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Solitary fibrous tumour of the pleura: an ultrastructural and immunohistochemical study

SARAH KEATING, G T SIMON, I ALEXOPOULOU, J MICHAEL KAY

From the Department of Laboratory Medicine, St Joseph's Hospital, and Department of Pathology, McMaster University, Hamilton, Ontario, Canada

ABSTRACT Solitary fibrous tumour of the pleura is a benign neoplasm differing from diffuse pleural mesothelioma. It was originally thought to be a variant of mesothelioma because it consists of a spindle cell stroma associated with branching tubular structures lined by cuboidal cells. In this study of two cases the tubular structures were lined with ciliated and non-ciliated cuboidal cells. Ultrastructurally most of the non-ciliated cells had the features of type II pneumocytes, while the stromal cells had all the characteristics of fibroblasts. Immunohistochemical staining showed the epithelial cells to be positive for both keratin and carcinoembryonic antigen, whereas the stromal cells were negative. The findings support the theory that these tumours are fibroblastic in origin, and that the biphasic pattern is due to entrapment of non-neoplastic bronchiolar and alveolar epithelial cells.

Solitary fibrous tumour of the pleura is a rare neoplasm that most often affects the visceral pleura. It was originally considered to be a type of mesothelioma, largely because of two histological elements—a spindle cell stromal component and branching tubular structures lined with cuboidal cells at the edge of the tumour and deep within it. A tissue culture study performed by Stout and Murray[1] and subsequent ultrastructural investigations[2–5] initially supported a mesothelial origin. This neoplasm, however, has a good prognosis,[6–8] and it is clinically separate from malignant mesothelioma.

The present study concentrates on establishing the histogenesis of the tumour by means of light microscopic, ultrastructural, and immunohistochemical methods. Although 52 reported cases of this neoplasm have been examined ultrastructurally,[2–13] most workers have concentrated on the stromal component alone. Three cases have been investigated immunohistochemically for keratin and factor VIII[12] and nine for keratins and vimentin.[5] In this paper the ultrastructure of the tubular lining cells and the stromal spindle cells in two cases is examined in detail. The results of immunohistochemical staining for carcinoembryonic antigen and keratin are also described.

Address for reprint requests: Dr J M Kay, Department of Laboratory Medicine, St Joseph's Hospital, Hamilton, Ontario, Canada L8N 4A6.

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Case reports

CASE 1

A 51 year old man developed chest pain and a cough productive of orange sputum in May 1984. He had smoked 25 cigarettes a day for 40 years and had worked for many years on a chicken farm. There was no history of asbestos exposure. Physical examination revealed only occasional rhonchi. A chest radiograph showed a nodule 8 × 4 mm in the left upper lobe which was interpreted as a granuloma, and a nodule 13 × 13 mm at the periphery of the right upper lobe overlying the anterolateral aspect of the right fifth rib. Review of a chest radiograph taken four months previously showed that the diameter of the latter lesion had been 7 mm. A needle aspiration biopsy yielded only small collections of histiocytes. At thoracotomy in July 1984 a nodule was found on the surface of the right upper lobe about 1·5 cm above the major fissure. A wedge resection was carried out. The patient was discharged five days after operation and had no respiratory complaints when seen six months later by his family doctor.

CASE 2

A 53 year old man was admitted to hospital for a cholecystectomy in June 1984. A routine preoperative chest radiograph showed a lesion 15 mm in diameter in the periphery of the right upper lobe close to the pleura. The patient worked in a car body shop doing car repairs. He had smoked 50 cigarettes a day for 20 years until 1983. Physical examination before operation showed nothing remarkable. Needle aspiration of the lesion yielded only scanty blood and macrophages. At thoracotomy in September 1984 a sessile, minimally pedunculated lesion was seen on the lung surface, and was removed by wedge resection. A good postoperative recovery ensued. He was seen by his family doctor one year later and had no respiratory complaints.

Methods

Formalin fixed tissue from both cases was embedded in paraffin, sectioned, and stained with haematoxylin and eosin and by the Miller elastic-Van Gieson method.[14] Immunoperoxidase staining for keratin and carcinoembryonic antigen was performed in both cases, a standard peroxidase-antiperoxidase technique being used. Controls included normal rabbit serum substituted for primary antibody with and without trypsinisation of the section, and with and without preabsorption of the normal rabbit serum with spleen homogenate. The carcinoembryonic antigen determination was performed with and without preabsorption of the primary antibody with spleen homogenate. The antibodies were obtained from Dako Corporation (Santa Barbara, California). The antikeratin antibody was a polyclonal antibody raised against stratum corneum. Fresh tissue for electron microscopy from both cases was cut into 1 mm^3 blocks, fixed in 2% glutaraldehyde, postfixed in 1% osmium tetroxide, dehydrated, and embedded in Spurr resin. Semithin sections were cut and stained with toluidine blue, after which areas were chosen for ultrathin sections. The latter were stained with uranyl acetate and lead citrate.

Pathological findings

The specimen from patient 1 consisted of a wedge of lung measuring 3·5 × 3·5 × 2·0 cm. On the cut surface a firm, beige, well circumscribed but non-encapsulated tumour, 1 cm in maximal diameter, was located immediately beneath the pleura. The specimen from patient 2 was a wedge of lung measuring 5·5 × 2·0 × 1·7 cm with a spherical firm, grey, well circumscribed nodule 1·5 cm in diameter located immediately beneath the pleura.

The histological appearances were similar in the two cases. The lesions were well circumscribed but non-encapsulated, and composed predominantly of spindle shaped cells varying from plump to elongated. Some areas were sparsely cellular with abundant hyalinised collagen. Other areas were moderately

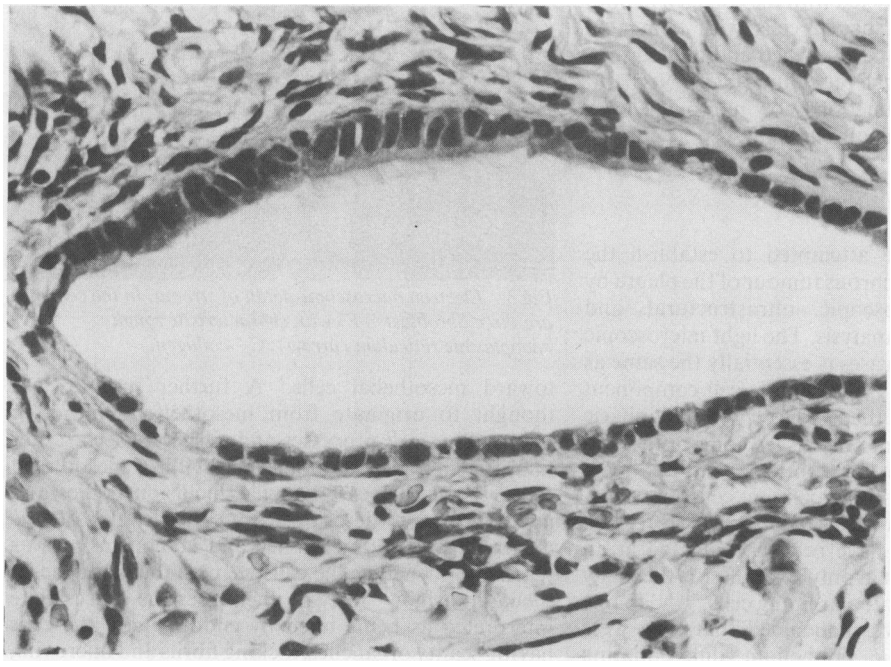

Fig 1 *A tubule lined by cuboidal and ciliated columnar cells. (Haematoxylin and eosin.)*

cellular. Nuclei varied from oval to fusiform and were bland in appearance, differing little in size. Mitoses were absent. Both tumours contained, in addition to capillaries, slit like tubular spaces lined with columnar or cuboidal cells, some of which were ciliated (fig 1). These spaces were just as numerous in the central portion of the tumours as near the margins. The adjacent lung parenchyma was moderately anthracotic.

With antikeratin antibody the lining cells of the tubular elements showed moderate positivity while the stromal cells were negative. Normal alveolar epithelium was weakly to moderately positive and normal bronchiolar epithelium was moderately to strongly positive. Normal mesothelium was moderately positive. Tubular lining cells were weakly positive for carcinoembryonic antigen, while the stromal component was negative. Normal alveolar epithelium was negative to weakly positive and normal bronchiolar epithelium moderately positive. Normal mesothelium was negative.

The tubular structures were easily found on electron microscopy. Numerous lining cells were examined and most contained the typical lamellar inclusion bodies of type II pneumocytes and a small to moderate amount of glycogen (fig 2). Others had short microvilli but lacked lamellar inclusion bodies. The characteristic long microvilli of mesothelial cells were not seen. In some tubules the epithelial cells formed several layers. Both types of cell lay on a well formed basal lamina (fig 2). Beneath the basal lamina abundant collagen fibrils were present. Admixed with the collagen in both tumours were spindle shaped cells with elongated cytoplasmic processes and branched and dilated profiles of rough endoplasmic reticulum (fig 3). No basal lamina, intercellular junctions, or microvilli were present, and no mesothelial cells were seen.

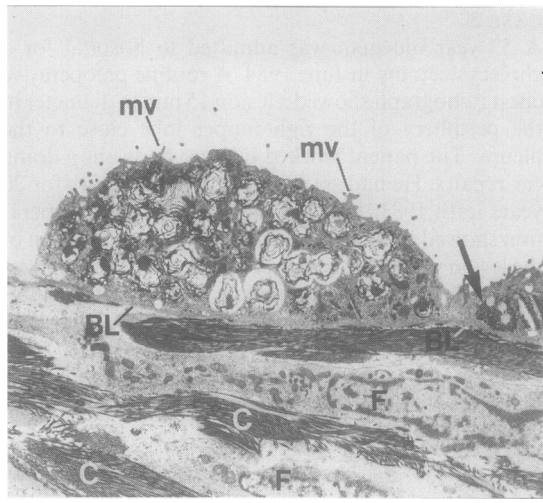

Fig 2 *Electron micrograph of two tubular lining cells with adjacent stroma. At their surface the cells show poorly developed microvilli (mv). In the cytoplasm numerous lamellar inclusions and some glycogen (arrow) are seen. BL—basal lamina; C—collagen; F—fibroblast.*

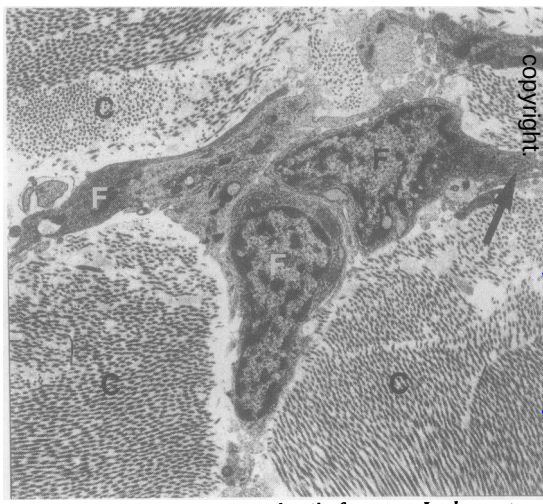

Fig 3 *Electron microscopic detail of stroma. In the centre are three fibroblasts (F) with characteristic rough endoplasmic reticulum (arrow). C—collagen.*

Discussion

In this paper we have attempted to establish the histogenesis of solitary fibrous tumour of the pleura by means of light microscopic, ultrastructural, and immunohistochemical analysis. The light microscopic appearance in our two cases is essentially the same as that reported previously, the spindle cell component making up the bulk of the lesion.[1-3 5-13] The biphasic morphology of these tumours has led some authors to conclude that they are of mesothelial origin.[1-3] The nature of the epithelial tubular lining cells, however, has not previously been adequately studied. Fifty two of the published cases have been investigated at an ultrastructural level, but in only 10 of these is there any specific mention of the tubular lining cells.[2 3 11 13] In one study of six cases it was concluded that they were derived from coelomic epithelium differentiating toward mesothelial cells.[2] A further tumour was thought to originate from mesothelium, although blunt villous cell processes and cilia were seen rather than the characteristic long microvilli of mesothelial cells.[3] In another case lamellar inclusion bodies and microvilli were described, but the length of the microvilli was not mentioned and no conclusion was reached on whether the cells were epithelial or mesothelial in origin.[11] In two other cases the spaces were interpreted as being lined by endothelium, the cells having scanty organelles, lacking fibrils and microvilli.

and resting on basement membranes with occasional desmosomal attachments between cells; Weibel-Palade bodies were not described.[13] The cells of the stromal component have been described as having features consistent with a fibroblastic origin in most cases, similar to the stromal cells seen in our two cases.[2-13] These features include branching rough endoplasmic reticulum and abundant intercellular collagen. In a recent series mesothelial differentiation was postulated because of the presence of some form of intercellular junction in seven of 10 cases, basal lamina deposition in three, and polarised microvilli in one.[5] On the basis of these findings the authors suggested that most localised tumours of serosal membrances are a subset of mesothelioma, while a minority are fibromas.

In our material most of the tubular lining cells showed features of type II pneumocytes, with short, blunt microvilli and characteristic lamellar inclusion bodies. Neither the stromal nor the epithelial like cells had the ultrastructural features of mesothelial cells. Some solitary fibrous tumours may contain entrapped mesothelial cells, especially those that have expanded out into the pleural cavity. Those tumours expanding deep to the visceral pleura would be more likely to entrap bronchioloalveolar epithelium, as in our two cases.

Only two previous immunohistochemical studies of this type of tumour have been reported. In one the epithelial like cells were found to be negative for keratins and factor VIII related antigen.[12] Surface mesothelial cells were positive for all keratins tested. In the other study[5] vimentin was present in four of 10 cases and cytokeratin in one. In our material anti-keratin antibody stained the tubular lining cells moderately but not the stromal cells. The antikeratin staining of the epithelial like elements was similar to that of normal epithelium and mesothelium. In addition, anti-carcinoembryonic antigen weakly stained the tubular lining cells and normal alveolar and bronchiolar epithelium. Non-neoplastic mesothelial cells and tumour stromal cells were negative.

From our study we conclude that the tubular structures of solitary fibrous tumour of the pleura are lined by alveolar and bronchiolar epithelium, which is entrapped in the tumour and is non-neoplastic, such as in metastatic smooth muscle neoplasms in the lung.[15] The neoplastic portion is the stromal component, the cells of which are fibroblastic and do not have the ultrastructural or immunohistochemical features of mesothelial cells. At present two main theories exist regarding the histogenesis of these tumours. Both hypotheses postulate an origin from submesothelial cells. One implicates a specialised cell capable of differentiation to surface mesothelium,[8] while the other suggests a derivation from fibroblasts.[9 11] Our histological, immunohistochemical, and ultrastructural findings support the latter hypothesis.

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