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Giant fibroma of the lung

A morphological study

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Summary. The authors report the case of a 78-year-old male patient with an inoperable giant lung tumour diagnosed 5 years prior to death. Fine needle cytological examination at that time was interpreted as indicative of malignancy. In the following years the tumour grew very slowly without signs of infiltration or metastatic spread. On radiological examination sharp limitation of the tumour was evident. Recurrent pleural effusions occurred and the patient died from cardiorespiratory insufficiency.

Autopsy revealed a giant fibroma, well vascularized but without signs of malignancy. The diagnosis was confirmed by immunohistochemical and electron microscopic examinations.

Key words: Lung fibroma – Immunohistochemistry

Introduction

Intrapulmonary fibromas are rare and uncommon mesenchymal lesions and constitute 2 to 7.5% of benign pulmonary tumours (Vogt Moykopf 1967). They are possible derived from cells of the fibrous lung stroma, the subpleural tissue, the bronchial wall or the interlobular visceral pleura (Eck et al. 1969; Michas 1953). Accordingly, they were classified as "pulmonary" and "pleural fibromas" by Spencer (1977).

Endobronchial fibromas are mostly small; pedunculated large tumours are rare (Schaudig 1970). Sizes vary between 1 cm in diameter up to a weight of 1 kg ("giant fibromas", Houyez 1938, Scheibe 1952). Most are located peripherally and there is no characteristic sex or age preference (Justich et al. 1976). At gross inspection, the gray-white firm tumours are well demarcated and the cut surface shows a fascicular and lobulated appearance. They are mostly richly vascularized, contain variable amounts of collagen fibres and fibroblast-like tumour cells. Highly cellular tumours are differentiated with great difficulty from sarcomas or neurogenic tumours, particularly in adolescent patients (Albertini 1955; Galy and Touraine 1965). Degenerative changes, like hyalinosis, calcification and cystic transformation are frequent (Liebow 1952; Scheibe 1952; Spencer 1977).

Malignant transformation is extremely rare (only 2 uncertain cases are described; Lyssunkin 1935; Scheidegger 1932).

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Case report

A 78 year old male patient was admitted to the hospital with dyspnoea and dry cough. At radiological examination of the thorax, first done 4 years prior to death, an opacity 10 cm in diameter was discovered in the lower lobe of the left lung, without connection with the pleura. The lesion did not involve the pleura, suggesting an intrapulmonal tumour. A fine needle biopsy was performed and the cytological pattern was considered to be malignant. Because of the large size of the tumour surgical intervention was not attempted, and conservative symptomatic therapy was initiated. Three years later radiological examinations revealed tumour progression towards the mediastinum, the pleural cavity and the upper lobe of the left lung. The general state of health was satisfactory. During the year prior to death the patient suffered from recurrent haemorrhagic pleural effusions and complained of pain in the left thorax, decreased appetite and loss of weight. During this time the tumour occupied about 80% of the left thoracic cavity. The cranial limitation was sharp. The mediastinal organs were displaced to the right. Finally, the patient suffered from intense dyspnoea, vertiginous attacks and convulsions, and brain metastases were suspected. He died of cardiorespiratory insufficiency.

At autopsy no metastases were found. There were signs of right ventricular failure with conspicuous venous enlargement. A well circumscribed tumour arising from the lower lobe of the left lung (Fig. 1a) filled the whole left thoracic cavity and displaced the mediastinal structures toward the right

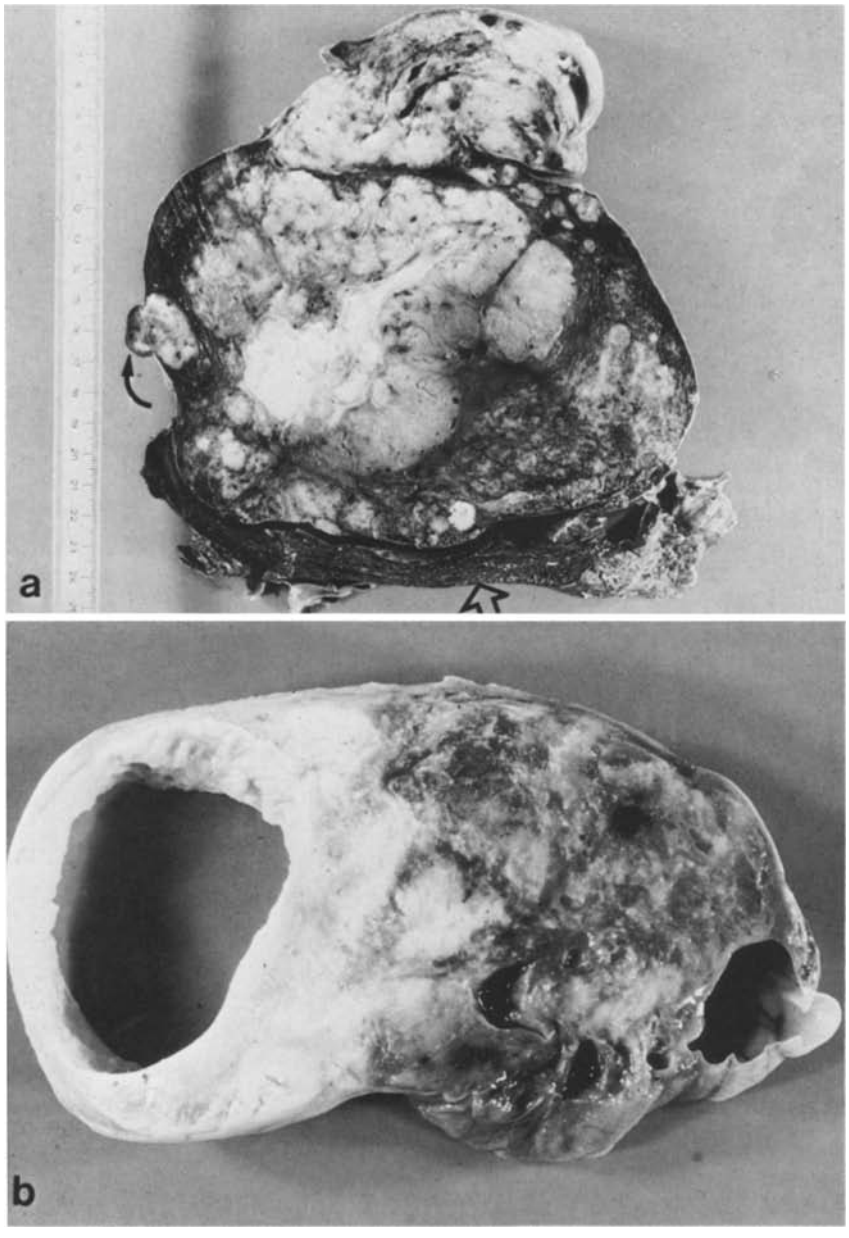

Fig. 1. a Gross section of the lung tumour: Note the fungiform process protruding from the surface of the tumour (curved arrow). Atelectatic lung tissue from the upper lobe partly covers the tumour mass (straight arrow). **b** Note cystic degeneration of the tumour simulating an echinococcus cyst. Part of the tumour is covered by visceral pleura

(Fig. 1, arrow). The tumour weighed 2,250 gm. It arose from the central portion of the left lung. A few fungiform processes covered by visceral pleura protruded from its surface and cystic spaces filled with gelatinous, yellow-white material were also seen (Fig. 1 b). The inner surface of the cysts were irregular. Cut surfaces showed gray-white tissue with areas of necrosis, haemorrhage, hyalinosis, and dense fibrosis. Bronchi could not be detected within the tumour. The vessels and the main bronchus at the hilum were compressed. There were no signs of infiltrative growth.

Methods

For histological studies tumour specimens were fixed in 10% buffered formaldehyde solution (pH 7.4), dehydrated in a series of graded alcohol and embedded in paraffin. 5 μm thick sections were stained with haematoxylin-eosin, van Gieson, periodic acid Schiff reagent, Congo red, Massons trichrome, Gomori and by Bodian's silver impregnation-method.

For electron microscopic examination specimens were fixed in 3% glutaraldehyde solution (in 0.1 M cacodylate buffer) for 2 h, washed thereafter in cacodylate buffer (0.1 M, pH 7.2) and precontrasted in 1% osmium tetroxide. After dehydratation in a series of graded alcohol the tissue blocks were embedded in Epon 812. Semithin sections were stained in alcoholic solution of toluidin-blue and ultrathin sections (Reichert OM U_2) were examined using a Philips EM 400 electron microscope.

For immunohistochemistry deparaffinized 5 μm thin sections were pretreated with 0.1% Pronase (Protease Typ VII, Sigma Chemical Comp. St. Louis MO, USA) for 20 min, washed in ice cold TRIS buffer (pH 7.6) and incubated with the following antibodies: rabbit-anti-human vimentin (Euro-

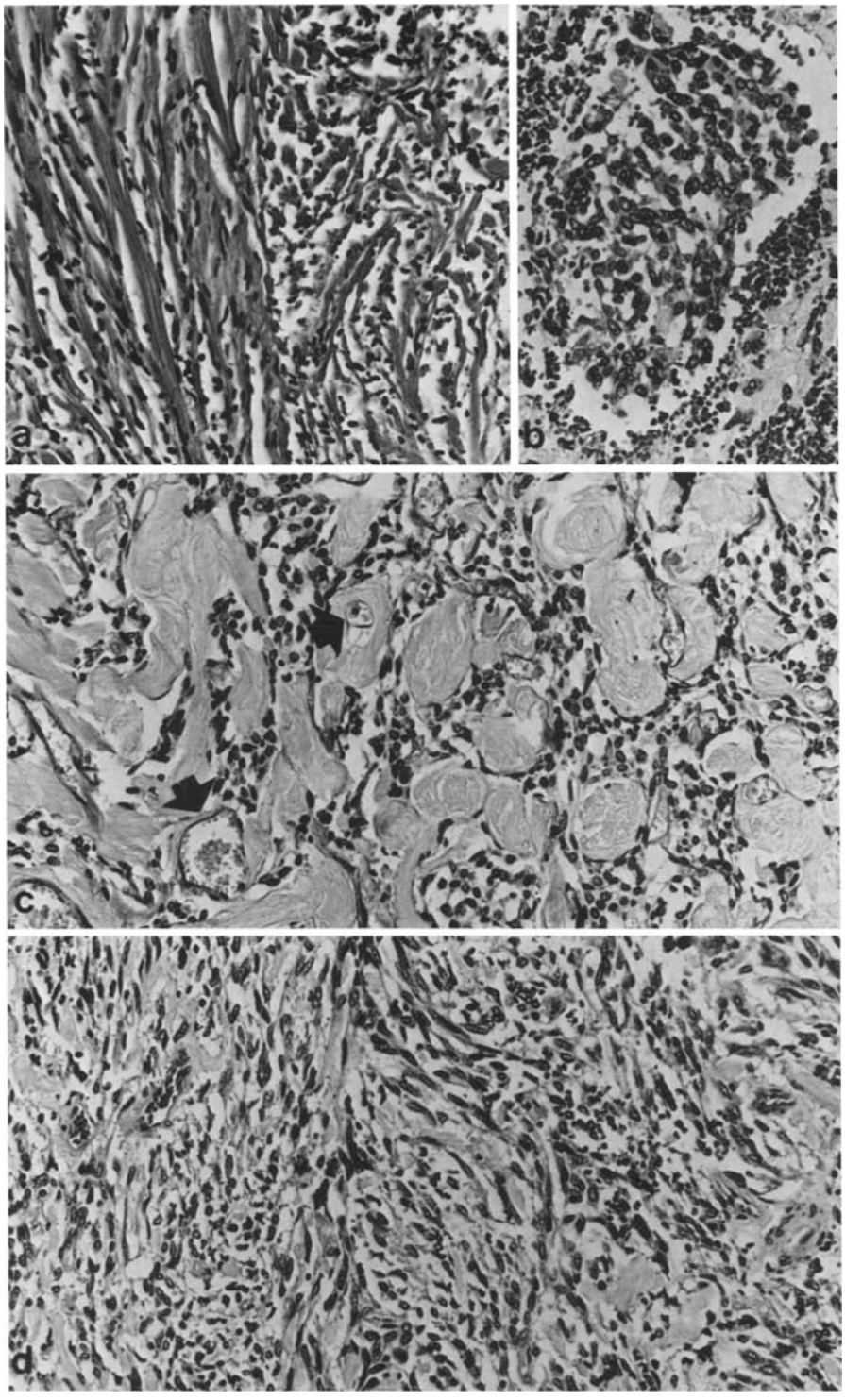

Fig. 2. a Tumour area mostly consisting of spindle cells arranged in interlacing fascicles with interspersed collagen fibre bundles. **b** Richly cellular area consisting of round cells with epitheloid phenotype and arrangement surrounded by lymphocytic infiltrate. **c** Thick hyalinized collagen fiber bundles are surrounded by tumour cells with round or oval nuclei, vessels are often present in the centres of the collagen fiber bundles (*arrows*). **d** Richly cellular tumour area simultating a storiform pattern. The tumour cells are arranged in fascicles and whorls. H & E, magnification 250 ×

diagnostics, Apeldoorn, NL), monoclonal mouse-anticytokeratin (Lab. System, Helsinki), rabbit-anti-lysozym (Dako, Copenhagen, Denmark), rabbit-anti-human F. VIII-antigen (Dako, Copenhagen, Denmark), rabbit-anti S-100-Protein (Dako, Copenhagen, Denmark), rabbit-anti-NSE (Dako, Copenhagen, Denmark), mouse-anti-neurofilament (kindly provided by J. Virtanen, Helsinki), rabbit-anti-human-Alpha$_1$-Antichymotrypsin (Dako, Copenhagen, Denmark), rabbit-anti-Alpha$_1$-Antitrypsin (Behring-Werke Marburg, Germany), mouse-anti-human-EMA (epithelial membrane antigen, Dako, Denmark), without pretreatment with pronase. Binding of primary antibodies was assessed with the ABC-method developed with 0.05% diaminobenzidine (DAB; Serva-Feinbiochemica, Heidelberg) and 0.01% H_2O_2 in 0.25 M TRIS-HCL-buffer (Hsu 1981). All antibodies were diluted with PBS containing sodium azide (2%) and human serum albumin (0.25%). After 5 min the specimens were washed with PBS and the DAB reaction was intensified with 1% osmium tetroxide for 10 sec.

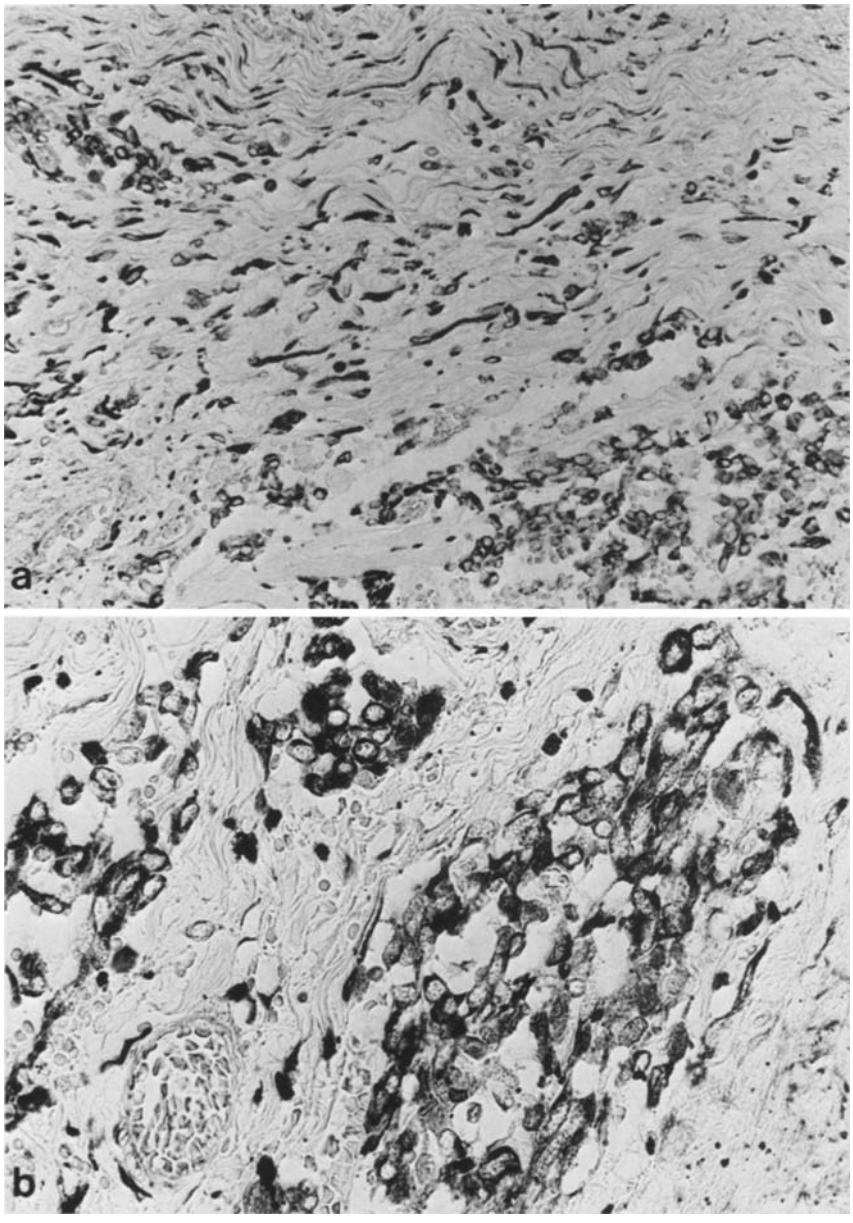

Fig. 3a, b. Demonstration of vimentin content in tumour cells of different morphology (spindle cells in upper left part of (**a**) cells with epitheloid morphology in lower right part of (**a**) and (**b**)). Note intensive staining of cytoplasmic processes of spindle cells (**a**). ABC method, (**a**) 250×, (**b**) 350×

Results

Histological examination revealed a richly cellular tumour with tumour cells arranged in fascicles and whorls. Most of the nuclei were oval or round, no mitoses, nuclear or cellular polymorphism, or nuclear hyperchromatism were present. Between the tumour cells there were collagen fibres and a few reticulin fibres. The tumour contained small and large blood vessels (Fig. 2). Degenerative changes including haemorrhages and necroses were frequent. There were no signs of malignancy. Due to the huge size of the tumour its precise origin from lung stroma or peribronchial tissue could not be identified. The main mass was within the lung parenchyma, therefore origin from the visceral pleura seems improbable. The tumour was covered by visceral pleura, no pleural invasion was seen.

The aim of the immunohistochemical study was to elucidate the histogenetic origin of the tumour. The tumour tissue was characterized by a distinct positive reaction with vimentin antibodies (Fig. 3). The vascularization of the tumour could easily be demonstrated by immunostaining of endothelial cells with F VIII antibodies. Histiocytic markers (Lysozym, $Alpha_1$-Antitrypsin, and $Alpha_1$-Chymotrypsin) as well as several neurogenic markers (NSE, neurofilament and S-100 Protein) were absent. Cytokeratin and EMA-reactions were also negative.

By electron microscopy of fixed tumor tissue collagen fibrils were demonstrable around tumour cells. Nuclei were characterized by prominent nucleoli and excentric arrangement of chromatin. There were no desmosomes between tumour cells. Neural structures were not seen within the tumour. There were no features suggesting a vascular origin. Ultrastructural examination was limited due to poorly preserved autopsy material.

The ultrastructure as well as the immunohistochemical results support a mesenchymal origin of this tumour and confirm the histologically suggested diagnosis of a giant fibroma of the lung.

Discussion

Intrapulmonary fibromas, expecially the large ones, are rare benign tumours. Only a few examples of "giant fibromas" are reported in the literature (Houyez 1938; Scheibe 1952). Characteristically they are located peripherally and are well delimited from the surrounding structures of the lung and visceral pleura. Additional features of diagnostic significance are circumscribed degenerative changes. The radiological findings reflect the size of the tumour, its clear delimitation and structure (a predominance of cellular or fibrous components).

Discrimination of pulmonary fibromas from localized fibrous mesotheliomas is difficult on histological grounds alone. Benign fibrous mesothelioma can be excluded in this case, because it arises predominantly from fibrous connective tissue of the pleura and seldom invades the lung (Bürrig et al. 1983; Doucet et al. 1986; Mark 1984; Spencer 1977). Moreover, mesotheliomas also express cytokeratin in addition to vimentin (Blobel et al. 1985). In our case the tumour arose from the central portion of the lung and grew towards the inner layer of the visceral pleura. Numerous gross sections through the tumour revealed that the maximum tumour mass was within the lung parenchyma. A further argument in favour of an intrapulmonary origin of the tumour is the sequential X-ray examinations performed during the 4 year-period prior to death of the patient, which revealed progressive tumour growth starting from the center of the left lower lobe and expanding peripherally. In the early stages of tumour growth no connection with the pleura was noted. Consequently, at that stage of examination the tumour was regarded as bronchial carcinoma by the radiologist, but tumour cells were cytokeratin negative.

Our report demonstrates that cytological investigation alone is inadequate especially in this tumour type and a biopsy is necessary to confirm the diagnosis. It should also be emphasized that frozen section diagnosis may be very difficult. Only thin and multiple sections from paraffin-embedded material provide the quality of information which will lead to an exact classification. Immunohistochemistry aids in the classification of these tumours, especially by separating them from neurogenic, myogenic, vascular and histiocytic tumours.

Our study demonstrates that close cooperation of various medical disciplines (pathologists, radiologists and surgeons) is necessary to avoid misinterpretation, particularly with giant-sized tumours.

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