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Case Report

Primary Clear Cell Adenocarcinoma of the Peritoneum

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TERADA, T. and KAWAGUCHI, M. *Primary Clear Cell Adenocarcinoma of the Peritoneum*. Tohoku J. Exp. Med., 2005, **206** (3), 271-275 —— We report on a very rare case of peritoneal clear cell adenocarcinomas. A 49-year-old Japanese woman underwent hysterectomy and bilateral salpingo-oophorectomy for endometrial endometrioid adenocarcinoma grade III, which was composed of undifferentiated carcinoma cells (98%) and tubular carcinoma cells (2%). No clear cell adenocarcinoma elements were noted in this tumor. Two peritoneal cystic tumors were detected by imaging modalities around the stomach and spleen, 15 months and 21 months after the follow-up period of the endometrial carcinoma, respectively. These two tumors were surgically resected. They were cystic tumors encapsulated by fibrous capsules and showed the same morphologies. They showed proliferation of carcinoma cells arranged in solid nest, tubular, and papillary patterns. They showed clear cytoplasm positive for periodic acid-Schiff stain, hobnail cells, and occasional hyaline globules. The morphologies fulfilled the criteria of clear cell adenocarcinoma. The morphologies and immunohistochemical findings of the two peritoneal clear cell adenocarcinomas were different from those of endometrial carcinoma. We believe that the two clear cell adenocarcinomas are not metastatic lesions from the endometrial carcinoma of the uterus, and that they are primary clear cell adenocarcinomas of the peritoneum. Our case was characterized by cyst formations and encapsulation in addition to the common histological features of clear cell adenocarcinoma of the uterus and ovary. ———— clear cell adenocarcinoma; peritoneum

Neoplasms of the peritoneal cavity are rare, but they are important because they may pose diagnostic challenges to clinicians and histological differential diagnosis to pathologists. Peritoneal neoplasms are diffuse or localized (Battifora and Elliot McCaughey 1994). Most diffuse neoplasms are malignant mesothelioma. Localized peritoneal neoplasms are classified into benign, intermediate and malignant tumors. Localized malignant tumors of the peritoneum include localized malignant mesothelioma, serous papillary adenocarcinoma, fibrosarcoma, angiosarcoma, solitary fibrous tumor, desmoplastic small round cell tumor, and other sarcomas (Battifora and Elliot McCaughey 1994). The most common of these are localized malignant mesothelioma and serous papillary adenocarcinoma (Battifora and Elliot McCaughey 1994). Clear cell adenocarcinoma is common in the ovary and endometrium. It is characterized by clear cells with glycogen

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and hobnail cells arranged in tubular, papillary and solid patterns (Scully 1982). Primary clear cell adenocarcinoma of the peritoneum is extremely rare; only two cases have been reported in the English literature to the best of our knowledge (Lee et al. 1991; Ichimura et al. 2001). We here report a case of primary clear cell adenocarcinoma of the peritoneum. This case report shows that clear cell adenocarcinoma may primarily occur in the peritoneal cavity, and the morphologies of such tumors.

Case Report

The publication of this case was approved by Shizuoka Municipal Shimizu Hospital Ethical Committee. A 49-year-old Japanese woman underwent hysterectomy and bilateral salpingo-oohorectomy for endometrial carcinoma. Pathological examination showed that the endometrial carcinoma was endometrioid adenocarcinoma grade III, exclusively composed of undifferentiated carcinoma cells. No clear cells or hobnail cells were recognized. The carcinoma was shown to have invaded the myometrium, but bilateral fallopian tubes and ovaries were free of carcinoma cells and showed normal histology. No metastases were noted in the dissected lymph nodes. No ascites was noted, and the cytologic examination of the peritoneal lavage fluid during surgery was negative for malignant cells. The patient was then followed up every three months. A peritoneal tumor was recognized at the peritoneum of the greater curvature of the stomach by computed tomography (CT) and positron emission tomography (PET) 15 months after the operation on the endometrial carcinoma, and resection of the tumor was performed. Another tumor was noted in the peritoneum near the splenic hilus by CT and PET six months after the first gastric peritoneal tumor, and resection of the tumor was performed. Blood laboratory data were within normal range during the entire follow-up period. The patient is now free of tumors 27 months after the initial uterus operation.

Pathologically, the gastric peritoneal tumor was a cystic one (3 cm in diameter) attached to the stomach (Fig. 1A). The splenic hilus peritoneal tumor (2 cm in diameter) was also a cystic one attached to the peritoneum (Fig. 1B). Microscopically, the gastric and splenic tumors were located in the peritoneum and subserosa (Fig. 2). They were cystic tumors encapsulated by fibrous capsules (Figs. 1A and 2). The two tumors showed almost the same histologies. The tumors showed proliferation of polygonal carcinoma cells arranged in solid nest (Fig. 3), tubular, or papillary patterns (Fig. 4). Approximately 50% of tumor cells showed a clear cytoplasm (Fig. 3).

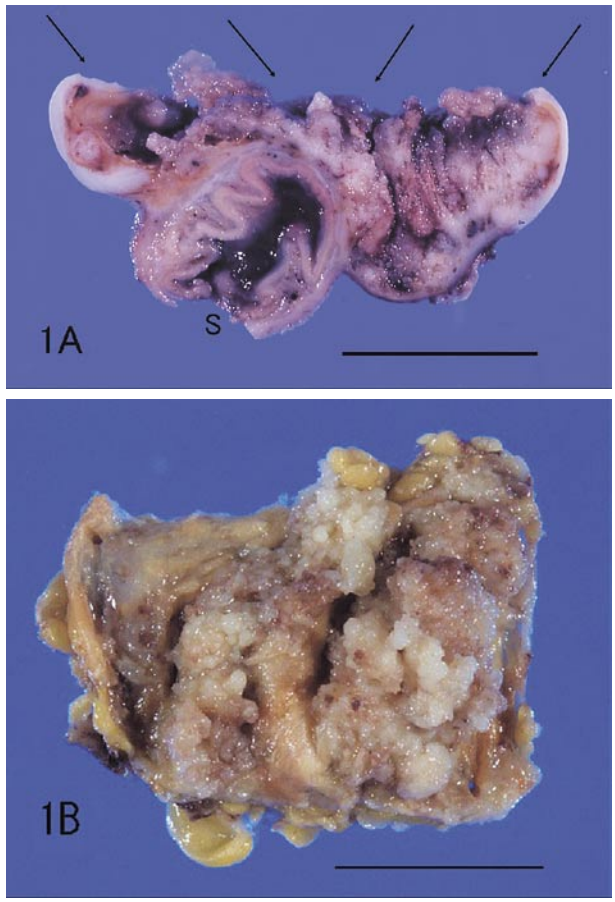

Fig. 1. (A) Gross appearances of a peritoneal tumor near the stomach. Cut surface of the peritoneal tumor (arrows) attached to the stomach (*S*). The cystic tumor is opened. The tumor is cystic with solid areas. Bar = 1 cm.
(B) Gross appearances of a peritoneal tumor near the splenic hilus. The tumor is cystic and the cyst is opened. The tumor shows solid and papillary areas in the inner cyst lumen. Bar = 1 cm.

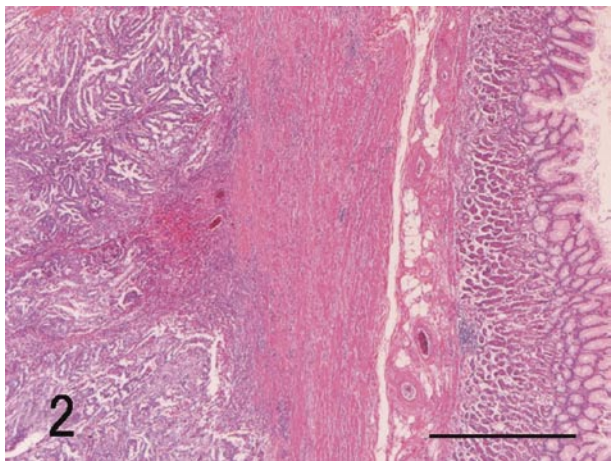

Fig. 2. Low power view of the peritoneal tumor (left) and stomach (right). The peritoneal tumor is located in the subserosal and peritoneum. HE, × 20. Bar = 1,000 μm.

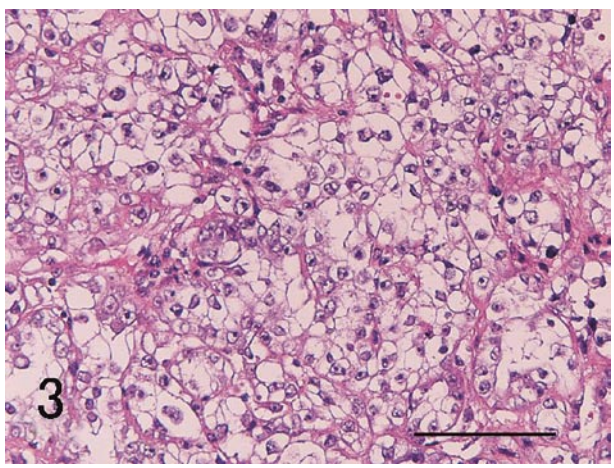

Fig. 3. High power view of a part of the peritoneal tumor. The tumor cells are polygonal in shape and arranged in solid nests. They have clear cytoplasm, hyperchromatic nuclei, and clear cell boundaries. HE, × 200. Bar = 120 μm.

Hobnail cells were noted in the papillary areas (Fig. 4). The stroma of the papillary areas showed hyalinous changes rich in mucinous substances positive for periodic acid-Schiff (PAS) and alcian blue. PAS-positive intracytoplasmic hyaline globules were recognized in a few areas. Mucins (neutral and acidic) were present in the surface of tumor cells. An immunohistochemical study was performed by Dako's ENVISION method, as previously described (Terada et al. 2002, 2004). The

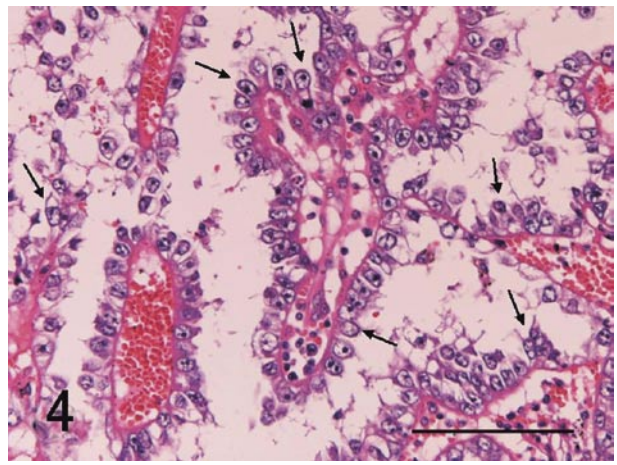

Fig. 4. High power view of a part of the peritoneal tumor. Tumor cells show papillary structures and hobnail appearances. Some hobnail cells are labeled by arrowheads. HE, × 200. Bar = 120 μm.

antibodies and the immunohistochemical results are shown in Table 1. Both tumors showed almost the same immunophenotypes.

The endometrial carcinoma was endometrioid carcinoma of grade III. Approximately 98% of the tumor was composed of undifferentiated cells (Fig. 5), and the remaining 2% of the tumor showed tubular structures resembling endometrial glands (Fig. 6). No clear cells, hobnail cells or papillary structures were recognized in this endometrial carcinoma. The immunohistochemical findings were different from the two peritoneal tumors (Table 1).

Discussion

Clear cell tumors of the female genital tracts are characterized by clear epithelial cells containing abundant cytoplasmic glycogen and hobnail cells, either alone or in combination (Scully 1982). They are classified as benign, intermediate, and malignant. The present two peritoneal tumors showed clear cells and hobnail cells arranged in papillary, solid nest, and tubular patterns. Much atypia, regarded as malignant cells, was recognized. Therefore, the authors diagnosed these tumors as clear cell adenocarcinoma of the peritoneum. The presence of hyalinous stroma in the papillae and cytoplasmic eosinophilic globules

TABLE 1. *Histochemical and Immunohistochemical Results in Two Peritoneal Tumors (Tumor 1, Peristomach: Tumor 2, Perisplenic) and Endometrial Carcinoma*

Antigens	Antibodies (clones)	Source	Tumor 1	Tumor 2	Endometrial carcinoma
PAS			+	+	-
Alcian blue			+	+	-
PAS/alcian blue			+	+	-
Cytokeratin	AE1/AE3	Dako Glostrup, Denmark	+	+	+
Cytokeratin	Polyclonal	Dako	+	+	+
Cytokeratin	MNF116	Dako	+	+	+
Cytokeratin	34βE12	Dako	+	+	-
EMA	E29	Dako	+	+	-
Vimentin	V9	Dako	-	-	+
S-100 protein	Polyclonal	Dako	-	-	-
Chromogranin A	DAK-A3	Dako	-	-	-
p53	DO-7	Dako	+	+	+
C-erbB2	Polyclonal	Dako	+	+	-
CA19-9	NS19-9	TFB Lab, Tokyo, Japan	+	+	-
CA125	M11	Dako	+	+	-
AFP	Polyclonal	Dako	-	-	-
CEA	Polyclonal	Kyowa Medical, Tokyo, Japan	-	-	-
Estrogen receptor	1D5	Dako	-	-	-
Progesterone receptor	1A6	Novocastra, Newcastle upon Tyne, UK	-	-	-
Ki67 labeling	MIB-1	Dako	40%	50%	90%

PAS, Periodic acid-Schiff.

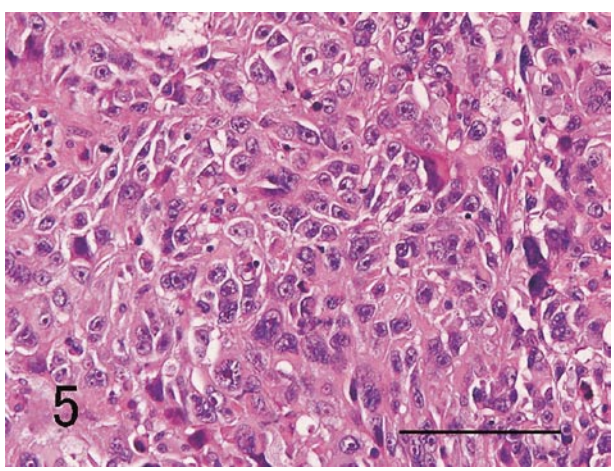

Fig. 5. High power view of a part of the endometrial carcinoma of the uterus. The tumor cells are composed exclusively of undifferentiated carcinoma cells. HE, × 200. Bar = 120 μm.

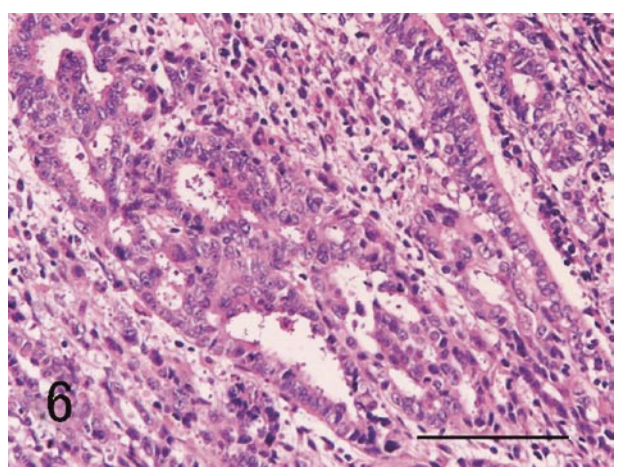

Fig. 6. High power view of a minor part of the endometrial carcinoma of the uterus. The tumor cells show focal tubular formations resembling endometrial glands. HE, × 200. Bar = 120 μm.

in the tumor cells also supports the diagnosis (Scully 1982).

Most of the malignant neoplasms of the peritoneum are malignant mesothelioma and serous papillary adenocarcinoma. The present case is histologically different from these tumors. The present case is also different from metastatic renal cell carcinoma and york sac tumor in terms of histology and immunohistochemical findings.

The present case had undergone total hysterectomy for endometrial carcinoma previously. The present two tumors were differentiated from metastatic endometrial carcinoma. The endometrial carcinoma in the present case was endometrioid adenocarcinoma grade III composed exclusively of undifferentiated cells. The areas of tubular formations were endometrioid adenocarcinoma composed of tubules resembling endometrial glands. No clear cells and hobnail cells were noted in the endometrial carcinoma. Therefore, the present two peritoneal tumors are histologically different from endometrial carcinoma. In addition, an immunohistochemical study showed that the two peritoneal tumors had immunophenotypes different from those of the endometrial carcinoma. Therefore, we think that the two peritoneal tumors were not metastatic endometrial carcinomas but primary clear cell adenocarcinomas of the peritoneum.

The two clear cell adenocarcinomas of the present case were morphologically characterized by encapsulation and cyst formations in addition to ordinary features of clear cell adenocarcinoma of the uterus and ovary.

In summary, we presented an exceedingly rare case of primary clear cell adenocarcinoma of the peritoneum. Our case was characterized by cyst formations and encapsulation in addition to the common histological features of clear cell adenocarcinoma of the uterus and ovary.

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