, the actual figures being (normal results in brackets): total protein, 6.9 g.% (albumin 59.6%, α_1 globulin 5% (3.5%), α_2 globulin 10.6% (8.5%), β globulin 9.9% (10.0%), and γ globulin 14.9% (14.5%)).

No L.E. cells were detected at one examination, and the erythrocyte sedimentation rate (Wintrobe) was 28 mm. in one hour.

Summary

A case of Caplan's syndrome in an asbestos worker is described. It differs from the first reported case of this association in the radiographic findings, namely, large cavitated nodules of unilateral distribution, in the absence of the classical features of pulmonary asbestosis, and in the late development of rheumatoid arthritis.

I am indebted to Dr. C. A. Mills for referring this patient, and to Professor Jethro Gough, who reviewed the case, and in fact made the diagnosis, during his Australian tour. It is a pleasure to express my thanks to my colleagues Dr. A. L. Waddington and Dr. F. W. Ross for their collaboration, and to Dr. Alan Bell and Mr. H. M. Whaite, of the Division of Occupational Health. The photomicrographs were provided by Dr. B. B. Turner, and the other photographs by Mr. R. A. Money, of Sydney Hospital.

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