Recurrence of a Germ Cell Tumor 12 Years After Initial Treatment: a Case Report

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Patients with testicular germ cell tumors who have disease-free remission for more than 2 years are usually considered to be cured of their disease. This report describes a case of a germ cell tumor recurring 12 years after initial diagnosis and its treatment in a 35-year-old man who developed a retroperitoneal mass adhering to the abdominal aorta with a bout of severe colic in the left flank. Although tumor markers were not elevated and histology of the biopsy specimen was initially diagnosed as adenocarcinoma, we finally concluded that the retroperitoneal tumor was teratoma developing as a recurrence of the germ cell tumor for the following reasons: (1) the histology of the specimen was similar to an epithelial component of teratoma found in the tissue resected 12 years before; (2) systemic survey failed to detect any other primary site; (3) the young age of this patient was consistent with germ cell tumor rather than adenocarcinoma; and (4) the retroperitoneum is the most frequent site of late recurrences of testicular cancer. He was treated successfully with combination chemotherapy of cisplatin, etoposide and bleomycin followed by surgery. It is important to differentiate this treatable disease from metastasis from an unknown primary, because the latter responds poorly to therapy and survival is usually short.

Key words: late relapse – testicular cancer – teratoma – chemotherapy – surgery

INTRODUCTION

Testicular cancer currently serves as the model of a curative neoplasm; about 95–100% of patients with early-stage disease and 70–80% in stage III disease are curable (1,2). Recurrences typically develop within the first 2 years after the initial diagnosis and treatment and patients who have had disease-free remission for this period are considered to be cured (2). A recent study showed that a late relapse could occur in about 3% of patients who had been free from their disease for more than 2 years. The recurrence rate, however, decreases with time and only a few cases of recurrence more than 10 years after the initial presentation have been reported (3,4).

Late relapse of testicular cancer has not been documented in Japan, probably because this disease is relatively rare there; the annual age-adjusted incidence rate for the disease between 1983 and 1987 was 1.4 per 100 000 men, which was about one third to one quarter of the incidence rate in western countries and accounted for 0.6% of all malignancies in Japanese men (5). This is, to our knowledge, the first report from Japan of a patient with germ cell tumor which relapsed 12 years after orchidectomy.
gastrointestinal tract. The ureter was dissected free of the lesion and a tissue sample was obtained for histological examination.

The patient was relatively well and without pain on admission to our hospital. Physical examination was unremarkable except for an operative scar in the abdomen. The right testis was normal on palpation. Complete blood count and biochemical studies were within normal limits. Serum tumor markers including CEA, CA19-9, AFP, hCG and β-hCG were not elevated. An MRI scan of the abdomen revealed a retroperitoneal mass, 3 x 2 cm in cross-section and 6 cm longitudinally, adhering to the abdominal aorta at the level of the lower pole of the left kidney and the dilated left ureter, but no tumorous lesion in the other organs (Fig. 1). The surveys for the chest, brain and bone and the systemic Ga scan yielded negative results for primary and metastatic tumors.

Histological review of the specimen from the left testis resected 12 years before showed that two-thirds of the tumor was necrotic and the remaining one third was viable, 90% of which was made up of yolk sac tumor. The remainder was comprised mainly of embryonal carcinoma and partly of glandular tissue with well differentiated epithelium, which was thought to be a component of the teratoma (Fig. 2). Immunohistochemically, positive staining for AFP and placental alkaline phosphatase was seen in the yolk sac tumor and predominantly in the embryonal carcinoma, respectively, and CEA-positive tumor cells were scattered throughout the tumor. The biopsy specimen taken from the para-aortic lymph node was replaced with well differentiated glandular epithelium, resembling the teratoma component in the original tumor (Fig. 3). These findings were consistent with the recurrence of the germ cell tumor. Immunohistochemically, the tumor was negative for AFP, hCG and CEA.

The patient was treated with two cycles of chemotherapy consisting of cisplatin 120 mg/m² on day 1, etoposide 100 mg/m² on days 1-5 and bleomycin 15 mg/body on days 2, 9 and 16, beginning on March 24. This treatment yielded only a minor response and the toxicity was severe: grade 4 neutropenia lasting for 3 days, grade 3 thrombocytopenia and grade 3 vomiting, but no life-threatening infection was noted.
Late recurrence of germ cell tumor

Adjuvant surgery was carried out on June 4, 1994. The peritoneal cavity was entered through a median skin incision. Exploration of the abdomen revealed an unremarkable stomach, duodenum and large and small bowels. The tumor was located in the retroperitoneum, adhering to the infrarenal abdominal aorta and inferior vena cava, but was successfully separated from the surface of these large vessels. The left-sided retroperitoneal dissection encompassed the left renal hilar area down to the common iliac artery with the right margin of the inferior vena cava.

The resected specimen was 6.3 x 4.2 x 1.8 cm in size. Histologically, the tumor was composed of teratoma showing cystic spaces lined by tall columnar cells forming papillary structures. The nuclei were atypical but the overall features of these cells resembled the teratomatous component of the testicular primary.

The patient was alive and well without recurrence at the last follow-up in December 1997.

**DISCUSSION**

It was difficult to establish the diagnosis in the current case because tumor markers were not elevated and histology of the biopsy specimen was initially interpreted as adenocarcinoma. However, we concluded that this case represented the recurrence of germ cell tumor for the following reasons: (1) the histology of the biopsy specimen was similar to an epithelial component of teratoma found in the tissue resected 12 years before; (2) systemic survey failed to detect another primary site; (3) the young age of this patient was consistent with germ cell tumor rather than adenocarcinoma (6); and (4) the retroperitoneum is the most frequent site of late recurrences of testicular cancer (3). It was important to differentiate this treatable disease from adenocarcinoma of an unknown primary site, which usually has a poor response to therapy and a short median survival of 3–4 months (6).

The possible mechanism of the late recurrence in this patient was that microscopically residual viable tumor after initial treatment persisted with an atypical biological behavior (4). The slow growth of teratomas might explain the long latent period in this patient, although it is not always the case. A review of the literature of 25 cases of testicular germ cell tumor relapsing after a remission period of more than 2 years showed that the histologies of the recurrent tumor were seminoma in two (8%), embryonal carcinoma in eight (32%), embryonal carcinoma and yolk sac tumor in two (8%), yolk sac tumor in one (4%), teratocarcinoma in seven (28%) and mature teratoma in five (20%) cases (3,4,7–10). Prophylactic radiotherapy after the first operation might have influenced the length of the latent period, although the late relapse rate did not increase in a randomized trial comparing orchidectomy alone with orchidectomy plus adjuvant radiotherapy with the para-aortic lymph nodes for stage I nonseminomatous testicular cancer (11). Development of a second primary lesion was also possible. Of consecutive patients with testicular germ cell tumor, 1–3% developed bilateral primary tumor, 20% of which occurred more than 10 years after

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**Figure 3.** Microscopic features of the biopsy specimen taken from the para-aortic lymph node. Well differentiated glandular epithelium resembling the teratoma component in the original tumor is seen (hematoxylin–eosin). (a) Low magnification, x25; (b) higher magnification, x100.
the first tumor (12). However, it seems reasonable to regard this case as metastatic because extragonadal germ cell tumors are extremely rare in adults (13).

A standard treatment for late recurring germ cell tumor has not been established. Only a minor response was achieved in this patient by combination chemotherapy of cisplatin, etoposide and bleomycin, which produced a complete response in 77% of patients at the initial treatment (14). Baniel et al. (4) reported that a complete response was observed in only 17 of 65 (26%) patients receiving chemotherapy and only two of these patients were cured with chemotherapy alone, whereas 11 of 16 (69%) patients managed by surgery alone were continuously disease free. Hence surgery is thought to make a significant contribution to the control of late relapse of germ cell tumor. At the same time, chemotherapy may also have a role in the management of these tumors, because heterogeneous germ cell tumors may include a chemosensitive component even if a biopsy fails to demonstrate this and it is often difficult to exclude micrometastasis to other organs. Baniel et al. (4) also noted a more favorable outcome in late relapse with histologically pure teratoma compared with carcinoma, which might apply in the present case.

In conclusion, germ cell tumors rarely relapse more than 10 years after the initial treatment. We should carefully differentiate these tumors from metastatic cancer of unknown primary site in patients with a previous history of germ cell tumor, because they are potentially treatable with chemotherapy followed by surgery.

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References