CASE REPORT

Extragonadal Retroperitoneal Embryonal Carcinoma Successfully Treated with Chemotherapy

Shoji HIRASAKI, Toshikazu MORIWAKI, Takao TSUZUKI, Ken HIRAO and Ichinosuke HYODO

Abstract

A 27-year-old Japanese man visited our hospital for further evaluation of multiple shadows on his chest X-ray. A 6 cm hard mass was palpable in the left lower abdominal region. Histological examination revealed that the lung tumor resected by the video-assisted thoracoscopic surgery was an embryonal carcinoma (EC). He was diagnosed as retroperitoneal EC with multiple lung metastases. He underwent chemotherapy with cisplatin, etoposide, and bleomycin, followed by 3 courses. A curative surgical operation revealed that there were no malignant cells in the lung lesions and primary lesion. This patient responded well to chemotherapy and achieved complete remission by chemotherapy.

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Key words: germ cell tumor, retroperitoneum, BEP therapy, alpha-fetoprotein, postchemotherapy resection

Introduction

Male germ cell tumors (GCTs) predominantly arise from the testis, however, a small subset of 1 to 5% is of extragonadal origin (1, 2). Primary embryonal carcinoma (EC) of the retroperitoneum is a relatively rare disorder. A review of the literature revealed only 9 cases of retroperitoneal EC in Japan in the past 15 years (3–10). EC is highly malignant, but it can be cured with chemotherapy even in advanced cases (11, 12). Herein we report the case of a Japanese man diagnosed as having retroperitoneal EC with multiple lung metastases that responded well to systemic combination chemotherapy consisting of cisplatin, etoposide and bleomycin.

Case Report

A 27-year-old Japanese man visited our hospital for further evaluation of abnormal findings of a chest roentgenogram from a yearly physical checkup on February 22, 2002. He had been in good health and no specific family or medical history was identified.

Multiple tumors were demonstrated on his chest X-ray, and a contrast-enhanced computed tomography (CT) scan (Fig. 1). These imaging examinations suggested metastatic lung tumors. A 6 cm hard mass was palpable in the left lower abdominal region. An abdominal contrast-enhanced CT scan (Fig. 2) and magnetic resonance imaging (MRI) revealed a space-occupying lesion in the retroperitoneum. Ultrasound examination of the testis revealed no abnormal findings. No other tumors were found elsewhere.

Laboratory findings showed a red blood cell count of 459 x 10^6/μl, a white blood cell count of 6,100/μl and a platelet count of 23.3 x 10^7/μl. The hemoglobin concentration was 14.4 g/dl. The levels of hepatic and biliary enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), leucin amino peptidase (LAP), and γ-glutamyltranspeptidase (γ-GTP) were normal except for lactate dehydrogenase (LDH) of 596 IU/l (normal, 150–425 IU/l). On renal function tests, blood urea nitrogen (BUN) and creatinine levels were normal. Tests for C reactive protein (CRP) revealed 0.27 mg/dl. Results of serological studies for hepatitis B and C viruses were negative. The levels of tumor markers were as follows: carcinoembryonic antigen, 1.3 ng/ml (normal <3 ng/ml); carbohydrate antigen 19–9, 27.9 U/ml (normal <24 U/ml); alpha-fetoprotein (AFP), 219 ng/ml (normal <8 ng/ml); human chorionic gonadotropin (hCG), 7.9 mIU/ml (normal ≤ 1.0 mIU/ml) and β-hCG, <0.2 ng/ml.

We clinically diagnosed this patient as having a primary retroperitoneal tumor with lung metastasis based on the CT and MRI findings. This tumor was thought to be nonsemino-
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Figure 1. Chest computed tomography on admission showed multiple nodular tumors in S^3, S^6, S^7, and S^9 of the right lung (white arrows).

Figure 2. Abdominal computed tomography on admission revealed a round cystic tumor, 6 cm in diameter, in the retroperitoneum.

Elevated serum AFP level indicated a immature germ cell tumor (GCT) since serum AFP level was elevated. A video-assisted thoracoscopic surgery (VATS) was performed for histological confirmation. The resected tumor in the right S^9, 20x17x11 mm in size, was a yellowish-white nodule and revealed central necrosis. Histological examination revealed large multangular tumor cells with bullous nucleus and clear nucleolus, which had a high nuclear-cytoplasmic ratio, were irregularly arranged and the border of tumor cells was unclear (Fig. 3). Mitotic figures were remarkable. The diagnosis, based on these histological findings, was EC.

The patient underwent chemotherapy with cisplatin (CDDP) 35 mg/ body (20 mg/m^2) i.v. days 1–5, etoposide 170 mg/ body (100 mg/m^2) i.v. days 1–5, and bleomycin 30 mg/ body i.v. days 2, 9, 16, (BEP regimen) repeated every 3 weeks, followed by 3 courses of chemotherapy. After 3 courses of BEP chemotherapy, serum levels of AFP and hCG were decreased to the normal range (AFP; 2.8 ng/ml, hCG <1.0 mIU/l). The patient’s response to chemotherapy was extremely good for a metastatic lung tumor and remarkable tumor regression was achieved (Fig. 4), although the
primary tumor in the retroperitoneum was only slightly reduced in size, from 6 cm to 5 cm. Thoracotomy with lymph node dissection was performed for decreased lung tumors in S3, S6, and S7 on May 31, 2002. Histological examination revealed multiple nodules with granulation and fibrosis in S3, S6, and S7. No malignant cells were seen in the resected lung tissues or lymph nodes. On June 13, laparotomy was performed for the primary lesion in the retroperitoneum. Histological examination of the resected tumor revealed necrotic tissue and no malignant cells were seen (Fig. 5). There was no mature teratoma component in the resected tumor. This patient seemed to have complete remission (CR). He has been under close periodic observation, and there was no evidence of disease 11 months after surgery.

**Discussion**

It is generally accepted that extragonadal GCTs, including those of retroperitoneal origin, arise as a result of malignant transformation of residual germinal elements that abnormally migrated during embryogenesis. Extragonadal GCTs account for only a small percentage, 1% to 5% of all GCTs (1, 2). EC accounts for 2.3% of retroperitoneal tumors, and primary EC of the retroperitoneum represents only 0.0077% of all tumor cases (13). A review of the English and Japanese literature revealed that only 10 cases of retroperitoneal EC including the present case have been reported over the last 15 years in Japan (3–10) (Table 1). Major symptoms of retroperitoneal EC include lumbago, back pain and abdominal pain. All 10 cases in Table 1 show elevation of serum AFP or hCG or both. Five cases achieved CR with chemotherapy and curative surgical resection, however, 4 cases
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Figure 5. Histological examination of the retroperitoneal tumor revealed necrotic tissue and no viable malignant cells were seen.

died of this disease. Recently Scholz et al (2) reported that all 25 testes explored in their patients with extragonadal retroperitoneal GCTs had pathological findings, 76% of which were either viable tumor or scars. They claimed that those so-called primary extragonadal GCTs in the retroperitoneum are very likely a rare or non-existing entity and should be considered as metastasis of a viable or burned-out testicular cancer until proven otherwise. In the present case, ultrasound examination of the testis revealed no abnormality and histological examination of the testis was not performed. Although we clinically diagnosed this patient as having a primary retroperitoneal tumor, we could not rule out the possibility of testicular origin.

Ninety percent of nonseminomatous GCT cases show elevation of serum AFP or hCG or both (14). These tumor markers are valuable not only for the presence of nonseminomatous GCT, but in monitoring the response to therapy. In the present case, serum levels of AFP and hCG improved to the normal range as the metastatic lung tumors decreased with chemotherapy. We should be attentive to recurrence and carefully follow these tumor markers.

Almost all GCTs possess high proliferative potential. Clinically, they are highly malignant and follow an acute course. They are generally associated with metastasis: 74% of patients had metastatic disease at the time of diagnosis, and 50% of these had distant metastasis (15). Recently, an international consortium collected clinical data on patients receiving platinum-based therapy for metastatic GCT to develop a new prognostic model for disseminated disease (16). Data on 5202 patients with nonseminomatous GCT and 660 patients with seminoma were analyzed and it was found that independent predictors of outcome in univariate analysis included mediastinal primary site, degree of AFP, hCG and LDH elevation and the presence of non-pulmonary visceral metastasis. Using these factors, prognostic categories were derived. Good risk nonseminomatous patients were those with a testis or retroperitoneal primary, favorable markers, and no non-pulmonary visceral metastasis (anticipated progression-free survival: 90%). According to the prognostic factor classification of the International Germ Cell Cancer Collaborative Group (IGCCG), the present case satisfied all aforementioned conditions of good prognosis, namely, 1) retroperitoneal primary, 2) no non-pulmonary visceral metastasis, and 3) good markers of all the following: AFP <1,000 ng/ml, hCG <5,000 IU/l, and LDH <1.5 upper limit of normal. As to the chemotherapy, the Southeastern Cancer Study Group performed a trial in which patients with good-risk disease were randomized to receive either 4 courses of BEP or

Table 1. Summary of 10 Cases of Retroperitoneal Embryonal Carcinoma Reported in Japan in the Past 15 Years

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Year</th>
<th>Symptoms</th>
<th>Size (cm)</th>
<th>AFP (ng/ml)</th>
<th>hCG (mIU/l)</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oda (3)</td>
<td>31</td>
<td>M</td>
<td>1987</td>
<td>abdominal pain</td>
<td>7</td>
<td>9,140</td>
<td>ND</td>
<td>operation</td>
<td>ND</td>
</tr>
<tr>
<td>Natori (4)</td>
<td>29</td>
<td>M</td>
<td>1987</td>
<td>lumbago</td>
<td>ND</td>
<td>2,700</td>
<td>12</td>
<td>CDDP+VCR+BLM</td>
<td>CR</td>
</tr>
<tr>
<td>Yasumoto (5)</td>
<td>27</td>
<td>M</td>
<td>1989</td>
<td>lumbago</td>
<td>ND</td>
<td>29</td>
<td>350</td>
<td>CDDP+VP-16, VAB-VI</td>
<td>death</td>
</tr>
<tr>
<td>Murao (6)</td>
<td>23</td>
<td>M</td>
<td>1990</td>
<td>epigastralgia</td>
<td>16x12</td>
<td>137</td>
<td>40,000</td>
<td>CDDP+VCR+PEP+VP-16+SO</td>
<td>death</td>
</tr>
<tr>
<td>Ohkubo (7)</td>
<td>32</td>
<td>M</td>
<td>1993</td>
<td>dull back pain</td>
<td>10x10</td>
<td>4,500</td>
<td>1,100</td>
<td>PVB</td>
<td>CR</td>
</tr>
<tr>
<td>Satake (8)</td>
<td>26</td>
<td>M</td>
<td>1994</td>
<td>lumbago, back pain</td>
<td>ND</td>
<td>48.1</td>
<td>31.3</td>
<td>PPV</td>
<td>death</td>
</tr>
<tr>
<td>Satake (8)</td>
<td>37</td>
<td>M</td>
<td>1994</td>
<td>fever, edema of legs</td>
<td>ND</td>
<td>17,700</td>
<td>WNL</td>
<td>PPV+ curative SO</td>
<td>CR</td>
</tr>
<tr>
<td>Hashimoto (9)</td>
<td>25</td>
<td>M</td>
<td>1998</td>
<td>back pain</td>
<td>ND</td>
<td>1,800</td>
<td>1.2</td>
<td>BEP+curative SO</td>
<td>CR</td>
</tr>
<tr>
<td>Tanaka (10)</td>
<td>29</td>
<td>M</td>
<td>2001</td>
<td>lumbago</td>
<td>30</td>
<td>elevated</td>
<td>elevated</td>
<td>BEP+curative SO</td>
<td>death</td>
</tr>
</tbody>
</table>

3 courses of the same 3 agents (17). There was no difference in the percentage of patients achieving CR with either 3 (98%) or 4 courses (97%) courses of therapy. Also, Nichols (18) described that good risk disseminated disease should be treated with 3 cycles of BEP regimen though postchemotherapy resection of residual disease is commonly necessary. In the present case, the response to systemic combination chemotherapy was extremely good for metastatic lung tumors and achieved remarkable tumor regression, although the primary tumor in the retroperitoneum remained. Finally, a subsequent curative surgical operation revealed that there were no malignant cells in the lung lesions, mediastinal lymph nodes, and primary lesion in the retroperitoneum. Thus, the present case was considered to have achieved CR by chemotherapy.

In conclusion, we reported a case of retroperitoneal embryonal carcinoma that responded well to BEP regimen. We emphasize that despite the highly malignant nature of EC, the survival of patients with EC has greatly improved because of the effectiveness of chemotherapies as in the present case.

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References