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CASE REPORT

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Pleural epidermoid carcinoma from displaced skin following extrapleural pneumothorax in a patient exposed to asbestos

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Abstract This report illustrates a rare case of primary epidermoid carcinoma of the pleura in a patient previously treated by artificial extrapleural pneumothorax for active tuberculosis. The patient had also been occupationally exposed to asbestos. Light microscopic examination showed two different lesions: laminar pleural fragments were covered by normal squamous epithelium that was similar in all respects to epidermis, whereas nodular fragments were composed of well-differentiated infiltrating carcinoma. These findings support the hypothesis that the carcinoma arose from normal epidermis seeded in the pleural cavity during multiple air refills to maintain the pneumothorax. A possible interaction between asbestos fibres and chronic inflammation might have potentiated tumour development.

Key words Pleura · Carcinoma · Pneumothorax · Asbestos

Introduction

Primary epidermoid cell tumours of the pleura identical to epidermoid carcinoma of the skin can occur in patients who have previously undergone therapeutic pneumothorax (intra- or extrapleural) for active tuberculosis [1, 3, 5, 9, 10]. Pleural carcinoma produces a dense effusion and clinical symptoms that can lead to an incorrect diagnosis of empyema. However, these primary pleural carcinomas have proved to have a better prognosis than malignant pleural mesotheliomas and pleural metastatic carcinomas [10].

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The origin and the cause of such tumours are not clear. Origins from heterotopic epithelial tissue or from squamous metaplasia of mesothelial cells have been suggested [8]. A possible association with occupational asbestos exposure might have important legal implications.

We report a new case of primary epidermoid carcinoma of the pleura and review the literature.

Clinical history

A 65-year-old man was referred to the hospital in March 1995 with dyspnoea and chest pain. The past medical history revealed that 48 years earlier the patient had been treated by artificial extrapleural pneumothorax for active tuberculosis; the subsequent collapse of the lung was maintained with repeated air refills in the extrapleural space. No foreign agent had been placed in the pleural cavity to induce pulmonary collapse. For 7 years, from 1964 to 1971, the patient had been occupationally exposed to asbestos as he was doing insulation work. However, asbestosis was never diagnosed.

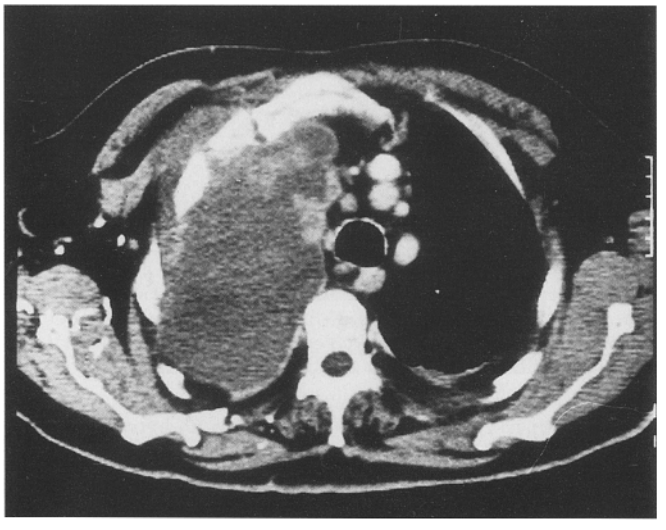

Fig. 1 Computerized tomography showing moderate thickening of the thorax wall and a large dense effusion in the right pleural cavity

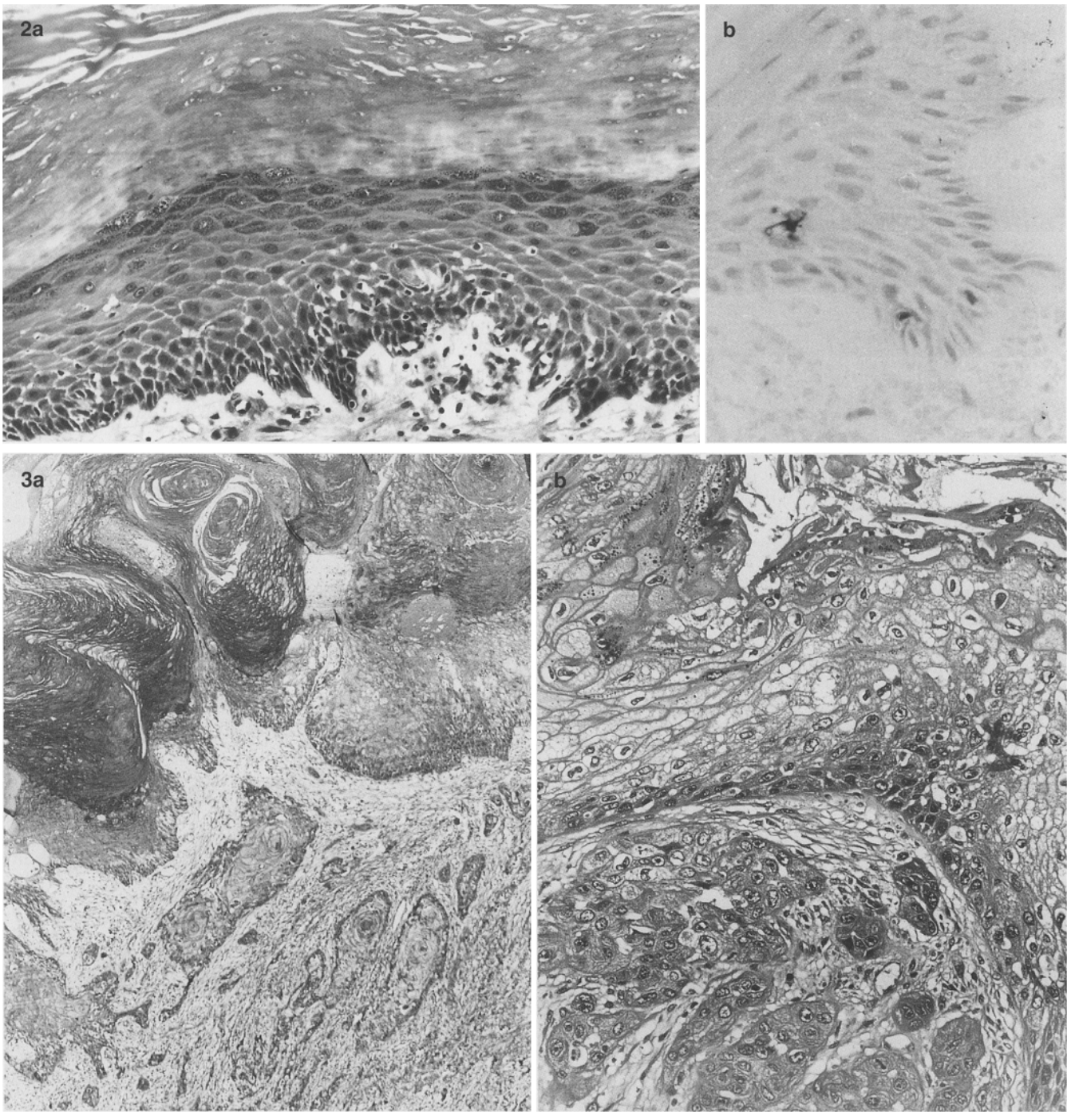

Fig. 2 **a** Squamous epithelium covers the pleural connective tissue. This epithelium shows the four layers typical of the epidermis. H&E. **b** Immunoperoxidase staining using S-100 monoclonal antibody shows up rare star-like cells similar to the dendritic Langerhans cells of the epidermis and basal melanocytes

Fig. 3 **a** Pleural epidermoid carcinoma has a verrucous appearance and a markedly papillomatous surface with hyper- and parakeratotic horns. **b** At higher magnification, rare vacuolized cells and coarse keratoyalin granules were seen. The neoplastic nests infiltrating the stroma are more undifferentiated. H&E

On admission, chest radiograph and CT scan (Fig. 1) showed moderate thickening of the thoracic wall and an abundant dense effusion, which was interpreted as pleural empyema of the right pleural cavity. The lung parenchyma was clear and the mediastinum was not enlarged. The pleural effusion was partially drained, but was not examined cytologically.

Four months later the patient was admitted to the Department of Thoracic Surgery of the University Hospital in Turin. There was an increase in the extent of the pleural effusion, despite the correct location of the drain. There was no evidence of recurrent tuberculosis infection, mediastinal enlargment, lung or abdominal masses. An open-window thoracotomy was performed and numerous pleural nodules were seen. Pathological material was obtained from these and from the effusion.

The patient died of cardiovascular failure 1 month after the diagnosis of pleural carcinoma. No autopsy was performed.

Table 1 Primary squamous carcinomas of the pleura following extrapleural pneumothorax for tuberculosis. Review of cases reported in the literature (*DOD*: dead of disease, *NED* evidence of disease)

Reference	Sex	Age[a] (years)	Interval between extrapleural pneumothorax and onset of carcinoma (years)	Follow-up and outcome
[1]	F	42	5	20 years NED[b]
	Man	48	3	3 years DOD[b]
	Man	41	9	1.5 years DOD[b]
	Man	29	10	3 years DOD[b]
	Man	63	10	Died of postoperative haemorrhage
[3]	F	43	17	Not available
[10]	Man	53	19	1.5 years DOD
[9]	F	43	22	5 years NED
Present case	Man	65	48	1 month DOD

[a] At onset of cancer
[b] Information taken from [10]

Materials and methods

Numerous fragments of the pleural tissue were fixed in formalin. Sections obtained from tissue paraffin blocks were stained with haematoxylin and eosin. For immunohistochemistry the avidin-biotin complex procedure [6] was performed and the following antisera were used: monoclonal antibody (mAb) against S100 protein (1:1500, Dakopatts, Glostrup, Denmark), mAb anti-CEA (1:50, clone TF3H8 Bio-Genex Sanramon, Calif.) mAb anti-cytokeratin (clone KL1, 1:200 Immunotech, Marseille, France), mAb anti-vimentin (clone V9, 1:30 Dakopatts), mAb AMAD2 [2] (1:50, BYK-Gulden, Milan, Italy).

Asbestos fibres were sought by light microscopy on the pleural fragments.

Pathological findings

Grossly, the specimen appeared as thick laminar fragments or as nodules of cheese-like friable material.

Microscopically, the laminar fragments were overlayed by a squamous epithelium. This epithelium was not neoplastic and in all respects was similar to normal epidermis. Accordingly it showed the four typical Malpighian layers (Fig. 2a). Dendritic cells consistent with Langerhans cells of the epidermis and rare clear basal cells similar to melanocytes were stained by S100 protein antiserum (Fig. 2b). The squamous "epidermoid" epithelium showed acanthosis with elongation and thickening of the rete ridges. Rare foreign body granulomas around squamous debris were also present in the stroma.

The nodular lesions, in contrast, showed areas of intraepithelial squamous cell carcinoma in continuity with infiltrating squamous carcinoma. The in situ area was markedly hyperkeratotic, while the invasive component was well differentiated (Fig. 3a,b). Squamous debris were free in the pleural cavity.

CEA was negative in the normal squamous epithelium and focally positive in areas of keratinization of the carcinoma. The anti-keratin mAb stained the normal and neoplastic epithelium, whereas anti-vimentin reacted mostly with the stromal component and with rare epithelial cells of the invasive carcinoma. The AMAD2, anti-mesothelioma antibody, failed to stain either the normal or the neoplastic tissue.

Microscopical search for asbestos fibres was negative.

Discussion

In this rare case of primary epidermoid carcinoma of the pleura, a metastic origin of the lesion can be excluded clinically. Similar primary pleural neoplasms have been described in patients subjected to extrapleural pneumothorax for pulmonary tuberculosis (Table 1), in whom the time interval between the induction of pneumothorax and the development of cancer has varied between 3 and 22 years [1, 3, 9, 10] In our case the latency was about 48 years. The finding of nonneoplastic squamous epithelium in all respects similar to normal epidermis supports the origin of this tumour from epidermal fragments implanted in the pleural cavity after repeated air refills. The needle punctures could produce seeding of the normal skin in the cavity, which could gradually replace the normal mesothelial layer and give rise to an epidermoid carcinoma. The immunocytochemical markers confirm the epithelial phenotype of the pleural neoplasm.

Malignant pleural tumours, unlike mesotheliomas, have been described in patients afflicted with chronic empyema or subjected to therapeutic pneumothorax for active tuberculosis, or carrying pleurocutaneous or bronchopleural fistulae [1, 5, 7, 9, 10]. The histological type of these tumours has varied from squamous cell carcinoma to sarcoma and, rarely, non-Hodgkin lymphoma. Apart from pleural lymphomas, which are due to clonal proliferation of viral-infected B lymphocytes [7], the pathogenesis of the other non-mesothelial pleural tumours is not clear. Asbestos exposure or chronic inflammation have been proposed as pathogenetic factors [4, 5, 9].

We cannot exclude a pathogenetic relation of the tumour with asbestos because our patient had been occupationally exposed to asbestos for 7 years. The cancerogenetic potential of asbestos, acting both as initiator and promoter, is well known [8]. Moreover, experimental data have already demonstrated metaplastic squamous changes in mesothelial cells after intrapleural injection

of different types of asbestos [4]. However, asbestosis was never diagnosed and we were not able to find asbestos fibres in the material examined. Whilst it is possible that both asbestos exposure and chronic inflammation contributed to the development of the squamous carcinoma, it might be that the asbestos exposure was coincidental and the tumour would have followed the extrapleural pneumothorax anyway.

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