Virchows Arch [Pathol Anat] (1981) 393:353–357

Virchows Archiv A

Case Report

Primary "Adenosquamous" Mesothelioma of the Pleura

W.S. Kwee[1], R.W. Veldhuizen[1], R.P. Golding[2], and R. Donner[1]
Departments of Pathology[1] and Radiology[2], Free University Amsterdam, The Netherlands

Summary. The case of a 64-year-old man with "adenosquamous" mesothelioma of the pleura is described. These two elements were intimately associated, which suggested that they formed an integral part of the tumor. To the authors, pluripotentiality of the mesothelium seems essential for the pathogenesis of this unusual neoplasm.

Key words: Mesothelioma – Pleural neoplasms – Pathology

Introduction

The microscopic features of mesothelioma create diagnostic problems because of their diversity, varying from epithelioid forms resembling carcinoma on the one hand, to mesenchymal or sarcomatoid tumors on the other. Epithelioid types are in the majority; pure sarcomatoid forms are the least common. The coincidence of epithelioid and mesenchymal differentiation, the so-called mixed or biphasic form, may serve as a clue to diagnosis in about one-fourth of the cases but these must be distinguished from other tumors of mixed histology (Hourihane 1964; Whitwell and Rawcliffe 1971; Shearin and Jackson 1976; Kannerstein and Churg 1977). These various expressions are attributable to the pluripotentiality of the mesothelial cells (Klemperer and Rabin 1937). Cases of squamous cell carcinoma in metaplastic pleura are described (Ender 1966; Willen et al. 1976; Rüttner and Heinzl 1977; Koss 1979). The incidence of primary pleural squamous cell carcinoma is certainly small. We describe a case of an epithelial mesothelioma of the pleura with a histological feature of "adenosquamous" neoplasm.

Clinical Data

A 64-year-old man was admitted to the hospital with a 6-month history of cough productive of yellow-green sputum and dyspnoea on effort for about 4-months. There was no history of

Offprint requests to: W.S. Kwee M.D., Department of Pathology, Free University Amsterdam, De Boelelaan 1117, 1007 MB Amsterdam, The Netherlands

0340-1227/0393/0353/$01.00

haemoptysis. He become orthopnoeic. His symptoms of orthopnoea and dyspnoea on effort gradually increased. He had worked as a furniture maker for about 33-years and he was uncertain about asbestos exposure. He smoked 12 cigarettes daily.

Physical examination revealed the signs of right sided pleural effusion.

Laboratory studies presented a moderate leucocytosis with shift to the left and ESR of 49 mm/h. A variety of biochemical studies of the blood showed pCO_2 48 mm Hg, base excess +2, creatinine 1.54 mg%, uric acid 6.8 mg%, alkaline phosphatase 3.2 mmol Bessey. The other values were within normal limits. The ECG was normal.

Serial *chest films* showed a large right pleural effusion gradually increasing with time. There was slight shift of the trachea to the right. No other pulmonary, pleural, bony or mediastinal features were evident. An IVP showed a reduction of calyceal excretion and a thin lobulated cortex of the right kidney: features suggestive of chronic pyelonephritis. The left kidney was normal with slight compensatory hypertrophy. Barium examinations of the stomach and colon were interpreted as normal.

The *sputum cytology* showed no malignant cells. The cytological diagnosis of the pleural effusion showed malignant cells, compatible with squamous cell carcinoma. Pleural biopsy confirmed squamous cell carcinoma. Bronchoscopy revealed deviation of the distal part of the trachea to the right. The right upper lobe bronchus was narrowed due to compression and the right lower lobe bronchus was laterally displaced. The mucosa showed no sign of malignancy, cytological examination of the bronchoscopical specimen also showed no malignancy. A diagnosis of squamous cell carcinoma of the right lung with pleuritis carcinomatosa was adopted.

The patient died despite chemotherapy and radiotherapy.

Results

Autopsy Findings. All the main airways were patent and mucoid secretions were present in various quantities. The lung parenchyma was congested on sectioning. There was no pulmonary fibrosis present on naked eye examination. On the right side, both parietal and visceral layers were grossly thickened. The right lung was collapsed and encased by hard white tumor of a thickness varying from 1 to 1.5 cm that had also invaded the right leaf of the diaphragm. The right hilar glands were enlarged and involved by tumor tissue. The appearance of the left lung was abnormal and showed multiple metastases with a diameter about 0.5 to 1 cm (Fig. 1).

Abdominal examination revealed enlarged para-aortic lymph nodes above the level of the renal arteries. The right kidney appeared hypoplastic with slight hydronephrosis, and the left kidney was hypertrophied. There was no other evidence of neoplasia.

Microscopic Findings. Microscopically, the tumor cells of the right pleura for the most part were pleomorphic and in many areas were relatively large and squamoid. The cytoplasm was abundant, deeply acidophilic and coarsely granular with well defined cell borders and hyperchromatic nuclei. Many mitotic figures were present. Intercellular bridges were identifiable. These portions of the tumor were intermengled with cell nests consisting of cells of smaller size and mucosubstance in and around these cells.

Sections of the tumor were stained with Alcian Blue at pH 2.5. In addition, sections were incubated with hyaluronidase from streptomyces hyalurolyticus (200 turbidity reducing units per 0.5 ml) in 0.02 M acetate buffer (pH 5.0) at 40° C for 2 h. There was marked reduction of Alcian Blue positivity after streptococcal hyaluronidase incubation.

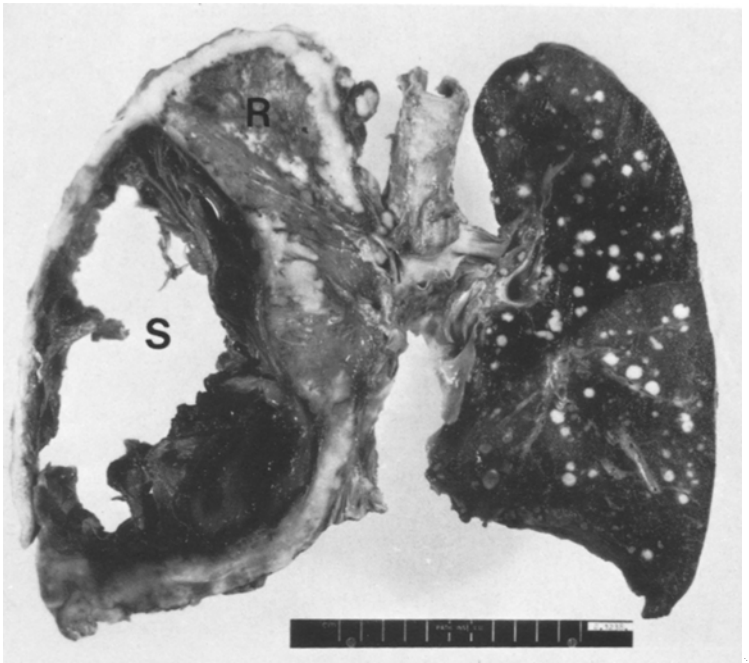

Fig. 1. Frontal slice of the right and left lungs, showing tumor involving the whole pleural surface of the collapsed right lung (*R*) with blood clot in pleural space (*S*). The left lung shows multiple metastases

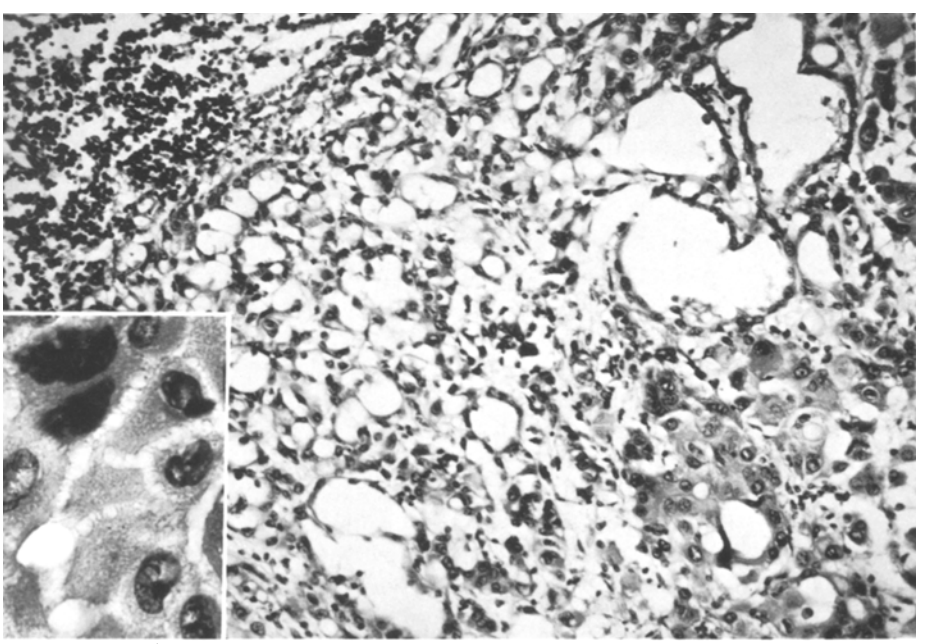

Fig. 2. Photomicrograph of lymph node tissue showing the metastases of two histological patterns. H+E, ×132. *Inset:* intercellular bridges. H+E, ×528

Many metastatic neoplastic deposits were present in the left lung and in hilar glands with two distinct malignant histological patterns (Fig. 2); one was the malignant squamous cell and the other was a more or less adenoid pattern with hyaluronic acid production.

The lung tissue showed no evidence of asbestosis and ferruginous bodies were not seen. There was a moderate deposition of carbon and haemosiderin particles. Three grams of pulmonary parenchyma was processed for ferruginous bodies, by the method of Smith and Naylor (1972). There were no ferruginous bodies observed in the filtrate.

Discussion

Mesothelioma is related to exposure to asbestos. An interesting piece of etiological evidence has come from the induction of tumors of mesothelioma histology after inoculation of experimental animals with asbestos fiber (Wagner and Berry 1969) but there are cases of mesothelioma without evidence of occupational exposure to asbestos (Roberts and Irvine 1970; Hasan et al. 1977; Vianna and Polan 1978). In this case there were no ferruginous bodies observed.

A feature that is of diagnostic value in many cases is the capacity of mesothelial cells to secrete the acid mucopolysaccharide, hyaluronic acid. This substance is not produced by tumors of intrinsically epithelial origin and its demonstration in tissue by chemical or histochemical methods can be decisive in diagnosis. Conversely the presence of neutral mucin as produced by native epithelial cells and adenocarcinomas and not by mesotheliomas excludes the diagnosis of the latter (Kannerstein et al. 1973). The presence of hyaluronic acid in the tumor was confirmed by means of histochemical methods and by application of hyaluronidase from streptomyces hyalurolyticus which is strictly specific for hyaluronic acid (Yamada 1973).

The histological picture of this tumor showed two elements: solid sheets of adenoid cells with hyaluronic acid production and squamous epithelial features. These latter included moderately differentiated squamous epithelium with malignant features and prominent intercellular bridging. Two separate neoplasms may have been present, an epithelioid mesothelioma and squamous carcinoma. This possibility cannot be excluded entirely but the intimate relationship of these two components both throughout all sections of the primary tumor encasing the right lung and also in the metastases in the contralateral lung and in the bilateral hilar lymph nodes is strongly against two different primary neoplasms.

Mesotheliomas arise from mesothelial cells and they possess the pluripotentiality of mesothelium. Liebow (1952) considered that squamous cell cancer was the most dubious form of pleural tumor. Mesothelium may give rise to metaplastic squamous features in conditions of chronic irritation and inflammation (Merlier and Orcel 1956; Ender 1966). Atypical squamous cell metaplasia may be difficult to differentiate from well differentiated squamous cell carcinoma.

Adenocarcinoma with a malignant squamous component has been described in many organs where adenocarcinomas commonly occur. For such tumors, various terms, such as adenoacanthoma, adenocarcinoma with squamous meta-

plasia, mucoepidermoid carcinoma and adenosquamous carcinoma have been applied. So, of these terms "adenosquamous" mesothelioma, meaning that the tumor contains both malignant glandular and malignant squamous elements, seems the most acceptable in this case (Poulsen et al. 1975). In adenoacanthomas the squamous part is considered to be metaplastic with benign features, whereas in adenosquamous carcinoma the squamous component is also thought to be malignant. Probably the pathogenesis of this tumor is related to the pluripotentiality of the mesothelial cells.

Because the pathogenesis of this tumor has yet to be ascertained, we feel that the term "adenosquamous mesothelioma" is most appropriate for the present.

Acknowledgments. Our thanks to Messrs. G.J. Oskam and J.T. van Veldhuisen for the photographs.

References

Ender A (1966) Ein Beitrag zum primären Pflasterzellkarzinom der Pleura nach extrapleuralem Pneumothorax. Thesis, University of Zürich

Hasan FM, Nash G, Kazemi H (1977) The significance of asbestos exposure in the diagnosis of mesothelioma: A 28-year experience from a major urban hospital. Am Rev Respir Dis 115:761–768

Hourihane DO'B (1964) The pathology of mesothelioma and analysis of their association with asbestos exposure. Thorax 19:268–278

Kannerstein M, Churg J (1977) Peritoneal mesothelioma. Human Pathol 8:83–94

Kannerstein M, Churg J, Magner D (1973) Histochemistry in the diagnosis of malignant mesothelioma. Ann Clin Lab Sci 3:207–211

Klemperer P, Rabin CB (1937) Primary neoplasms of the pleura. A report of five cases. Arch Pathol 11:385–412

Koss LG (1979) Diagnostic cytology and its histopathologic bases, 3rd edn. JB Lippincott Company, Philadelphia, Toronto

Liebow AA (1952) In: atlas of tumour pathology, Sect V, fasc 17: Tumours of the lower respiratory tract, Armed Forces Institute of Pathology, Washington, p 177

Merlier M, Orcel L (1956) Pachypleurite chronique avec revêtement épithelial des deus feillets de la plévre. La Semaine des Hôpitaux de Paris. Arch Anat Pathol 32:127–128

Poulsen HE, Taylor CW, Sobin LH (1975) Histological typing of female genital tract tumours. World Healt Organization, Geneva, p 59

Roberts GH, Irvine RW (1970) Peritoneal mesothelioma. Br J Surg 57:645–650

Rüttner JR, Heinzl S (1977) Squamous-cell carcinoma of the pleura. Thorax 32:497–500

Shearin JC, Jackson D (1976) Malignant pleural mesothelioma: Report of 19 cases. J Thorac Cardiovasc Surg 71:621–627

Smith MJ, Naylor B (1972) A method for extracting ferruginous bodies from sputum and pulmonary tissue. Am J Clin Pathol 58:250–254

Vianna NJ, Polan AK (1978) Non-occupational exposure to asbestos and malignant mesothelioma in females. Lancet 1 (8073):1061–1063

Wagner JC, Berry G (1969) Mesothelioma in rats following inoculation with asbestos. Br J Cancer 23:567–581

Whitwell F, Rawcliffe RM (1971) Diffuse malignant pleural mesothelioma and asbestos exposure. Thorax 26:6–22

Willen R, Bruce T, Dahlström G, Dubiel WT (1976) Squamous epithelial cancer in metaplastic pleura following extrapleural pneumothorax for pulmonary tuberculosis. Virchows Arch A Path Anat and Histol 370:225–231

Yamada K (1973) The effect of digestion with streptomyces hyaluronidase upon certain histochemical reactions of hyaluronic acid-containing tissue. J Histochem Cytochem 21:794–803

Accepted July 20, 1981