

Dedifferentiated primary mediastinal liposarcoma mimicking a thymic tumor

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Key words

Liposarcoma • Mediastinal liposarcoma • Thymic tumor

Summary

Mediastinal tumors are heterogeneous and the diagnosis depends on their location in the mediastinum. The most frequent tumors are germinal tumor, lymphoma and thymoma. The clinical and radiological aspects are often not sufficient to orient the diagnosis and biopsy is necessary to confirmed it. Here, we present a rare case of an anterior mediastinal mass incidentally detected in

a 63 years old man during assessment for asthma. The lesion was presumptively diagnosed as a thymic epithelial tumor based on location and radiological characteristics. Surgical biopsy revealed a primary dedifferentiated mediastinal liposarcoma with multiple lung metastases.

Introduction

Mediastinal tumors are rare and most of them occur in the anterior mediastinum corresponding to thymomas, lymphomas or germ cell tumors. Otherwise, primary liposarcoma of the mediastinum is an extremely rare tumor, accounting for 0.13% to 0.75% of all mediastinal tumors ¹. On the other side, these neoplasms usually arise from the lower extremities and the retroperitoneum, while the mediastinal localization is very rarely reported in clinical practice (about 1% to 2% of all liposarcomas) and usually at the level of the posterior mediastinum ^{2,3}. According to the most recent classification by the World Health Organization, liposarcomas are classified histologically into well-differentiated liposarcoma (accounting for 40% to 45% of liposarcomas); myxoid liposarcoma (accounting for 15% to 20%); dedifferentiated liposarcoma (arising de novo and occurring in up to 10% of well-differentiated liposarcomas); and pleomorphic liposarcomas (rarest, accounting for 5%) ⁴. Here, we report and discuss an unusual dedifferentiated liposarcoma presenting as an anterior mediastinal mass and mimicking a thymic epithelial tumor.

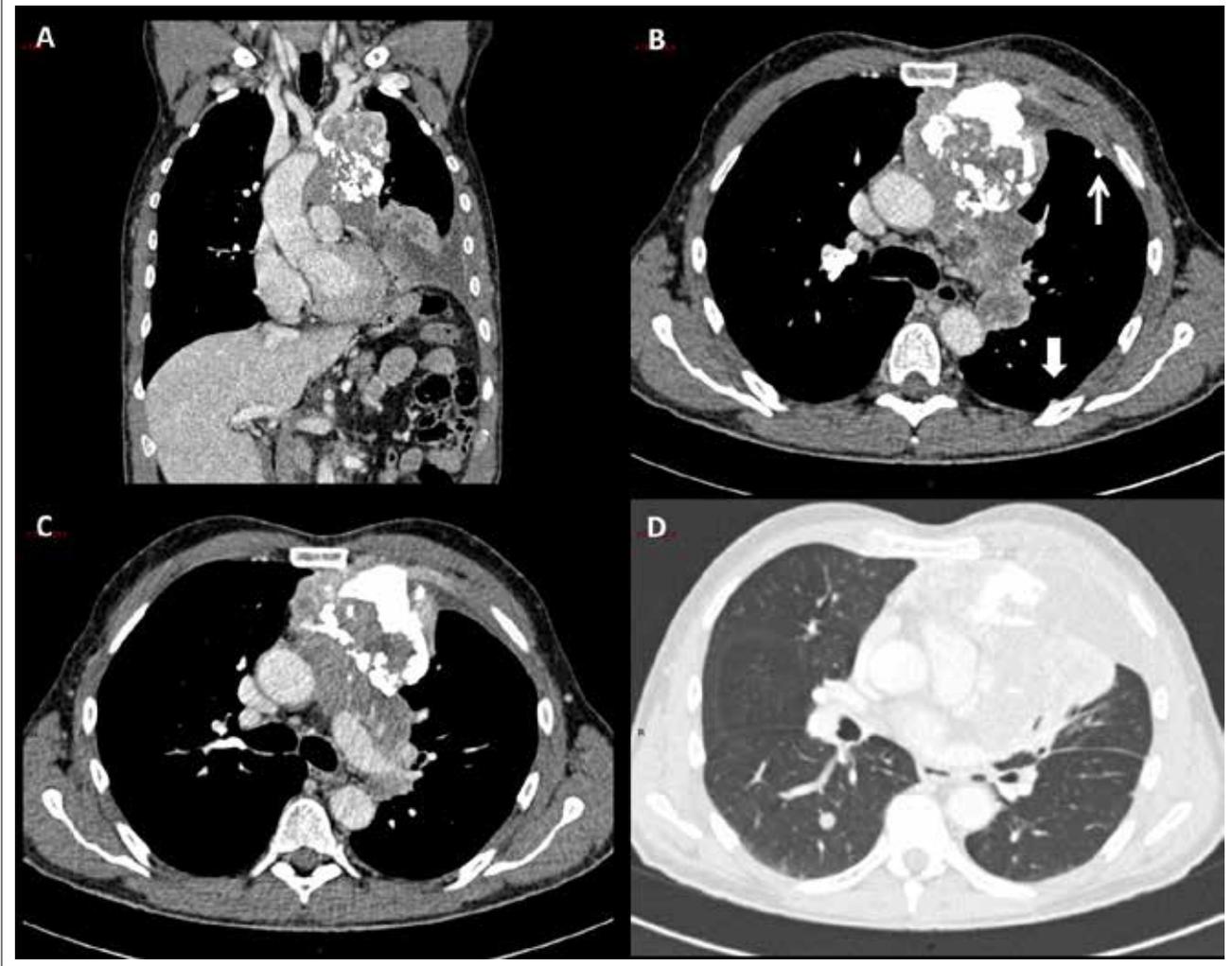
Clinical case

An anterior mediastinal mass was discovered in a 63 years old man during assessment for asthma. The patient had no relevant clinical history and complained about dyspnea and weight loss (10% over the last 6 months). Thoracic Computerized Tomography (CT) scan revealed a left anterior mediastinal mass with a large central calcified area (Fig. 1). The tumor measured 11 cm in the main axis and had an aggressive and infiltrant behavior (lung parenchyma, phrenic nerve). It was associated to multiple pleural nodules and a moderate pleural effusion. No nodal enlargement was seen, but there were several contro-lateral lung micronodules, consistent with metastatic spreading (Fig. 1). These radiologic findings suggested a thymic tumor. Clinical examination revealed no sign of myasthenia. Serum markers of germinal tumors were not elevated (Human Chorionic Gonadotropin or Alpha Foetoprotein). During video-assisted thoracoscopy, we confirmed diffuse pleural extension. The biopsy of a pleural nodule and talc poudrage were performed. Histologic examination showed a malignant tumor with two different parts. The most abundant

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Fig. 1. A. Chest CT scan (coronal view) showing a large anterior mediastinal mass with central ossification. Elevation of left diaphragm and pleural effusion are evident. B. Chest CT scan (axial view, mediastinal window) showing the anterior mediastinal mass and calcified (thin arrow) and uncalcified (fat arrow) pleural nodules. C. Chest CT scan (axial view, mediastinal window) showing the large mediastinal mass encasing main elements of left lung hilum. D. Chest CT scan (axial view, lung window) showing one of the contro-lateral lung nodules.

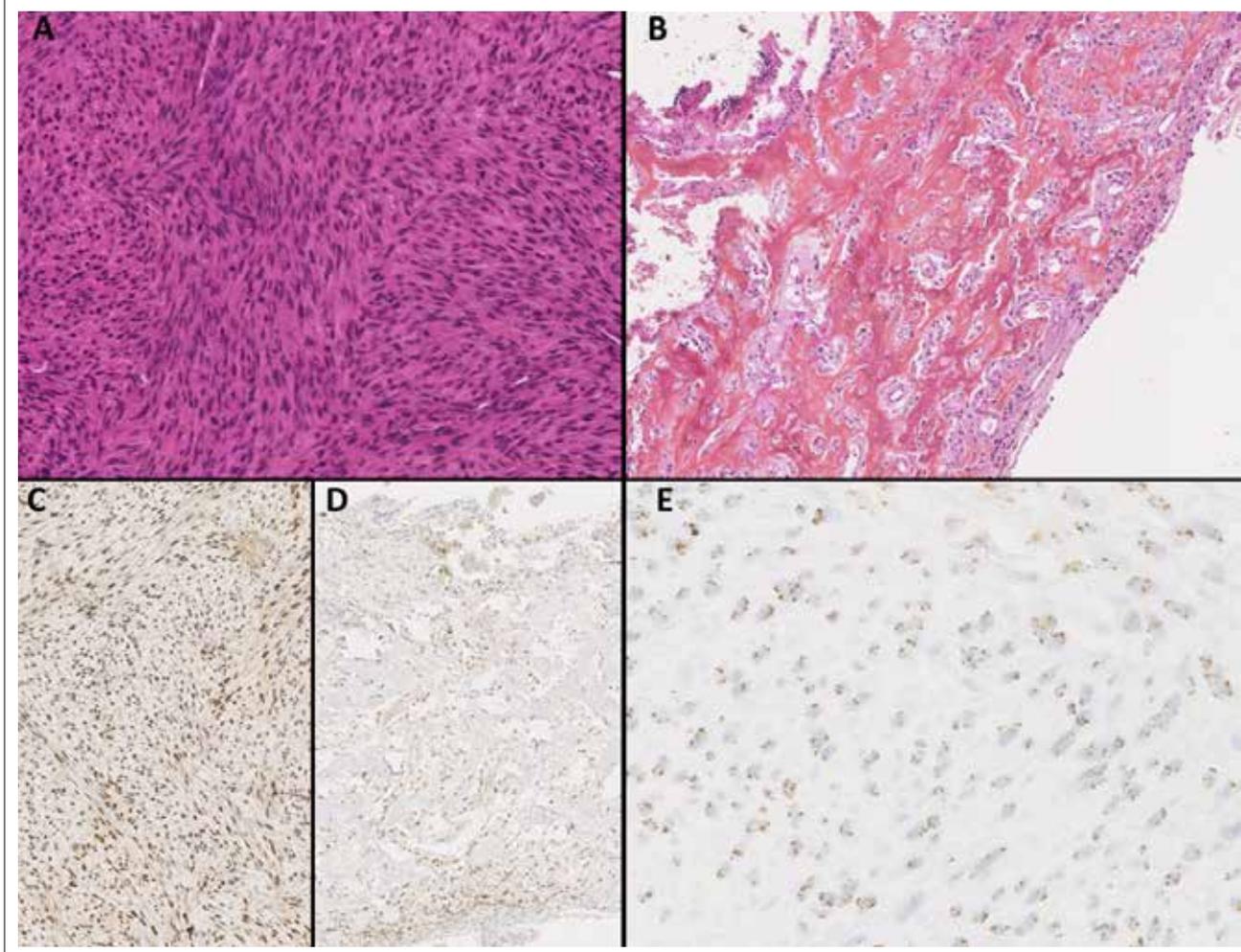


component was an undifferentiated high-grade spindle-cell proliferation organized in storiform pattern, with moderate mitotic activity (10 mitoses/10 HPF). Another component consisted of bone-forming tumor (Fig. 2). Tumor cells were negative for immunostains with smooth muscle actin, desmin, CD34, S100 protein, AE1/AE3 and EMA antibodies. MDM2 antibody revealed nuclear staining in both tumor areas (Fig. 2). Chromogenic in Situ Hybridization (CISH) performed with a *MDM2* probe on formalin-fixed paraffin-embedded tissue sample showed amplification of *MDM2* gene (Fig. 2). Although no well-differentiated liposarcoma component was found in the biopsy samples, dedifferentiated liposarcoma was final diagnosis according to histological features and molecular pattern. Because of metastatic disease at presentation, the tumor was not considered as resectable and chemotherapy based on doxorubicin and ifosfamide was started.

Discussion

We report an unusual case of large anterior mediastinal mass corresponding to dedifferentiated liposarcoma. The most common tumors of the anterior mediastinum include thymic tumor, lymphoma and germ cell tumors. As remarked by Grobmyer and co-workers⁵, fewer than 150 cases have been reported in the medical literature. In our case, these diagnoses were rapidly infirmed on the basis of clinical, laboratory and pathologic grounds. The hypothesis of dedifferentiated liposarcoma was not suggested by radiologic findings, because of the absence of fatty component. Moreover, mediastinal liposarcomas are rarely encountered in clinical practice representing 1% to 2% of all liposarcomas; anyway they are the most common sarcomas of the mediastinum, particularly in the anterior location². As primary mediastinal liposarcomas are rare, it is mandatory to exclude a metastatic disease from a primary liposarcoma of the retroperitoneum or soft tissues.

Fig. 2. Dedifferentiated liposarcoma (A, HES staining, x200) containing metaplastic woven bone (B, x100). Strong nuclear expression of MDM2 antibody in both tumor components (C and D). The diagnosis of dedifferentiated liposarcoma was confirmed with CISH, showing *MDM2* amplification.



Three main histologic types with different prognostic behavior are described: well-differentiated/dedifferentiated liposarcoma, myxoid liposarcoma, and pleomorphic liposarcoma². In anterior mediastinum, the most frequent type is well-differentiated/dedifferentiated liposarcoma, whereas pleomorphic liposarcomas are uncommon, and myxoid liposarcomas are exceptional³. Liposarcoma classification has been improved by advances in the molecular characterization of soft tissue tumors³. Less than 200 primary mediastinal liposarcomas have been reported to date, either in case reports or in series³⁻⁶, but in the majority of these reports molecular analysis was not used to confirm diagnosis⁴⁻⁷. A recent series of 24 cases of intrathoracic liposarcomas showed that mediastinal liposarcomas present a preponderance of uncommon subtypes and unusual morphologic variants, including, for example, myxoid well-differentiated liposarcoma mimicking myxoid liposarcoma, as well as differentiated myxoid liposarcoma mimicking well-differentiated liposarcoma⁴. In these cases diagnosis was confirmed by molecular genetic testing. Thus, accurate histopathologic and molecu-

lar classification is essential to distinguish relatively indolent well-differentiated and dedifferentiated liposarcomas from much more rapidly progressive histotypes, such as myxoid and pleomorphic liposarcoma.

Conclusion

Although infrequent, primary mediastinal liposarcoma should be considered in differential diagnosis of anterior mediastinal masses. Molecular characterization should be made, as different subtype of liposarcoma have different prognosis. Exhaustive clinical and pathological work-up are necessary to best characterize and manage this unusual tumor.

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