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【 CASE REPORT 】

Resection for Primary Retroperitoneal Serous Adenocarcinoma and Liver Metastasis

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Abstract:
Primary retroperitoneal serous adenocarcinoma (PRSA) is a rare malignancy of which only seven cases have been reported in the literature. The clinical features and outcomes of PRSA are not well understood. We herein report a case of PRSA with liver metastasis in a 74-year-old woman who was treated with surgical excision. The tumor cells were positive for estrogen receptor, Wilms tumor 1, PAX8, p53, and cytokeratin AE1/AE3. The final diagnosis was PRSA and liver metastasis. The pathological features of PRSA resemble those of ovarian serous carcinoma, which suggests that a combination of surgical excision with adjuvant chemotherapy may be the best option.

Key words: primary retroperitoneal serous adenocarcinoma (PRSA), liver metastasis

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Introduction

Primary retroperitoneal serous adenocarcinoma (PRSA) is a rare malignant neoplasm. Only seven reports of surgery in patients with PRSA have been published in the English literature as of 2016 (Table 1) (1-7). In addition, there have been no reports of hepatectomy for liver metastasis. All seven tumors affected women. Because of the rarity and the unknown biological behavior of PRSA, its clinical features are not well understood. Establishing a treatment modality in patients with PRSA has been challenging. We herein report a patient with PRSA and liver metastasis who underwent surgical resection.

Case Report

A 74-year-old woman was admitted to our department for the evaluation and treatment of a retroperitoneal tumor and a tumor of the liver in the segment (S) 6 area. Her medical history included a right adrenocortical adenoma (Cushing's syndrome, resected at 69 years) and pancreatic mass (suspected mucinous cystic neoplasm) on follow-up. After resection of the adrenocortical adenoma, no recurrence was detected for five years. Liver dynamic computed tomography (CT) during the course of our observations showed a low-density mass with internal enhancement in the S6 area in the arterial and delayed phase (Fig. 1a-c). Magnetic resonance imaging (MRI) showed a mass in the S6 area with low-intensity T1-weighted signals and high-intensity T2- and diffusion-weighted signals. In the arterial, portal, delayed, and hepatobiliary phases of gadolinium ethoxybenzyl diethylene triamine pentaacetic acid (Gd-EOB-DTPA)-enhanced MRI, the mass exhibited poor contrast enhancement, and during the hepatobiliary phase, contrast between the mass and liver was clearly seen (Fig. 1d). Contrast CT showed a low-density mass located at the right retroperitoneal cavity (Fig. 1e). On positron emission tomography (PET)-CT, the maximum standard uptake value of the tumor in S6 of the liver was 7.3 (Fig. 1f), and that of the retroperitoneal tumor was 3.8 (Fig. 1g).

Upon presentation, the patient was afebrile and had no history of weight loss, and her appetite was good. On a preoperative indocyanine green (ICG) test, the ICG retention rate at 15 minutes (ICG R15) was 5.6%. The total bilirubin level was 0.6 mg/dL. The serum albumin level was 4.2 g/

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dL, and the prothrombin activity was 94.7%. The Child-Pugh score was 5 points, signifying a grade of A, and the degree of liver damage was equivalent to A in accordance with the scoring system of the Liver Cancer Study Group of Japan. Table 2 shows the patient's laboratory data on admission. Her laboratory test results did not show any evidence of liver dysfunction. Antibodies against hepatitis B virus and hepatitis C virus surface antigens were negative. The serum tumor markers alpha-fetoprotein, protein induced by vitamin K absence-II, carcinoembryonic antigen, and cancer antigen 19-9 levels were within the normal range. Given the patient's medical history, we suspected liver metastasis of an adrenal gland tumor or other cancer.

Table 1. Laboratory Data on Initial Visit.

WBC	7,700 /μL	AFP	5.1 ng/mL
RBC	424 /μL	CA19-9	5.8 U/mL
Hb	12.8 g/dL	CEA	1 ng/mL
Plt	19.3 μL	PIVKA-II	15 U/mL
PT	94.7 %		
APTT	33.8 s	HBs-Ag	(-)
TP	6.8 g/dL	HBs-Ab	(-)
Alb	4.2 g/dL	HCV-Ab	(-)
BUN	20 smg/dL		
Cre	0.84 mg/dL	ICG R15	5.6 %
Na	143 mmol/L		
K	4.8 mmol/L	GSA-Rmax (mg/min)	
Cl	107 mmol/L	Total: 0.397	
AST	12 U/L	Anterior segment: 0.145	
ALT	11 U/L	Posterior segment: 1.29	
ALP	158 U/L	Lateral segmental: 0.063	
LDH	155 U/L	Medial segment: 0.060	
T-Bil	0.6 mg/dL		
D-Bil	0.1 mg/dL		
γ-GTP	17 U/L		
ChE	323 U/L		
CRP	0.111 mg/dL		

ICG R15: indocyanine green retention rate at 15 minutes, GSA-Rmax: maximal removal rate of ^{99m}Tc-galactosyl human serum albumin

Performing a liver biopsy was difficult. Therefore, the patient underwent laparoscopic surgical resection of the retroperitoneal tumor and partial hepatectomy (S6) (Fig. 2a and b). There appeared to be no involvement of the retroperitoneal tumor with the ipsilateral kidney or liver. The tumor was removed en bloc, and no major findings were observed in the peritoneal cavity, uterus, or ovaries. After the operation, the postoperative course was uneventful, and the patient was discharged on the sixth postoperative day.

A pathological examination of the resected retroperitoneal tumor showed papillary proliferation with hierarchical branching (Fig. 2c and d). These neoplastic cells had large round-to-oval nuclei with conspicuous nucleoli. The histopathological features of the liver tumor were fundamentally the same as those of the retroperitoneal tumor (Fig. 2d-g). Immunohistochemical analyses showed that estrogen receptor, PAX8, p53, cytokeratin (AE1/AE3), and Wilms tumor 1 were diffusely positive in the neoplastic cells of the liver

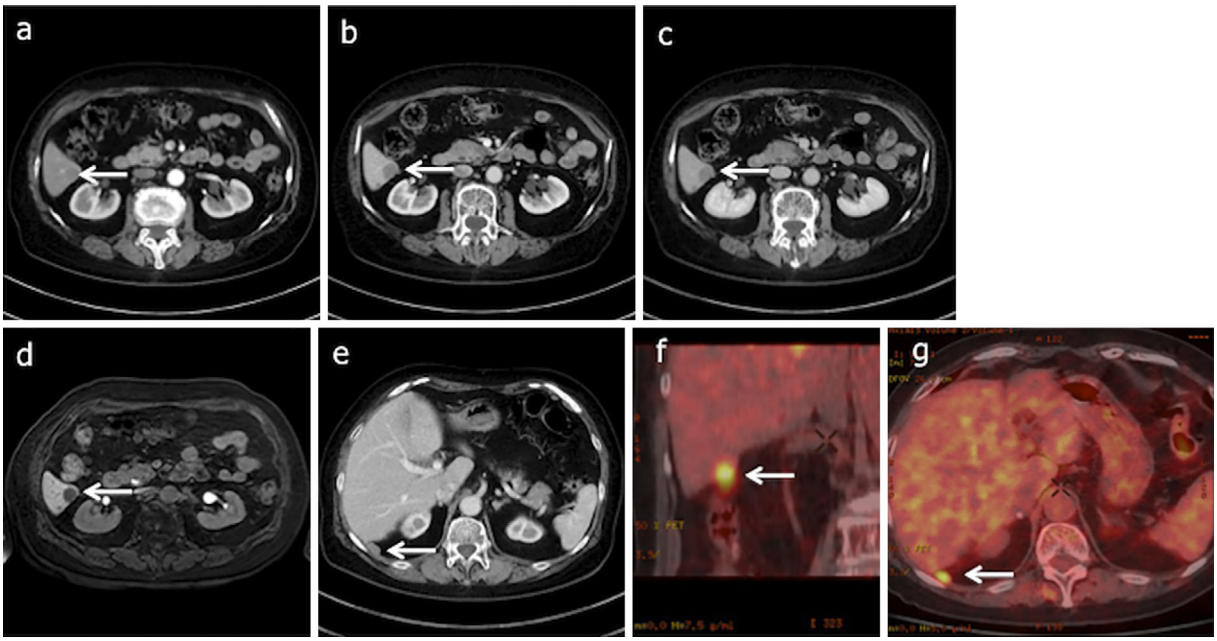

Figure 1. (a-c) Liver dynamic CT. (a) Arterial phase, (b) portal phase, and (c) delayed phase. Dynamic CT of the liver showed a low-density mass with internal enhancement in the S6 area in the arterial and delayed phase (arrows). (d) The hepatobiliary phase of Gd-EOB-DTPA-MRI shows a single nodule in the liver S6 (arrow). (e) Contrast CT showed a low-density mass located at the right retroperitoneal cavity (f, g) PET-CT. The SUV_{max} of the tumor in S6 of the liver was 7.3 (f, arrow), and that of the retroperitoneal tumor was 3.8 (g, arrow).

Table 2. Previously Reported Cases of Retroperitoneal Serous Adenocarcinoma.

	Reference	Age/ Sex	Site	Size (mm)	Elevated tumor markers	Operation	Chemotherapy	Outcomes
1	1	11/F	Encased the right common iliac artery	180×130×110	None	Partial resection	Chemotherapy	NED 10 months
2	2	49/F	Adjacent to the kidney	90×60×50	CEA	Partial resection	None	Not mentioned
3	3	38/F	Adherent to the kidney	60	CEA	Complete resection with partial nephrectomy	None	NED 24 months
4	4	54/F	Adjacent to the aorta	Not mentioned	CA125	None	Chemotherapy	DOD 24 months
5	5	44/F	Adjacent to the left psoas major muscle	60×35×30	CA125, CA19-9	Complete resection with a partial resection of the psoas muscle	None	AWD 23 months
6	6	66/F	Adherent to the ileocecum	200×95×85	CA125, CA19-9	Complete resection with a partial resection of the ileocecum	Adjuvant chemotherapy	AWD 32 months
7	7	75/F	Adherent to the diaphragm	38×47×50	CA125	Complete resection with a partial resection of the diaphragm	Adjuvant chemotherapy	NED 6 months
8	Our case	74/F	Right retroperitoneal cavity and liver (S6)	150 and 200	None	Complete resection with partial hepatectomy	None	NED 12 months

AWD: alive with disease, DOD: died of disease, NED: no evidence of disease

(Fig. 2h-l). The immunohistochemical findings of the retroperitoneal lesion were similar. Because of the single tumor, the liver mass was diagnosed as metastasis rather than a disseminated tumor. Given these results, a diagnosis of PRSA with liver metastasis was made. The metastatic route from the primary lesion was considered hematogenous, as tumor cells were present in the hepatic vein (Fig. 2g). The resection margins were tumor-free (R0 resection). The patient did not wish to receive adjuvant chemotherapy. One year after surgery, the patient remains alive with no clinical evidence of tumor recurrence and is in good general health.

Discussion

The histological findings of PRSA resemble those of ovarian serous carcinoma. The exact origin of PRSA remains unclear, although several possibilities have been postulated, including coelomic metaplasia, extra-ovarian endometriosis, supernumerary ovary, teratoma, and enterogenic cyst (1, 2, 4, 5, 8, 9). The female peritoneum has been considered a secondary Müllerian system with the potential to differentiate into various types of epithelium derived from the Müllerian duct. Pennell and Gusdon reported that small clusters of coelomic epithelial cells could be deposited along the embryonic descent of the ovary to proliferate and/or undergo metaplastic changes to develop into cystic tumors (10). However, in most patients, no ovarian stroma was found surrounding the tumor, which may conflict with the hypothesis of heterotopic ovarian tissue.

Almost all of the reported patients showed elevated tumor markers (Table 2), such as CEA, CA125, and CA19-9 (2-7), which are often elevated in patients with ovarian serous carcinoma. In the present case, the CA125 levels were not measured before the operation, but no elevated tumor markers, including CA125, have been noted thus far. Observation of tumor markers is necessary to screen for recurrence.

There is no standard therapy of PRSA. At present, complete resection with a safe margin is the only curative option and provides the most favorable outcome. However, the long-term survival of PRSA cannot be discussed because of its rarity. In the literature, there are four cases of PRSA that were surgically managed by simultaneous tumor excision in adjacent organs (3, 5-7). Assuming that PRSA shares the biological potential of epithelial ovarian cancer, adjuvant chemotherapy after surgical excision should be the top priority (7). Kaku et al. reported the aggressive phenotype of PRSA with an emphasis on adjuvant chemotherapy, especially in patients with positive surgical margins, local tumor infiltration, and locoregional lymph node involvement (5). Surgical resection for PRSA may be an independent predictor of the survival. However, surgery alone is hardly curative, so adjuvant chemotherapy after curative resection should be considered, although no prospective studies are available to support this practice.

The majority of cases of ovarian high-grade serous carcinoma are thought to arise from the fallopian tube (11). Therefore, the possibility of metastatic high-grade serous carcinoma in the retroperitoneum and liver from the primary fallopian tube must be considered in the current case. Although hysterectomy and bilateral salpingo-oophorectomy

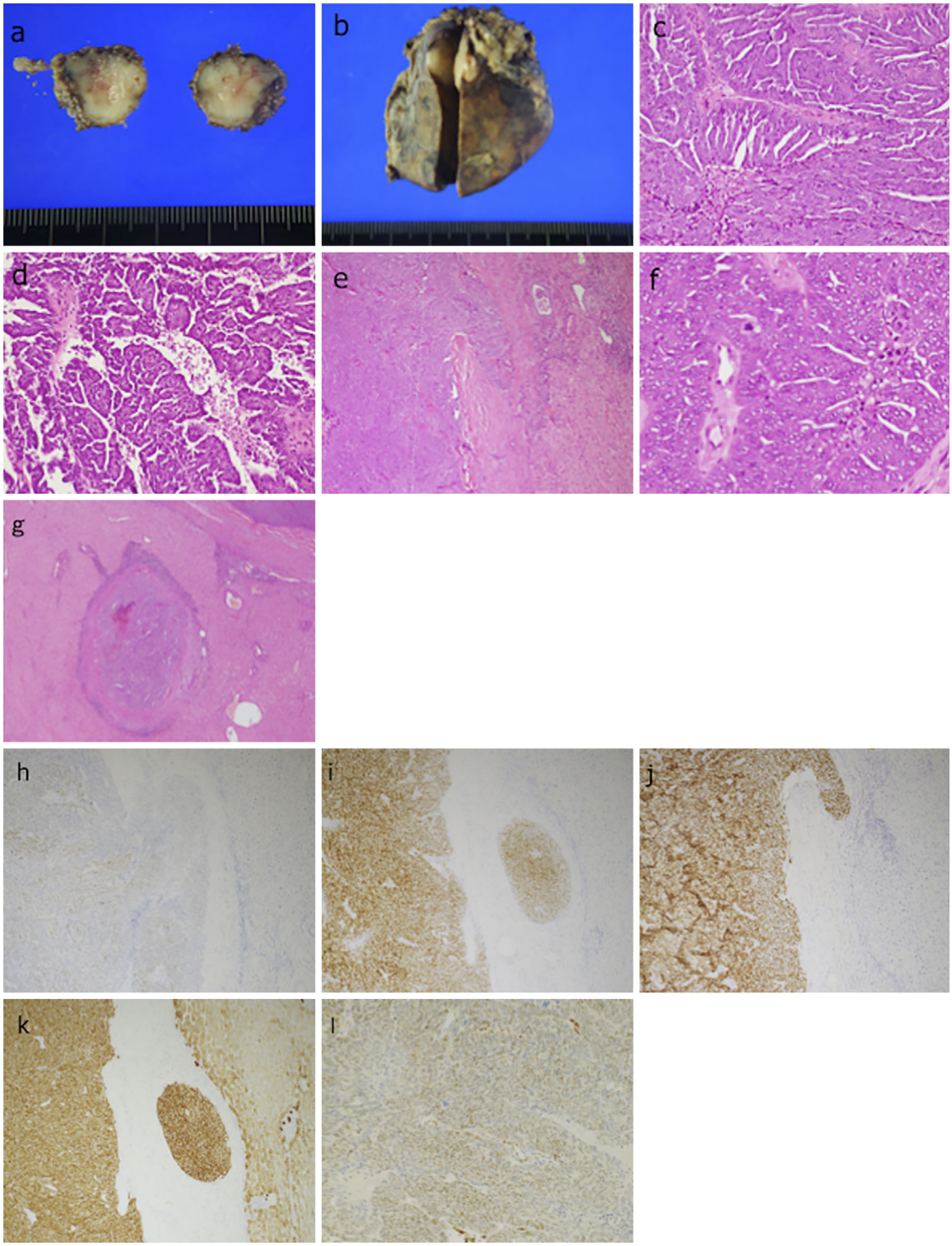

Figure 2. **(a, b) The cut surface of the resected retroperitoneal (a) and liver (b) tumors. (c-f) Hematoxylin and Eosin staining of the retroperitoneal (c: ×200 and d: ×400) and liver (e: ×200, f: ×400 and g: ×40) tumors showed funicular and alveolar proliferation of atypical cells. The metastatic route from the primary lesion was considered hematogenous, given that tumor cells were present in the hepatic vein (g). (h-l) The immunopathological examination of the liver tumor (×40). The tumor cells were positive for estrogen receptor (h), p53 (i), PAX8 (j), WT1 (k), and cytokeratin AE1/AE3 (l). The immunohistochemical findings of the retroperitoneal lesion were similar.**

were not performed, neither a tumorous lesion nor an uptake on PET in the fallopian tube or ovary was observed. For patients with peritoneal serous carcinoma with a lesion in the ovary or fallopian tube, references 12-14 can be cited as diagnostic criteria (12-14). When tumors are simultaneously present in the peritoneum and ovary, the ovarian tumor is considered to have been seeded in the peritoneum. When an ovarian tumor is <5 mm, it is defined as a peritoneal carci-

noma. The primary site (i.e. ovary, fallopian tube, or peritoneum) should be identified if possible. In some cases, it may be impossible to definitively identify the primary site; such cases should therefore be listed as "undesignated." Estrogen receptor expression is most common in serous carcinoma, and PAX8 can be used to help identify cells of Müllerian origin. Because the tumor in the present case was considered a histologically high-grade serous lesion, we performed an immunohistochemical analysis of the p53 expression to distinguish between high-grade and low-grade serous carcinomas. Cytokeratin (AE1/AE3) can be useful for distinguishing epithelial tumors from other tumors. WT1 is useful for distinguishing serous tumors (both high-grade and low-grade) (15). These examinations in the present study revealed the same findings as those for high-grade serous carcinoma derived from the Müllerian duct. Therefore, a diagnosis of PRSA was made.

Conclusion

In conclusion, PRSA is a rare retroperitoneal primary tumor with unique specificity regarding its occurrence and development. There are still no reports of liver metastasis of PRSA. We performed surgical excision and obtained an excellent clinical outcome. Although the optimum therapeutic strategy for PRSA has not been established, the combination of surgical excision with adjuvant chemotherapy for curative treatment is recommended at present.

The authors state that they have no Conflict of Interest (COI).

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