Retroperitoneal extragonadal germ cell tumor without distant metastasis: A case report.

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Abstract

A 66-year-old man was referred to our hospital for an incidentally detected 40-mm mass located at the inter-aortocaval area around the renal hilum. Positron emission tomography CT revealed high accumulation (SUVmax 12.382) without distant metastasis. Bilateral testes were normal by ultrasonography and physical examination, but the serum AFP level was increased to 1161 ng/mL. The pathology based on trans-duodenal needle biopsy demonstrated a yolk sac tumor; therefore, we diagnosed him with retroperitoneal primary germ cell tumor. Due to old age, the potential toxicity of systemic chemotherapy, and no significant signs of invasion to adjacent organs, we performed surgical resection. Although the AFP level decreased to 13.2 ng/mL postoperatively, it increased to 553 ng/mL two months after surgery without clinical recurrence on imaging studies. Four cycles of a VIP regimen (VP-16, ifosfamide, and CDDP) was performed, and the AFP level normalized to 2.4 ng/mL. The patient is now disease-free 1 year and 6 months after surgery.

Introduction

Extragonadal germ cell tumor (EGCT) are rare, accounting for approximately 5% of the germ cell tumors among males [1]. In general, EGCT are treated by chemotherapy because most patients present with large retroperitoneal lymph node metastasis or distant organ metastasis. Solitary retroperitoneal EGCT without distant metastasis are rare, and to our knowledge, there is no treatment consensus as to surgery first or chemotherapy first in these rare cases. We report a case of solitary EGCT treated by surgery and subsequent systemic chemotherapy.

Case report

A 66-year-old man (height 162.8 cm, weight 66.85 kg, body mass index 25.2) was referred to our hospital because of an asymptomatic retroperitoneal tumor of 40 mm in diameter incidentally detected by computed tomography (CT). His medical history included appendectomy, hypertension, hyperuricemia, and dyslipidemia. Physical examination did not reveal any significant abnormalities, and the bilateral testes were normal. He was a current smoker (100-150 packs/year), and on the respiratory function test, his %VC was 102%, FEV 1.0 was 2.59 L (72.58%), and mild obstructive ventilatory disorder was noted. Blood analysis revealed increased levels of serum alpha-fetoprotein (AFP) (1161 ng/mL) and the AFP-L3 fraction (54.7%). CT and MRI demonstrated a 44-mm mass located between the aorta and IVC around the renal-hilum level without any signs of invasion to adjacent organs. On PET-CT, accumulation with an SUVmax 12.382 in the retroperitoneum was observed (Figure 1). Abdominal ultrasonography revealed

a low echoic solid nodule. Respiratory synchronization between adjacent organs and retroperitoneal lesions was not observed, which further supported the absence of invasion into adjacent organs. Taken together, the differential diagnosis includes metastasis of testicular tumor, schwannoma with cystic degeneration, leiomyosarcoma, Castleman's disease, and paraganglioma.

Based on the recent General Rule for Clinical and Pathological Studies on the Testicular Tumor 4th version [2], we decided to perform the biopsy of the retroperitoneal tumor endoscopically through the duodenum. Histology revealed a small atypical epithelioid cell cluster and mature cartilage tissue, with abundant necrotic tissue. Immunohistochemistry suggested the atypical cells to be a yolk sac tumor. Considering 1) his old age, 2) heavy smoking history, 3) solitary, non-metastatic lesions with a smooth margin, which we considered possible to be resected with a good margin, we decided to proceed with surgery and reconsider the indication of systemic chemotherapy as two courses as adjuvant following the normalization of the AFP level after surgery. Retroperitoneal tumor resection with modified right template retroperitoneal lymph node dissection was performed through a midline abdominal incision. However, the tumor was firmly adhered to the duodenum (possibly due to adhesion associated with needle biopsy), which caused duodenum injury. It was repaired using primary sutures and cholecystectomy + C tube drainage by the general surgeon. The operative time was 7 hours 2 minutes and the amount of blood loss was 739 cc, requiring no blood transfusion. The surgical margin and invasion into the duodenum were negative. On pathology, the resected tumor was 110 × 85 mm in size and surrounded by thick fibrous capsule. The cut surface was a greyish-white colored solid tumor with marked hemorrhage and central

necrosis. Histologically, the vacuolated tumor cells formed a micro cystic/reticular, glandular, and solid pattern. On immunohistochemistry, the tumor cells were immunoreactive for SALL4, AFP, and Glypican 3, consistent with a yolk sac tumor (Figure 2). Mature cartilaginous tissues were also found, but other teratomatous elements were not evident except for the cartilage. Moreover, no other germ cell tumor component was identified. Based on these findings, we conclusively diagnosed it as a yolk sac tumor with cartilaginous tissue.

After surgery, the AFP level decreased to 13.2 ng/mL in 1 month, but it increased to 553 ng/mL 2 months after surgery (hCG is <0.5 mIU/mL, hCG-β is <0.5 mIU/mL, LDH is 137 U/L, IGCCC good risk group). Although imaging studies (CT) showed no recurrent disease, we decided to start chemotherapy including VP-16, ifosfamide, and CDDP (VIP) based on stage IS treatment algorithm. After careful discussion about his unusual clinical course, we did not regard him as IGCCC good risk and we did not treat him with four courses of etoposide and cisplatin (EP). In addition, we avoid using bleomycin due to lung toxicity for his slightly deteriorated respiratory disease. After 2 courses of VIP, the AFP level was still above the normal limit. After a total of 4 courses of VIP, the AFP level normalized to 3.6 ng/mL. During the treatment, the patient developed Grade 4 (CTCAE. ver 4.0) neutropenia, anemia, and thrombocytopenia, which were managed conservatively granulocyte colony-stimulating factor and blood transfusion. He is now disease-free 1 year 6 months after surgery (Figure 3).

Discussion

EGCT are reported to account for approximately 5% of GCTs in males, and the retroperitoneum is the second most common site of origin (13–45%) after the mediastinum (35–54%) [1,3]. Nonseminomatous EGCT were reported to have a 5-year survival rate of 20-30%[4], with poorer outcomes than those of primary testicular germ cell tumors. One of the reasons for this is delayed diagnosis due to the lack of initial symptoms, which results in advanced disease in most patients with EGCT at the first visit. For example, Bokemeyer et al. reported that 76% of 227 patients with nonseminomatous EGCT had metastases to other areas [3].

In this case, he was classified into the IGCCC good risk group after surgery and his treatment options were three courses of bleomycin, etoposide, and cisplatin (BEP) or four courses of EP. But we thought that this treatment options were not appropriate for this unusual case. One of the reasons is that the tumor marker gradually declined during the course until before surgery. The other is that non-seminomatous EGCT is generally known as poorer outcomes than those of primary testicular germ cell tumors. Therefore, we decided to treat him with VIP therapy as intermediate risk group after a careful discussion.

In the Japan Urological Association (JUA) testicular tumor clinical practice guidelines 2015, systemic chemotherapy (i.e. BEP) is recommended for nonseminomatous EGCT according to the IGCCC prognostic classification, and residual tumor resection should be considered after the normalization of tumor markers [5]. On the other hand, we performed surgical resection for the following reasons: First, due to the patient's age and heavy smoking history, the risks of systemic chemotherapy, especially the

pulmonary toxicity of bleomycin, which may cause early withdrawal of treatment, were of concern. Second, we were reconsidering systemic chemotherapy after surgery as two courses of adjuvant systemic chemotherapy following the normalization of the AFP level. Third, based on preoperative imaging studies, we considered the tumor to be resectable. However, due to adhesion that was likely caused by the needle biopsy procedure, duodenum injury and subsequent repair were required during surgery.

The tumor pathology was confirmed to be pure yolk sac tumor. The incidence of pure yolk sac tumor is relatively low in adult-onset germ cell tumors. In this case, AFP, SALL4, and Glypican 3 are positive. Although KIT, and OCT3/ 4 were focally positive, PLAP, CD30, D2-40, and hCG are negative in immunohistochemical staining. Other germ cell tumor components (germinoma, embryonal carcinoma) have not been identified pathologically. Yolk sac tumor may be accompanied by differentiation into cartilage [6], so our diagnosis was yolk sac tumor with cartilage differentiation..

As described above, we introduced a VIP regimen after the postoperative increase in AFP considering the potential pulmonary toxicity of bleomycin. VIP regimens are often used as salvage therapy for germ cell tumors, and adverse events, especially hematological toxicity, are more frequent than during BEP therapy[7]. Indeed, Grade 4 neutropenia, anemia, and thrombocytopenia developed in our patient, but they were safely managed by G - CSF and blood transfusion. After 4 courses of chemotherapy, the serum AFP level normalized. The patient is now disease-free 1 year and 6 months after surgery.

Conclusion

Although primary systematic chemotherapy is the gold standard treatment for serum AFP-positive EGCT, primary surgery for solitary lesions may be an alternative for elderly patients for whom chemotherapy administration carries high risks.

Compliance with Ethical Standards

Funding: None

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: For this type of study formal consent is not required.

Informed consent: Informed consent was obtained from the patient included in the study.

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Figure legends

Figure 1: Pretreatment CT, MRI, and PET-CT showed a retroperitoneal tumor between the aorta and inferior vena cava at the renal level.

Figure 2: Histology of the tumor revealed reticular formation (a). The tumor cells were focally positive for AFP (b).

Figure 3: The AFP level first gradually declined. It rapidly decreased from the postoperative day, but increased again. After 4 courses of VIP, the AFP level decreased.

Figure 1

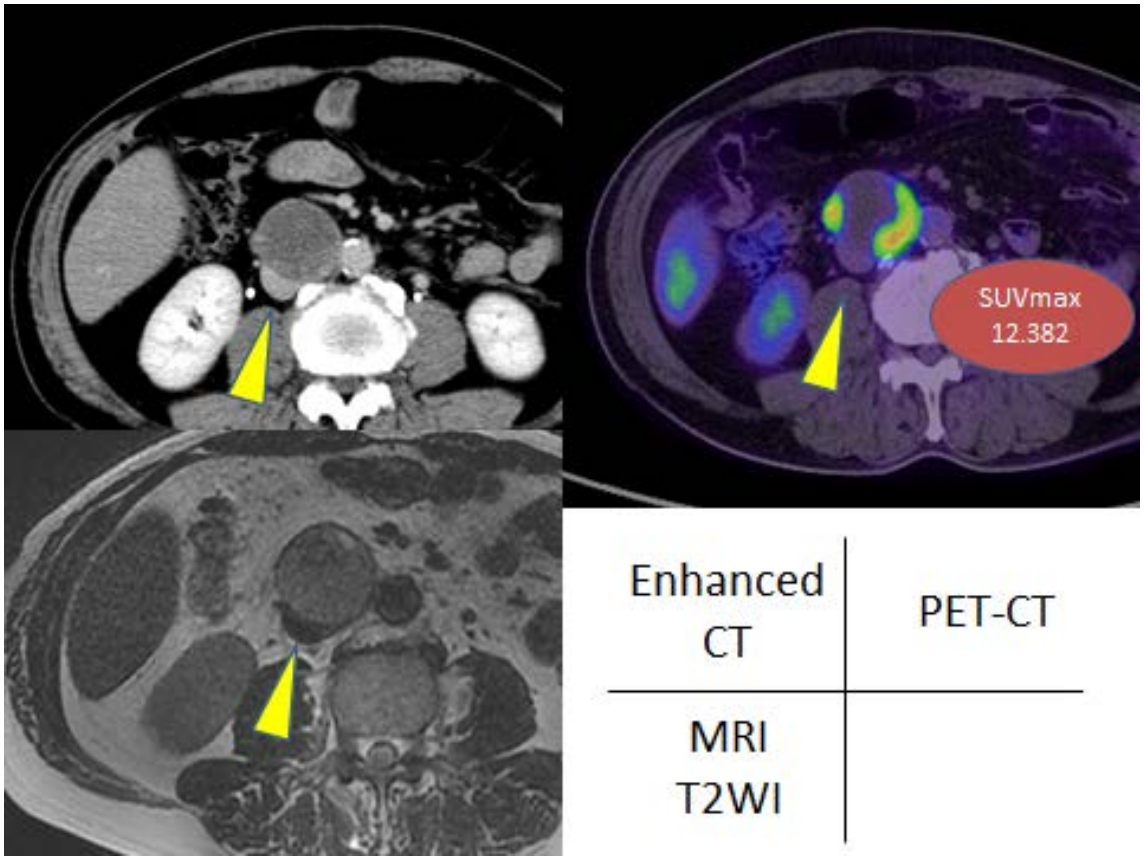
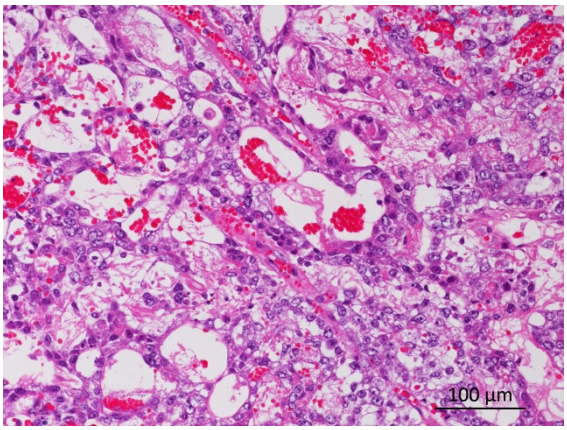


Figure 2

(a)



(b)

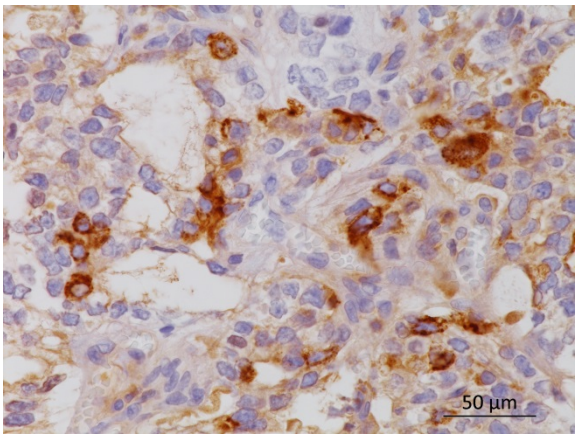
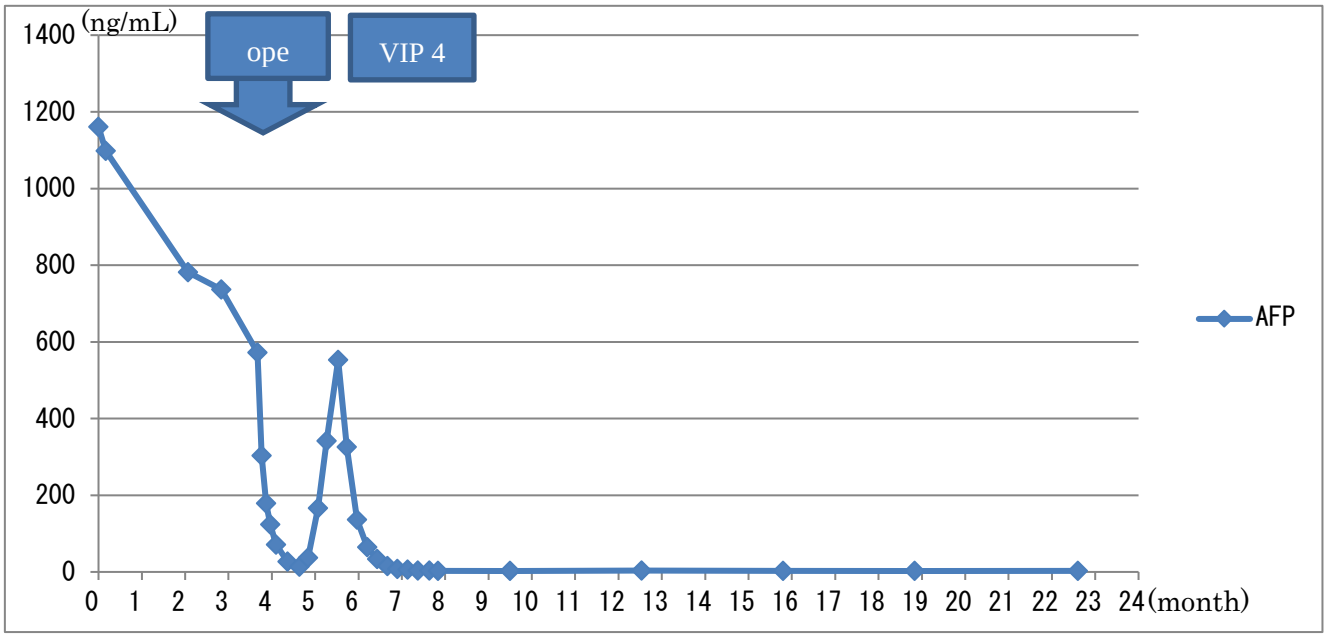


Figure 3


(ng/mL)
1400
1200
1000
800
600
400
200
0
ope
VIP 4
AFP
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24(month)