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CASE REPORT

Radiological-pathological correlation of malignant teratoma with liposarcomatous transformation: Proven by repeated transthoracic needle biopsy

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Abstract

A mediastinal germ cell tumor with a sarcomatous component is extremely rare and is accompanied by a poor prognosis. Clinical and radiologic diagnosis is very difficult. Herein, we report a rare case of anterior mediastinal malignant teratoma containing a growing liposarcomatous component and detail the diagnostic process. The case was diagnosed by repeated transthoracic needle biopsy and correlated with changes in follow-up chest computed tomography and serum tumor markers. We also provide a review of the literature.

Introduction

Germ cell tumors (GCTs) usually originate in the gonad. Mediastinal GCTs represent approximately 1–3% of all GCTs.[1] Mediastinal GCTs with a sarcomatous component are extremely rare and have a poor prognosis because the sarcomatous component appears to be highly resistant to the chemotherapy regimen for GCTs.[2] Furthermore, differentiating GCT with a sarcomatous component from GCT without a sarcomatous component is very difficult, both clinically and radiologically.

Case report

A 43-year-old man was admitted to our hospital for evaluation of a huge anterior mediastinal mass and a complaint of anterior chest pain. Laboratory tests taken at the time of admission showed elevated levels of alpha-fetoprotein (AFP; 3413 IU/mL vs. normal level 0–5.8 IU/mL) and β-human chorionic gonadotropin (β-hCG; 444 mIU/mL vs. normal level 0–5 mIU/mL). The initial contrast-enhanced chest computed tomography (CT) images revealed a 9 × 7 cm mass in the anterior mediastinum showing heterogeneous enhancement (Fig 1). On follow-up testicular ultrasonography, there was no evidence of GCT. Based on laboratory test results and imaging findings suggesting an invasive anterior mediastinal tumor, we presumed that the mass was a primary non-seminomatous malignant GCT and transthoracic needle biopsy (TTNB) confirmed that the specimen was teratoma with suspicious immaturity (Fig 2a–c).[3]

The tumor was considered an immature teratoma and the patient underwent two cycles of chemotherapy with bleomycin, etoposide, and cisplatin (BEP) and a third cycle of chemotherapy with etoposide, ifosfamide, and cisplatin (VIP). During treatment, AFP and β-hCG levels gradually decreased and normalized. However, a follow-up CT series taken one month later showed that the tumor had

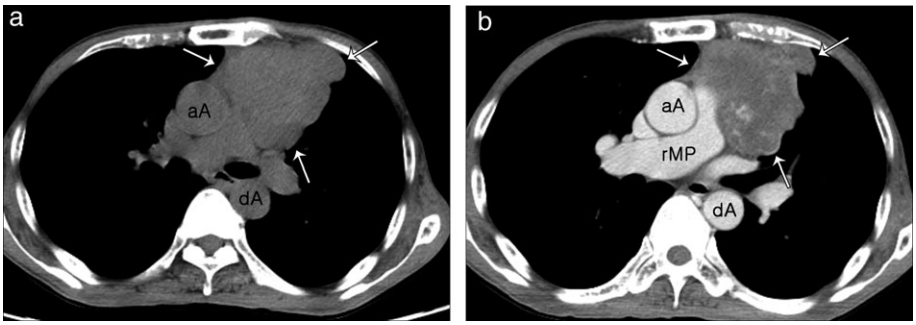

Figure 1 (**a**) Unenhanced and (**b**) contrast-enhanced images of initial chest computed tomography. There is a 9 × 7 cm mass (arrows, **a,b**) in the anterior mediastinum, which had a lobular margin and showed heterogeneous enhancement without a demonstrable fat component, with extrinsic compression and/or early invasion of adjacent mediastinal great vessels and left upper lobe. aA, ascending thoracic aorta; dA, descending thoracic aorta; rMP, right main pulmonary artery.

markedly increased in size (data not shown) and contrast-enhanced magnetic resonance imaging revealed a huge heterogeneous anterior mediastinal mass with marked interval growth (Fig 3). The fat component within the tumor, which was not clear on baseline CT, was clearly demonstrated on follow-up contrast-enhanced CT images at three months (Fig 4). In spite of an additional three months of chemotherapy, the tumor showed slight growth. Because of the conflicting results between laboratory testing and imaging findings, we considered the possibility of teratoma with growing lipogenic tissue, even though it has rarely been reported. We performed another TTNB, which targeted the growing fat component. This specimen pathologically revealed a well-differentiated liposarcoma (Fig 2d–e). From the clinical course including laboratory data, and imaging and pathologic findings, we diagnosed malignant teratoma with liposarcomatous transformation. The patient underwent palliative radiotherapy, but the disease showed poor prognosis.

Discussion

Extragonadal GCTs are uncommon and the mediastinum is the most common location.[4,5] This type of tumor occurs

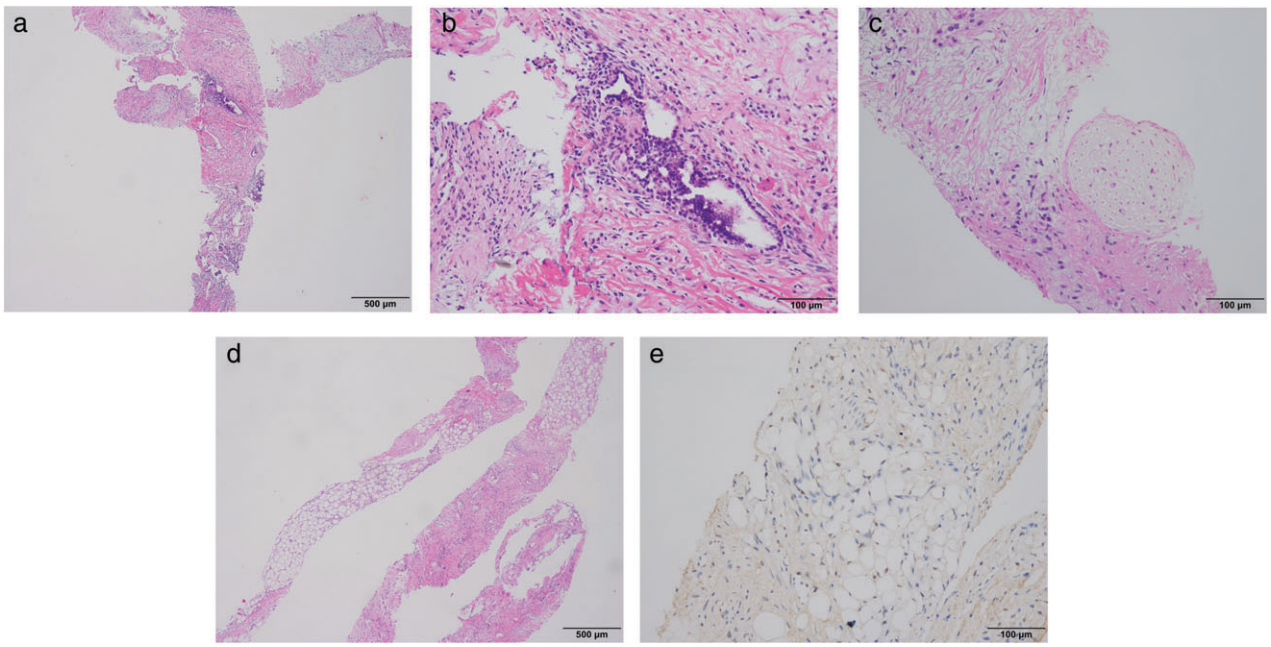

Figure 2 Microscopic findings of malignant teratoma in (**a–c**) first transthoracic needle biopsy (TTNB) and liposarcoma in (**d–e**) second TTNB. The tumor (**a**) had teratomatous features (hematoxylin–eosin [HE], original magnification x40), and showed (**b**) immature neuroepithelial components (HE, original magnification x200), (**c**) an immature cartilage component (HE, original magnification X200), and (**d**) several lipogenic tissues with dense collagenous tissue (HE, original magnification x40). (**e**) The fat cells showed immunoreactivity for MDM2 (original magnification x200).

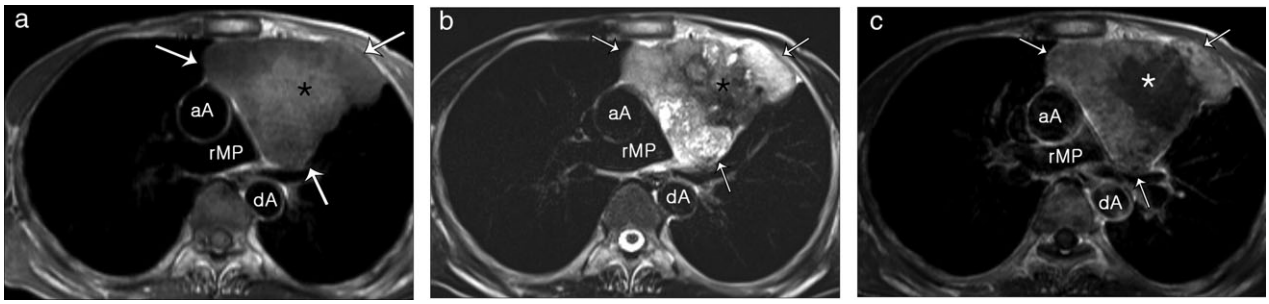

Figure 3 Double inversion-recovery (IR) (**a**) T1 weighted, (**b**) T2-weighted, and (**c**) gadolinium-enhanced T1 weighted chest magnetic resonance imaging at one month follow-up. A huge, prominent heterogeneous anterior mediastinal mass (arrows, **a–c**) contains a relatively large hemorrhagic and necrotic portion, which shows subtle high signal intensity on T1 weighted image (asterisk, **a**), a heterogeneous mixed area of strong high and dark signal intensities on T2 weighted imaging (asterisk, **b**), and low signal intensity without contrast enhancement on contrast-enhanced T1 weighted image (asterisk, **c**). (**c**) The remaining portion of the mass shows heterogeneous enhancement, which is suggestive of malignant potential. aA, ascending thoracic aorta; dA, descending thoracic aorta; rMP, right main pulmonary artery.

more frequently in men and often invades adjacent vasculature.[6] Malignant GCTs secrete tumor markers, such as lactic dehydrogenase, AFP, and β-hCG, which are useful for diagnosis and follow-up of the disease.[4]

In the present case, the tumor was initially diagnosed as malignant teratoma with immaturity, in association with tumor markers and imaging findings. Malignant teratoma can be classified as an immature teratoma, teratocarcinoma, or teratoma with malignant transformation (TMT).[7,8] Teratocarcinoma refers to a mixture of teratoma with undifferentiated stem cells of embryonal carcinoma or choriocarcinoma, or both.[9] TMT refers to a GCT containing a non-germ cell malignant component.[10] The tumor in this case could not be thoroughly distinguished after the first biopsy, but the patient initially underwent chemotherapy for an immature teratoma. While receiving treatment, the patient showed resistance to both BEP and VIP chemotherapy regimens. A follow-up CT series showed that the invasive anterior mediastinal tumor was deteriorating with an obvious fat component. During that time, AFP and β-hCG levels gradually decreased and normalized.

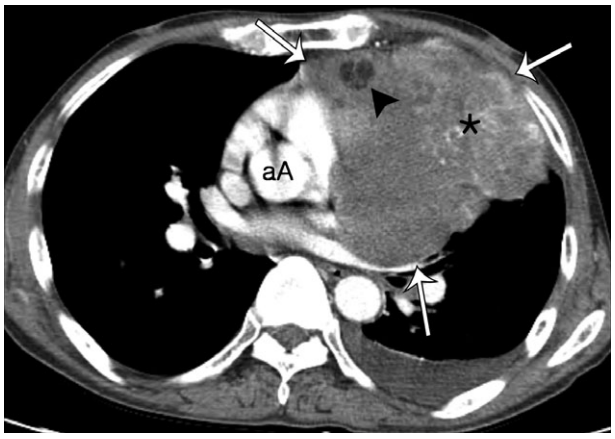

Figure 4 Follow-up contrast-enhanced computed tomography (CT) imaging at three months. The anterior mediastinal mass (arrows) also shows marked interval growth and heterogeneous enhancement with a marked hypervascular portion (asterisk). Also the fat component within the tumor (arrowhead), which was not clear on baseline CT, is clearly demonstrated.

Because of the contradictory results between the laboratory tests and follow-up imaging, we inferred that there was a sarcomatous component rather than AFP-producing cells, which is one of the causes of poor prognosis in teratomas.[11] We repeated TTNB and the liposarcomatous component inside the teratoma was diagnosed by immunohistochemical staining. Although immunohistochemistry with MDM2 can indicate false positives, the growing tendency and invasive imaging features of the tumor indicate malignant potential, such as atypical lipomatous tumor or liposarcoma, rather than benign lipoma.[12] Therefore, we made a diagnosis of teratoma with liposarcomatous transformation among the categories of malignant teratoma.

Two different mechanisms for TMT have been noted: totipotential embryonal cells might be differentiated into malignant somatic elements, or mature teratomas can be transformed into a malignant element.[13] Because TTNB cannot represent the entire tumor, we could not ensure that the liposarcomatous component was emerging rather than inherent, which is one of our limitations. However, TMT is more likely to be the correct diagnosis in this case rather than teratocarcinoma or growing teratoma syndrome, which refers to an enlarging metastatic mature teratoma during or after chemotherapy for the treatment of non-seminomatous GCT.[14] The development of a somatic (or non-germ cell) malignant component is rare, but has been previously reported.[2,11,15–18] There is no known hypothesis regarding the development of a sarcomatous

component. Our case supported a "selection" phenomenon with further development of chemotherapy-resistant clones.[2,15]

In conclusion, when patients display no response to chemotherapy for malignant teratoma and laboratory and imaging findings are conflicting, growing teratoma syndrome and also teratoma with a sarcomatous component should be included in differential diagnosis. When GCT with sarcomatous transformation is highly suspected, repeat biopsies should be performed, especially in patients ineligible for surgery.

Disclosure

No authors report any conflict of interest.

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