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A CASE OF BERYLLIUM DISEASE

BY

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Beryllium disease was first described in 1933 by Weber and Engelhardt working in Germany, and has since been reported from many other countries. In Great Britain it is rare, but in the United States of America more than 500 cases have been reported. Seventy-five per cent. of these cases arose in beryl smelting plants and during fluorescent lamp manufacturing where, for a time, a phosphor containing 13% beryllium by weight was used.

The three principal syndromes of the disease, namely, chronic pulmonary, acute pulmonary, and dermal, have been described in patients in this country (Agate, 1948; Royston, 1949; Lederer and Savage, 1954; Sneddon, 1955; Rogers, 1957). The reported incidence of the chronic pulmonary type of disease has been low possibly because, in the absence of epidemiological evidence, it is not suspected. A further difficulty is the absence of good diagnostic tests that can safely be applied. The first patients who had this form of beryllium disease in the U.S.A. were diagnosed as sarcoidosis, miliary tuberculosis, or silicosis until the true nature of the condition was recognized.

The case now reported is believed to be one of chronic beryllium disease, although the histological findings are not entirely typical. The history of a mixed exposure to coal dust, mesothorium, and silica illustrates some of the difficulties of investigation and diagnosis in this type of case.

Case Report

In May, 1951, a chemical worker, aged 36, was admitted to hospital with a diagnosis of bronchopneumonia.

Occupational History.—From the age of 14 to 18 he worked underground in a Nottinghamshire coal-mine and then went into domestic service for five years. At the age of 23 he went to work for a small chemical firm where he stayed 11 years and was exposed to a variety of toxic substances. For the first three years (aged 23 to 26) he was making granules for absorbing toxic gases. He had to grind silica gel in hand-operated coffee mills. This was a very dusty process. During this time he also had contact with cement, barium hydrate, and zinc chloride and was extracting mesothorium. The latter became his main occupation for the next three years (aged 26 to 29). Aged 29 to 34 he was making a fluorescent powder for tubular lights. He collected beryllium oxide from a ball mill, mixed it with silica gel and heated it to 1,200 to 1,800° C. After firing he tipped the mix into bins, broke up the lumps by hand, sieved it, and then tipped the powder into bags. In 1949 he left this job because of shortness of breath and general malaise and worked as a clerk for a year.

Medical History.—In 1943, at the age of 28, he developed painful indolent ulcers on his arms and legs. These were attributed to mesothorium. In 1946, after he had been working with beryllium oxide for two years, he began to get short of breath. This increased and he developed a dry cough. By 1950 a chest radiograph showed "diffuse reticulation throughout both lung fields, increasing towards the lower zones with some fine nodulation".

He was admitted to hospital in May, 1951, having spent most of the previous year in bed. He had lost 2½ st. in weight. He produced 2 to 4 oz. of sputum daily and was dyspnoeic on the slightest exertion. He had a low-grade fever. On examination he was thin and cyanosed, and his fingers were grossly clubbed. Fine rales were present in all areas of the chest. Scars of the ulcers could be seen on his arms and legs.

Investigations.—A blood count gave Hb. 102%; white cells 13,500 per c.mm.; E.S.R. 42 mm. in one hour (Westergren); serum protein 7·0 g. per 100 ml. Vital capacity was 1,420 ml. A radiograph of the chest at this time showed extensive reticulation throughout both lung fields with early nodulation (Figs. 1 and 2). Analyses of 24-hour specimens of urine were performed on 13 occasions during his stay in hospital. On two occasions 5·8 and 4·5 μg. of beryllium were found; on four occasions, though detected qualitatively, the amount was below the level of quantitative estimation (0·7 μg. per 24-hour specimen) and on seven occasions no beryllium was found.

Progress.—During the first few weeks in hospital he improved only slightly. He was given streptomycin

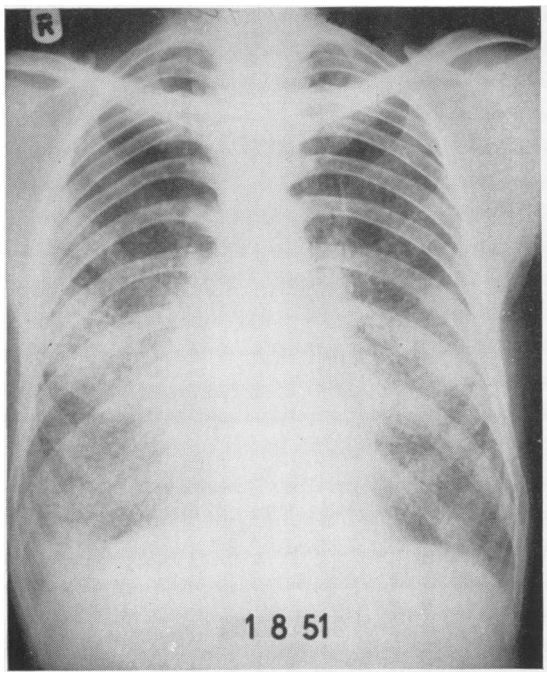

FIG. 1.—Chest radiograph in May, 1951, the patient aged 36, showing extensive reticulation and early nodulation.

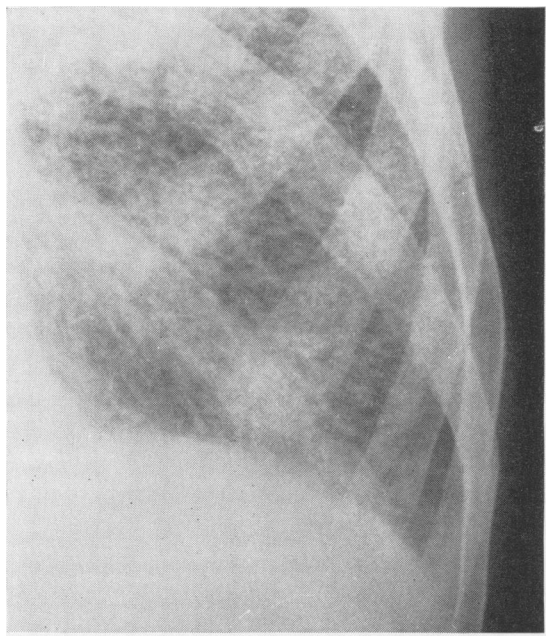

FIG. 2.—An enlargement of the left lower zone from Fig. 1.

penicillin, and chloramphenicol with little decrease in the amount of sputum.

He was then started on corticotrophin, 20 mg. six hourly. Three days later he could talk and move about in bed without gasping. There was a marked improvement in his appetite. After one week his sputum was greatly reduced and he could walk for 300 yards. Improvement continued for three weeks and his condition then remained stationary. His vital capacity had risen from 1,420 ml. to 2,300 ml. After five weeks corticotrophin was stopped (total given 1.68 g.). During the next four weeks he became steadily more dyspnoeic. A further course of corticotrophin was started and the dosage gradually increased to 150 mg./day but no further improvement occurred. After 27 days, treatment was again stopped (total given 2.01 g.) and he was discharged.

During the next four years he remained completely disabled. He complained of a feeling of severe fatigue and his breathlessness was such that he was seldom able to leave his bed. He had a troublesome cough. He was treated to relieve bronchospasm and to prevent infection, but this did not affect the progress of the disease. Chest radiographs showed an increase in the nodulation and he developed right heart failure from which he died in September, 1955.

Necropsy.—The body was poorly nourished and there was marked clubbing of the fingers.

The pertinent internal findings were an excess of free fluid (4 oz.) in the pericardial sac and a dilated and thickened right ventricle, which was tough and firm. The peritoneal cavity contained 1 pint of fluid and the liver had the typical nutmeg appearance of chronic congestion. The other organs showed no significant changes. Microscopical examination of brain, kidneys, and adrenal tissues showed congestion in the small blood vessels. In the liver chronic congestive changes were well marked with the appearances of early cardiac cirrhosis.

Lungs.—Scattered adhesions were present over the posterior aspects of both lungs and there was a little free fluid within the pleural cavities. The lungs showed a gross degree of emphysema (Fig. 3) and their substance contained numerous hard, shotty nodules, maximal in their posterior halves, with bronchopneumonia in both lower lobes.

The lung sections showed an overall picture of acute congestion, small areas of pneumonic consolidation and lakes of fibrin together with emphysema. The outstanding feature was the presence of numerous small nodules composed chiefly of mononuclear cells of endothelial type with an intermingling of plasma cells and lymphocytes. No caseation was seen. Giant cells of both Langhans and foreign body type were present in moderate numbers with inclusion bodies, both within the giant cells and extracellularly in the granulomatous areas. The inclusion bodies were seen both as long refractile needles and as conchoidal bodies, the latter consisting of a central body of irregular shape which was either a deeply stained amorphous mass or colourless plates not refractile to polaroids (Fig. 4). Towards the central body there was a series of concentric lines, the outer line being

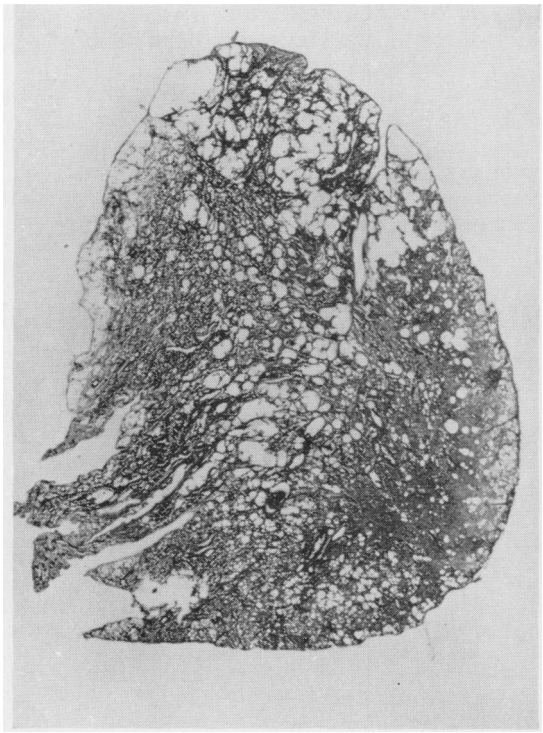

FIG. 3

FIG. 3.—Whole section of left lung showing widespread emphysema and consolidation in the lower zone. (Prepared by the method of Gough, James, and Wentworth, 1949.)

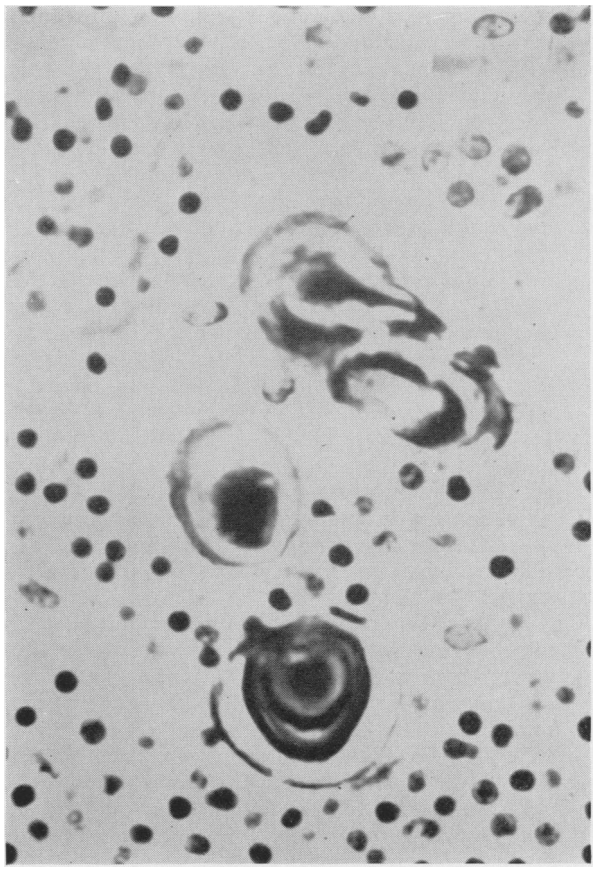

FIG. 4

FIG. 4.—Part of a nodule showing typical conchoidal body, surrounded by mononuclear cells × 600.

heavy and the inner ones thinner. When these bodies were digested by hydrogen-peroxide and stained for the presence of calcium and iron they gave positive reactions.

Fibrosis was not a feature, which is perhaps surprising in view of the length of the clinical history. Sections of lymph node showed discrete areas of hyalinization and fibrosis together with scattered conchoidal bodies. The other tissues examined microscopically showed no evidence of involvement.

The histopathology, as described, is that of a diffuse and focal chronic sarcoid-like pulmonary granulomatosis similar to that seen in cases of chronic beryllium disease as described by Dutra (1948).

Chemical Analysis.—Chemical analysis of a sample of lung showed a concentration of 0·22 g. of silicon dioxide per 100 g. of dry lung. This figure is slightly above the normal but does not approach the amounts which are found in silicosis (King, Maguire, and Nagelschmidt, 1956). No beryllium was detected.

Discussion

One of us (C. H. W.) has recently had the opportunity of examining the records of over 500 American cases, including 300 chronic cases, which are being collected in a beryllium case registry by Dr. Hardy at the Massachusetts General Hospital. The clinical features of the case described were indistinguishable from those of the severe cases of the chronic pulmonary syndrome recorded in the beryllium registry.

By the nature of the processes for which beryllium is used, there is frequently a history of exposure to other hazards at the same time, such as silica and gamma radiation. The striking similarity of the clinical picture of these cases occurring in beryllium workers engaged in different processes is an important diagnostic feature. Proof of the diagnosis may be impossible. The discovery of beryllium in the urine is evidence of exposure to beryllium but not of disease: many beryllium workers excrete beryllium in their urine for years without developing any disease. Acting on the principle that beryllium disease is an allergic response to beryllium or a beryllium-protein allergen, patch testing has been

tried (Curtis, 1951). De Nardi, Van Ordstrand, Curtis, and Zielinski (1953) claim consistent results with this diagnostic test; but others, in view of the theoretical danger of producing a severe reaction or of provoking an exacerbation of the disease, have been reluctant to perform this test. Sneddon (1955) found that, for several days after patch testing a patient, dyspnoea appeared to be worse than usual and moist rales were heard over both lungs for the first time.

The demonstration of a granulomatous reaction together with the presence of beryllium in biopsy and necropsy specimens has sometimes supported the diagnosis. Possibly however, once the pathological process has been initiated, the offending agent may disappear. Also the difficulties of detecting trace quantities of beryllium are considerable and complete reliance should not be placed on the results of such examinations, especially when performed only on rare occasions. In this case the microscopical picture was one of chronic sarcoid-like granulomatosis, but no beryllium was found in the sample of lung analysed.

The rapid subjective and objective improvement of the patient with corticotrophin was striking. Relapse followed withdrawal and a subsequent course of treatment for 27 days failed to produce a further remission. The fatality rate among those patients with chronic beryllium disease reported to the case registry has fallen during the past eight years. While this may be due, in part, to the more frequent diagnosis of milder cases now that the syndrome is better known, Hardy (1955) believes that the introduction of steroid therapy is also important. There were only two deaths among 101 patients treated with steroids between 1950 and 1955. In many of these, treatment was started earlier than was possible in the patient described in this paper and was continued for several years.

The potential field of usefulness for beryllium is expanding and opportunities for exposure exist in this country. Further sporadic cases or small outbreaks are therefore still possible and will provide a challenge for diagnosis if they cannot more properly be prevented.

Summary

The occupational and clinical histories and post-mortem appearances of a man who developed dyspnoea and cough while working with beryllium oxide are reported. The disease progressed, and, despite a temporary remission under treatment with corticotrophin, he died at 40 years of age after having been bedridden with dyspnoea for four years.

Some of the difficulties of confirming the diagnosis of beryllium disease are discussed.

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