CASE STUDY

Clear cell sarcoma: an extremely rare cause of pleural disease

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Clear cell sarcoma: an extremely rare cause of pleural disease. Th. Bury, G. Hermans, R. Alexis-Agnant, Ph. Chevalier, R. Limet, P. Bartsch. ©ERS Journals Ltd 1997.

ABSTRACT: We present the case of a 36 yr old woman with a persisting complaints of left chest pain. A chest radiograph revealed multiple left pleural thickenings. Classical exploration was negative. Thoracic surgery allowed the subtotal removal of a huge pleural tumour. The histological examination revealed a clear cell sarcoma. The literature on this extremely rare tumour is reviewed.

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Clear cell sarcoma is a rare tumour first described by ENZINGER [1] in 1965. It has a uniform and distinctive clinical and morphological pattern which distinguishes it from other groups of sarcoma. The principal sites of this neoplasm are the extremities. Clear cell sarcoma is usually deeply situated and often has a close association with tendons and aponeuroses. Recently we have observed a similar tumour presenting as a pleural disease. The findings in this unusual location are presented below.

Case report

In May 1994, a 36 yr old Caucasian woman was admitted to hospital for investigation of a pleural disease. She had a 10 yr history of smoking eight cigarettes per day. There was no evidence of professional respiratory risk (e.g. asbestos exposure) and she had never had any serious past illness, except an excision of a congenital pigmented nevus with hairs (hair nevus) in 1974.

In February 1994, the patient complained of left chest pain and had lost 5 kg over a 4 month period. Routine laboratory examination results were normal, except for

the presence of a moderate inflammatory syndrome. Tumour markers were negative. Chest radiography revealed multiple left pleural thickenings. This was confirmed by a chest computed tomography (CT) scan. Indeed, the chest CT showed an extensive, irregular, circumferential left pleural thickening with a diaphragmatic involvement (fig. 1). This type of radiological presentation suggested firstly a mesothelioma. Bronchoscopic exploration with bronchoalveolar lavage and cytological analysis revealed no abnormalities. Pleural needle biopsy suggested a benign inflammatory condition. Therefore, open thoracotomy was performed to rapidly obtain an adequate specimen. Pathological examination of the pleural biopsy material revealed a massive infiltration by a tumoural tissue which was difficult to precisely qualify at the first microscopic examination. The tumoural cells were of epithelial monotonous appearance, arranged in cohesive sheets and lobules surrounded by fibrous septa of various thickness (fig. 2). The clear or eosinophilic cytoplasm contained a small amount of glycogen. There was no mucin secretion, keratinization, or pigment deposits. Routine immunohistochemistry was useless in the diagnosis, but electron microscopic examination disclosed numerous melanosomes in the cytoplasm (fig. 3). There were also rudimentary cell junctions and a discontinuous basal lamina around the tumoural cells. These characteristics are the ultrastructural features of clear cell sarcoma [2, 3]. Subsequent immunostaining with S-100 protein and anti-Melanoma (HMB45) antibodies was positive (fig. 4).

Biopsy material disclosed all the characteristics of the so-called "clear cell sarcoma" or "malignant melanoma of soft parts". An extensive workup was realized to exclude a metastatic disease. It included CT of the upper and lower abdomen, liver ultrasonography, *i.v.* pyelogram, thyroid, lung and bone scintigraphy; all of which were normal. A whole-body 18-F-fluorodeoxyglucose (FDG) positron emission tomography (PET) was also realized and showed moderate FDG uptake within the diffuse pleural thickening.

As treatment, a preoperative radiotherapy (40 Gy) was applied to the mediastinal pleural involvement followed

Fig. 1. — Computed tomographic image of the thorax, at first presentation. The left hemithorax demonstrates an irregular circumferential pleural thickening.

Fig. 2. – Histological appearance of the pleural biopsy: monotonous epithelial-like cells with clear or slightly granular cytoplasm and rounded vesicular nuclei (haematoxylin and eosin stain, internal scale bar = 50 μ m).

Fig. 3. – Electron microscopy of the pleural biopsy showing numerous premelanosomes of various sizes and configuration in the cytoplasm of tumoural cells. Some show the characteristic internal periodic structure (internal scale bar = 500 nm).

by a left pleuropneumonectomy (September 1994). Pathological observations confirmed the proposed diagnosis: the tumour was firm with a nodular surface; its distribution was circumferential and invaded the adjacent pulmonary tissue.

At present, the clinical course is satisfactory with a probable complete remission supported by a negative PET and CT findings (February 1997).

Discussion

Malignant neoplasms that originate from soft tissue are rare and clear cell sarcoma of tendons and aponeuroses is a rather rare type of soft tissue sarcoma [4, 5].

The clinical and histological findings in this patient are in agreement, except for the localization, with the

Fig. 4. – Immunohistochemistry using Amyl-Ethyl Carbazole staining (internal scale bar = 25 μ m). Anti-Melanoma (HMB45) is strongly positive, whilst cytokeratin (CK) shows a slight positivity. S-100 protein and Vimentine were also weakly positive.

symptomatology and pathology reported in the literature. In 1965, ENZINGER [8] was the first to describe it as a distinct entity and several reports on occasional cases of this tumour have been published since (about 200 published cases) [1, 6–8]. This rare tumour mainly afflicts young adults. The principal sites of the neoplasm are the extremities, especially the region of the foot and ankle. The trunk is only rarely involved. Clear cell sarcoma is a relatively slow-growing tumour with occasional symptoms reported by the patient, complaints beginning a few months to several years before the diagnosis. In our patient, there was a history of nonexplored left chest pain which started at least 4 yrs preceding consultation. The clinical course of this tumour is slow and progressive with recurrences and metastases. Most often, the metastases involve the regional lymph nodes, lungs and bones [9]. In previous literature, the treatment applied to this tumour varied greatly, but generally consists of radical excision, combined eventually with radiotherapy and/or chemotherapy.

To the best of our knowledge, this report is the first description of a clear cell sarcoma invading the pleural membrane. Its origin was probably from the connective tissue layer of the parietal pleura or by contiguous extension from a tendon or aponeurose of an intercostal muscle. It is also interesting to underline the possible theoretical relationship between the hair nevus excised in 1974 and this type of sarcoma. Indeed, it has been suggested that clear cell sarcoma was related to tumours of melanocytic origin [2]. However, in our case, the delay between nevus excision and the evidence of a pleural lesion was very long (more than 20 yrs) making unlikely any relationship between these two lesions; furthermore dermatological examination was and remains negative.

The histology of clear cell sarcoma displays distinctive features, which makes the pathological diagnosis easy, provided that the pathologist is aware of the enti-

ty. The characteristic microscopic pattern includes: epithelioid cellular appearance with clear cytoplasm; clear nuclei with dispersed chromatin; homogeneous growth pattern; scarce mitotic figures; absence of intracellular mucin; presence of intracellular glycogen or melanosomes; and abundant collagen fibres in the extracellular spaces [2, 3, 9, 10]. Recently, a primary chromosomal aberration (translocation 12;22) has been described in the majority (65%) of those cases [11].

Malignant pleural lesions are usually metastatic disease (lung, breast, *etc.*) and the most common cause of primary pleural neoplasm is the mesothelioma. Confronted with a malignant pleural disease, our pathologists in the first instance suggested a metastatic renal cell carcinoma or an epithelial mesothelioma. However, the search for a primary renal tumour was negative and complementary techniques (electron microscopy, immunohistochemistry) led us to exclude the diagnosis of mesothelioma and to confirm the diagnosis of "clear cell sarcoma". This term is descriptive and reflects the uncertainty of histogenesis [3, 5, 12]. Twenty eight months after the radical excision, the follow-up of our patient failed to reveal recurrent disease. Indeed morphological (CT scan) and metabolic (PET) imaging are negative and the weight of the patient remains stable.

In conclusion, clear cell sarcoma is a rare homogeneous entity among soft tissue sarcomas showing a strong predilection for tendons and aponeuroses of the extremities. The present case is of interest because it is the first description of a pleural invasion. The treatment applied was radical excision. Follow-up observation after 28 months shows no recurrence.

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