Two malignant pleural mesotheliomas with unusual histological features

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**ABSTRACT** Morphologically, mesotheliomas may be composed of epithelial and/or sarcomatous elements with various patterns, such as tubular, papillary, tubulopapillary, and diffuse epithelial or mixtures of these. Two cases are described in which, in addition to typical mesothelioma, there was cartilage with foci of calcification and ossification, and fibrochondrosarcomatous tissue. These foci were intimately associated with the mesothelioma, which suggested that they formed an integral part of the tumour. One of the cases also showed a cuff of cartilage and bone round blood vessels and bronchioles in the lung parenchyma. The pathogenesis could be explained if the mesothelial cell is considered to be totipotent and able to give rise to epithelial and connective tissue elements. Other theories that must be considered are: that there are two separate neoplasms; that there is a circulating substance, perhaps induced by the mesothelioma, which stimulated the cartilage and bone formation; and that the cartilage and bone were due to a previous or associated infection such as tuberculosis. Calcification is also common in asbestotic pleural plaques.

Several authors (Hourihane, 1964; Whitwell and Rawcliffe, 1971; Shearin and Jackson, 1976; Kannerstein and Churg, 1977) have described the pathological features of mesothelioma, and the tumour has been classified into epithelial, sarcomatous, and mixed types. The morphological features are usually distinctive, but in some cases a secondary carcinoma or a sarcoma arising from one of the connective tissue elements must be excluded.

The sarcomatous or fibrous types usually show a range of appearances from a cellular fibrosarcomatous pattern to relatively acellular collagen, but as the mesothelial cell is capable of differentiating, other connective tissue elements could occur but have not been recorded. Two cases with unusual features are presented in this report.

**Case 1**

A 35-year-old black woman was admitted to hospital with generalised slight oedema and lumps under the skin of the left chest. These were attached deeply but were not adherent to skin. Grossly distended superficial neck veins were present. The patient had lived in the Kuruman area of the NW Cape Province but no history of asbestos exposure could be elicited. She died soon after admission.

At necropsy both parietal and visceral pleural layers of the left lung were grossly thickened and infiltrated by neoplasm that had also invaded the pericardium and left leaf of the diaphragm. In parts the growth was "boney" in consistency. Over the right lung there were a few adhesions but no other significant changes were noted. The liver was grossly enlarged and had a nutmeg appearance.

The hilar glands were slightly enlarged and slightly pigmented but not fibrosed. The bronchi and pulmonary vessels showed no gross changes. The left lung was encased in neoplasm up to about 2 cm thick, and calcification was present in this tissue (fig 1). A few metastatic neoplastic deposits were present in the right lung, which also contained a focus of encapsulated necrosis 3 mm in diameter. The epicardium contained a few metastatic neoplastic deposits.

On microscopy, sections of the encapsulated necrosis showed the features of active fibrocaseous tuberculosis. The lung tissue showed no evidence of asbestosis, and ferruginous bodies were not
observed. After digestion and concentration of lung tissue, however, examination with the electron microscope microprobe analyser showed several crocidolite asbestos fibres.

Sections of the pleura showed relatively acellular fibrous tissue in which there were cleft-like spaces lined by atypical flattened or cuboidal cells occurring as one or more layers. In some of the clefts the cells were detached from the wall. The nuclei of these cells were pleomorphic and contained a prominent nucleolus. The features of this tissue were typical of a mesothelioma. Parts of the neoplasm were, however, more cellular consisting of atypical spindle-shaped cells with sarcomatous features (fig 2).

In other sections there was fibrous tissue with proliferating tumour cells on the inner surface adjacent to the lung parenchyma. In this fibrous tissue there were islands of cartilaginous tissue separated by a spindle cell stroma that appeared to merge into the cartilage (fig 3). Some of the spindle cells and cartilage cells were atypical, and a few mitotic figures were seen consistent with fibrochondrosarcomatous change. An occasional focus of ossification was also present in the cartilaginous tissue (fig 4).

Another unusual feature was the formation of cuffs of bone or cartilage around blood vessels and bronchi in the lung parenchyma. The bone appeared to be forming in a matrix of fibrous tissue. Cement lines were visible on the periphery of some of the bone trabeculae consistent with intramembranous ossification. Where cartilage occurred, the foci of ossification appeared to be endochondral in nature (figs 5, 6).

**Case 2**

A 38-year-old black man had complained of
swelling of the face for two months and cough productive of greenish sputum. He was well-nourished. There was swelling of the neck caused by distended non-pulsatile external jugular veins, and this was more pronounced on the right side. The right side of the chest was dull to percussion, and breath sounds were absent. The pulse rate was 88 beats/min, the volume was good but pulsus paradoxus was present. The blood pressure was 130/100 mmHg. Chest radiographs showed dense opacification over the whole of the right lung.

He had been admitted to a hospital two years earlier when radiography showed pleural thickening over the right apex and base but three consecutive sputum examinations did not show acid-fast bacilli. He was, however, treated with streptomycin, isoniazid, and PAS, but there were no records to indicate whether there was any improvement in the chest radiographs.

The industrial history, so far as could be determined, indicated that he worked on an amosite mine as an underground lasher for 1140 shifts and as a surface lorry loader for 540 shifts. He also had one year’s service each in gold and coal mines.

At necropsy it was reported that the right pleural space was filled with dense, hard, white, homogeneous tumour about 5 cm thick, covering and compressing the underlying lung. The tumour invaded the superior vena cava and extended into the right atrium. A small metastatic nodule was present on the upper surface of the liver. In compliance with the Occupational Diseases in Mines and Works Act (Goldstein and Webster, 1976) the cardiorespiratory organs were removed and sent to this institute.

Macroscopic examination of the lungs showed thickening of the pleurae over both lungs. Over the right lung the thickening was pronounced and consisted of white tissue adherent to the lung and extending in parts into the adjacent lung tissue. Foci of calcification were also present. On section the lungs were slightly pigmented and there was a nodule of tumour tissue 1.5 cm in diameter in the right lower lobe. The bronchi showed no evidence of a bronchogenic carcinoma. Microscopically, there was a moderate deposition of carbon and haemosiderin particles, and a few asbestos fibres were seen in sections of the hilar glands.

Microscopic examination of sections from both lungs showed numerous asbestos bodies and asbestos fibres in the air-spaces and interstitial tissues with an associated moderate degree of interstitial fibrosis.

The sections from the right lung showed well-marked hyaline fibrous thickening of the pleura, and in parts there was a cellular infiltrate near the
junction with the underlying lung parenchyma. These cells were atypical, cuboidal or flattened, and varied in size and shape, while the nuclei were either vesicular or pyknotic, with 2–3 mitoses per high-power field. The cells formed thin cords, mostly one cell thick, but sometimes they lined clefts in the fibrous tissue. Occasional acinar formation was also present (fig 7).

In addition to these typical features of a mesothelioma, there were foci of cartilage in which bone formation with cement lines was occurring (fig 8). Bone trabeculae also occurred in a loose connective tissue stroma, and there were a few associated multinucleated giant cells (fig 9).

In some parts the cartilage was extensive but did not stain well, suggesting necrosis of the tissue. In other areas the chondrocytes were atypical and had the features of a chondrosarcoma. Fibrosarcomatous areas merged into the chondrosarcoma giving the appearance of a fibrochondrosarcoma. This tissue also contained foci of bone and multinucleated giant cells (fig 10). Some of the spindle cells resembled smooth muscle but myofibrils could not be shown by special stains.

Sections of the tumour nodule in the right lower lobe showed a focus of chondrosarcoma in the lung parenchyma affecting the air-spaces and containing entrapped ferruginous bodies. Tumour emboli were seen in some of the blood vessels and perivascular lymphatics on the periphery of this mass (fig 11).

The metastatic nodule found on the liver surface was not submitted for examination.
The findings in these two cases are unusual, although small foci of cartilage can occasionally be seen in a mesothelioma. The tissues found in the two tumours described could be explained in several ways.

(1) The cartilage and bone developed separately from the neoplasm. This could have resulted from a previous tuberculous pleurisy, and although the second patient had a clinical history of tuberculosis and the first had a small active tuberculous lesion at the time of death, there was no evidence of tuberculous involvement of the pleura at necropsy. It is highly likely that the pleural thickening found on the initial radiographs of case 2 was due to tumour growth, which later progressed to affect the entire pleura.

(2) The mesothelioma may have been producing a substance that promotes cartilage and bone formation, directly or by stimulating the parathyroid glands. Biochemical studies had, however, not been carried out. The perivascular bone and cartilage in case 1 and the bone trabeculae in case 2 did not appear to be malignant and could possibly be explained in this way. That mesotheliomas may secrete biologically active substances was recently suggested by Perks et al (1978), who described a case of malignant mesothelioma with inappropriate secretion of antidiuretic hormone. It is therefore possible that other active substances may also be secreted.

(3) The cartilage and bone were part of the neoplastic process. Several features appear to favour this view. The bone and cartilage appeared to be integral components of the neoplasm and in parts the spindle cells appeared to be merging or transforming into the cartilage. Chondrosarcomatous metastases in the lung parenchyma and in some of the vessels in case 2 also indicated that this was part of a malignant tumour. This combination of epithelial and connective tissue elements can be explained if it is accepted that the mesothelial cell can differentiate into epithelial as well as connective tissue elements.

(4) Two separate neoplasms may have been present, a mesothelioma with classical tubular formation and a fibrochondrosarcoma. This possibility cannot be excluded entirely but the intimate relationship of the various components tends to be against this.

(5) Asbestotic pleural plaques often undergo calcification but the bone and cartilage in our cases do not appear to be related to this process.

These two cases thus illustrate a mesothelioma with typical features as well as areas of fibrochondrosarcoma and the formation of bone and cartilage.

References


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