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Case Reports

ASBESTOSIS ASSOCIATED WITH BRONCHOGENIC CARCINOMA

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HOLLEB and Angrist [1] in 1942 reported two cases of bronchiogenic carcinoma in association with pulmonary asbestosis. The first case of carcinoma of the lung in association with pulmonary asbestosis was reported in 1935 by Lynch and Smith.[2] In that year Gloyne reported two cases and in 1936 another.[3] Egbert and Geiger [4] reported one case in 1936. Nordmann [5] presented two cases in 1938. One year later Lynch and Smith [6] added another. Of these, six were of squamous-cell carcinoma, one of squamous-cell carcinoma with glandular features, two of oat-cell carcinoma, one of glandular carcinoma, and another of squamous-cell nonkeratinizing carcinoma. The age of the patients ranged from 35 to 71 years, and the duration of exposure, from 19 months to 25 years. All but two had metastases. Freedom from exposure before death varied from four months to 15 years. We have found four additional cases not mentioned in the report by Holleb and Angrist.[1] Two cases reported by Koelsch [7] in 1940 were in an oral communication, and no details are known. Two more cases were reported by Linzbach and Wedler [8] in 1941, one of which was of a squamous-cell carcinoma in a man 61 years old, exposed for at least three years to asbestos; of the other, no details were known.

In 1941 also Desmeules [9] added two more cases to the literature, one of a man 57 years old in whom alveolar-cell carcinoma was found and who had been exposed

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1. Holleb, H., and Angrist, A.: Bronchiogenic Carcinoma in Association with Pulmonary Asbestosis: Report of 2 Cases, Am. J. Path. **18**:123-135, 1942.

2. Lynch, K. M., and Smith, W. A.: Pulmonary Asbestosis: III. Carcinoma of Lung in Asbesto-Silicosis, Am. J. Cancer **24**:56-64, 1935.

3. Gloyne, S. R.: Two Cases of Squamous Carcinoma of the Lung Occurring in Asbestosis, Tubercle **17**:5-10, 1935; Case of Oat Cell Carcinoma of Lung Occurring in Asbestosis, ibid. **18**:100-101, 1936.

4. Egbert, D. S., and Geiger, A. J.: Pulmonary Asbestosis and Carcinoma: Report of a Case with Necropsy Findings, Am. Rev. Tuberc. **34**:143-150, 1936.

5. Nordmann, M.: Der Berufskrebs der Asbestarbeiter, Ztschr. Krebsforsch. **47**:288-302, 1938.

6. Lynch, K. M., and Smith, W. A.: Pulmonary Asbestosis: V. A Report of Bronchial Carcinoma and Epithelial Metaplasia, Am. J. Cancer **36**:567-573, 1939.

7. Koelsch: Lungenkrebs und Beruf, abstracted in Zentralbl. Gewerbehyg. **27**:32-33, 1940.

8. Linzbach, A. J., and Wedler, H. W.: Beitrag zum Berufskrebs der Asbestarbeiter, Arch. path. Anat. **307**:387-409, 1941.

9. Desmeules, R.; Rousseau, L.; Giroux, M., and Sirois, A.: Amiantose et cancers pulmonaires, Laval méd. **6**:97-108, 1941.

to asbestos for 23 years. The other was of a man of 50 with squamous-cell carcinoma who had been exposed for 22 years. Both had metastases to the pleura.

Since 1941, a number of similar cases has been reported. In 1942 Homburger [10] reported three cases in men 45, 43, and 49 years of age. In two, squamous-cell carcinoma was found; in the other, an anaplastic carcinoma. One had been exposed to asbestos for five years, another for 20 years. The duration of exposure in the third was not known. All three had metastases. In Homburger's laboratory from 1918 to 1938, in 4,137 autopsies, asbestosis was diagnosed in eight cases. Pulmonary carcinoma was found in four of these.

Wedler [11] in 1943 collected 92 postmortem reports of cases of asbestosis from different parts of the world and found an incidence of 16% with associated pulmonary carcinoma.

In 1947 Merewether [12] reviewed the accumulated data over a period of 22 years (1924 to 1946) in the "Annual Report of Chief Inspector of Factories in England." In 235 cases asbestosis was found, and in 31 of these pulmonary carcinoma was also present, an incidence of 13.2%. The incidence of pulmonary carcinoma in the general adult population was 1.0%.

Lynch and Cannon in 1948,[13] reported that among 40 cases of asbestosis over a period of 18 years in their postmortem series a total of 3 cases of carcinoma of the lung was encountered, an incidence of 7.5%. Each of these three cases showed medium to advanced grades of asbestosis.

Wyers in 1949 [14] reported on a series of 115 cases of asbestosis. Pulmonary carcinoma was present in 17, an incidence of 14.8%. Squamous carcinoma was present in nine cases, oat-cell carcinoma in five, and columnar-cell carcinoma in one.

REPORT OF CASE

D. L., a white man 40 years old, was admitted to Queens General Hospital complaining of cough, fever, and weakness of two weeks' duration. For four to five months prior to admission he felt weak and slightly anorectic, with a weight loss of about 10 lbs. (4.5 kg.). Two weeks prior to admission his weakness became more marked, and he began having a dry persistent cough which was nonbloody. He visited his local physician at that time and was found to be febrile. A roentgenogram was taken, and he was told he had viral pneumonia. He was treated with penicillin, sulfonamides, chloramphenicol (chloromycetin®), and aureomycin without a fall in temperature, and with persistence of the cough. His local physician then advised hospitalization. There was no history of previous illness.

From 1925 to 1940 he had worked as a plumber but did not use asbestos in his work. In 1940 he obtained a job with the Works Progress Administration as a pipe coverer in which he worked with asbestos exclusively for one and a half years. For the next four and a half years he continued to work as a pipe coverer in a shipyard, where he again used asbestos only. During this time he was told to wear a mask while working but neglected to do so and complained that the smell always made him sick.

10. Homburger, F.: Co-Incidence of Primary Carcinoma of Lungs and Pulmonary Asbestosis: Analysis of Literature and Report of 3 Cases, Am. J. Path. 19:797-807, 1943.

11. Wedler, H. W.: Asbestose und Lungenkrebs, Deutsche med. Wchnschr. 69:575, 1943; abstracted, Bull. Hyg. 19:363, 1944.

12. Merewether, E. R. A.: Annual Report of the Chief Inspector of Factories, London, His Majesty's Stationery Office, 1947.

13. Lynch, K. M., and Cannon, W. M.: Asbestosis: VI. Analysis of 40 Necropsied Cases, Dis. Chest 14:874-880, 1948.

14. Wyers, H.: Asbestosis, Post-Grad. M. J. 25:631-638, 1949.

Physical examination revealed a well-developed, well-nourished, moderately ill white man lying in bed and coughing. Examination of his chest disclosed a slightly diminished percussion note with depressed breath sounds and occasional expiratory wheezes at the base of the right lung. There were no unusual findings in the heart, abdomen, extremities, or venous system.

Laboratory Data.—The temperature was 102.4°; the pulse rate, 104 per minute, and the blood pressure, 120/76. The urine was normal. The hemoglobin concentration was 15.5 gm. per 100 cc. and the white blood cell count 10,000 per cubic millimeter, of which 75% were polymorphonuclear cells. The Wassermann reaction was negative, and blood chemical values were within the normal range. Examination of the bone marrow revealed clumps of malignant cells. An electrocardiogram was normal.

A chest roentgenogram taken shortly after admission showed generalized, large discrete oval shadows of increased density throughout both lung fields indicative of pulmonary metastases. A bone survey revealed multiple osteolytic lesions in the cranial vault in the frontal and parietal regions. The long bones and pelvis showed no lesions. The appearance on retrograde urography and on a gastrointestinal series was normal. Proctoscopy revealed no abnormal findings.

Throughout the patient's hospital stay the temperature continued to range from 101 to 104 F. On the ninth hospital day he complained of numbness of the right arm, with definite weakness of the right peripheral facial nerve. There were no definite motor changes in the extremities. A spinal tap performed at this time revealed crystal-clear fluid under no increased pressure. The cell count was 0; sugar measured 72 mg., proteins, 28 mg., and chlorides, 115 mg., per 100 cc. On the 28th hospital day the patient displayed Babinski's sign with hyperreflexia on the right side. On the 31st hospital day a course of treatment with nitrogen mustard (methyl-*bis* or *tris*[2-chloroethyl]amine hydrochloride) was started and given for three days without improvement. His condition went gradually downhill, and he died on the 54th hospital day.

The final clinical diagnosis was metastatic carcinoma to lung and bone, primary site unknown.

Postmortem Observations.—There were no adhesions or fluid in either pleural space. The pleural surface of the lung was studded with nodules varying to 2 cm. in diameter. These were yellow, slightly raised, and roughly rounded in outline. The cut surface of the lung showed these nodules to be scattered throughout both lungs and varying to 4 cm. in diameter. The right lower bronchus opened into a cavity about 2 cm. in diameter which was filled with necrotic material. The right upper bronchial site of tumor tissue was not discovered.

Interstitial fibrosis was present throughout the lung, with areas of chronic pneumonitis. In addition, there was an area in the upper part of the middle lobe of the right lung which was dark red and noncrepitant, measuring about 2 cm. in diameter. This resembled infarct in the gross, but on microscopic section it was seen to be atelectasis and pneumonitis. At the upper pole of the right kidney, a nodule measuring 2 cm. in diameter was noted. This was raised, rounded, firm, and yellow. A similar nodule was observed in the lower pole of the left kidney. Several swollen nodules were seen scattered through the remainder of both kidneys.

In each frontal lobe of the brain was seen an oval-shaped area, 2 cm. in diameter, containing small hemorrhages, which was slightly paler than the surrounding tissue. These areas were surrounded by a small area of softening.

In the liver occasional small, white, discrete nodules were noted. The largest of these measured 0.5 cm. in diameter.

The other organs appeared normal.

Microscopic Study.—The neoplasm was composed of loosely arranged cells, irregular in shape, varying in size, and staining quite markedly. Many mitoses were seen. There was no regular arrangement of these cells into any pattern. These cells were mingled in an unusual manner with plasma cells, lymphocytes, and fibroblasts, and many giant multinuclear cells were noted. Large areas of necrosis were seen throughout the lung.

Typical club-shaped brown asbestos bodies were seen throughout the lung in the tumor and outside the tumor areas.

Metastases observed in the kidneys, brain, and liver showed a similar histological appearance, including extensive areas of necrosis.

Chemical examination yielded 30 mg. of silicon dioxide per 100 gm. of tissue.

The final diagnoses were (1) anaplastic carcinoma of the lung with possibility of multicentric origin, with metastases to kidney, brain, and liver, and (2) pulmonary asbestosis.

COMMENT

The diagnosis of pulmonary asbestosis is based primarily on a history of a long exposure to asbestos dust. The most consistent complaint is dyspnea. Other symptoms are a chronic cough, weight loss, fatigue, and occasionally chest pain. Examination of sputum may disclose asbestos bodies. A roentgenogram may reveal little or show a haziness only.

In regard to the mechanism of the malignant change in asbestosis, it is questionable whether the silicate in asbestos itself is directly carcinogenic or whether the silicate causes bronchiectasis with metaplasia due to irritation of the bronchial epithelium, thus leading to carcinoma. The former mechanism seems significant, since this high an incidence of carcinoma does not occur in other forms of silicosis, though they do tend to produce an equivalent degree of bronchitis and bronchiectasis.

CONCLUSIONS

A case of bronchogenic carcinoma in association with pulmonary asbestosis is presented.

The importance of this association of carcinoma in cases of asbestosis is indicated from the review of the literature presented.

This association emphasizes the hazards of industrial exposure, the compensability of the cancerous process as well as the asbestosis, and the need of careful preventive measures.