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Carcinoma of the Lung in Asbestosis: Report of Two Additional Cases*

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The possible relationship of pulmonary carcinoma to asbestosis is as yet unsettled. Statistics would indicate a probable association.

As CARCINOMA of the lung has assumed a foremost position in the field of neoplastic disease, both from the standpoint of incidence and causation, it appears desirable to describe two additional cases involving the coexistence of an external irritant, asbestos. Since the original report from this department in 1935,¹ the number of reported cases with autopsy has grown to twenty-one.² That form of pneumoconiosis produced by the asbestos fiber and known as asbestosis has probably been the subject of more comment and investigation in relationship to carcinoma of the lung than any of the other dust diseases. This appears to be related to the fact that the incidence of coexistence of asbestosis and carcinoma is fairly high when compared to the incidence of carcinoma of the lung in autopsies at large, as well as its incidence in such other diseases as silicosis and tuberculosis.

The average of five analyses of the incidence of asbestosis and carcinoma of the lung as recorded in the literature is 13.8 per cent.² The incidence of carcinoma of the lung in routine necropsies ranges from 0.8 to 2.1 per cent. Data compiled by Merewether³ and the Miners Phthisis Medical Bureau of South Africa⁴ disclosed an incidence of carcinoma of the lung of 1.32 and 0.7 per cent in a large series of patients with silicosis. We have had

four instances of carcinoma of the lung in an autopsy series of 49 cases from workers in an asbestos manufacturing plant who showed demonstrable deposits of asbestos in their lungs. This is an incidence of 8.2 per cent of carcinoma and asbestosis in this series. The general incidence of carcinoma of the lung in the hospital service during the same period and in the same age range as the cases of asbestosis was 1.5 per cent. This incidence of 8.2 per cent is by far the lowest incidence recorded among the five significant series relating to this problem. Merewether³ found 31 instances of carcinoma of the lung among 235 patients with asbestosis or an incidence of 13.2 per cent. Wedler⁵ had 92 patients who died with asbestosis among whom there were 15 with carcinoma of the lung or an incidence of 16.3 per cent. At the present moment the available evidence is not conclusive as to whether asbestosis may play an etiological role in the occurrence of carcinoma of the lung. However, the evidence at least does not allay the suspicion, chiefly from statistical evidence, that there may be a cause and effect relationship.

Case Reports

Case 1. A 46 year old white man, who had been employed as a labor foreman for 25 years in an asbestos plant was admitted to the hospital in June, 1913, complaining of pain and soreness in the left side of his chest. About 10 weeks previously he caught cold which was accompanied by a hacking cough productive of a small amount of tenacious blackish sputum. He remained about the same until

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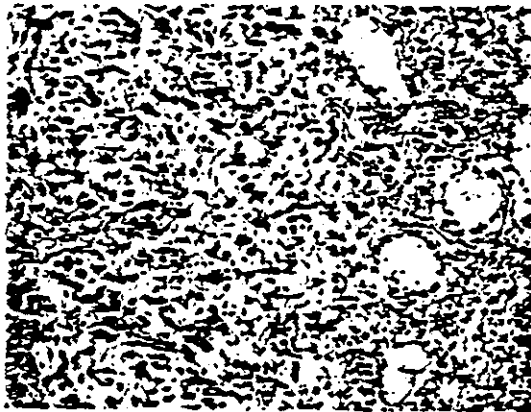
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three weeks before admission when he noticed soreness and pain throughout both sides of his chest and he had to go to bed. He remained essentially the same until four days before admission when he noted that the pain had localized in the left side of his chest. The cough had improved.

Physical examination revealed signs which were limited to the left side of the thorax. Breath sounds over the left base were decreased and there was decreased resonance in the same area. A roentgenogram revealed a bilateral increase in lung markings of a fine granular type. There was partial atelectasis of the left lower lobe and a definite enlargement of the left hilar region, the left with a marked increase in density.

Bronchoscopy revealed a tumor in the left lower main stem bronchus. A biopsy of this lesion revealed a nonkeratinizing epidermoid carcinoma (Fig. 1). Material aspirated from the bronchial tree at the time of bronchoscopy as well as a subsequent specimen of sputum reveal numerous typical asbestos bodies (Fig. 2).

FIG. 1



Nonkeratinizing squamous cell carcinoma in bronchial biopsy from case 1. Hematoxylin and eosin stain, X200.

FIG. 2



Asbestos bodies and carbon particles in sputum treated with potassium hydroxide from case 1. Stained, X400.

The patient was discharged on May 2, 1943. He returned to the hospital on June 10 with story that his legs began to give away about three weeks previously and at the present time he could move them scarcely at all. At the same time he also began having trouble urinating and had been constipated. Examination revealed paralysis of both legs from his hips downward. He was examined by a urologic consultant who found a markedly distended bladder and gave the opinion that this was a cold bladder due to carcinomatous involvement of the spine. Severe pain, increasing dyspnea and cyanosis developed and he pursued a steady downhill course and died on July 17, 1943.

Case 2. A 55 year old white man had been employed as a spinner in an asbestos factory for approximately 36 years. During the winter of 1932 he experienced several respiratory infections accompanied by pleuritic pains and cough. The cough never cleared and became productive of rather large quantities of grayish sputum which was occasionally flecked with blood. Increasing weakness, afternoon fever, severe night sweats, exertional dyspnea and orthopnea followed. He had lost 33 pounds in weight during the last two years. Some shortness of breath had been present for 20 years.

FIG. 3



R. LUNG: Ant.

Ill-defined, grayish, nodular neoplastic mass in the upper and middle lobes from case 2.

FIG. 4



Neoplasm of hilar region of left lung with extension into pericardium and heart of second case.

Röntgenographic examination revealed a diffuse granular infiltration of the lungs with a lesion in the right middle lobe which was thought to be either carcinoma or chronic bronchiectasis and pneumonitis. Bronchoscopic examination was negative, but cytologic study of the sputum revealed neoplastic cells as well as asbestos bodies. His vital capacity was 48 per cent of normal and exercise produced marked dyspnea so that the thought of pneumonectomy was abandoned and he received x-ray therapy. The diagnosis had been definitely established by examination of the sputum on July 1, 1952, and the patient died on December 12, 1952.

Necropsy. There were dense pleural adhesions present so that the lungs were removed with difficulty. The pericardial sac was also partially obliterated. The lungs together weighed 1600 Gm. They held their shape well and on palpation had an irregular nodular and leathery quality. An ill-defined neoplastic mass was present in the lower portion of the right upper lobe and in the right middle lobe (Fig. 3). In the hilar region of the left lung there was a neoplastic mass 5 cm. in diameter which obliterated the bronchi to the upper and lower lobes with the exception of the superior branches to these lobes (Fig. 4). This extended into the pericardial sac and involved the posterolateral aspect of the left ribular wall. A polypoid tongue of tumor pro-

truded into the lumen of the bronchus of the lower lobe on the left so that the point of this polypoid protrusion extended towards the tracheobronchial bifurcation. Cystic and dilated alveoli were present in considerable numbers, particularly in the right lung and most marked in its upper lobe (Fig. 5).

Histologic Study. Two outstanding features were immediately apparent upon microscopic examination. These consisted of extensive infiltration of a well differentiated squamous carcinoma with conspicuous keratinization and pearl formation (Fig. 6). The

FIG. 5



52-330

Pleural thickening and marked emphysema in case 2.

FIG. 6



Plexiform squamous cell carcinoma with group of asbestos bodies from case 2. Hematoxylin and eosin stain, X200.

... tumor was present not only in the hilar region of the left lung and the midportion of the right lung, but was present in the alveoli in many areas where the neoplastic cells lay either in clusters or formed a sort of alveolar lining. The second notable feature was the extensive fibrous thickening of the alveolar walls with clumps and balls of fibrous tissue and macrophages lying in the alveolar spaces. Numerous asbestos bodies were embedded in the fibrous tissue and were also present in the alveolar spaces either as single bodies or in clusters.

Discussion

The tissue reaction produced by asbestos dust is believed to be due to the physical nature of the asbestos particle rather than to any chemical constituent. The asbestos fiber causes desquamation of the bronchiolar epithelium and an outpouring of numerous macrophages in an attempt to phagocytize the fibers (Fig. 7). Fibroblastic proliferation and collagen deposition in the walls of alveoli and about the terminal bronchioles follow at a later stage. Theoretically it is an attractive hypothesis to believe that the mechanical irritation of the asbestos fibers produces hyperplasia of bronchiolar epithelium which eventually escapes from the realm of normal biologic control and becomes neoplastic. There is at least some histologic evidence of epithelial hyperplasia (Fig. 7), but experimental proof of progression from hyperplasia to neoplasia is difficult to produce. The experimental animal in this case, as in many others, does not necessarily respond in a fashion that is comparable to human tissue behavior. Mice exposed to con-

centrations of asbestos dust having the proper specifications as regards particle volume and size do not develop asbestosis or carcinoma, although the ubiquitous pulmonary adenoma is frequently present. In fact bronchogenic carcinoma of man has no counterpart in other animals. It appears that the pulmonary tissue of dogs may respond to asbestos dust in a manner somewhat more closely analogous to man. Until a valid biologic experiment can be evolved, it appears that the evidence for or against the possible carcinogenic effect of the asbestos fiber will rest primarily on statistical evidence and personal opinion.

Conclusions

We have described two additional cases of asbestosis and bronchogenic carcinoma. A total of four cases showing the coexistence of these diseases have occurred in our series of 49 cases having asbestosis at necropsy, an incidence of 8.2 per cent. Statistical inference from this and other series does not allay the suspicion that there may be an association between the two conditions. Animal experimentation has not yet provided any conclusive evidence of this.

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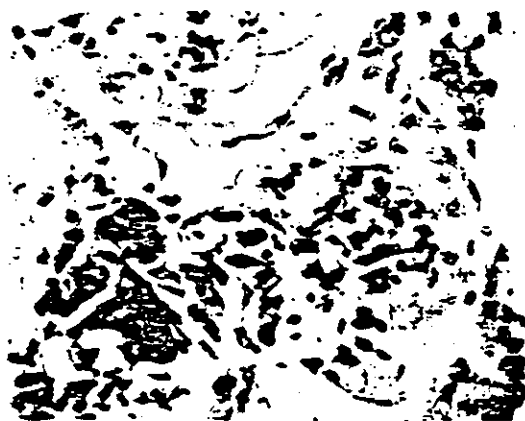
Discussion (Abstract)

Dr. Gretchen F. Squires, Pensacola, Fla. I would like to ask Dr. Pratt-Thomas, what is the present industrial compensation status of the coexistence of these two diseases? As pathologists we are quite frequently called upon to give an opinion in an industrial compensation case on such individuals who have coexistent disease.

Dr. Pratt-Thomas. My impression is that it may not matter what opinion you give as I have testified quite volubly on one side or the other, and the industrial commission always decides in the opposite direction. They would much rather listen to a doctor who has never done an autopsy but who has had 75 years of clinical experience render an opinion which they will always "buy," rather than to a so-called specialist.

Seriously, in our experience we have seen cases in which at least partial compensation has been allowed.

FIG. 7



Collection of asbestos bodies in alveolar duct. Note intense macrophage activity and hyperplasia of bronchiolar epithelium, particularly on right. Hematoxylin and eosin, X100.

It was thought they might not have died quite as fast if they had not gotten carcinoma and that the evidence for asbestosis producing cancer, though not proven, was sufficiently questionable so the cases were judged in favor of the plaintiff, or at least partially so.

Dr. Albert E. Casev, Birmingham, Ala. I would like to ask Dr. Pratt-Thomas, what is the incidence of asbestosis over the country? I am afraid we have been missing some in Birmingham, at least I have, if it is as much as you report there. Also I ask whether the effect of a carcinogen with a nonspecific foreign body reactor might not be the answer to the increased incidence. Another question is, what is your autopsy routine for demonstrating asbestosis?

Dr. Pratt-Thomas (closing). I take it you do not have any asbestos plants in Birmingham. Well, that's your misfortune. We happen to have quite a big fabricating plant outside of Charleston and, of course, that is the reason Dr. Lynch originally became interested in the problem and did much of the first and basic work which has been done on this particular form of pneumoconiosis.

It is estimated that there are about 10,000 people in the United States who are at the present moment

potentially industrially compensable as far as asbestosis is concerned. In other words, they are being exposed to the dust. In addition to the 10,000 in the United States there are approximately 5,000 to 6,000 others in the British Isles who are exposed to this hazard at the present time.

Though I cannot answer your question in overall statistics, this gives you an idea as to the incidence. You will not see it unless you are in a community or area in which there is either mining or fabrication of the product.

The asbestos fiber is quite easy to find in sputum. One uses the simple sodium or potassium hydroxide liquefaction technique with centrifugation and study of the concentrates. In sections they show up beautifully and do not require any special staining technique. The only trouble is that there are occasional things that look like asbestos fibers though they are not. That, of course, is a subject within itself as to the proper identification. But the classical asbestos fiber can certainly be detected in the sputum very simply as well as in tissue sections. Of course, the presence of asbestos bodies in tissue sections do not necessarily mean that the patient is really suffering from true asbestosis. They may have an occasional one scattered around and no reaction to it.

Malignant Tumors of the Superior Maxilla*

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Recent advances in anesthesia and radiation-therapy, along with the antibiotics, permit a radical attack upon malignant lesions of the superior maxilla not possible in the past.

IN SCANNING the medical literature of the past 15 years one finds more and more about malignant lesions of the head and neck and less about the medical and surgical treatment of infectious conditions. There are two main reasons for this. Over a period of years the technical difficulties of, and indications for surgical procedures have been generally and in most instances specifically ironed out. Also, the principles and rationale of medical therapy and the availability of antibiotics have greatly decreased the indications for

surgical treatment of infections. Thus the pendulum has swung more nearly to the perpendicular in regard to the infectious conditions. Secondly, with the increase in life expectancy and the additional facilities for diagnosis, malignant disease is becoming increasingly a more prominent problem in medical practice.

With the advances that have been made in anesthesiology and in preoperative and postoperative care, surgical procedures are being done today that were not possible formerly. The radical surgical procedures necessary in dealing with malignant tumors are now feasible in many instances, and the possibility of

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