Primary Mucinous Cystic Neoplasm of the Retroperitoneum
- A Report of Three Cases -

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The primary mucinous cystic neoplasm of the retroperitoneum is rare. Only 29 cases have been reported in literature to date, including 2 cases in domestic literature. They encompass benign, borderline and malignant varieties and show a histologic similarity to the ovarian mucinous tumors. Although several theories have been proposed, the histogenesis of this neoplasm is still uncertain. Mucinous or coelomic metaplasia of the retroperitoneal mesothelium, proposed by Lauchlan, has gained wide acceptance. We report three cases of primary retroperitoneal mucinous cystic neoplasm ranging the spectrum from benign to malignant histologic features, and discuss the histogenesis and appropriate treatment for these rare neoplasms.

CASE 1

A 50-year-old woman was admitted to our hospital. She complained of a palpable abdominal mass in the left upper quadrant that she had had for one month. The previous routine gynecological examination had revealed no abnormalities. On ultrasonography, a huge multiseptate cystic mass with a few mural nodules was discovered in the retroperitoneum below the left kidney. On abdominal and pelvic computed tomography (CT) with contrast, this tumor was found to be located around the pancreatic tail portion and had lobulating contour (Fig. 1). The laboratory data showed a slight elevation of CA-125 (41 UI/mL) and marked elevation of CA 19-9 (1,510 UI/mL). The levels of CEA (4.7 ng/mL) and α-fetoprotein (1.4 ng/mL) were within normal limits. The cystic mass was located in the mesentery, and no anatomical connections with the pancreas including the tail portion, ovaries, or small bowel were found. It was initially intact and was removed by laparoscopic procedure after the aspiration of the cyst content to reduce the tumor volume.

Grossly, the tumor was a lobulated multiseptate cystic mass (10 × 9 × 5 cm and 238 gm), filled with white to yellow thick mucoid material (Fig. 2). The outer surface was grayish tan and glistening, and showed a fibrous adhesion site. The inner surface was pinkish tan, glistening, and irregular with frond-like areas and a few solid mural nodules.

Microscopically, the tumor was composed of irregular multilocular cysts lined by columnar cells with mucinous or eosinophilic cytoplasm, which were flat or piled up with micropapillary pro-

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trusions showing benign to borderline appearances (Fig. 3A). The adenocarcinoma components were well differentiated with a cribriform pattern (Fig. 3B). The stroma consisted of hypocellular fibrous or cellular ovarian stroma-like tissue. There were a few anaplastic mural nodules consisting of spindle or multinucleated cells with malignant features, including marked cellular pleomorphism and high mitotic activity, mixed with mucinous glandular components (Fig. 3C). Some tumor cells lining the cyst showed strong positivity for Alcian-blue and periodic acid schiff (PAS) stainings, but negativity for calretinin by immunohistochemical staining. The only mucinous glandular components in the anaplastic mural nodules showed strong positivity for cytokeratin by immunohistochemical staining (Fig. 3D). This tumor was diagnosed to be a primary retroperitoneal mucinous cystadenocarcinoma.

After the laparoscopic operation, the level of CA 19-9 decreased to 26.5 IU/mL at the two months follow-up, but re-increased to 41.9 IU/mL at the four months follow-up. It increased up to 549 IU/mL at the ten months follow-up. The follow-up CT at postoperative six and eight months revealed neither local recurrence nor distant metastasis despite increased levels of CA 19-9. But, it revealed thickening of the walls of the cecum and ascending colon with pericolic fat infiltration: both paracolic gutters had thickened and there was a presence of multiple mesenteric lymphadenopathy at the ten months follow-up, which were suggestive of peritoneal seeding. No recurred mass was identified around the previous operation site, and the remaining solid organs showed no metastasis. The patient received chemotherapy using Taxol, but expired ten months after the operation.

**CASE 2**

A 31-year-old woman was admitted to our hospital. She complained of abdominal distension in the right lower quadrant that she had for one year. On abdominal and pelvic computed tomography with contrast, a multiseptate cystic mass with calcifications was detected in the right retroperitoneum. The laboratory data for CA 72-4 in serum was within the normal limit (1.9 µ/mL). At excision, using a mid-line incision, a well-encapsulated, soft and glistening cystic mass was found in the right retroperitoneal space behind the ascending colon. The mass was easily separated from the ascending colon without adhesion. Other solid organs including both ovaries were intact. Incidental appendectomy was also performed.

Grossly, the tumor was a smooth-surfaced, multilocular cyst (21 × 16 × 10 cm and 210 gm), filled with grayish green turbid fluid. The inner surface was grayish tan and glistening, and showed calcified septa without any solid nodules.

Microscopically, the cyst was mostly lined by single layered low cuboidal or tall columnar cells with mucinous or eosinophilic cytoplasm (Fig. 4A). In addition, small papillae or glands com-
posed of stratified hyperchromatic nuclei were occasionally observed (Fig. 4B). The stroma consisted of cellular ovarian stroma-like tissue or collagenous tissue with multifocal calcifications. Obvious malignant features or stromal invasion were not present. Immunohistochemistry showed a negative reaction for calretinin in the nucleus and cytoplasm of low cuboidal cells. This tumor was diagnosed to be a primary retroperitoneal mucinous cystic neoplasm of borderline malignancy. The appendix was normal. The post-operative gynecological examination revealed no abnormalities.

CASE 3

A 67-year-old woman was admitted to our hospital. She complained of abdominal discomfort in the right upper quadrant that she’s had for several months. On abdominal and pelvic computed tomography with contrast, a 5.1 cm sized cystic mass with homogeneous low attenuation was detected in the posterior lateral side of the ascending colon. There was no lymphadenopathy and the liver showed a tiny nodule in segment VIII, which was too small to characterize. The laboratory data for CEA in serum was within the normal limit (1.9 ng/mL). At laparotomy,
a well-defined, soft and round cystic mass was found in the right retroperitoneal space behind the paracolic gutter. Grossly, the tumor was a smooth-surfaced unilocular cyst (7.5 × 5 × 5 cm and 170 gm), filled with slight yellow serous fluid. The inner surface was whitish tan, smooth and glistening without any solid portions or papillary excrescences.

Microscopically, the cyst was lined by a single layer of flattened low cuboidal or tall columnar cells with mucinous cytoplasm (Fig. 5A). The tumor cells showed no evidence of stratification, pleomorphism, or papillary arrangement. The stroma consisted of hypocellular collagenous tissue with multifocal calcifications. PAS and alcian-blue stainings showed a strong positive reaction in the cytoplasm of tall columnar cells. Immunohistochemistry showed positive reaction for calretinin in the nucleus and cytoplasm of some low cuboidal cells (Fig. 5B). This tumor was diagnosed to be a primary retroperitoneal mucinous cystadenoma. The patient was lost to follow-up 3 months after the operation.

**DISCUSSION**

Primary retroperitoneal mucinous cystic neoplasms in women are rare. There have been 29 cases reported to date.\(^1\)\(^-\)\(^20\) This neoplasm covers the spectrum from benign to malignant, and a case with distant metastasis was reported by Banerjee and Gough.\(^1\)

The origin of this rare neoplasm has been a matter of debate because of its location and its histologic features being similar to that of its ovarian counterpart. The precise histogenesis of this neoplasm has not been defined; however, several hypotheses are proposed in literature.

Frank\(^5\) reported a papillary cystadenoma in a retroperitoneal supernumerary ovary as early as 1909. Wharton\(^7\) documented the presence of accessory and supernumerary ovaries at autopsy and postulated the possibility of heterotopic ovarian tissue as an ori-
gin. Meyer considered these neoplasms to represent the monodermal variant of retroperitoneal teratomas. Hansmann and Budd proposed the development to be from the embryonal urogenital remnants and the possibility of a mesonephric origin for the neoplasm. Abascal suggested an enterogenous origin from intestinal duplication. Recently, Lauchlan postulated that the peritoneal mesothelium retains the potential for mullerian differentiation, with the possibility that the development of the tumor shows the same histologic features as ovarian tumors. During embryogenesis, the coelomic epithelium is multipotential and gives rise to the peritoneum as well as the germinal epithelium of the ovary. As in the ovary, this epithelium may undergo mucinous metaplasia with cyst formation and gain the potential for malignant transformation. In a recent study by Tenti et al., two cases of primary retroperitoneal mucinous cystadenocarcinomas revealed a similarity to their ovarian counterpart by immunohistochemical stainings for gastroenteropancreatic antigens and DNA analysis for point mutation of K-ras oncogene.

We could not find the heterotopic ovarian tissue, teratoid component, or digestive tract remnants in any of our cases. The positive immunoreactivity for calretinin of some low cuboidal cells in case 3 demonstrates its being of mesothelial origin and suggests that this neoplasm may have arisen from mesothelial cells through subsequent mucinous metaplasia. Thus, mucinous metaplasia of the retroperitoneal mesothelium, by Lauchlan, is considered to be the most possible histogenesis in case 3.

The histologic features such as ovarian-like stroma and anaplastic mural nodules in case 1 are reminiscent of both pancreatic and ovarian mucinous cystadenocarcinomas. The tumor in case 1 showed a strong correlation with the level of CA 19-9 in the initial diagnosis, treatment, and follow-up. Thus, we could not entirely exclude the possibility that the undetected heterotopic pancreas might be the origin of the tumor in case 1, but no pancreatic tissue was detected in the specimen of case 1. The tumor showed no anatomical connection with the pancreas, ovaries, or the adjacent gastrointestinal tract at the operation field; and the tumor markers, except for CA 19-9, did not significantly increase. Therefore, we concluded the tumor of case 1 to be of primary retroperitoneal origin, excluding the possibility of a distant metastasis.

The treatment for primary retroperitoneal mucinous neoplasms is considered to be similar to their ovarian counterparts. It is definitely important to remove these tumors without rupture, and laparoscopic removal should be avoided if the histology of the tumor is unclear. The peritoneal seeding in the patient of case 1 might be a result of laparoscopic removal including the aspiration procedure to reduce the tumor volume. If the malignant cyst ruptures or invasive foci are microscopically noted, adjuvant therapy with cis-platinum-based chemotherapy or radiation, or a combination of both, may be required. Re-exploration laparotomy with complete surgical staging for the mucinous cystadenocarcinoma, as in the ovarian counterpart, is controversial for its benefit; but it is recommended because of rare local recurrences and distant metastases.

REFERENCES