A Mediastinal Somatic-type Germ Cell Tumor with Hepatic Metastasis Successfully Treated by Multiple Modalities

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Abstract. *Rhabdomyosarcoma in the mediastinum coexisting with metastatic non-seminomatous germ cell tumor, so-called somatic-type malignancy, is a rare carcinoma and has poor survival. This study reports a case of diffuse and huge hepatic metastasis of non-seminomatous germ cell tumor associated with coexisting embryonal rhabdomyosarcoma in the mediastinum. A 31-year-old man presented with abdominal pain and was found to have multiple abnormal hepatic masses on abdominal computed tomography (CT). Concomitantly, an anterior mediastinal mass was found on chest CT. Chemotherapy was initiated because the hepatic lesion was diagnosed as choriocarcinoma, based on histological findings and the elevation of chorionic gonadotropin β-subunit and α-fetoprotein. After six cycles of bleomycin, etoposide and cisplatin chemotherapy the metastatic liver tumors showed complete response. The remaining mediastinal tumor was completely and successfully resected. The histological findings revealed mature teratoma with embryonal rhabdomyosarcoma. The patient has remained well for over six years after the treatment without any signs of disease recurrence.*

A non-germinal tumor, such as embryonal rhabdomyosarcoma, occurring in a germ cell tumor (GCT) is a rare but well-described entity during the clinical course of non-seminomatous GCTs. Mediastinal rhabdomyosarcoma in GCT, a so-called somatic-type malignancy, has a poorer prognosis than its gonadal counterpart and patients generally have survival of less than two years (1-3). This study reports a case of mediastinal somatic malignancy which presented initially as a diffuse and huge hepatic metastatic tumor. The hepatic lesion was diagnosed as choriocarcinoma based on histological findings and the elevation of chorionic gonadotropin β-subunit (β-HCG) and α-fetoprotein (AFP). The patient was treated with adequate chemotherapy and, subsequently, underwent thoracic surgery for a coexisting anterior mediastinal tumor. The pathological findings were mature teratoma with embryonal rhabdomyosarcoma. The patient remains alive without any signs of recurrence over six years after therapy. This study describes this case and presents a review of the relevant literature.

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Key Words: Mediastinal germ cell tumor, rhabdomyosarcoma, BEP chemotherapy, positron-emission tomography, hepatic metastasis.

Case Report

A previously healthy 31-year-old man was admitted to a local hospital in February 2005 because of intermittant abdominal pain and fever. A physical examination revealed hepatomegaly with tenderness located five finger-widths below the right costal margin. Computed tomography (CT) disclosed multiple liver tumors with high vascularity and concomitant presence of a heterogeneously enhanced anterior mediastinal tumor 52 mm in diameter (Figure 1A). The laboratory findings on admission indicated a mild liver dysfunction, including an alanine aminotransferase level of 301 U/l, an aspartate aminotransferase level of 239 U/l, an alkaline phosphatase level of 1,519 U/l and a lactate dehydrogenase level of 1,254 U/l, but a normal total bilirubin level of 0.94 mg/dl. Serum β-HC) and AFP were elevated to 2,300 ng/ml (cut-off value <0.1 ng/ml) and 20.7 ng/ml (cut-off value <10.0 ng/ml), respectively. The histological findings by fine-needle biopsy from the liver tumor revealed

choriocarcinoma with positive staining for anti-HCG in an immunohistological study (Figure 1C). A systemic review confirmed the absence of testicular disease and a retroperitoneal lymph node adenopathy. Thus, a clinical diagnosis of primary mediastinal nonseminomatous GCT with multiple liver metastases was made. Chemotherapy was started with the standard bleomycin, etoposide and cisplatin (BEP) regimen (30 mg bleomycin on days 1, 8 and 15 and 100 mg/m^2/day etoposide and 20 mg/m^2/day cisplatin from day 1 to day 5 every three weeks). After six cycles of chemotherapy, the liver tumor showed a marked shrinkage on an abdominal CT scan and the increased tumor makers were normalized. However, there was little effect on the mediastinal tumor even after chemotherapy (Figure 1B). ^{18}F-Fluorodeoxyglucose positron-emission tomography (FDG-PET) revealed no abnormal findings in the liver on completion of chemotherapy (Figure 2), suggesting a complete response to chemotherapy in the hepatic lesions. The patient was referred to Shinshu University Hospital and underwent thoracic surgery. Although the tumor was adherent to the anterior aspect of the pericardium and right mediastinal pleura, the mediastinal mass was completely resected *en bloc* including the pericardium, mediastinal pleura and thymus. The postoperative course was uneventful. The final pathological diagnosis was mature teratoma with embryonal rhabdomyosarcoma (mediastinal germ cell tumor with somatic-type malignancy) (Figure 3). The patient remains well without any evidence of recurrence, including tumor markers, over six years after the thoracic operation.

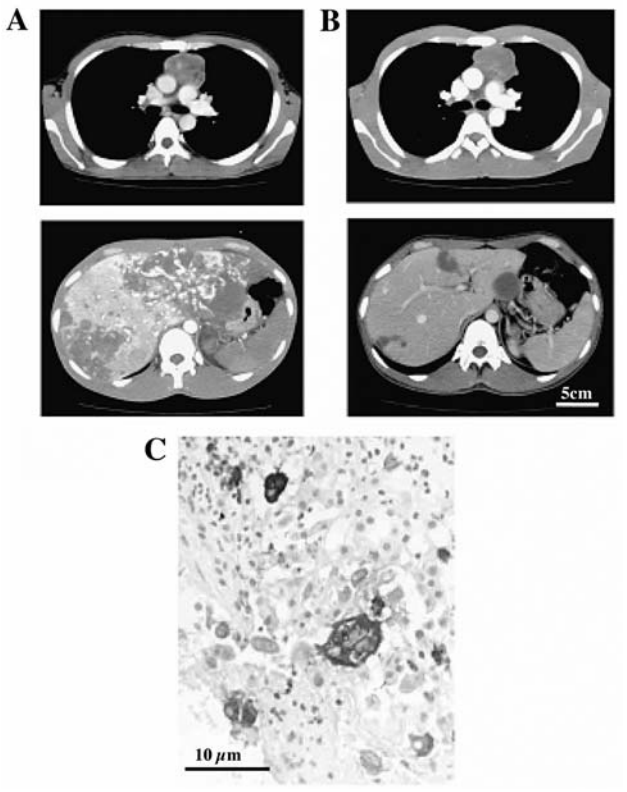

Figure 1. *CT images depicting the anterior mediastinum (top) and the liver (bottom) (A) before and (B) after chemotherapy. C: The histological findings of liver specimens demonstrated choriocarcinoma. Anti-HCG staining.*

Discussion

This study describes a case of mediastinal teratoma with embryonal rhabdomyosarcoma associated with diffuse and huge hepatic metastasis. The initial clinical manifestation was hepatic involvement and the histological findings indicated choriocarcinoma. The hepatic lesions were treated successfully with chemotherapy and the concomitant presence of mediastinal mass was treated by thoracic surgery.

Malignant GCTs have the capacity to display other types of malignant transformation (1-4). Examples of histologically transformed cell types include rhabdomyosarcoma, primitive neuroectodermal tumor and enteric adenocarcinoma and they are known as GCTs with somatic-type malignancy. These tumors account for fewer than 2% of all GCTs (4) and are more common in mediastinal non-seminomatous GCTs than in gonadal or retroperitoneal primary tumors. Although a somatic-type malignancy commonly arises after chemotherapy and/or recurrence (4), sarcoma may be coexisting or may develop after a short latent interval from the initial presence of GCT (3-8). As the mediastinal mass in the present case failed to respond to chemotherapy, it is postulated that a sarcomatous transformation developed concomitantly from pre-existing teratomatous elements or choriocarcinoma components disseminated into the liver. Therefore, the presence of GCT with somatic-type malignancy must be considered, when the disease progresses or fails to respond to standard chemotherapy.

The outcome of non-seminomatous GCTs has improved dramatically since the introduction of cisplatin-based chemotherapy. However, the five-year overall survival rate for patients with mediastinal non-seminomatous GCT remains at only 40% (4). In addition, patients with mediastinal rhabdomyosarcoma usually have poor prognosis and die due to regional and distant metastases (1, 3, 5-8). Omezzine *et al.* reviewed 16 patients with mediastinal rhabdomyosarcoma and demonstrated a poor prognosis; only one of the patients was cured (6). Gonzalez-Vela *et al.* reported that of fifteen patients with mediastinal GCTs, four with a sarcomatous component died of the disease; the prognosis was markedly different from that of cases without a sarcomatous component (7). A recent study by Makagón *et al.* (8) showed that most patients with mediastinal GCT associated with sarcomatous components died within an average of 14 months. Thus, the presence of a sarcomatous component is an important prognostic factor.

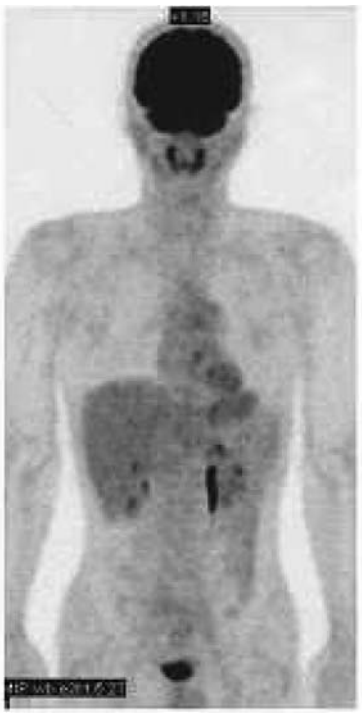

Figure 2. *FDG-PET showed negative findings for hepatic lesions after chemotherapy.*

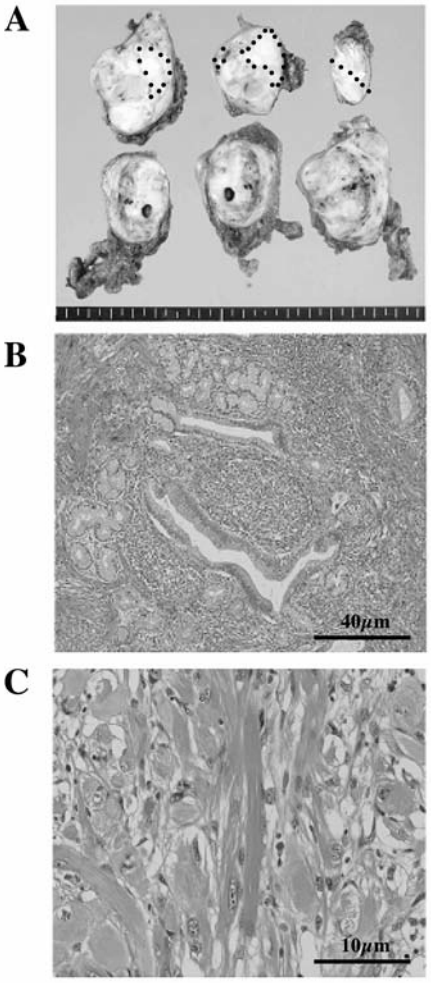

Figure 3. *A: Macroscopic features of resected mediastinal teratoma with embryonal rhabdomyosarcoma. The areas marked by dotted lines indicate the focus of embryonal rhabdomyosarcoma elements. B: Mediastinal teratoma. Hematoxylin and eosin staining. C: Part of teratoma composed of numerous spindle cells and large round rhabdomyoblasts. Hematoxylin and eosin staining.*

Furthermore, the present case was associated with diffuse hepatic metastasis. A total of six cycles of standard BEP chemotherapy were performed and the abnormal findings in the liver disappeared. The hepatic lesions were also negative on FDG-PET. With regard to the management of metastatic GCTs, many authors have recommended the excision of all residual tumors after chemotherapy, if technically feasible. However, as hepatic involvement of GCTs is not common, the therapeutic strategy remains controversial. Copson *et al*. reported that there was no difference in survival between cases with immediate resection of isolated hepatic masses after initial treatment and those given conservative management with regular follow-up assessment by CT (5). Thus, the 'watch and wait' approach to residual hepatic lesions does not adversely affect survival in patients with hepatic metastasis in GCTs. The present case has had a long disease-free survival period of about 6 years. It is, therefore, suggested that adequate neoadjuvant chemotherapy for the liver involvement may have contributed to the good outcome in the present case. In addition, the present case indicated that complete removal of the mediastinal mass after systemic chemotherapy is a very important part of treating a teratoma with somatic-type malignancy. In general, the diagnosis of teratoma with malignant transformation is found incidentally at the time of surgery. Therefore, the possibility of somatic malignancy should be considered in patients with GCTs who have failed to respond to systemic chemotherapy.

In summary, patients with GCTs, in particular those associated with somatic malignancy, exhibit a variety of clinical features. The present case demonstrated that even in a patient with diffuse and huge metastatic GCT at presentation, long-term survival may be achieved by adequate chemotherapy followed by local surgical treatment.

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Received October 19, 2010
Revised November 15, 2010
Accepted November 18, 2010