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.

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Case Report

An 81-year-old woman was referred to our department because of a casual finding of left pleural effusion. The patient underwent thoracentesis with negative cytological and microbiological examination. Two months before, in another hospital situated in a foreign country, the patient had a diagnosis of malignant neoplasm not well characterized (myoepithelial tumor *vs.* extraskeletal 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 computed tomography (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. We chose to try another faster way to get neoplastic material. In particular, we identified our target in the pleural lesions described on the 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, and the surface of the lung was altered with 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 were observed. Necrosis was absent.

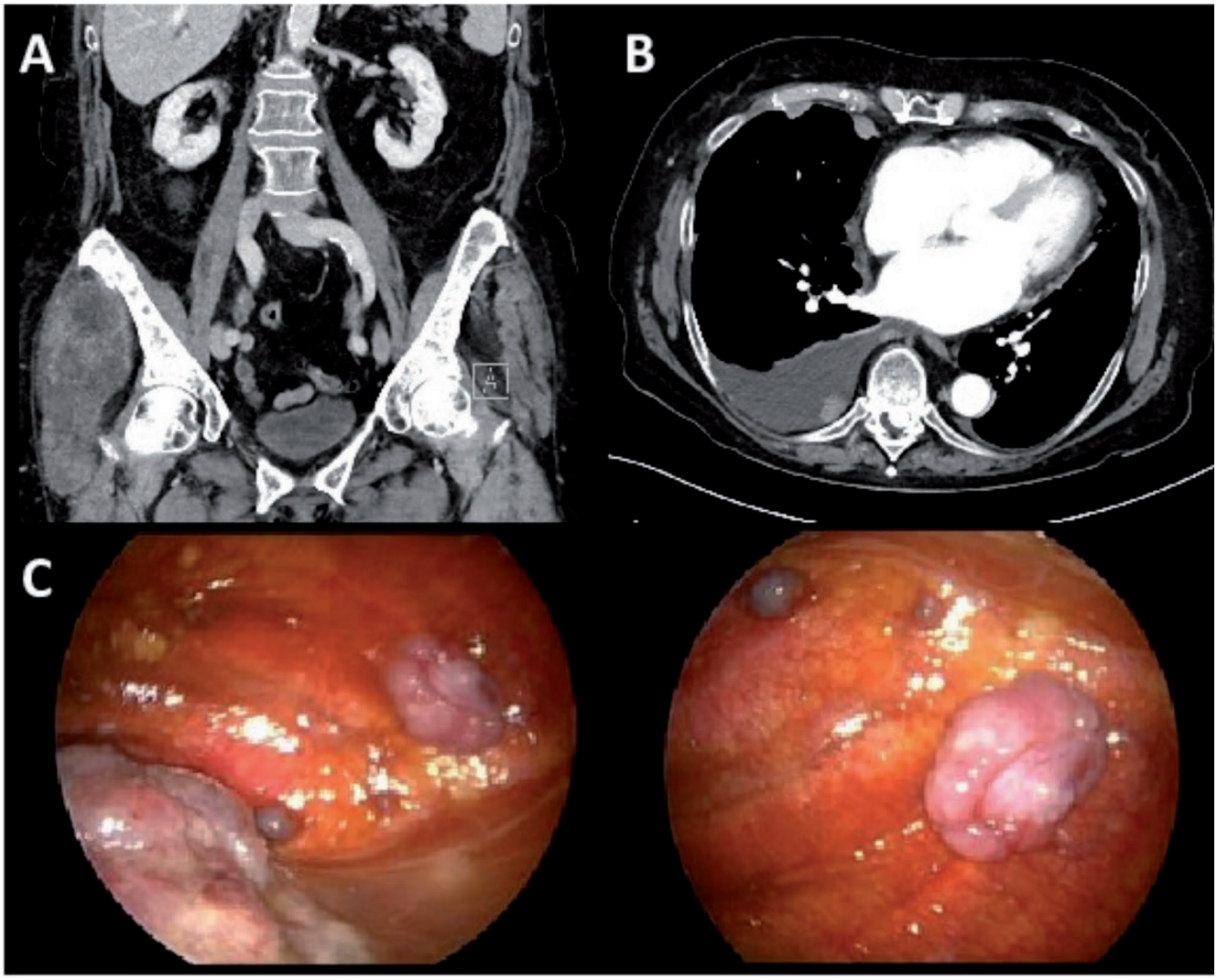

Figure 1. A) Right gluteus solid neoformation; B) right pleural effusion and pleural neoformations; C) pleural exophytic lesions.

Proliferative index, measured by immunohistochemical staining for Ki67, was 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 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 malignant pleural mesothelioma (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, 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 World Health Organization (WHO) classification defines it as a proliferation of spindle cells arranged in fascicles or 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

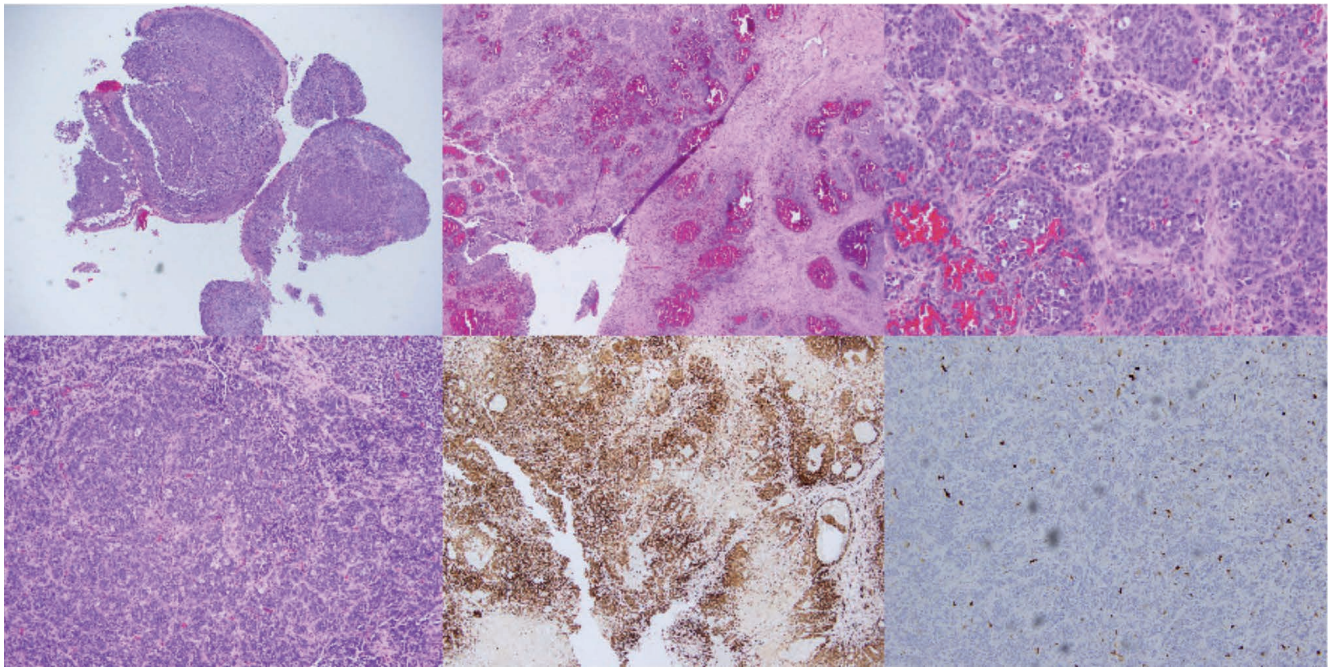

Figure 2. Histological and immunohistochemical features of the pleural biopsies.

molecular, and radiologic findings. MPM diagnosis is usually challenging for pathologists because its phenotype varies among patients and mimics benign reactive mesothelial proliferations and other cancers [5]. 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 with 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 workup. 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 of 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 *post-mortem* 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 MPM. 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.

References

1. Micolucci L, Akhtar MM, Olivieri F, et al. Diagnostic value of microRNAs in asbestos exposure and malignant mesothelioma: systematic review and qualitative meta-analysis. Oncotarget 2016;7:58606-37.
2. Chen KB, Huang YJ, Huang Y, et al. Metastasis of sarcomatoid malignant mesothelioma with p16/CDKN2A deletion manifested as a subcutaneous mass in the back: a case report and review of literature. Int J Surg Pathol 2021;29:856-63.
3. Beasley MB, Galateau-Salle F, Dacic S. Pleural mesothelioma classification update. Virchows Arch 2021;478:59-72.
4. Travis WD, Brambilla E, Nicholson AG, et al; WHO Panel. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. J Thorac Oncol 2015;10:1243-60.
5. Alì G, Bruno R, Fontanini G. The pathological and molecular diagnosis of malignant pleural mesothelioma: a literature review. J Thorac Dis 2018;10:S276-84.
6. Monaco S, Mehrad M, Dacic S. Recent advances in the diagnosis of malignant mesothelioma: focus on approach in challenging cases and in limited tissue and cytologic samples. Adv Anat Pathol 2018;25:24-30.
7. Travis WD. Sarcomatoid neoplasms of the lung and pleura. Arch Pathol Lab Med 2010;134:1645-58.
8. Berg KB, Churg A. GATA3 immunohistochemistry for distinguishing sarcomatoid and desmoplastic mesothelioma from sarcomatoid carcinoma of the lung. Am J Surg Pathol 41:1221-5.
9. Galetta D, Catino A, Misino A, et al. Sarcomatoid mesothelioma: future advances in diagnosis, biomolecular assessment, and therapeutic options in a poor-outcome disease. Tumori 2016;102:127-30.
10. Ward RE, Ali SA, Kuhar M. Epithelioid malignant mesothelioma metastatic to the skin: A case report and review of the literature. J Cutan Pathol 2017;44:1057-63.
11. Kant S, Verma SK, Sanjay. Malignant pleural mesothelioma without asbestos exposure with distant metastasis in a peripheral lymph node: a case report. Lung India 2008;25:31-3.
12. Zardawi SJ, Li BT, Zauderer MG, et al. Localized malignant pleural mesothelioma with renal metastasis. Oxf Med Case Reports 2015;2015:170-2.
13. Finn RS, Brims FJH, Gandhi A, et al. Postmortem findings of malignant pleural mesothelioma: a two-center study of 318 patients. Chest 2012;142:1267-73.
14. Grellner W, Staak M. Multiple skeletal muscle metastases from malignant pleural mesothelioma. Pathol Res Pract 1995;191:456-62.
15. Akyurek S, Nalca Andrieu M, Hicsonmez A, et al. Skeletal muscle metastasis from malignant pleural mesothelioma. Clin Oncol (R Coll Radiol) 2004;16:585.
16. Kong L, Ren D, Chen S, Duan G. A case report of breast metastasis from malignant pleural mesothelioma invading the rhabdoid muscle. Asian J Surg 2023;46:2067-8.