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Mucinous Cystadenocarcinoma of the Retroperitoneum: Report of a Case

SATOSHI SUZUKI[1], TAKESHI MISHINA[1], DAI ISHIZUKA[1], MASAYUKI FUKASE[2], and YO-ICHI MATSUBARA[1]

Departments of [1]Surgery and [2]Pathology, Tsuruoka Municipal Shonai Hospital, 2-1 Baba-cho, Tsuruoka, Yamagata 997-0035, Japan

Abstract Retroperitoneal mucinous cystadenocarcinomas are extremely rare. A 40-year-old Japanese woman was found to have a retroperitoneal mucinous cystadenocarcinoma of ovarian type. Both ovaries were normal. Concentrations of carcinoembryonic antigen and carbohydrate antigen 19-9 in the cyst fluid were extremely high (810 000 ng/ml and 8 082 000 IU/l, respectively). The tumor varied from benign to borderline and malignant in microscopic appearance, and the lesion was composed of mesothelium-like cells. The histologic and immunohistochemical findings suggested that the tumor developed from mucinous metaplasia of the coelomic mesothelium.

Key words Cystadenocarcinoma · Retroperitoneum · Mucinous metaplasia · Coelomic mesothelium

Introduction

Retroperitoneal cystadenocarcinomas are extremely rare. We present herein the clinical and pathologic features of a case that we encountered and discuss the likely origin of this tumor.

Case Report

A 40-year-old Japanese woman with progressive abdominal distension of 2 months' duration was admitted to our hospital. A large palpable mass in the right flank region of the abdomen had been noted by a gynecologist at another hospital when she gave birth to a child 1 month before admission.

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The patient was asymptomatic except for distension. A physical examination suggested the tumor to be a large intra-abdominal cyst. Laboratory results were within the normal limits except for increased serum concentrations of carbohydrate antigen (CA) 19-9 (74 U/ml, normal <37) and tumor-associated galactosyltransferase (14.8 U/ml, normal <13.6). Computed tomography showed a large unilocular cyst measuring $10 \times 10 \times 15$ cm in the right retroperitoneal space. This mass displaced the right colon ventromedially, and the right iliopsoas muscle and lower pole of the right kidney dorsally. The cyst was encapsulated and contained fluid (Fig. 1).

At laparotomy a large cystic tumor adherent to the cecum was seen in the right retroperitoneal space. The cyst was completely resected including a portion of the ileocecal region accompanied with the appendix. The ovaries, fallopian tubes, appendix, kidneys, and pancreas all appeared normal. The patient required no further treatment. She was discharged and has shown no evidence of recurrence for 15 months.

Macroscopically, the cystic mass measured $12 \times 12 \times 15$ cm and was unilocular, with a wall varying in thickness from 0.1 to 2 cm and a weight of 1300 g including 1000 ml of dark, viscous fluid. The external surface of the tumor was smooth; the tumor adherence to the cecum had resulted from colonic diverticulitis, not tumor invasion. Two papillary mural nodules measuring 2.5–3.0 cm protruded into the cyst (Fig. 2). In the cystic fluid the concentration of carcinoembryonic antigen was 810 000 ng/ml while that of CA19-9 was 8 082 000 U/ml.

A microscopic examination showed a fibrous cyst wall consisting of collagen and fibroblasts. The cyst was lined by tall columnar epithelial cells with basal nuclei, indicating a mucinous tumor. The columnar epithelium was simple in some areas and stratified in others, and also exhibited varying degrees of differentiation. Alcian blue staining showed a strong positive reaction in the

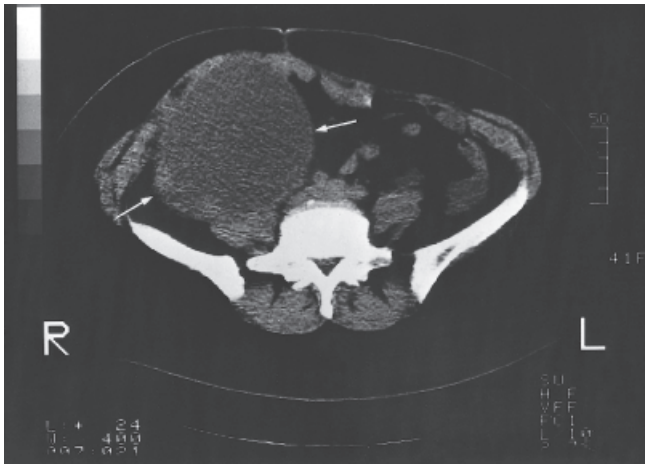

Fig. 1. Computed tomography showing a large unilocular cyst measuring 10 × 10 × 15 cm in the right retroperitoneal space. The cyst was encapsulated and contained fluid (*arrows*)

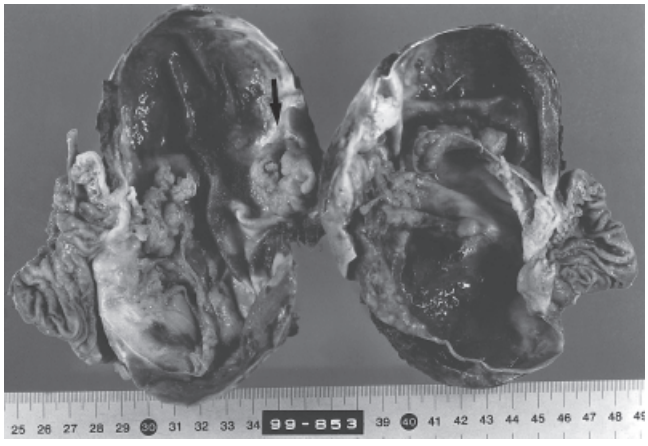

Fig. 2. Following a resection, the retroperitoneal cyst, which measured 12 × 12 × 15 cm, was confirmed to be unilocular. The mass weighed 1300 g including 1000 ml of dark, viscous fluid. Two papillary mural nodules measuring 2.5–3.0 cm protruded into the cyst (*arrows*)

cytoplasm of some tumor cells. Immunohistochemical staining for epithelial membrane antigen (EMA) showed cytoplasmic reactivity in most tumor cells. Reactivity for vimentin was absent. In some areas the tumor was very well differentiated and had the appearance of a mucinous cystadenoma, while other areas had the appearance of a papillary mucinous cystadenocarcinoma; still others showed features of borderline malignancy (Fig. 3). The malignant areas demonstrated infiltration into the fibrous cyst wall but not full-thickness invasion. A careful microscopic examination showed no evidence of ovarian tissue in the cyst wall, and the resected appendix was normal on multiple sections.

Discussion

Primary tumors of the retroperitoneal area include many types.[1] Beginning with the first description of the retroperitoneal mucinous cystadenocarcinoma of the ovarian type by Lawrence and Clarence in 1977,[2] we know of only 14 cases previously reported in English. All patients were female. The mean age was 45 years, with a range from 35 to 69. The cysts ranged in diameter from 11 to 24 cm, with a mean of 19.1. These tumors are clinically unilocular or multilocular cysts with several mural nodules protruding into the cyst. The histologic appearance within the mass varied from a benign mucinous cystadenoma to an anaplastic tumor. The connective tissue resembled ovarian stroma, although no ovarian tissue could be identified, and they all were demonstrated in the presence of two normal ovaries. Concerning the origin of retroperitoneal mucinous tumors, Roth and Ehrlich reported a case of primary retroperitoneal mucinous cystadenocarcinoma of ovarian type which was thought to have arisen from either a displaced coelomic epithelium or from a supernumerary ovary.[3] On the other hand, a case studied by light and electron microscopy by Fujii et al. demonstrated that the morphological features of the tumor resembled those of an ovarian mucinous tumor, and they concluded that histogenetically the tumor appeared to be derived from a mesothelial inclusion cyst.[4]

Mucinous cystadenocarcinomas are not uncommon in the liver, pancreas, or ovary; the relative rarity of similar lesions in the retroperitoneum probably has resulted in an underdiagnosis.[5] Two main hypotheses have been advanced concerning the origin of this tumor. One is that the tumors arise from heterotopic ovarian tissue,[6] even though accessory and supernumerary ovaries are rare. A more likely explanation is that tumors arise from invaginations of the peritoneal mesothelial layer that undergo metaplasia either at the same time or subsequently. As a result, the coelomic epithelium, which invaginates during embryonic growth, might undergo mucinous metaplasia with cyst formation in a retroperitoneal location.[7]

A recent study demonstrated that immunohistochemical evaluations facilitated the histological determination and the establishment of histogenetic correlations of this tumor. Park et al. stressed that the positive reaction to EMA and the selective positive reaction to vimentin are significant factors in determining the histogenesis of the primary retroperitoneal mucinous cystadenocarcinoma.[8] Mesothelial tumor cells which actively proliferate produce enough vimentin to react positively to this stain, whereas benign mesothelial cells do not produce enough vimentin for the positive reaction. Although such histochemical staining is not a specific finding for mesothelial tumors, they are very

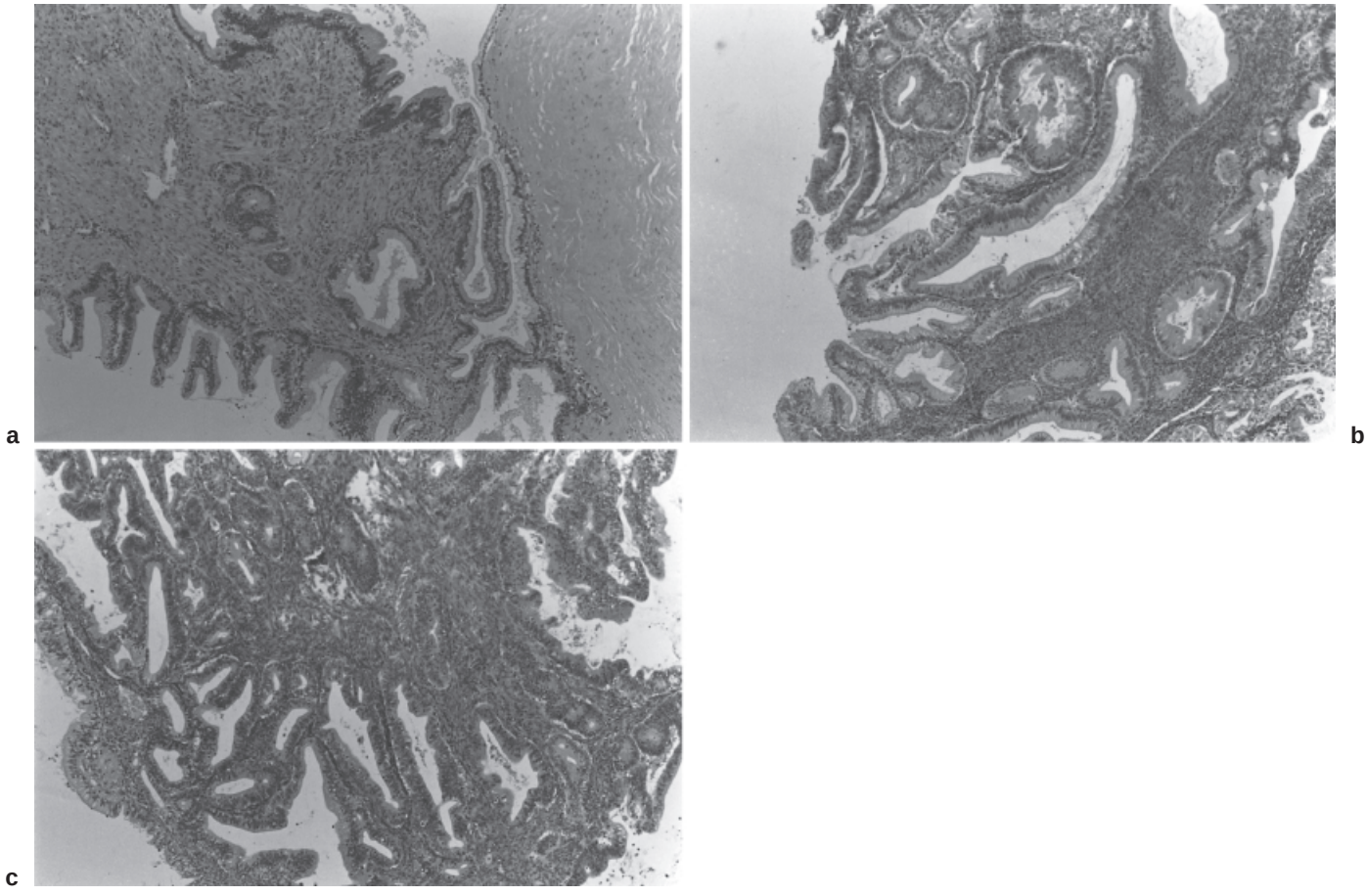

Fig. 3. Microscopic examination showed that in some areas the tumor was very well differentiated and had the appearance of a mucinous cystadenoma **a**. Other areas had the appearance of a papillary mucinous cystadenocarcinoma **c**, while still others showed borderline malignancy **b** (H&E, ×20)

helpful for the diagnosis of this tumor.[9] In contrast, Tenti et al. reported two cases of primary retroperitoneal mucinous cystadenocarcinomas by an immunohistochemical and molecular study.[10] These tumors have patterns similar to ovarian mucinous tumors as a result of special immunohistochemical staining for the gastropancreatic antigen, markers of pyloric-type gastric mucosa differentiation, intestinal cell markers, and DUPAN-2. The activation of the K-ras oncogene which in particular has been identified in ovarian mucinous adenocarcinomas is detected in one case of primary retroperitoneal mucinous cystadenocarcinomas. Accordingly, Tenti et al. conclude that whatever the histogenesis of primary retroperitoneal mucinous cystadenocarcinoma, whether from teratomas, from ectopic ovarian tissue or from mucinous metaplasia of the coelomic epithelium, their morphological and biological similarities to ovarian mucinous tumors suggest that the process of tumor formation follows similar steps.[10]

In our case, the retroperitoneal tumor was mainly composed of mesothelium-like cells. The lesions demonstrated a spectrum of microscopic appearances from that of cystadenoma to those of borderline tumors and cystadenocarcinoma. These histologic features indicated that the lesions in this case resembled those of ovarian mucinous tumors. Accordingly, the absence of ovarian tissue in the cyst wall, as well as epithelial immunoreactivity for EMA without staining for vimentin, strongly suggest an origin from mucinous metaplasia of coelomic epithelium.

Primary retroperitoneal tumors are usually mucinous or serous cystadenocarcinoma, although endometrioid carcinoma, clear cell carcinoma, and Brenner tumor may occur in the retroperitoneum. Papillary serous carcinomas of the retroperitoneum indicated the metaplastic process of coelomic epithelium into serous tumors, taking place in the development of cystomas, as the same process as mucinous tumors. Serous and mucinous tumors have the same clinical imaging characteristics as corresponding tumors of the ovary.[11] The differential diagnosis includes mesothelial cysts, cystic mesothelioma, lymphangioma, enteric duplication cysts, enteric

cysts, and nonpancreatic pseudocysts. A mesothelial cyst is a thin-walled unilocular cyst which may be difficult to distinguish from serous cystadenoma. Cystic mesothelioma and lymphangioma tend to be multiloculated masses which resemble a mucinous tumor. Enteric cysts and enteric duplication cysts are closely related to the parent gut with a uni- or multilocular appearance. Nonpancreatic pseudocysts with thin-walled uni- or multilocular cysts may be difficult to distinguish from serous and mucinous cystadenoma, respectively.

The preoperative course of these cysts appears obscure, yet the overall prognosis is poor. Based on the histogenesis, these tumors should be treated in the same manner as a primary ovarian tumor of the same grade and comparable stage.[12] In our present case, the tumor was completely resected and chemotherapy was not planned during the follow-up period. The patient has shown no evidence of recurrence for 15 months after surgery.

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