

CASE STUDY

Mesenchymal chondrosarcoma of the pleura

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Mesenchymal chondrosarcoma of the pleura. G. Luppi, A.M. Cesinaro, A. Zoboli, U. Morandi, L. Piccinini. ©ERS Journals Ltd 1996.

ABSTRACT: A 52 year old man developed an extraskeletal mesenchymal chondrosarcoma (ESMC) arising from the pleura. Clinically, the tumour mimicked a mesothelioma. Fine needle biopsy was consistent with the diagnosis of sarcomatoid mesothelioma.

Histological examination of multiple tumour samples, supported by immunohistochemical characterization, made it possible to correctly diagnose extraskeletal mesenchymal chondrosarcoma.

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Mesenchymal chondrosarcoma is a rare variant (1%) of chondrosarcoma, characterized clinically by an aggressive behaviour and histologically by a proliferation of undifferentiated cells organized in a haemangiopericytoid pattern with nodules of cartilaginous tissue.

Mesenchymal chondrosarcoma may develop in the skeleton and, more rarely, in soft tissues, the most common sites being the muscles of the lower extremities, central nervous system (CNS) and orbit [1-3]. Unusual localizations of extraskeletal mesenchymal chondrosarcoma (ESMC) in the kidney [4], lung [5] and lumbar nerves [6] have also been reported.

We report a case of ESMC arising from the pleura, which is to our knowledge the first described in the literature.

Case report

A 52 year old male clerk, who was a nonsmoker, was admitted to another hospital in February 1990 because of fever, dry cough, and pain in the right chest of recent onset. On physical examination, a pleural effusion was diagnosed. Chest radiography followed by computed tomographic (CT) scan of the thorax disclosed a 6 cm pleural mass located next to the anterior-basal segment of the lower right pulmonary lobe (fig. 1). A fine needle biopsy of the mass was performed and a diagnosis of malignant sarcomatoid mesothelioma was made.

Surgical removal of the mass was not possible and three courses of chemotherapy with cisplatin (60 mg·m⁻² on day 1) and epirubicin (60 mg·m⁻² on day 1) were administered every 28 days. CT scan at the end of chemotherapy documented an increase of the pleural mass, combined with new solid nodules, 1 cm in diameter, located in the right parietal pleura. Bronchoscopy and bone scan were also performed, but no mediastinal, lung or rib lesions were detected.

Because of the lack of response to treatment, the patient was then referred to a department of surgery and underwent thoracotomy. The pleural origin of the mass

was confirmed and a partial resection was performed. Histological examination revealed a high-grade mesenchymal chondrosarcoma of the right pleura.

After surgery, the patient was admitted to our institution and received chemotherapy with mithoxantrone (12 mg·m⁻² on day 1) and ifosfamide (2,500 mg·m⁻² on day 1-3). After two courses of chemotherapy the chest roentgenogram (fig. 2) showed no response. The patient's condition rapidly worsened and he died from disease progression in March 1991, 13 months after initial diagnosis. For the last few months, the patient had been in the care of another hospital and no autopsy was made. It was reported that the disease had metastasized to the liver and adrenal glands.

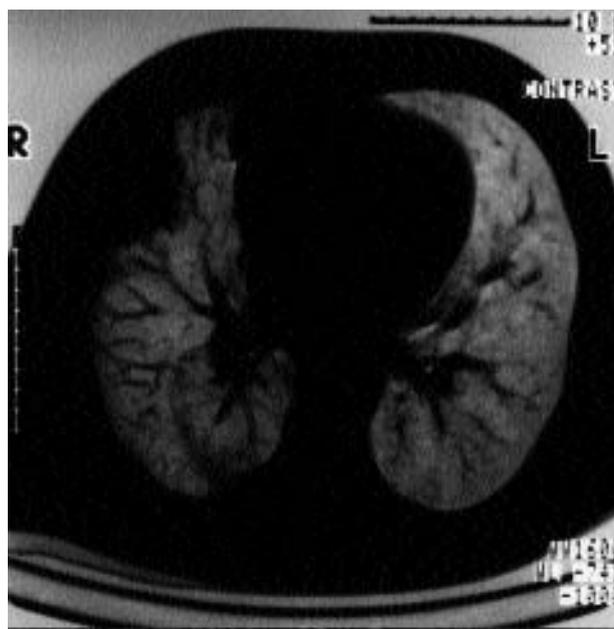


Fig. 1. - Computed tomographic scan of the chest: solid non-homogenous mass (6 cm diameter) on the chest wall, close to the anterior basal segment of the right lower pulmonary lobe, of probable pleural origin.

Histopathology

Multiple specimens of the tumour mass were fixed in 10% buffered formalin, routinely processed and embedded in paraffin. Sections 4 μ m thick were stained with haematoxylin and eosin. Histochemical reactions were also performed (Alcian blue pH 0.5 and pH 2.5, both with and without hyaluronidase digestion; periodic-acid-Schiff (PAS) and PAS-diacetate) and immunohistochemistry was carried out utilizing the avidin-biotin complex (ABC) method. The following antibodies were employed: anti-low and high molecular weight cytokeratins (AE1 and AE3) (monoclonal, Biomed), smooth-muscle actin (monoclonal, Biogenex Laboratory), vimentin (monoclonal, Biomakor), desmin (monoclonal, Eurodiagnostica), lysozyme (monoclonal, Dako), S-100 protein (polyclonal, Immunon) and Factor VIII-Rag (polyclonal, Dako).

The tumour consisted of several samples of soft, greyish-white tissue with foci of necrosis and small areas of haemorrhage. The largest surgical sample measured 5 \times 2 \times 1 cm.

Microscopy revealed a proliferation of round or spindle-shaped cells with scanty cytoplasm and small round-to-ovoid hyperchromatic nuclei, representing the main part of the tumour. The round cells were arranged in aggregates and in a haemangiopericytoid pattern around vascular spaces (fig. 3), sometimes in an abundant mucinous matrix. The areas composed of spindle cells displayed a storiform pattern. Few mitoses were present. Small areas of cartilaginous tissue constituted the second component (fig. 4). No foci of calcification or ossification were present. Alcian blue pH 0.5 and 2.5 stained the chondroid and mucinous matrix, but the staining was consistently reduced after hyaluronidase digestion. PAS and PAS-diacetate stains revealed small granules of glycogen in the cytoplasm of the undifferentiated cells. Immunohistochemistry showed a positive reaction for S-100 protein in the chondrocytes and in some undifferentiated

cells. Moreover, tumour cells reacted positively for vimentin, actin and lysozyme. Reactions for desmin, Factor VIII-Rag and cytokeratins were negative. On the basis of these findings, the diagnosis of ESMC was made.

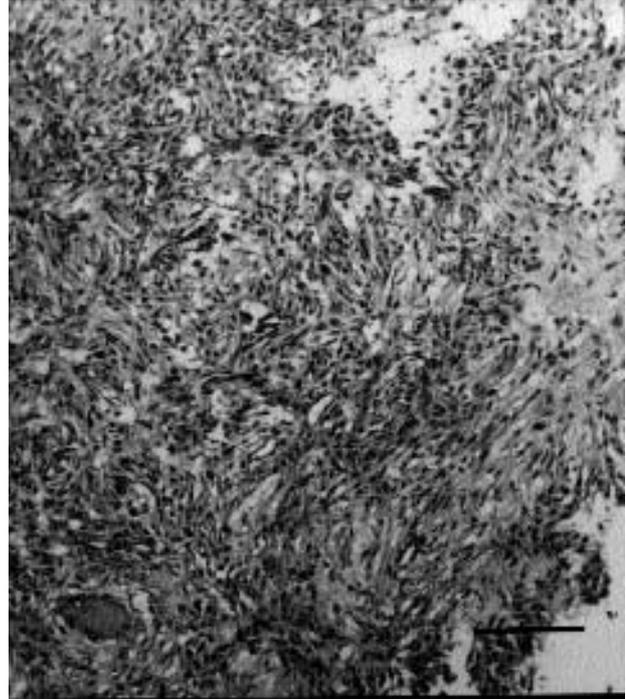


Fig. 3. – Undifferentiated component with small cells surrounding narrow vascular spaces in a haemangiopericytoid pattern. (Internal scale bar= 150 μ m).

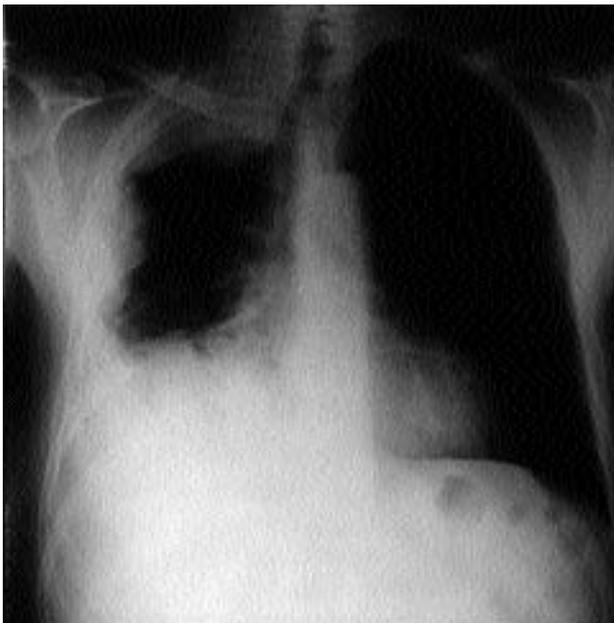


Fig. 2. – Chest radiograph: large parietal nodules of the right pleura and a pleural effusion.

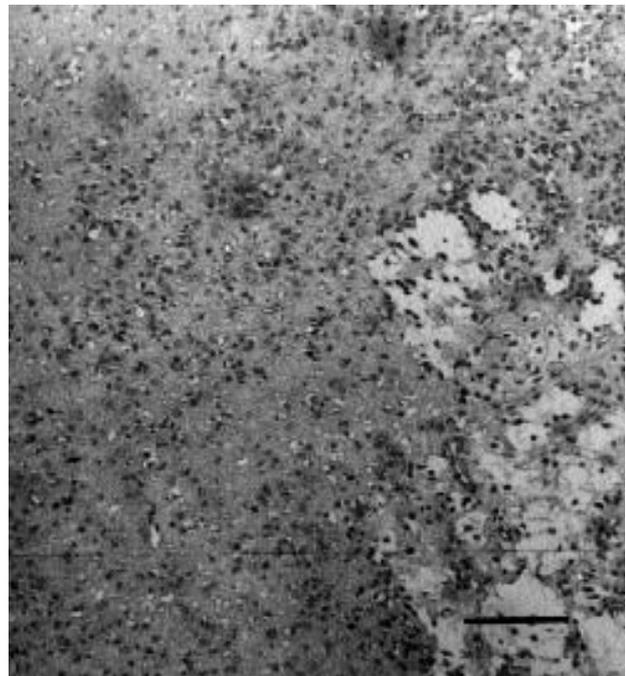


Fig. 4. – Area of cartilaginous tissue merging with the undifferentiated component. The chondrocytes reacted positively with S-100 protein (Internal scale bar=150 μ m).

Discussion

Mesenchymal chondrosarcoma is an uncommon, highly malignant neoplasm, which rarely occurs in extra-skeletal sites. In a review of the literature, LOUVET *et al.* [7] reported 63 cases of ESMC, 29 of which were localized in the central nervous system (14 meningeal, 8 cerebral, 7 orbital) and 34 in the skeletal muscles. In a review of 111 mesenchymal chondrosarcomas, NAKASHIMA *et al.* [8] reported 38 cases of extraskeletal localization. ESMC seems to occur more frequently in younger people (in their teens and twenties), particularly in CNS localizations, whereas skeletal muscles are the site of preponderance in older people [7].

Histologically, mesenchymal chondrosarcoma can be difficult to differentiate from malignant haemangiopericytoma and synovial sarcoma [9]. However, the presence of cartilaginous tissue is a diagnostic clue for mesenchymal chondrosarcoma, since it is absent in haemangiopericytoma [10]. On the other hand, the immunohistochemical positivity for S-100 protein and the negativity for cytokeratins differentiate ESMC from synovial sarcoma, for the spindle cell variant, which is usually focally positive for cytokeratins.

In our case, the tumour clinically mimicked a mesothelioma, and a fine needle biopsy was consistent with this diagnosis. A partial resection enabled the pathologist to examine multiple samples of the tumour. Its histological and immunohistochemical features ruled out mesothelioma. Mesenchymal chondrosarcoma is positive for vimentin, but negative for cytokeratin [11], whereas mesothelioma reacts positively both with vimentin and cytokeratin, even in the sarcomatoid variant [12]. Our case was completely negative for cytokeratins and positive for vimentin and S-100 protein. Moreover, the histochemistry demonstrated a high content of chondroitin 4- and 6-sulphate, which is Alcian blue pH 0.5 and 2.5 positive, but is digested by hyaluronidase. This mucosubstance is characteristic of foetal cartilage and poorly differentiated chondrosarcomas [13]. The immunohistochemical features and the morphological findings also supported the differential diagnosis between ESMC and mesothelioma with cartilaginous differentiation. Furthermore, in the series of malignant mesotheliomas with osseous and cartilaginous differentiation reported by YOUSEUM and HOCHHOLZER [14], a history of asbestos exposure was common.

Mesenchymal chondrosarcomas primarily arising from the lung [5], as well as from the chest wall [1, 2, 8] and mediastinum [15], have been reported. In our case, the origin of the neoplasm from parietal pleura was established by means of CT, bone scan and bronchoscopy.

Different types of sarcoma may originate from the pleura [16]. A case of myxoid chondrosarcoma, clinically simulating a mesothelioma, has been described [17]. BAILEY and HEAD [18] reported a well-differentiated chondrosarcoma, which exhibited a benign behaviour. The pathogenesis of mesenchymal chondrosarcoma is still unknown, but aetiological factors have been suggested. SEARS *et al.* [19] observed a case occurring in the lumbar vertebrae 12 yrs after radiotherapy for Wilm's tumour. In a series of 17 sarcomas of the pleura, MYOUI *et al.* [16] documented previous episodes of nonspecific or tuberculous pleuritis and empyema in eight cases. In the

case of myxoid chondrosarcoma reported by GOETZ *et al.* [17], the patient had a history of asbestos exposure. In our case, no possible aetiological factors could be identified.

ESMC is a neoplasm that frequently recurs and metastasizes. Radical excision is the treatment of choice. Radiotherapy may improve the outcome of the disease when a complete resection of the tumour is not possible [8, 9]. The role of chemotherapy is not clear, since very few data are reported in the literature, but it seems that ESMC shows poor sensitivity to drugs [7]. Our patient was completely nonresponsive to chemotherapy.

BUCHON *et al.* [6] stressed the importance of a wide sampling of the tumour mass, in order to detect the cartilaginous islands that are diagnostic for ESMC. In our case, the fine needle biopsy was inadequate, suggesting sarcomatoid mesothelioma. Surgical resection and subsequent histological examination allowed the correct diagnosis of ESMC. Immunohistochemistry is particularly useful in that it enables a differential diagnosis to be made between this tumour and other pleural neoplasms, which are all characterized by very similar clinical appearance and behaviour.

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