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PULMONARY ASBESTOSIS AND CARCINOMA

Report of a Case with Necropsy Findings¹

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Although there is a steadily growing recognition of pulmonary asbestosis as a disease entity and industrial hazard, the number of reported cases is still small. In a recent review by Egbert (1), in which 28 fatal cases were collected, pulmonary tuberculosis was found to be a common complicating disease. The following report was deemed especially interesting since it is apparently the first to describe primary carcinoma of the lung as an associated condition.

Case Report

History: J. V., a 41-year-old Hungarian factory-hand, was admitted to the Tuberculosis Ward of the New Haven Hospital, May 11, 1934, complaining of long-standing breathlessness and cough, and a recent disabling pain in the back.

The patient's mother had died at the age of 33 with a protracted "cold in the chest"; his father had met death by accident. Two siblings, as well as the patient's wife and two children, were well. No family history of tuberculosis or of carcinoma was obtainable.

The patient had immigrated in 1911, when he was 18 years old. Five years later he secured employment as a weaver in an asbestos factory, and he continued at this occupation uninterrupted for 18 years. He had considered his general health good until 1925, when he suffered a febrile illness of sudden onset and associated with pain in the left chest; the diagnosis had been "pneumonia." Although the acute illness subsided within a week, the patient was left with distressing dyspnoea on exertion and a moderately productive cough which prevented his returning to work for five months. X-ray examination of the lungs at this time was reported to have revealed nothing abnormal, and the patient resumed his occupation. His symptoms, however, persisted unabated for the next seven years. At the end of this time which was two years before the present hospitalization, alterations at the asbestos factory led to a great reduction in the amount of atmospheric dust to which the patient was daily exposed and his respiratory symptoms disappeared almost completely.

During the eight months preceding his hospital admission the patient de-

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veloped an insidious, gradually increasing pain of aching character throughout the back. Although the removal of five allegedly bad teeth and the application of heliotherapy to the back were followed by temporary amelioration of the pain, its recurrence with gradually increasing severity soon resulted in the patient's complete incapacity for work.

During the month before admission the dyspnoea, cough and expectoration had returned along with pain of pleural character in the left axilla. The sputum was described as white and heavy, but not foul. The patient had lost 40 lbs. in the last several months.

Physical examination: A lean male of sallow complexion with anxious, careworn expression. He looked chronically ill and his loose skin suggested that weight loss had been considerable. The patient's movements in bed were cautious and deliberate, apparently to avoid pain.

The respirations were regular, 30 per minute, and notably shallow. The lips were cyanotic. A frequent, loose cough "raised" thick, yellowish and blood-streaked sputum in abundance. Dirty teeth, a lightly coated tongue, and injected tonsils were observed incidentally. The chest, with barely perceptible respiratory movements, was definitely asymmetrical, with the left side flatter and less mobile than the right. No measurable diaphragmatic excursion could be demonstrated. Both sides of the chest were dull over the lower lobes, and numerous crepitant and medium moist râles were scattered from scapular angles to bases. The heart did not appear displaced or enlarged and, except for tachycardia of 110 beats per minute, no abnormal signs were noted.

A firm, subcutaneous nodule, about 1 cm. in diameter, was found in the left flank. Movement and manipulation of the lower spine and flexion of the thighs caused agonizing pain in the back with radiation down the thighs. The extremities were remarkable only for moderate clubbing of the fingers with double curvature of the nails, and the nail-beds were cyanotic. The hands, though calloused, presented no "asbestos corns."

Laboratory studies: The red blood cell count was 5,400,000, with 92 per cent haemoglobin; the leucocytes, 13,550, of which 89 per cent were polymorphonuclears. No tubercle bacilli were found in any of the 6 specimens of sputum examined. The urine was normal, and Kahn test of the blood negative. Because of extensive bone disease seen by X-ray, chemical examination of the blood was incidentally carried out, with the following results: The serum's calcium content was 9.27 mgm. per cent, and the phosphorus 4.05 mgm. per cent, with a total protein level of 6.14 per cent, of which 3.19 per cent and 2.45 per cent were made up of albumen and globulin respectively. The icteric index was 4.

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Stereoradiographic examination of the chest revealed a narrowing of the posterior intercostal spaces in the lower left hemithorax. The tracheal, mediastinal and cardiac shadows were normal in character and position, but the hilar shadows on both sides were increased in size and density. The bronchovascular markings throughout both lung-fields were obscured by a coarse, rather dense, nodular infiltration, which roughly followed the course of the linear markings and was symmetrically distributed throughout both entire lung-fields. In the left lower lobe was an associated haziness, with a poorly defined area of complete opacity between the left heart border and lateral chest-wall. The latter change suggested partial atelectasis or a pneumonic process in the left lower lobe. In view of the additional discovery of widespread destructive bone lesions of the pelvis and lumbar spine, which were characteristic of metastatic carcinoma, the pulmonary findings were summarized as pneumoconiosis and additional infiltration of the left lower lobe due probably to a malignant bronchogenic tumor.

Course: Throughout the ten days of hospitalization there was fever ranging continuously between 100° and 103°F., with the heart rate varying between 100 and 130. The patient complained repeatedly of distressing pains in the back and thighs, and analgesics had to be administered liberally. A steady and profuse perspiration sometimes required several changes of clothing daily. After a few days, patchy signs of pulmonary consolidation and pleurisy appeared over the lower lobe of the left lung; with this, the cyanosis grew deeper and the dyspnoea became so extreme that the patient found it difficult to take his meals. A loose cough produced bloody sputum in moderate amounts. On the last day, after a series of particularly violent coughing spells, the patient's pulse suddenly weakened, the skin grew clammy, and he complained of a smothering sensation in his chest. In spite of stimulating measures, including adrenalin and caffeine hypodermically, death ensued within a few minutes of the onset of collapse.

Necropsy: The report of the necropsy findings will be limited to the pertinent changes in the lungs. Both pleural cavities were completely obliterated by firm fibrous adhesions. The lungs, after removal from the body, retained almost the shape which they had while *in situ*. With the parietal pleura and part of the adherent diaphragm attached, the right lung weighed 1,179 and the left 1,128 gm. They were both fairly noncrepitant and of a rubbery firmness which rendered sectioning unusually easy. The grayish-red surfaces, which were mottled with large amounts of black pigment, revealed a large, solid tumor in the periphery of the lower lobe of the left lung (figure 1). The mass measured approximately 5 x 5 x 4 cm., its edges were well demarcated, and it was light gray with mottled zones of black pigmentation. A few tumor nodules,

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about 1 cm. in diameter, were scattered through the remainder of the lungs and had a mucinous appearance on section. At the hilum of the left lung was a large, firm lymph node measuring $2 \times 1.5 \times 1$ cm., which revealed about half



Fig. 1. Pulmonary asbestosis with bronchogenic carcinoma: B, primary site in main bronchus of left lower lobe. Photomicrograph of this region is shown in figure 2.

its substance to be occupied by tumor metastasis. A lymph node of similar dimensions was present at the hilum of the right lung, but it contained no tumor. Careful examinations of the bronchi revealed the primary site of the tumor to

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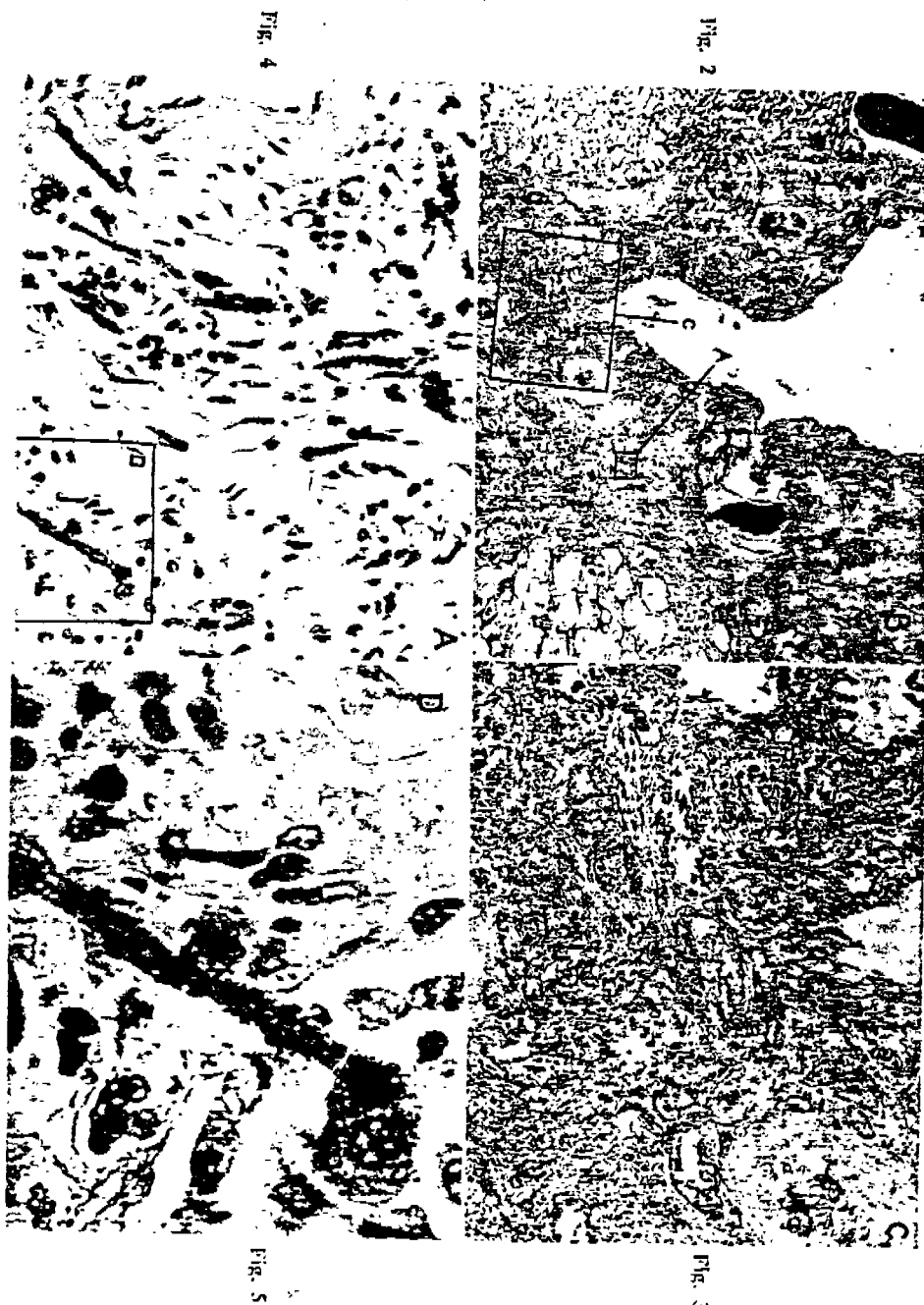


Fig. 2. Carcinoma of bronchus in figure 1: C, area shown in figure 3; A, area shown in figure 4. $\times 12$.
 Fig. 3. Carcinoma of bronchus probably arising from submucosal glands, area C in figure 2. $\times 40$.
 Fig. 4. Asbestotic body, area B in figure 1. $\times 12$.
 Fig. 5. Asbestotic body, area D in figure 1. $\times 40$.

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be in a large branch of the main bronchus of the left lower lobe (see B, figure 1). At this point the mucosal surface was roughened and finely nodular; the bronchial wall was thickened and infiltrated by firm, grayish tumor tissue. The bronchus itself led directly into the large tumor mass described in the left lower lobe.

Microscopic examination of fresh fluid scraped from the cut lung surfaces showed large numbers of typical asbestosis bodies.

Histological sections confirmed the primary site of the tumor in the bronchus of the lower lobe of the left lung (figure 2). Here in the submucosa and in a considerable zone of the peribronchial tissue were groups of carcinoma cells arranged in well-formed acinous structures which varied greatly in size and shape (figure 3). The neoplastic cells lining the acini were one to several layers in thickness. They were almost all hyperchromatic, varied considerably in size and shape, and exhibited very few mitotic figures. The arrangement and appearance of these cells were quite similar to those of submucosal bronchial glands. There was a tendency for the nuclei to be located at the base of the cells similar to their position in normal submucosal glands. Many of the carcinomatous acini were filled with a pale, gray-staining mucinous material, and in some of the preparations of the bronchus apparently normal submucosal glands could be seen merging with carcinomatous growth.

Asbestosis bodies were scattered throughout the pulmonary parenchyma, in alveoli for the most part and also extending through the carcinomatous zones (figure 4). The color of these bodies was yellowish-brown to brownish-black. They had varying shapes, but tended to be in the form of nodular rods with enlarged rounded heads. In many of the bodies a central somewhat paler and translucent core apparently represented the original asbestos fibre (figure 5). These asbestosis bodies did not give a positive iron reaction. In many instances they were enclosed in the cytoplasm of the macrophages, which were very numerous in the alveoli. Many of the macrophages were multinucleated and extremely large.

There was some diffuse, fibrous thickening of the alveolar walls, and the regions around the bronchi and bronchioles contained a large amount of fibrous tissue. The pleura in all the preparations was thickened, dense and hyalinized.

Tumor metastases, besides those in the lungs and tracheobronchial lymph nodes, were also present in the aortic lymph nodes, the right adrenal gland, the left external oblique abdominal muscle, and in the bony pelvis, vertebrae and skull.

DISCUSSION

Pulmonary asbestosis, a form of pneumoconiosis which is growing in medical and industrial importance, has been fully discussed in a

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recent review by Gloyne (2). Clinically, the condition is characterized chiefly by dyspnoea, by the appearance of a fine, diffuse fibrosis, and by asbestosis bodies demonstrable in the sputum. A review of the fatal cases reported in the literature up to 1932 (1) indicates that the condition comes on slowly and requires an average of 9 years of exposure to the dust before the onset of symptoms. The total time of exposure in uncomplicated cases with fatal terminations was found to average 16 years. Pathologically, the pulmonary fibrosis is diffuse and is most marked around bronchioles and bronchi. This is in distinction to the fibrosis of silicosis, which consists of discrete, dense, hyalinized connective-tissue nodules around and in the pulmonary lymphoid tissue. Asbestosis bodies are always demonstrable in the microscopic sections.

The association between the pulmonary asbestosis and carcinoma in this case is unique and the possible interrelationship of the two processes offers interesting speculation. Gloyne (2) mentions one case of pulmonary asbestosis with carcinoma of the pleura and adds, "There is no evidence at the moment that this is in any way related to the asbestosis." Otherwise, no mention of any such associated pulmonary malignant tumor has been found in the literature.

The relationship between exposure to irritating dusts and malignancy of the lung has aroused a great deal of comment, especially since various statistics would tend to show that the incidence of pulmonary cancer is increasing. Recently, Hrubby and Sweany (3) have analyzed the incidence of cancer of the lung and they conclude that not only has there been an approximately tenfold increase in the number of cases coming to autopsy within the last forty years, but that a twofold increase has occurred in the last ten years alone.

Reports of other forms of pneumoconiosis in which carcinoma of the lung has occurred are fairly numerous. It is not uncommon in silicosis (4). The incidence (10 per cent) of carcinoma of the lung found at autopsy among the cobalt miners in Schneeberg is well known (5).

That the irritating effects of the inhaled asbestos particles may in this case have been a significant factor concerned in the development of the primary lung cancer seems sufficiently plausible to be worthy of consideration.

SUMMARY

1. The clinical and anatomical findings are presented in a case of pulmonary asbestosis with an associated primary carcinoma of the lung.

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2. The associated incidence and possible aetiological relationships of pneumoconiosis to carcinoma of the lung are discussed.

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