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Lymphogenous Spread of an Intravascular Bronchioloalveolar Tumour

Case Report and Review of Literature

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Summary. A 56-year-old lady with distinct clinical symptoms was found to have an intravascular bronchioloalveolar tumour. The aetiology and pathogenesis of this disease are unknown; both a bronchoalveolar and a vascular origin of the tumour are discussed in the literature. For the first time, lymphatic spread of tumour to the lymphatic nodes of the hili of the lungs was encountered.

Key words: Intravascular bronchioloalveolar tumour – Histological findings – Lymphatic spread.

Introduction

The intravascular bronchioloalveolar tumour is an uncommon clinical and pathological entity (Spencer, 1977). The clinical differential diagnosis of the tumour is difficult, its histological features are very characteristic and its aetiology is unknown. Recently a vascular origin of the tumour was postulated by Corrin et al. (1979), whereas Dail and Liebow (1975) considered the tumour to be of bronchioloalveolar origin.

The following report describes another case of intravascular bronchioloalveolar tumour. Histological investigations showed tumour masses in both lungs and in the regional lymph nodes. Our findings are compared with those in the literature.

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Case Report

A female patient, born in 1921, was found in June 1977 to have dysponoea and pretibial oedema, and had been suffering from a decrease of physical performance. In July 1977, multiple round lesions in both lungs were found on radiography. They were interpreted as metastases of a carcinoma of unknown origin. The Westergren sedimentation rate was highly accelerated (72/100 mm). The pulmonary airways expiratory resistance showed an increase. Clinically a primary carcinoma could not be found. Intravascular bronchioloalveolar tumour was detected histologically in a biopsy of the right lung (N: HD 33960/77). There was no specific therapy. In October and December 1977, growth of the pulmonary lesions was found. In addition, an enlargement of both lung hili was detected by radiography. In February 1978, the patient died following a myocardial infarction.

Autopsy Findings

At autopsy multiple small grey-white nodules up to 1.5 cm in diam. were found in the peripheral parts of both lungs. The lymphatic nodules of both lung hili were occupied by tumour. Other metastases were not found. The coronary arteries displayed moderate atherosclerotic lesions. The anterior-septal part of the myocardium was infarcted. Patchy fibrosis could be seen in other parts of the left cardiac muscle. The large conducting arteries were affected by atherosclerosis.

Methods

Tissue specimens taken from both lungs and the trachea were embedded in paraffin. 5 µm thick paraffin sections were stained with haematoxylin eosin, elastin van Gieson, Congo red, Masson-Goldner's stains and by the periodic acid-Schiff reaction.

For electron microscopy, some formalin-fixed specimens were postfixed for 2 h with 1% OsO_4 and embedded in Epon® after washing. Ultrathin sections were stained with lead citrate and uranyl acetate. A Zeiss EM 9 was used for investigation.

Histological Results

The tumour nodules consisted of hyaline fibrous tissue with sparse vesicular cells containing large nuclei and pale-staining characteristics. The tumour occupied a large number of alveoli preserving the fibers of the alveolar walls (Fig. 1a). Central necrosis of tumour was seen. The tumour interstitium had PAS positive staining characteristics. Sometimes the lumina of small arteries, veins and bronchioli embedded in the tumour nodules were filled with tumour tissue (Fig. 2a and b). Elastin staining was helpful to demonstrate the well preserved vessel walls. In the periphery of the tumour nodules, protrusions of the alveolar wall consisting of a hyaline fibrous tissue were found. They were covered by hypertrophied alveolar epithelial cells. The tumour seemed to spread through the pores between the alveoli (Fig. 1b). The pulmonary tissue surrounding the tumor nodules was atelectatic. Non-specific round cell infiltrations were found in the vicinity of the tumour.

The lymph nodes and lymphatic vessels of both lung hili contained tumour tissue (Fig. 3a and b). The walls of the lymphatics were well preserved. In the lymph nodes the tumour displayed histological features which differed from those in the lung. The cellular elements were increased in number. The tumour cells were smaller and arranged in chains with gaps in between. The fibrous capsules of the lymph nodes were well preserved. In the central parts of the tumour large necrotic areas were found.

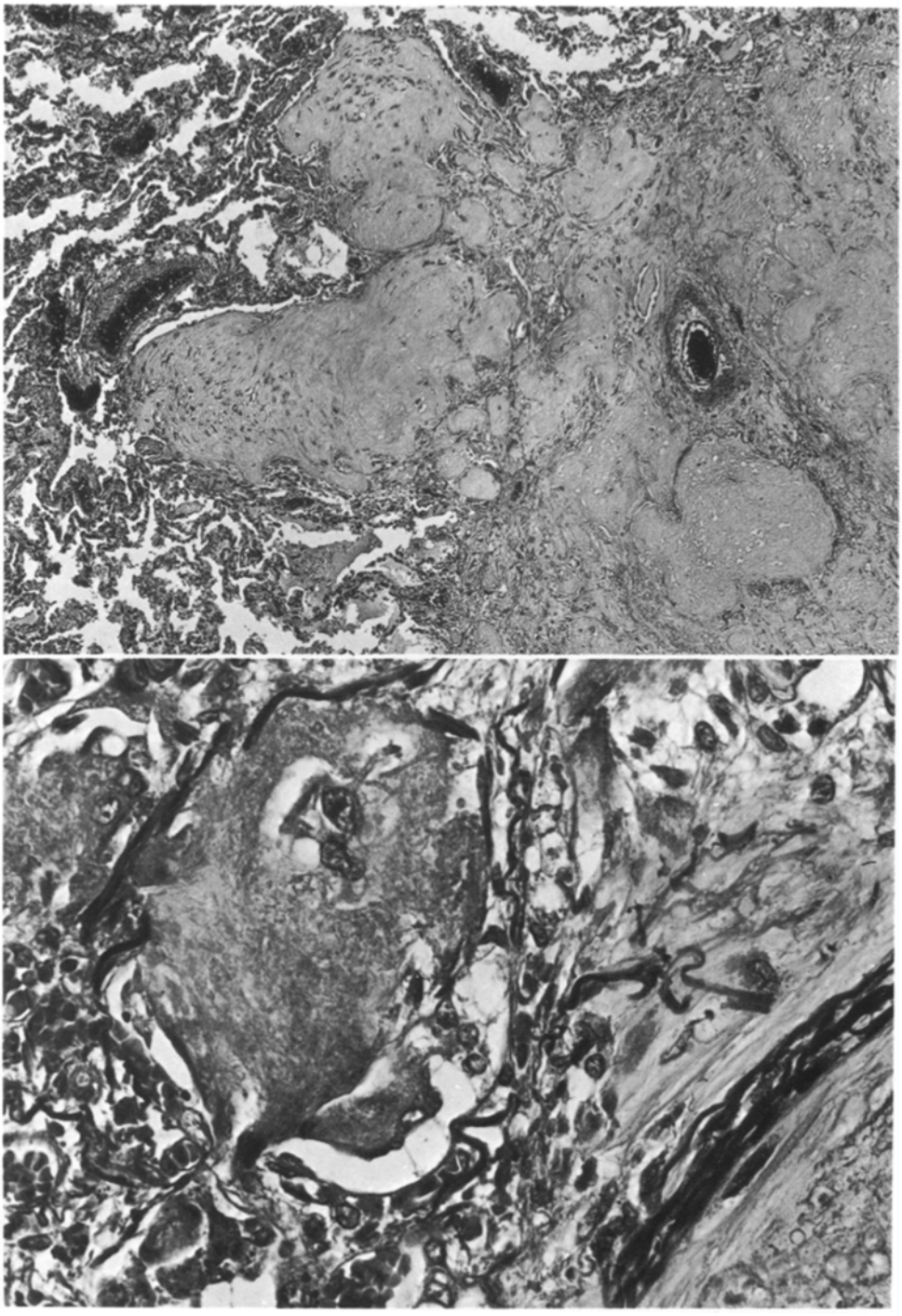

Fig. 1. a Photomicrograph, H.E. 1:40, right lung. Borderline of an intravascular bronchioloalveolar tumour lesion. The tissue contains broad interstitial spaces and few cells. The alveolar walls are recognizable. The tumour spreads in continuity. It is surrounded by atelectatic pulmonary tissue containing hyperemic capillaries. **b** Photomicrograph, EvG 1:350, right lung. Well preserved alveolar wall. The alveolus is filled with tumour tissue. Some of the alveolar cells are intact. The tumour displays contacts with other parts of the lesion through an alveolar pore

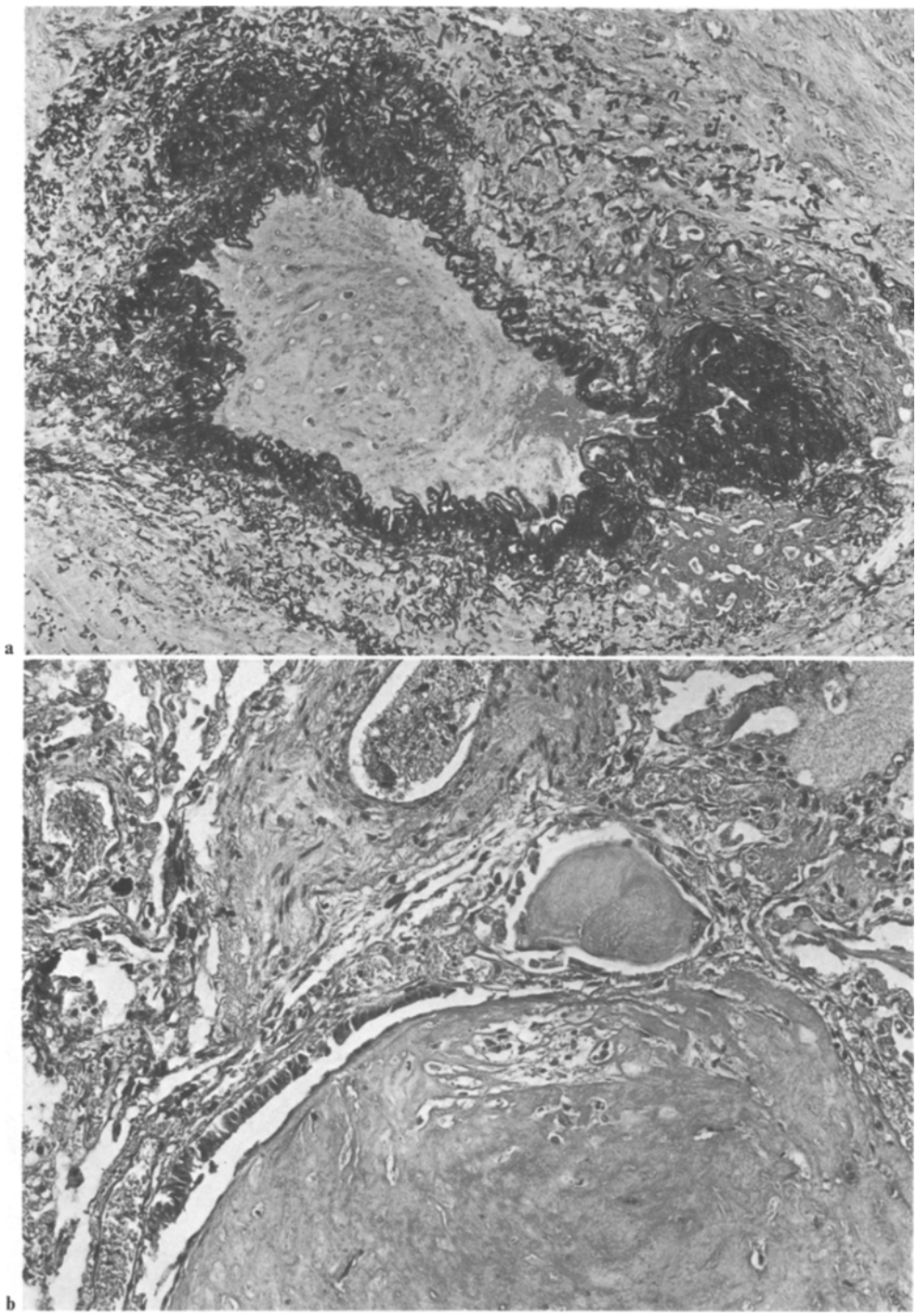

Fig. 2. **a** Photomicrograph, EvG 1:100, left lung. A small pulmonary artery is embedded in tumour. The elastic vessel wall components are well preserved. The lumen is completely occupied by the tumour. **b** Photomicrograph, PAS 1:150, right lung. A small bronchiolus is obliterated by typical tumour tissue. On the left, the bronchial epithelial cells are well preserved. The surrounding pulmonary tissue is atelectatic

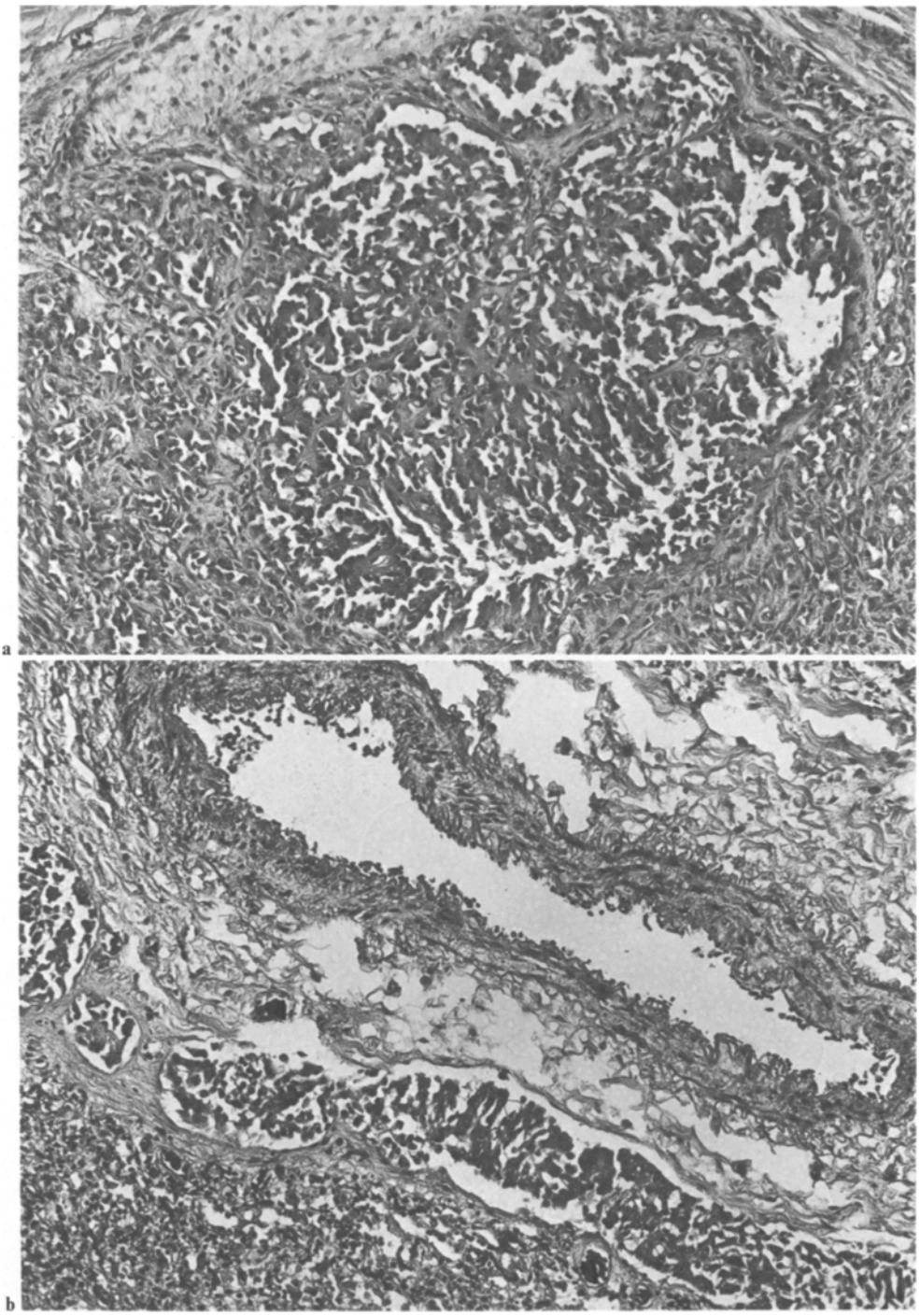

Fig. 3. a Photomicrograph, HE 1:150, lymph node of the left lung hilus. Infiltration by intravascular bronchioloalveolar tumour. The tissue appears trabecular and contains many clefts. Compared with the nodules found in the lungs, the number of cells is increased. The fibrous capsule of the node is well preserved. **b** Photomicrograph, HE 1:150, left lung hilus. A small lymphatic vessel in the vicinity of a pulmonary artery is occupied by intravascular bronchioloalveolar tumour. The histological features are similar to those in a. The wall of the lymphatic is well preserved

Because the specimens were kept in formaldehyde for a long period, the analysis of the tumour by electron microscopy was of minor value; the cells were autolytic, nuclei could be differentiated, but they displayed no specific characteristics. The cytoplasmic organelles were destroyed, large vacuoles found in the cytoplasm of the tumour cells did not permit any interpretation. In the interstitium a large amount of typical collagen fibers were found. They were partly arranged in bundles and partly haphazardly disseminated in the interstitial spaces.

Discussion

Farinacci et al. (1973) described so-called pulmonary deciduosis in a 28-year-old lady and Liebow commented that the lesion was better described as bronchioloalveolar tumour (compare Farinacci et al., 1973).

Dail and Liebow (1975) gave a survey of the characteristics of the tumour found in 20 cases accruing from 1962. Histologically, the epithelial-like tumour cells become more and more embedded in a hyalinized stroma during the course of tumour growth. In early stages, the stroma displays PAS-positive and Alcian blue staining characteristics. The central parts of the tumour nodules may undergo calcification (Table 1). In our case, the tumour stroma was focally PAS positive and Congo red negative. Calcification was not seen. The spread of the tumour inside small vessels and bronchioli with preservation of their fibrous walls, which was stated by Dail and Liebow (1975) to be highly characteristic for the intravascular bronchioloalveolar tumour, was found in our case. Tumour tissue was also detected in the regional lymph nodes of both lung hili and in the small lymphatics of both lungs, which may be interpreted as direct extension following infiltration of the pulmonary lymphatic system. No other metastases could be found in our patient although distant metastases in bones and liver were described by Liebow (citated by Corrin et al. 1979).

The clinical course of the disease in our patient was very characteristic for the intravascular bronchioloalveolar tumour. The correct diagnosis is usually only made following an open lung biopsy (Spencer, 1977). Often the tumour nodules are wrongly regarded as secondary deposits of a carcinoma as in the present case. Our patient was a female like most of the previous cases (Table 1). When compared with other reported cases, the growth of the tumour in our case seemed to be relatively fast, although death was caused by myocardial infarction. Usually the course of the disease is slow, and the patients may survive for up to 12 years, some have eventually died of subsequent pulmonary fibrosis (Dail and Liebow, 1975). Dail and Liebow suggested a bronchioloalveolar origin of the tumour, but as the ultrastructural features of smooth muscle, myofibroblast and endothelial cell differentiation were seen by electron microscopy, a vascular origin for intravascular bronchioloalveolar tumour from precursor mesenchymal cells (vasoformative reserve cells) was suggested by Corrin et al. (1979). We could not get any further information on the subcellular structure of our specimens by electron microscopy, although the collagen fibers of the interstitium were found to be well preserved. These results are in accordance with Spencer (1977). The clefts in the metastases of the hilar lymph

Table 1. Review of the cases of Intravascular Bronchioloalveolar Tumour described in the literature and their morphological characteristics (in accordance with Dail and Liebow, 1975; Spencer, 1977; Corrin et al., 1979)

Number of cases	Totally 26	Farinacci et al.	(1973)	1
		Dail and Liebow	(1975)	20
		Spencer	(1977)	2
		Corrin et al.	(1979)	3
Sex distribution	> 2/3 females			
Onset of the disease	4–70 years; > 1/3 of the patients < 30 years			
Time course of the disease	Up to 12 years			
Death rate	3 patients 2, 8 and 12 year from time of dicovery of the lesions			
Causes of death	Pulmonary insufficiency			
Morphological features				
Macroscopic characteristics	Multiple small nodules spread over both lungs			
Microscopic characteristics				
Initial change	Polyploidal protrusion of the alveolar wall by myxoid fibrous Tissue covered by hypertrophied type II alveolar epithelial Cells, lymphocytic infiltration of the alveolar interstitium			
Mature form	Hyalinous fibrous tissue with embedded scattered pale-staining Vesicular cells, filling the whole alveolus preserving the Alveolar walls, central necrosis and calcification			
Late form	Pulmonary fibrosis			
Spread of the tumour	Per continuitation along the bronchioloalveolar system, in The lumina of small arteries and veins preserving the fibrous Vessel walls			
Postulations of histogenesis	Bronchioloalveolar origin (Dail and Liebow, 1975) Vascular origin from vasoformative reserve cells Corrin et al., 1979)			

nodes of our case might be interpreted as an indicator of a vascular origin of the lesion.

Following the histological evolution of these tumours described by Spencer (1977) we classify our case as a mature late form of the tumour. Spencer considered the nomenclature of intravascular bronchioloalveolar tumour to be only descriptive and provisional and that when the true nature of the lesion was better understood it would almost certainly be renamed. Our case shows a new feature course of the disease – the possibility of infiltrating regional lymph nodes, which should be taken into consideration in future cases.

References

Corrin, B., Manners, B., Millard, M., Weaver, L.: Histogenesis of the so-called „intravascular bronchioloalveolar tumour". J. Pathol. **128**, 163–167 (1979)

Dail, D., Liebow, A.A.: Intravascular bronchioloalveolar tumour. Am. J. Pathol. **78**, 6a–7a (1975)

Farinacci, C.J., Bluaw, A.S., Jennings, E.M.: Multiple pulmonary lesions of possible decidual origin (so-called pulmonary deciduosis) Report of a case. Am. J. Clin. Pathol. **59**, 508–515 (1973)

Spencer, H.: Pathology of the lung, Volume II, pp. 907–908, 3rd Ed. Oxford-New York-Toronto-Sydney-Paris-Frankfurt: Pergamon Press 1977

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