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
markedly increased in size (data not shown) and contrast-
enhanced magnetic resonance imaging revealed a huge het-
erogeneous anterior mediastinal mass with marked interval
growth (Fig 3). The fat component within the tumor, which was not clear on baseline CT, was clearly demon-
strated 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 imag-
ing 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 under-
went 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 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.

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).
more frequently in men and often invades adjacent vasculature. Malignant GCTs secrete tumor markers, such as lactic dehydrogenase, AFP, and $\beta$-hCG, which are useful for diagnosis and follow-up of the disease.

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). Teratocarcinoma refers to a mixture of teratoma with undifferentiated stem cells of embryonal carcinoma or choriocarcinoma, or both. TMT refers to a GCT containing a non-germ cell malignant component. 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 $\beta$-hCG levels gradually decreased and normalized.

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. 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. 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. 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. The development of a somatic (or non-germ cell) malignant component is rare, but has been previously reported. 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.

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.

**References**

1. Rosado-de-Christenson ML, Templeton PA, Moran CA. From the archives of the AFIP. Mediastinal germ cell tumors: Radiologic and pathologic correlation. *Radiographics* 1992; 12: 1013–30.
2. Malagón HD, Valdez AM, Moran CA, Suster S. Germ cell tumors with sarcomatous components: A clinicopathologic and immunohistochemical study of 46 cases. *Am J Surg Pathol* 2007; 31: 1356–62.
3. Chetaille B, Massard G, Falcoz PE. Mediastinal germ cell tumors: Anatomopathology, classification, teratomas and malignant tumors. *Rev Pneumol Clin* 2010; 66: 63–70. (In French.)
4. Lau S, Yeung WH, Kwan WH, Cheng CS, Lam HS. Computed tomography of anterior mediastinal masses. *Hong Kong J Radiol* 2003; 6: 100–6.
5. Strollo DC, Rosado de Christenson ML, Jett JR. Primary mediastinal tumors. Part 1: Tumors of the anterior mediastinum. *Chest* 1997; 112: 511–22.
6. Tecce PM, Fishman EK, Kuhlman JE. CT evaluation of the anterior mediastinum: Spectrum of disease. (Published erratum appears in Radiographics 1994;14:1404. *Radiographics* 1994; 14: 973–90.

7. Jung JL, Park SH, Park JG, Lee SH, Lee KY, Hahn ST. Teratoma with malignant transformation in the anterior mediastinum: A case report. *Korean J Radiol* 2000; 1: 162–4.
8. Abid H, Neji H, Haddar S et al. [Mediastinal mature teratoma with spontaneous malignant transformation.] *Rev Mal Respir* 2013; 30: 424–8. (In French.)
9. Newman RC, Bezirdjian L, Steinbock G, Finlayson B. Complications of extracorporeal shock wave lithotripsy: Prevention and treatment. *Semin Urol* 1986; 4: 170–4.
10. Skeehan P, Storeng R, Scudiero D et al. New colorimetric cytotoxicity assay for anticancer-drug screening. *J Natl Cancer Inst* 1990; 82: 1107–12.
11. Motzer RJ, Amsterdam A, Prieto V et al. Teratoma with malignant transformation: Diverse malignant histologies arising in men with germ cell tumors. *J Urol* 1998; 159: 133–8.
12. Weaver J, Rao P, Goldblum JR et al. Can MDM2 analytical tests performed on core needle biopsy be relied upon to diagnose well-differentiated liposarcoma? *Mod Pathol* 2010; 23: 1301–6.
13. El Mesbahi O, Terrier-Lacombe MJ, Rebischung C, Theodore C, Vanel D, Fizazi K. Chemotherapy in patients with teratoma with malignant transformation. *Eur Urol* 2007; 51: 1306–11.
14. Scaivuzzo A, Santana Rios ZA, Noverón NR, Jimenez Rios MA. Growing teratoma syndrome. *Case Rep Urol* 2014; 2014: 139425.
15. Guo CC, Punar M, Contreras AL et al. Testicular germ cell tumors with sarcomatous components: An analysis of 33 cases. *Am J Surg Pathol* 2009; 33: 1173–8.
16. Iwasa A, Oda Y, Kaneki E et al. Squamous cell carcinoma arising in mature cystic teratoma of the ovary: An immunohistochemical analysis of its tumorigenesis. *Histopathology* 2007; 51: 98–104.
17. Preissig SH, Smith MT, Huntington HW. Rhabdomyosarcoma arising in a pineal teratoma. *Cancer* 1979; 44: 281–4.
18. Rim SY, Kim SM, Choi HS. Malignant transformation of ovarian mature cystic teratoma. *Int J Gynecol Cancer* 2006; 16: 140–4.