Virchows Arch [Pathol Anat] (1981) 394:167–176

Virchows Archiv A

Case Report

Malignant Fibrous Histiocytoma of the Lung

S.M. Paulsen[1], K. Egeblad[2], and J. Christensen[2]

[1] Institute of Pathology
[2] Department of Thoracic and Vascular Surgery, Aalborg sygehus, DK-9000 Aalborg, Denmark

Summary. A case of malignant fibrous histiocytoma of the lung is reported. The tumour margin was well circumscribed, showing an expanding border and no capsule. The main part of the tumour was composed of spindle-shaped fibroblast-like cells arranged in broad fascicles with a partially storiform pattern. Other parts of the tumour were arranged in a haphazard pattern, containing many mononucleated and multinucleated giant cells. Ultrastructurally six differnt cell types were encountered. The dominant type was a fibroblast-like cell; also present were many giant cells and some histiocyte-like cells, together with their intermediate forms, and few undifferentiated mesenchymal cells. We consider this tumour to have developed from the peribronchial connective tissue; it has the same cellular composition as the malignant counterpart arising in soft tissues.

Key words. Malignant fibrous histiocytoma – Sarcoma – The lung – Ultrastructure

Introduction

Primary sarcoma of the lung is a rare disease. Nine cases were collected from the Royal Infirmery in Edinburgh during a period of 18 years. In the same period 6,000 cases of bronchial carcinoma were encountered (Cameron 1975).

Malignant fibrous histiocytoma is now a well described and distinct form of soft tissue sarcoma, especially common in late adult life (Weiss and Enzinger 1978). Within recent years variations in the morphological pattern have been noted (Kyriakos and Kempson 1976; Weiss and Enzinger 1977; Enzinger 1979).

Only three cases of malignant fibrous histiocytoma of the lung have been reported and studied by electron microscopy (Kern et al. 1979, Bedrossian et al. 1979). The main purpose of this report is to describe the ultrastructure of

Send offprint requests to: S.M. Paulsen, at the above address

0340-1227/81/0394/0167/$02.00

a case of malignant fibrous histiocytoma of the lung, and to compare the findings with the ultrastructure of the same tumour type occurring in soft tissues.

Case Report

A 53-year old woman, who was a non-smoker, had always enjoyed good health. A routine X-ray of the chest was performed as a part of a health certification examination. The roentgenogram demonstrated a mass in the left lung, localized at the left heart border. On specific questioning she denied any pulmonary symptoms. The physical examination, blood and urine analyses were all normal. On 12/9/79 she underwent a left thoracotomy. A tumour was located centrally in the left lower lobe and a lobectomy was performed. The lymph nodes were free of metastases. The post operative period was uneventful, and she was discharged 11 days after surgery. The microscopic diagnosis was a malignant fibrous histiocytoma of the lung. She was followed as an outclinic patient, and 11 months after the operation an X-ray of the chest revealed a mass in the left upper lobe. A second thoracotomy was performed, and the tumour was removed. The histological pattern of this tumour was the same as the tumour removed from the left lower lobe. A throughout examination revealed no primary tumour or metastases elsewhere in the body. Six months after the second operation she is well and no further tumor tissue has been detected.

Materials and Methods

Tumour tissue from the first and second operation was fixed in 10% neutral buffered formalin, embedded in paraffin and sections were stained with hematoxylin-eosin, van Gieson-Hansen's connective tissue stain, Masson-trichrome and Gordon and Sweet's method for reticulin. Tumour tissue from the frist operation was fixed for electron microscopy in cacodylate-buffered 2.5% glutar-aldehyde, post-fixed in cacodylate-buffered 1% Osmium tetroxyde, dehydrated in ethanol and embedded in Epon. One μm sections for orientation were stained with toluidine blue and ultrathin sections were mounted on formvar coated copper grids and stained with uranyl acetate and lead citrate.

Results

Gross Pathology

The material consisted of a left lower lobe, containing a well demarcated tumour measuring 4 cm in its greatest diameter. The tumour was located close to the first division of the main lower lobe bronchus, but did not invade the bronchial wall. The tumour was rubbery-firm, and the cut surface was grey-tan and had a whorled fibroid appearance.

Light Microscopy

The tumour margin was well circumscribed showing a expanding border and no capsule (Fig. 1). At the periphery of the tumour, spaces lined by cuboidal or cylindrical epithelium which partly desquamated into the lumina, were seen (Fig. 1). These spaces were regarded as trapped pulmonary parenchyma within the tumour tissue. The sections revealed a tumour with a varied histological pattern. The main part of the tumour was composed of spindle-shaped fibroblast-like cells arranged in broad fascicles, with a partial storiform pattern (Fig. 2). The fibroblast-like cells had centrally placed nuclei and were surrounded by

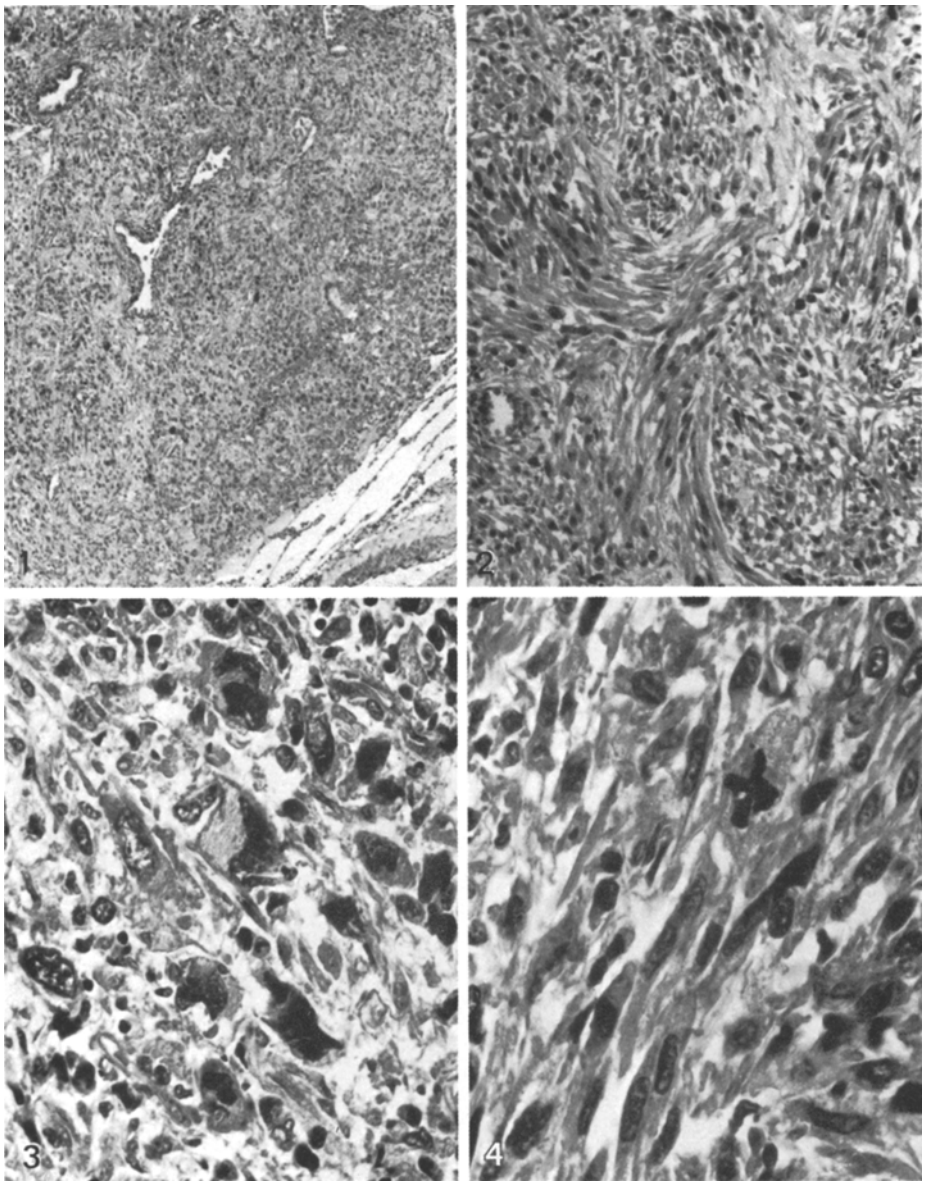

Fig. 1. Well circumscribed tumour margin showing a expanding border and no capsule. Spaces within the tumour tissue are regarded as trapped lung tissue. H & E ×40

Fig. 2. Spindle-shaped cells arranged in a storiform pattern. H & E ×100

Fig. 3. Bizzare giant cells arranged in a haphazard pattern. H & E ×250

Fig. 4. Spindle-shaped cells with an atypical tetrapolar mitosis. H & E ×400

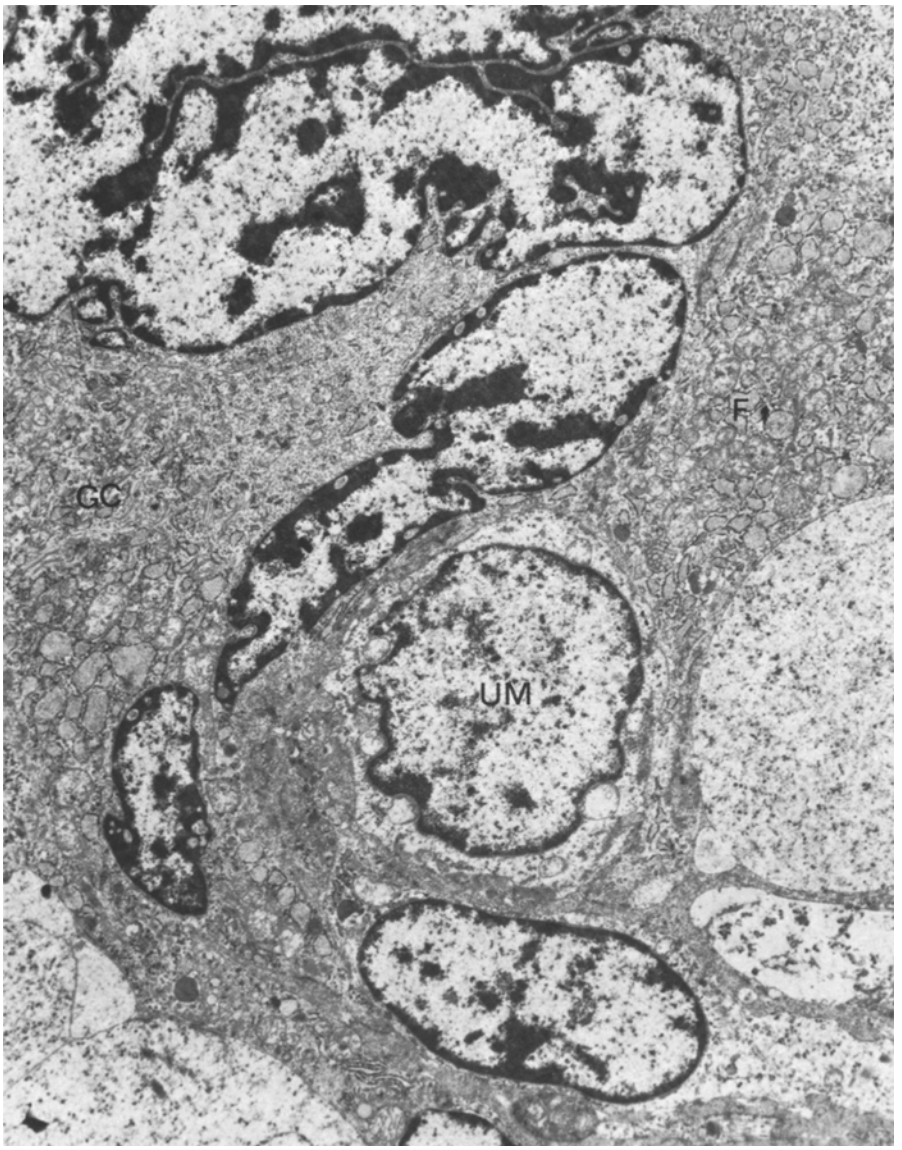

Fig. 5. Electron photomicrograph showing three different cell types. (*UM*) undifferentiated mesenchymal cell containing few cytoplasmic organelles. (*F*) fibroblast-like cells dominated by dilated rough endoplasmic reticulum containing granular material. (*GC*) part of a giant cell. H & E ×8,000

a sparse amount of collagen and reticulin fibres. Other parts of the tumour were arranged in a haphazard pattern, containing many mononucleated and multi-nucleated giant cells (Fig. 3). The nuclei of the giant cells were vesiculated with a coarse chromatin pattern and prominent nucleoli. Many mitoses, some atypical, could be demonstrated easily (Fig. 3 and Fig. 4). Very few xanthomatous cells were seen.

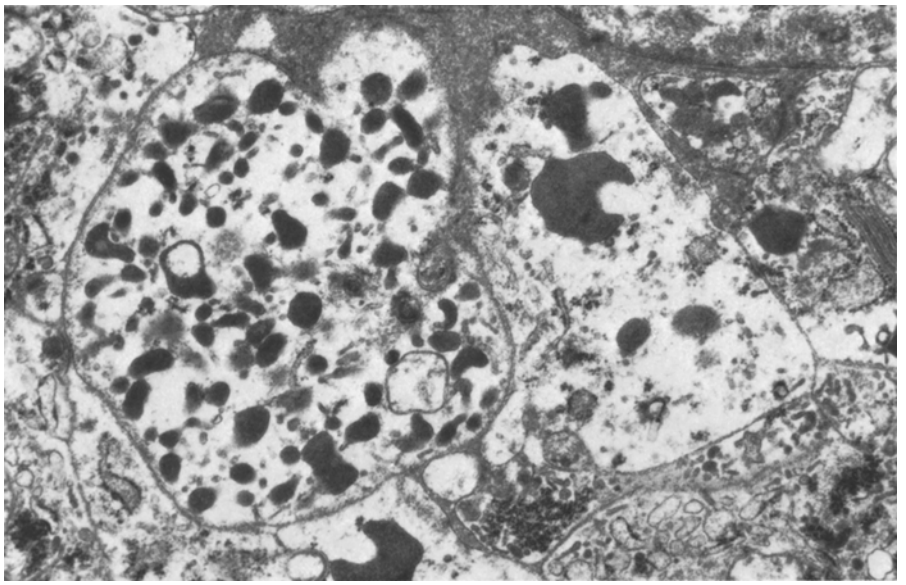

Fig. 6. Histiocyte-like cells containing large number of electron dense bodies of lysosomal character. H & E ×20,000

Electron Microscopy

Ultrastructurally, six different cell types were encountered.

The predominant cell was a fibroblast-like cell with a centrally placed nucleus, having a mostly smooth nuclear membrane and a prominent nucleolus. The cytoplasm contained abundant rough endoplasmic reticulum, often with dilated cisternae containing granular material, many ribosomes and mitochondria and a prominent Golgi apparatus (Fig. 5). A few undifferentiated mesenchymal cells with large nuclei containing a sparse amount of marginal heterochromatine were seen (Fig. 5). The cytoplasm contained scanty organelles, mostly ribosomes and polyribosomes, a few short rows of rough endoplasmic reticulum and occasional mitochondria. There were many giant cells with an irregular nuclear membrane showing deep cytoplasmic invaginations (Fig. 5). Some nuclei showed cytoplasmic pseudoinclusions. The plasma membrane was often ruffled with many cytoplasmic projections. The cytoplasm contained many ribosomes, mitochondria, abundant rough endoplasmic reticulum and many Golgi zones. There was a variable number of electron dense bodies of lysosomal character, localized in the peripheral part of the cytoplasm. Histiocyte-like cells often with a ruffled cell border containing numerous electron dense bodies of lysosomal character were found (Fig. 6). Two types of intermediate cells were encountered. The first, was a fibrohistiocyte containing a rich amount of granular endoplasmic reticulum as well as many electron dense bodies of lysosomal character (Fig. 7), and there was a myofibroblast with very much the same appearance as the fibroblast-like cells, but also containing filaments with dense bodies localized predominantly in the peripheral part of the cytoplasm close to the plasma membrane (Fig. 8). Between some tumour cells desmosome-like attachments were seen (Fig. 8). No xanthomatous cells were detected.

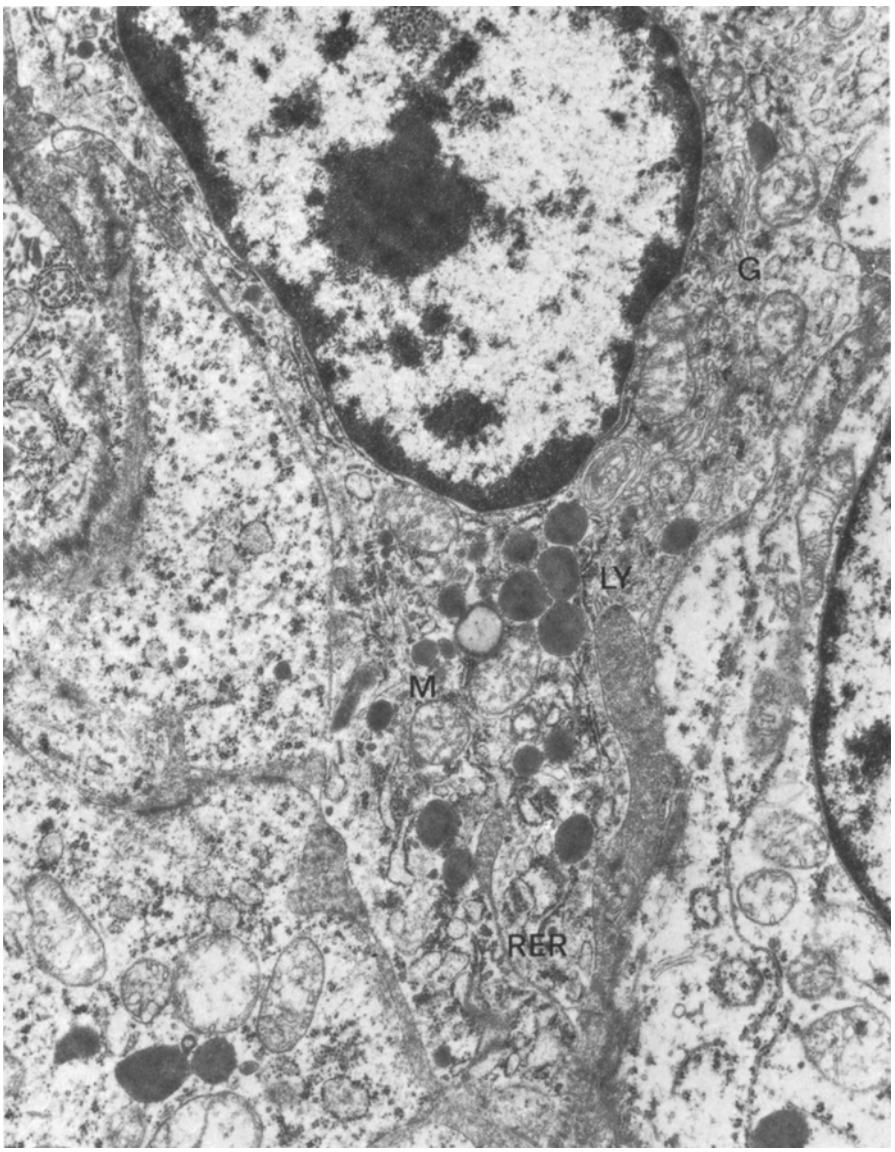

Fig. 7. Fibrohistiocyte containing round to oval mitochondria (*M*) rough endoplasmic reticulum (*RER*) large number of electron dense bodies of lysomal character (*LY*) and a prominent Golgi apparatus. (*G*) H & E ×20,000

Discussion

Only three cases of malignant fibrous histiocytoma of the lung have been reported. The clinical data of these cases have been set out in Table 1. From these reports, the impression is gained, that malignant fibrous histiocytoma of the lung is a serious disease, but definite conclusions as to the prognosis can only be drawn after further cases have been reported.

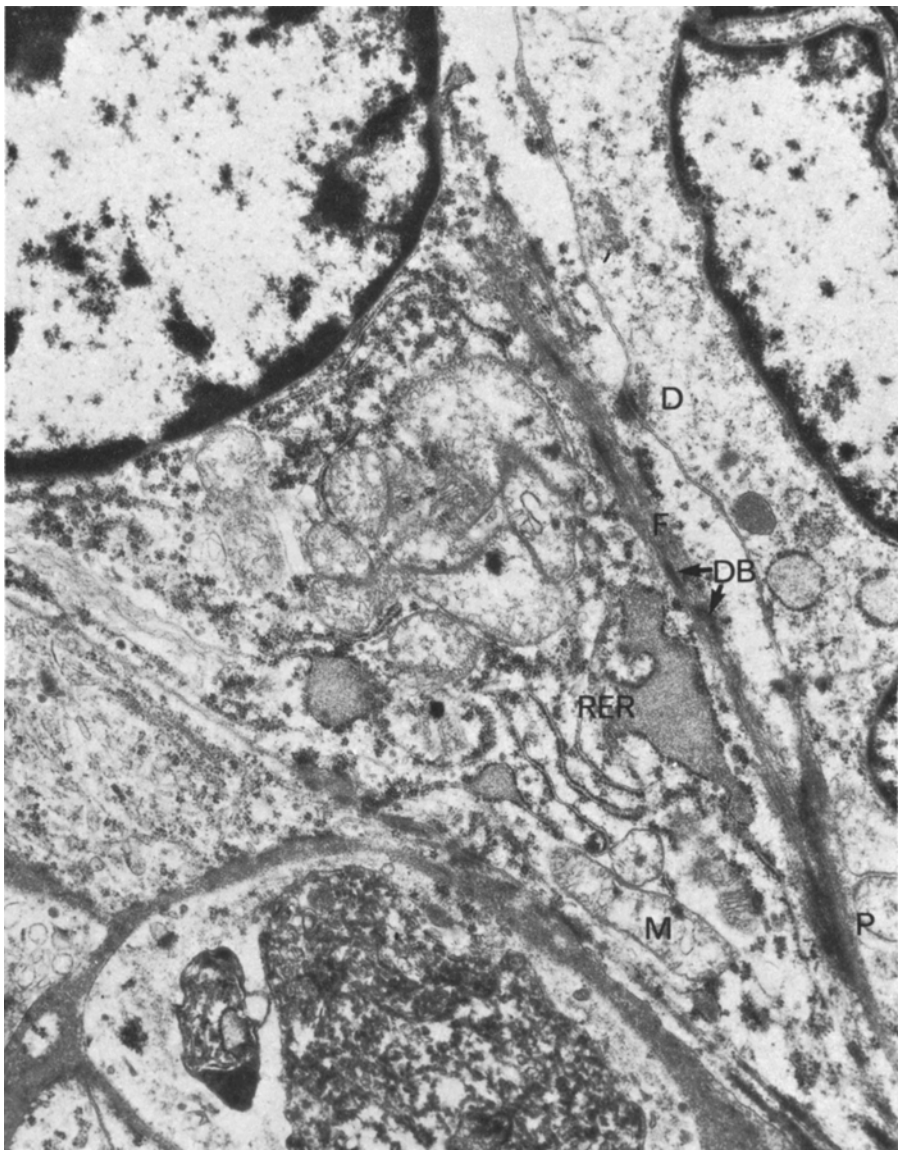

Fig. 8. A myofibroblast containing a large number of mitochondria (*M*), dilated rough endoplasmic reticulum (*RER*), and filaments (*F*) with dense bodies (*DB*) localized at the periphery of the cytoplasm. At the plasma membrane a plaque (*P*) and a desmosome-like attachment (*D*) between two adjacent cells are seen. H & E ×20,000

The cellular composition of the lung tumour reported here, which we have called a malignant fibrous histiocytoma of the lung, is in accordance with other descriptions of the electron microscopic appearances of malignant fibrous histiocytoma of soft tissues (Fu et al. 1975; Taxy and Battifora 1977; Harris 1980). The terms myofibroblast and fibrohistiocyte used by Harris (1980) are not mentioned by other authors (Fu et al. 1975; Taxy and Battifora 1977),

Table 1. Clinical data of four patients with malignant fibrous histiocytoma of the lung

Case/ref.	Age/ sex	Tumour location	Operation	Follow up
1. Bedrossian et al. (1979)	51/M	Right midlung and left lower lobe	Lobectomy, left lower lobe Tumour 2 × 2 cm	Radiotherapy to the right midlung. Died 12 months after the operation. No autopsy
2. Kern et al. (1979)	53/M	Right lower lobe	Lobectomy Tumour 8 × 6 cm	Four months postoperative a brain metastasis was removed. Reported alive
3. Kern et al. (1979)	25/F	Central part of the left lung	First operation tumourectomy, greatest diameter 3 cm Second operation left pneumectomy	Four months after the first operation (a.f.op.) symptoms of brain metastases. Twelve months a.f.op. left pneumectomy because of residual tumour. Fifteen months a.f. op. explorative thoracotomy. No residual tumour. Radiotherapy. Died 22 months a.f.op. Autopsy showed metastases in the right lung and in the brain
4. Present case	53/F	Right lower lobe	Lobectomy Tumour's greatest diameter 4 cm	Eleven months postoperative a solitar metastasis in the left upper lobe was removed. Six months after the second operation alive and well

but they describe cells of intermediate form corresponding to the myofibroblast and the fibrohistiocyte of Harris (1980).

The myofibroblast has been described in a number of different benign and malignant conditions e.g. Dupuytrens contracture (Gabbiani and Majno 1972), nodular fasciitis (Wirman 1976), circumscribed fibromatosis (Feiner and Kaye 1976), fibrosarcoma in the male breast (Crocker and Murad 1969) and myofibroblastic sarcoma (Vasudev and Harris 1978). Recently Lagacé et al. (1980) have advanced the hypothesis that the myofibroblasts observed within collagenized regions of soft tissue sarcomas may constitute an expression of a host response to neoplasia. The histogenesis of the myofibroblast is controversial. There seems to be three possibilities, that it is: 1) an undifferentiated mesenchymal cell, 2) a smooth muscle cell, or 3) a fibroblast. In an experimental study of avascular fibrous tissue, cells with features intermediate between fibroblasts and smooth muscle cells were noted (Ryan et al. 1973). These cells contained numerous filaments, which gave a positive reaction with a antiserum against actin and showed an ability to contract after pharmacological stimuli. The authors favour the suggestion that the myofibroblast derives from the tissue fibroblast. On the other hand, Murry et al. (1966) in an ultrastructural study of the healing process following injury to arteries, concluded that smooth muscle cells from the uninjured arterial media migrated into the injury zone where they developed the structural features of fibroblasts. Similar structural changes were noted in uterine smooth muscle cells in response to estrogen stimulation

(Ross and Klebanoff 1967; Ross and Klebanoff 1971). It is possible that myofibroblasts can derive from both smooth muscle cells and fibroblasts. In the case of malignant fibrous histiocytoma the latter possibility is the most logical, since genuine smooth muscle cells have not been demonstrated in the tumour. The derivation from undifferentiated mesenchymal cells is unlikely because of their very small number, but it cannot be totally ruled out.

The giant cells in malignant fibrous histiocytoma are regarded as being derived from histiocyte-like cells (Fu et al. 1975; Taxy and Battifora 1977; Lagace et al. 1979; Harris 1980). This assumption is based on the ruffled cell border with many cytoplasmic projections, and the content of lysosomes. In our case of malignant fibrous histiocytoma of the lung we found giant cells with very few or no lysosomes, and rather smooth plasma membranes. We would, therefore, suggest the possibility that fibroblast-like cells may also transform into giant cells.

The histogenesis of malignant fibrous histiocytoma is based on two theories. The first favours a derivation from primitive mesenchymal cells (Fu et al. 1975; Lagacé et al. 1979) and the second favours an origin from tissue histiocytes, these cells being regarded as facultative fibroblasts. The latter theory is based mainly on tissue culture findings (Ozzello et al. 1963).

In conclusion, the malignant fibrous histiocytoma of the lung we describe has a varied histological pattern. The dominant cell type is a fibroblast-like cell, and is combined with many giant cells and some histiocyte-like cells and intermediate forms, together with a few undifferentiated mesenchymal cells. We regard this tumour to have developed from the peribronchial connective tissue; it has the same composition as malignant fibrous histiocytoma of soft tissues. We are unable, on the basis of morphology alone, to decide, which of the two theories of the histogenesis of malignant fibrous histiocytoma ought to be prefered.

References

Bedrossian CWM, Verani R, Unger KM, Salman J (1979) Pulmonary malignant fibrous histiocytoma. Chest 75:186–189

Cameron EWJ (1975) Primary sarcoma of the lung. Thorax 30:516–520

Crocker DJ, Murad TM (1969) Ultrastructure of fibrosarcoma in a male breast. Cancer 23:891–899

Enzinger FM (1979) Angiomatoid malignant fibrous histiocytoma. Cancer 44:2147–2157

Feiner H, Kaye GI (1976) Ultrastructural evidence of myofibroblasts in circumscribed fibromatosis. Arch Pathol Lab Med 100:265–267

Fu Yao-Shi, Gabbiani G, Kaye GI, Lattes R (1975) Malignant soft tissue tumours of probable histiocytic origin (malignant fibrous histiocytomas): general considerations and electron microscopic and tissue culture studies. Cancer 35:176–198

Gabbiani G, Majno G (1972) Dupuytren's contracture: fibroblast Contraction? Am J Pathol 66:131–146

Harris M (1980) The ultrastructure of benign and malignant fibrous histiocytomas. Histopathology 4:29–44

Kern WH, Hughes RK, Meyer BW, Harley DP (1979) Malignant fibrous histiocytoma of the lung. Cancer 44:1793–1801

Kyriakos M, Kempson RL (1976) Inflammatory fibrous histiocytoma. Cancer 37:1584–1606

Lagacé E, Delage C, Seemayer TA (1979) Myxoid variant of malignant fibrous histiocytoma. Cancer 43:526–534

Lagacé R, Schürch W, Seemayer TA (1980) Myofibroblast in soft tissue sarcomas. Virchows Arch [Pathol Anat] 389:1-11
Murray M, Schrodt GR, Berg HF (1966) Role of smooth muscle cells in healing of injured arteries. Arch Pathol 82:138–146
Ozzello L, Stout AP, Murray MR (1963) Cultural characteristics of malignant histiocytomas and fibrous xanthomas. Cancer 16:331–344
Ross R, Klebanoff SJ (1967) Fine structural changes in uterine smooth muscle and fibroblasts in response to estrogen. J Cell Biol 32:155–167
Ross R, Klebanoff SJ (1971) The smooth muscle cell. J Cell Biol 50:159–171
Ryan GB, Cliff WJ, Gabbiani G, Irle C, Statkov PR, Majno G (1973) Myofibroblasts in an avascular fibrous tissue. Lab Invest 29:197–206
Taxy J, Battifora H (1977) Malignant fibrous histiocytoma. Cancer 40:254–267
Vasudev KS, Harris M (1978) A sarcoma of myofibroblasts. Arch Pathol Lab Med 102:185–188
Weiss SW, Enzinger FM (1978) Malignant fibrous histiocytoma. Cancer 41:2250–2266
Weiss SW, Enzinger FM (1977) Myxoid variant of malignant fibrous histiocytoma. Cancer 39:1672–1685
Wirman JA (1976) Nodular fasciitis, a lesion of myofibroblasts. Cancer 38:2378–2389

Accepted August 28, 1981

Note Added in Proof

Since this paper was submitted, we have noted the publication of two further cases of malignant fibrous histiocytoma of the lung. Chowdhury LN, Swerdlow MA, Jao W, Kathpalia S, Desser RK (1980) Postirradiation malignant fibrous histiocytoma of the lung. Am J Clin Pathol 74:820–826. Sajjad SM, Begin LR, Dail DH, Lukeman JM (1981) Fibrous histiocytoma of lung – a clinicopathological study of two cases. Histopathology 5:325–334.