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Gluteal muscle metastases from malignant pleural mesothelioma: a case report

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Abstract

Malignant pleural mesothelioma (MPM) is a rare malignancy arising from the mesothelial or subthelial layer of the pleura, and it has increased in recent decades, mainly associated with asbestos exposure. Sarcomatoid mesothelioma is the second-most common subtype of MPM. It is usually difficult to differentiate MPM from benign mesothelial pleural proliferations or other cancers. Because of its nonspecific symptoms, MPM is often diagnosed at a late stage with distal metastases. However, it is extremely rare to see a metastatic lesion within subcutaneous tissue and muscles, which is most likely caused by hematogenous spread. We present a case of sarcomatoid mesothelioma with a metastatic lesion of the right gluteal muscles.

Key words: malignant pleural mesothelioma, sarcomatoid mesothelioma, muscle metastases.

Case Report

An 81-years old woman was referred to our department because of casual finding of left pleural effusion. The patient undergone thoracentesis with cytological and microbiological examination negatives. Two months before, in another hospital situated in a foreign country, the patient had a diagnosis of malignant neoplasm not well characterized (myoepithelial tumor versus extraskelatal myxoid chondrosarcoma) of the right gluteal region muscles. As the sample had been taken abroad, the patient only had written documentation of the examinations performed. In our department, the total body CT-scan showed a solid neoformation at right gluteus medius and gluteus maximus muscles (Figure 1A), with regional lymphadenopathies and infiltration of the ipsilateral iliac bone, multiple repetitive solid lesions in the lung parenchyma bilaterally and mediastinal lymphadenopathies, a large right pleural effusion with atelectasis of lung parenchyma and pleural lesions (Figure 1B). These findings suggested that the lesions described were the manifestation of a single pathology. As the disease seemed to be progressing rapidly, we decided not to ask to see the first biopsies performed in another hospital, as this would have led to a longer diagnosis time. Therefore, we chose to try another faster way to get neoplastic material. In particular, we identified our target in pleural lesions described on CT scan, and the patient then underwent a medical thoracoscopy. The examination showed the presence of brown and white exophytic lesions throughout the parietal pleura, the surface of the lung was altered as a neoplastic appearance (Figure 1C). The histological features of the pleural biopsies revealed a poorly differentiated malignant neoplasm consisting of pleomorphic cellular elements, sometimes polygonal in

shape, sometimes elongated, vaguely spindle-shaped, scarce cytoplasm, nucleus with thickened chromatin, sometimes with prominent nucleolus, and with a mostly solid architecture, sometimes organized in nests and pseudoglandular structures, sometimes with vascular-like organization, infiltrative pattern with associated desmoplasia in the absence of frank deposition of stromal matrix. Numerous mitoses. Necrosis absent. Proliferative index, measured by immunohistochemical staining for Ki67: 75%. Immunophenotypic characterization of the neoplasm gave the following results: Cytokeratin CAM5.2 (+/-), CD 31 (-/+), WT1 (+), CD 117 (-/+), CD 99 (+) (Figure 2). The definitive diagnosis was sarcomatoid pleural mesothelioma. The case was discussed in the multidisciplinary tumor board, and the patient was eligible for a systemic therapy with a combination of platinum and a third generation antifolate. The patient was finally entrusted to the care of the oncology department.

Discussion

Diffuse mesothelioma is a rare malignancy arising from the mesothelial or subthelial layer of the pleura (80-90%), peritoneum (10-15%), pericardium, and tunica vaginalis testis (<5%), and most cases arise in the pleura. It has increased during the last decades mainly associated with asbestos exposure [1]. It is usually difficult to differentiate MPM from benign mesothelial pleural proliferations or other cancers. Because of its nonspecific symptom, MPM is often diagnosed at a late stage with distal metastases including lymph nodes, lung, liver, adrenal glands, and kidney. However, it is very rare to see a metastatic lesion within subcutaneous tissue and muscles, which is most likely via hematogenous spread [2]. Sarcomatoid mesothelioma is the second most common subtype of MPM, and it has been associated with only 4-month survival in patients who underwent surgical treatment [3]. The WHO classification defines it as a proliferation of spindle cells arranged in fascicles or in haphazard patterns invading the adipose tissue or lung parenchyma. Necrosis and atypical mitoses are frequently present. Heterologous elements such as osteosarcoma, rhabdomyosarcoma, or chondrosarcoma can be present in rare cases. Sarcomatoid mesothelioma is morphologically heterogeneous, and the upcoming WHO classification includes variants (desmoplastic mesothelioma, sarcomatoid) and cytologic features (transitional, pleomorphic) [3,4]. Our case is of interest for two reasons. The first concerns the diagnosis of sarcomatoid mesothelioma. Diagnosis may be challenging, given the need for a multidisciplinary correlation among clinical, histologic, immunohistochemical and/or molecular, and radiologic findings. MPM diagnosis is usually challenging for pathologists [5] because its phenotype varies among patients and mimics benign reactive mesothelial proliferations and other cancers. In many cases, only cytological material or a limited

amount of tissue is available for pathological evaluation [6]. In our case, we performed a medical thoracoscopy, thus being able to take several pleural biopsies and collect sufficient material for histological analysis. The typical macroscopic appearance of malignant mesothelioma is a diffuse pleural thickening by a white-brown compact mass. Rarely, malignant mesothelioma may present as a localized mass [7]. Indeed, we observed during the thoracoscopic examination exophytic and of different colors (white and brown) pleural lesions. The differential diagnosis of sarcomatoid mesotheliomas usually requires extensive immunohistochemical and molecular work up. After determination of the malignant process, the differential diagnosis includes other sarcomatoid tumors, such as sarcomatoid carcinomas of the lung and other sites (e.g., renal cell carcinoma). The distinction from carcinomas can be challenging, as expression of specific differentiation markers may be negative and mesothelial markers (WT-1, calretinin) can tend to be weakly expressed or even negative [8]. Histologically, sarcomatoid mesothelioma presents features like a soft tissue sarcoma, with 90% of tumor cells spindle shaped. In general, sarcomatoid mesothelioma expresses cytokeratins, while calretinin and WT1 are expressed in 31% and 33% of samples, respectively. In most cases, immunostaining of keratin and calretinin is a useful and sensitive assay for differentiating sarcomatoid mesothelioma from other sarcomas [9]. The biopsy of the right gluteal region, performed elsewhere, had not been conclusive. In fact, on the one hand, the relatively clear positivity of CD117 in a considerable proportion of tumor cells and the positivity of S100 tended to support the diagnosis of extraskeletal myxoid chondrosarcoma. On the other hand, speckled keratin positivity was supportive for a myoepithelial tumor. Immunohistochemical analyses performed on pleural biopsies taken at our institute, while showing a clear positive for WT1, were negative for Calretinin and D2-40 (two of the most sensitive mesothelioma markers along with WT1).

The second reason for interest in this case concerns the site of the metastases. The natural history of MPM varies but may involve an initial presentation of locally invasive disease followed by hematogenous metastases. MPM typically spreads by local invasion or extension. Distant metastatic disease is unusual in mesothelioma but may involve the liver, bone, brain, adrenal gland, kidney, pancreas, thyroid, spleen, skin, and lymph nodes. It is common to see MPM with lymph nodes and organ involvement. The tumor disseminating routes are direct invasion, lymphatic, and hematogenous spread [10]. Hilar and mediastinal lymph node involvement occurs in less than 50% of patients. Extrathoracic lymph node involvement is very rare. Cervical lymph node metastasis has been reported at autopsy. Clinically documented distant lymph node metastasis from pleural mesothelioma is very rare [11]. In most of the cases reported in the literature, the patients underwent surgical resection with varying uses of adjuvant radiotherapy and chemotherapy. Disease recurrence after

surgical resection can be in the local chest wall as well as a variety of distant sites including lung parenchyma, mediastinal and abdominal lymph nodes, stomach, small bowel, axial skeleton, skin, and brain [12]. The postmortem records of 318 patients with MPM demonstrated that extrathoracic metastasis was observed in the liver (31.9%), peritoneum (24.4%), and bone (13.8%). In these records, metastasis was found in many organs that are not usually regarded as sites of MPM metastasis, including the adrenals (10.2%), spleen (10.8%), and brain (3.0%) [13]. To our knowledge there are in literature three papers describing muscle metastasis of MPM [14]; a case of multiple skeletal metastases of biphasic type MPM; a case of left vastus lateralis muscle metastases of epithelioid MPM [15]; a case of epithelioid mesothelioma with invasion of transverse muscle tissue of the chest [16].

Conclusions

Diffuse mesothelioma is a rare malignancy and the sarcomatoid mesothelioma is the second most common subtype of malignant pleural mesothelioma. The diagnosis may be challenging, given the need for a multidisciplinary correlation among clinical, histologic, immunohistochemical and/or molecular, and radiologic findings. In these cases, muscle metastases are very rare.

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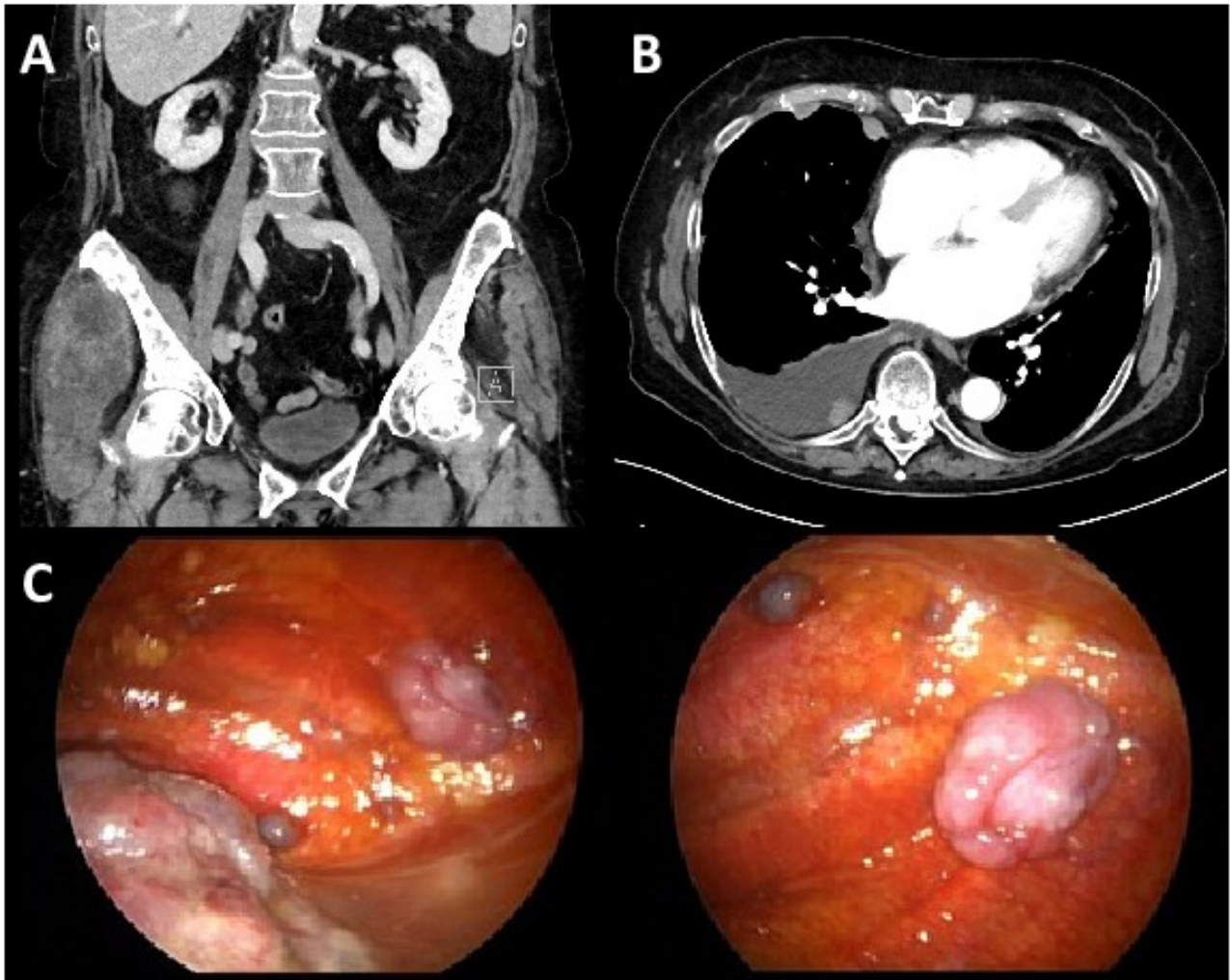


Figure 1. A) Right gluteus solid neoformation; B) right pleural effusion and pleural neoformations; C) pleural exophytic lesions.

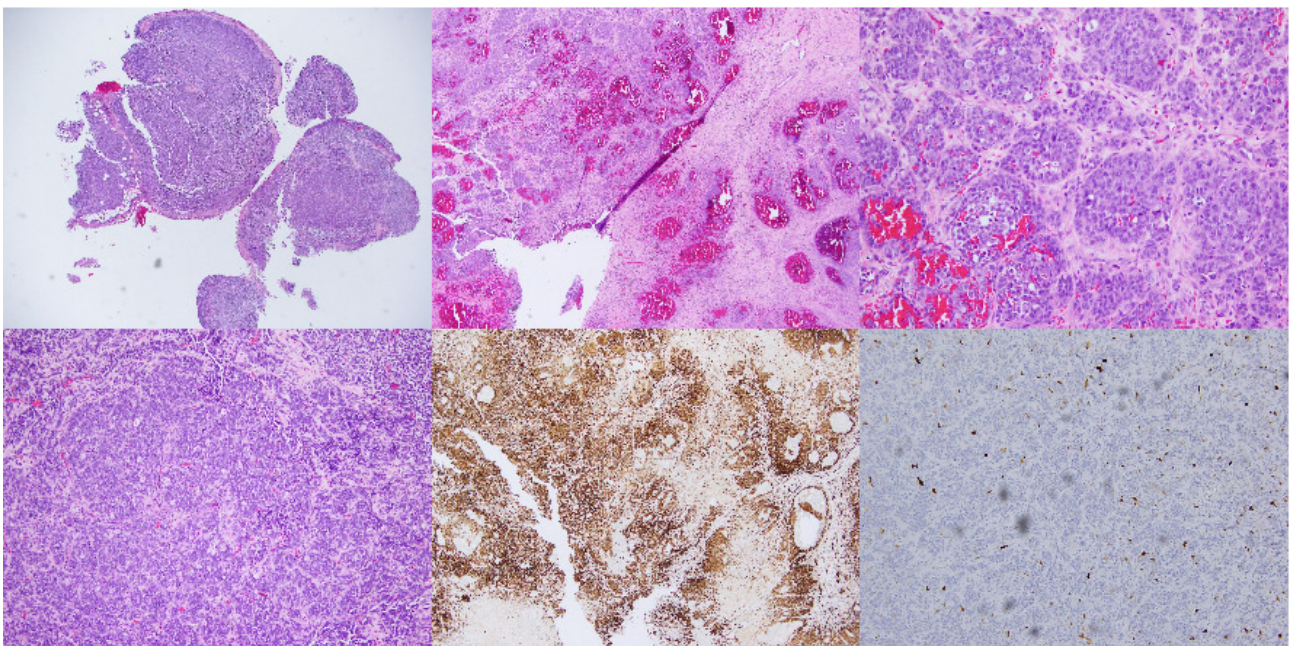


Figure 2. Histological and immunohistochemical features of the pleural biopsies.