Relapse with Malignant Transformation After Chemotherapy for Primary Mediastinal Seminoma: Case Report

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This case report details a relapse with malignant transformation after the completion of bleomycin, etoposide and cisplatin chemotherapy for primary mediastinal seminoma, although the residual mass after chemotherapy was <3 cm in size and did not display an increased uptake of fluorodeoxyglucose when examined using positron emission tomography.

Key words: germ cell tumor – seminoma – relapse – malignant transformation – mediastinum

INTRODUCTION

Primary mediastinal seminoma without metastases generally has a good prognosis, according to the International Germ Cell Cancer Collaborative Group (1) criteria, and the relapse of germ cell tumors (GCTs) after cisplatin-based chemotherapy is rare, with a reported relapse rate of approximately 6% (2). Moreover, malignant transformation from pure seminoma is extremely rare, and most cases have a past history of radiotherapy (3–5).

CASE REPORT

A 36-year-old man complaining of progressive facial and upper extremity swelling for 1 month visited our hospital. A computed tomography (CT) scan of the chest revealed a mediastinal mass 6.5 × 4.0 cm in size that had almost completely compressed the superior vena cava (Fig. 1). A CT scan of the chest and abdomen did not show metastases in the lung, liver or lymph nodes. A testicular ultrasound did not reveal a gonadal mass. The serum alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β-hCG) levels were within the normal limits. The lactate dehydrogenase level was slightly elevated at 266 U/L. A percutaneous core needle biopsy (CNB) of the mediastinal mass was performed. The specimen contained large oval nuclei with prominent nucleoli surrounded by pale cytoplasm and lymphoid infiltrates in the background; these infiltrates did not have teratomatous components (Fig. 2). An immunohistochemistry examination showed the malignant cells to be positive for placental alkaline phosphatase (PLAP) and c-kit. The patient was diagnosed as having a primary mediastinal seminoma and received three cycles of bleomycin, etoposide and cisplatin (BEP). After three cycles of BEP, the mediastinal mass had shrunk to a size of 2.3 × 1.5 cm. The patient received one more cycle of etoposide and cisplatin because of a planned follow-up without surgical treatment strategy. Four weeks after the completion of four cycles of chemotherapy, positron emission tomography (PET) imaging did not show a significant standard uptake value. A CT scan of the chest showed the residual mass to be 1.1 × 0.9 cm in size (Fig. 3). The patient underwent surveillance using monthly chest X-rays and serum AFP and β-hCG examinations during the first year and every 3 months thereafter. Eighteen months after the completion of chemotherapy, the patient complained of chest pain. An X-ray and CT scan of the chest showed an anterior mediastinal mass of 7.5 × 6.5 cm in size (Fig. 4). The patient’s serum AFP and β-hCG levels were within the normal limits. On the basis of his clinical history, the patient was diagnosed as having a mediastinal seminoma recurrence after chemotherapy. As a salvage treatment, he underwent four cycles of etoposide, ifosfamide and cisplatin chemotherapy and achieved a partial response. The residual ...
mass, which was 4.5 × 3.5 cm in size, was then resected en bloc along with the right upper lobe of the lung and part of the superior vena cava. A histological examination of the resected mass did not show a seminomatous component when the specimen was immunostained for PLAP, c-kit and Octamer-4. Necrosis was observed in most parts, and the sarcomatous components comprising chondrosarcoma (Fig. 5), leiomyosarcoma, malignant nerve sheath tumor and liposarcoma were positive when immunostained for desmin, alpha-smooth muscle actin and S-100 protein. In addition, the specimen was positive for cytokeratin (AE1/AE3). An isochromosome of the short arm of chromosome 12 was observed using fluorescence in situ hybridization.

The final histological diagnosis was a GCT with somatic-type malignancy. The patient is presently progression-free at 10 months after the salvage surgery.

DISCUSSION

Among primary mediastinal GCTs, pure seminoma accounts for 37%. On the other hand, teratoma or mixed GCTs containing teratoma account for 43% (6). The treatment and prognosis of patients with mediastinal GCTs differ according to whether the tumor contains non-seminomatous components.

At the time of the histological diagnosis of a primary mediastinal tumor, a percutaneous CNB is commonly performed. Hsu et al. (7) reported that the diagnostic rate of CNB for mediastinal tumors was 75%, but this report did not specify whether a clear differentiation of histological subtypes of the tumors was obtained. On the other hand, Fang et al. (8) reported that the histological diagnostic rate of CNB for mediastinal tumors was relatively low, being only 41.7%. When a biopsy is performed, the target area should be close to the center of the tumor. The biopsy site can lead to sampling errors. Therefore, accurate diagnosis using CNB might be difficult in the case of mixed GCT. Actually, this patient had a relapse after the completion of...
chemotherapy, although residual mass of this patient was 3 cm in size and negative for PET as discussed in more detail below. We eventually feel that this patient had non-seminomatous components other than seminoma in the tumor at initial presentation; that is to say, the specimen obtained by CNB was a sampling error.

Residual masses after chemotherapy are found in 56–78% of patients with bulky seminomas (9). The approach to treating residual seminoma masses after chemotherapy remains controversial. Although not proved, the size of a residual mass may predict residual disease, since large residual masses may have a greater chance of containing viable tumor cells. Investigators at the Memorial Sloan-Kettering Cancer Center reported that patients with residual masses >3 cm in size had a 30% incidence of harboring viable cells, whereas none of the patients with residual masses <3 cm harbored viable cells. Patients with residual masses of >3 cm should undergo surgical resection of the residual mass. However, the surgical options for removing post-chemotherapy residual seminoma masses are still quite limited. Surgery after the completion of chemotherapy may be technically difficult in seminoma patients because of the presence of extensive fibrosis and may be limited to multiple biopsies without attempted resection. In fact, 42% of 55 patients who underwent surgery for a residual mass ultimately received multiple biopsies and no attempt at resection was made (10). Moreover, a seminomatous component in patients undergoing post-chemotherapy resection is associated with a higher rate of additional intraoperative procedures and postoperative complications than in patients without seminomatous components (11). We did not select surgical treatment due to the low rate of viable cells in residual massed of <3 cm and the risk of surgical complication.

Meanwhile, PET imaging has emerged as a valuable staging tool for cases of seminoma because seminoma is a pure histological entity and viable tumor cells can be discriminated from necrotic cells in all cases. In the SEMPET trial (9), the sensitivity, specificity, positive predictive value and negative predictive value were determined to be 80%, 100%, 100% and 96%, respectively. In this series, PET imaging was more accurate for predicting residual disease than for determining the size of the residual mass (>3 cm versus ≤3 cm), and the management strategy for patients with pure seminoma after chemotherapy should be surveillance, rather than surgery, if the residual mass has negative PET findings. However, this strategy demands a reliable histology of the primary tumor, with the exclusion of teratoma and other non-seminomatous components. On the other hand, a single center study concluded that PET imaging was not helpful for distinguishing necrosis from viable seminomas because out of the 29 patients who had negative PET findings after primary or salvaged chemotherapy for seminoma, 5 (17%) relapsed (12). Among patients with residual masses of <3 cm, the false-negative rate for PET imaging is reported to be approximately 5–6.5% (9,13).

We diagnosed mediastinal seminoma with the pathological finding gained by CNB and provided chemotherapy as a good risk GCT in our case. However, this patient had a relapse with malignant transformation after the completion of chemotherapy. We ultimately judged that local recurrence might arise from the malignant dedifferentiation of residual, occult teratoma or from the proliferation of previously occult, dormant non-seminomatous components which could not be detected by CNB at presentation.

In conclusion, this patient had the relapse with malignant transformation, but could undergo salvage chemotherapy and surgery. We recommend that post-chemotherapy residual masses in seminoma patients should not necessarily be resected because of surgical complications and low probability of viable tumor for residual mass if it is <3 cm and negative of PET study, but closely followed using imaging examinations and tumor markers.

Conflict of interest statement
None declared.
References


