Primary Peritoneal Serous Papillary Carcinoma Presenting as a Single Colonic Mass without Peritoneal Dissemination

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Abstract
Peritoneal serous papillary carcinoma (PSPC), a rare primary malignancy arising from the abdominal and pelvic peritoneum, is characterized by peritoneal carcinomatosis with ascites and a histological pattern similar to that of papillary serous ovarian carcinoma. We herein describe a rare case of PSPC with unusual clinical presentations involving a single primary tumor originating from the peritoneal lining of the sigmoid colon with no evidence of intraperitoneal spread, pelvic lymph node involvement or distant metastasis. Awareness of such unusual presentations of PSPC should assist in the diagnosis of this disease, thereby improving the management of patients with this condition.

Key words: serous papillary carcinoma, peritoneum, ovary, malignant peritoneal mesothelioma, immunohistochemistry

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Introduction
Peritoneal serous papillary carcinoma (PSPC), a rare primary malignancy that arises from the peritoneal lining of the abdomen and pelvis, and it is similar to papillary serous ovarian carcinoma (PSOC) with respect to clinical presentation, histological appearance, pattern of spread, treatment and prognosis (1). Furthermore, it is essentially impossible to distinguish PSPC from PSOC based on clinical and imaging findings alone. Specifically, PSPCs are typically characterized by either peritoneal carcinomatosis with either no or minimal involvement of the ovaries and no identifiable primary tumor (2). In almost all cases of PSPC, extensive intraperitoneal spread is detected at the time of diagnosis, even in the absence of evidence of a primary ovarian tumor. Interestingly, however, there are two previous cases of PSPC that presented as localized pelvic masses without peritoneal dissemination (3, 4). Although rare, such unusual presentations of PSPC might make determining a definitive diagnosis even more difficult. We herein describe a very rare case of PSPC with an unusual clinical presentation in which a single primary tumor originated from the peritoneum lining the sigmoid colon with no evidence of intraperitoneal spread, pelvic lymph node involvement or distant metastasis. To the best of our knowledge, a localized form of PSPC without peritoneal dissemination and distant metastasis has not yet been reported.

Case Report
A 48-year-old woman arrived at the emergency department complaining of abdominal pain and hematochezia for the previous three days. She indicated no presence of any past medical problems, or remarkable gynecological or family history. A physical examination revealed a large, solid, non-tender mass in the lower abdomen; no other masses were detected. A laboratory examination revealed an elevated level of serum cancer-associated antigen 125 (CA 125) of 44.6 IU/mL. The serum levels of CA 19-9, α-fetoprotein and carcinoembryonic antigen were within the normal ranges. Colonoscopy revealed a large, ovoid vascular mass with oozing of blood and mucosal erosions located 40 cm from the anal verge (Fig. 1A). The overlying mucosa was severely congested with dilated, tortuous veins (Fig. 1B). Although the lumen of the sigmoid colon was narrowed due...
to mucosal edema as well as external compression by the tumor, a colonoscope could be successfully passed through the narrowed colonic lumen. The endoscopist did not biopsy the lesion due to the risk of massive bleeding. Dynamic computed tomography (CT) scans were obtained 30 seconds (early phase; Fig. 1C) and 90 seconds (late phase; Fig. 1D) after starting the injection of contrast material. There was a large mass (white arrow) with attenuation similar to that of blood vessels that tightly adhered to and externally compressed the colonic wall. In the early phase, the mass was strongly and rapidly enhanced.

Grossly, a relatively well-circumscribed, firm, slightly lobulated tumor measuring 11.5×6.5×6.0 cm was located on the peritoneum lining the sigmoid colon (Fig. 2A). As observed on colonoscopy, the overlying mucosa was flattened and congested with tortuous veins (Fig. 2B). No infiltrative lesions of mucosal origin were observed; however, transmural infiltration of the tumor caused a 2.0×1.5 cm-sized mural defect and thus exposure to the lumen (Fig. 2C). Upon sectioning, the tumor had a gray-to-yellow, solid cut surface and extended through the colonic subserosa and muscularis propria into the mucosa (Fig. 2D). A few foci of necrosis and hemorrhage were identified within the tumor. No ascites were observed, and intraoperative peritoneal washing cytology was negative for malignant cells. The surgical specimen was fixed in 10% neutral buffered formalin and embedded in paraffin for histopathological examination and immunohistochemical staining.

Microscopically, the tumor originated from the peritoneum lining the sigmoid colon (Fig. 3A) and involved the colonic wall. The subserosa showed marked desmoplastic reactions. The tumor tissue mostly consisted of several layers of monotonous neoplastic epithelial cells covering papillary structures (Fig. 3B). In some areas, the tumor cells formed interconnecting cords or irregular clusters. Within each of these cells, a combination of different growth patterns was present, including solid, cribriform and cystic patterns with

Figure 1. Imaging findings. (A) Colonoscopy demonstrated a large vascular mass with mucosal erosion. (B) The overlying mucosa showed congestion and edema with tortuous veins. (C-D) Dynamic CT scans were obtained 30 seconds (early phase; C) and 90 seconds (late phase; D) after starting the contrast material injection. There was a large mass (white arrow) with attenuation similar to that of blood vessels that tightly adhered to and externally compressed the colonic wall. In the early phase, the mass was strongly and rapidly enhanced.
Figure 2. Gross findings. (A) Grossly, the resected specimen showed a relatively well-circumscribed, firm, protruding mass on the serosal aspect of the sigmoid colon, measuring 11.5×6.5×6.0 cm. (B) The overlying mucosa was flattened and congested with tortuous veins. (C) Transmural extension of the tumor formed a 2.0×1.5 cm-sized mural defect. The appearance of the exposed tumor tissue corresponded well to the colonoscopic findings. (D) The tumor had a gray-to-yellow, solid cut surface and extended through the colonic subserosa and muscularis propria into the mucosa.

Central necrosis. The tumor had grown into the mucosa through all layers of the colon; however, no lymphovascular invasion was detected. Cytologically, the tumor cells were polyhedral with indistinct cell borders, exhibiting finely granular cytoplasm and a high nuclear-cyttoplasmic ratio. The nuclei were of high grade, large and pleomorphic with conspicuous nucleoli, vesicular chromatin and frequent mitotic figures (up to 20/10 high-power fields; Fig. 3C). Scattered psammomatous microcalcifications were occasionally noted. Seven pericolic lymph nodes were free of tumors. The histopathological findings observed in the peritoneum-based mass were consistent with both PSOC and PSPC, which are morphologically indistinguishable from each other. Furthermore, the possibility of malignant peritoneal mesothelioma (MPM), the microscopic features of which are almost identical to those of both PSOC and PSPC, could not be eliminated. Immunohistochemical staining demonstrated that the tumor cells were positive for pan-cytokeratin (Fig. 3D; 1:400, clone AE1/AE3, Dakocytomation, Glostrup, Denmark), epithelial membrane antigen (1:1,500, clone E29, Dakocytomation, Glostrup, Denmark) and estrogen receptor (Fig. 3E; 1:100, clone 6F11, Novocastra, Newcastle upon Dyne, UK) and negative for calretinin (Fig. 3F; 1:400, clone 5A5, Novocastra, Newcastle, UK), D2-40 (Fig. 3G; 1:200, clone D2-40, Signet Laboratories Inc., Dedham, MA), podoplanin (1:400, clone D2-40, Dakocytomation, Glostrup, Denmark) and progesterone receptor (1:800, clone 16, Novocastra, Newcastle upon Dyne, UK). The absence of pathologic abnormalities in the bilateral ovaries, which had retained their normal size and shape, excluded a diagnosis of PSOC. Furthermore, the absence of immunoreactivity for mesothelioma markers calretinin, D2-40 and podoplanin excluded a diagnosis of MPM. Therefore, a pathological diagnosis of PSPC was made. The patient’s postoperative recovery was uneventful. She did not receive adjuvant chemotherapy or radiotherapy. Five years after diagnosis, she remains in complete remission with negative abdominopelvic CT scans and normal CA 125 levels.

Discussion

We herein described a case of localized PSPC presenting as a single colonic mass with hematochezia. The histopathological findings of the tumor were consistent with the diagnosis of serous papillary carcinoma and mesothelioma, but not colonic adenocarcinoma. The immunohistochemical results excluded the possibility of the tumor cells being of mesothelial origin. The absence of ovarian disease indicated a primary peritoneal origin. The tumor was localized in the sigmoid colon peritoneum, but without the presence of
spreading in the pelvic cavity or distant metastasis. Tumoral infiltration of the entire colonic wall led to a mural defect, bleeding and hematochezia.

The most remarkable aspect of the present case was its unusual pattern of spread. Typically, PSPC gives rise to dissemination on the peritoneal surface and greater omentum in its early phase of growth. Furthermore, it is not uncommon to observe tumor implants on the surface of the liver, diaphragm or mesentery (5). The most common symptom of PSPC is abdominal discomfort, including pain, distension or expansion due to diffuse peritoneal involvement. The most common finding is ascites, reported in approximately 85% of cases (2). In the present case, there were no disseminated peritoneal lesions, ascites or omental involvement, but rather a single, large mass that had locally invaded the surrounding tissues. To date, only two cases of PSPC without peritoneal dissemination have been reported in the literature (3, 4). Interestingly, in both of these cases, metastases at distant lymph nodes were found, even though the primary tumors were localized in the pelvic peritoneum. In other words, the previously reported cases of PSPC were not truly localized. To the best of our knowledge, this is the first report of a localized form of PSPC arising in the colonic serosa without peritoneal dissemination or distant metastasis.

It is also uncommon for PSPC to arise from the peritoneum that covers the sigmoid colon and manifest as hematochezia. Direct invasion of the gastrointestinal tract by PSPC is even more rarer. To date, only 10 cases of invasion of the colon by PSPC have been reported in the literature (6-11). In all of these patients, omental tumors with dissemination
to the abdominal and pelvic peritoneum were found. Our patient represents an extremely unusual pattern of localized colonic involvement from PSPC without any evidence of intraperitoneal spread.

The differential diagnosis of PSPC includes PSOC, MPM and metastatic peritoneal carcinomatosis. In order to distinguish PSPC from PSOC, the Gynecologic Oncology Group developed concise criteria for the diagnosis of PSPC: (1) both ovaries must be either physiologically normal in size or enlarged by a benign process; (2) the involvement in extra-ovarian sites must be greater than the involvement on the surface of either ovary; (3) microscopically, the ovarian component must be (a) nonexistent, (b) confined to the ovarian surface epithelium with no evidence of cortical invasion, (c) involving the ovarian surface epithelium and underlying cortical stroma with any given tumor smaller than 5×5 mm or (d) a tumor less than 5×5 mm within the ovarian substance associated with or without surface disease; and (4) the histological and cytological characteristics of the tumor must be predominantly of the serous type and either similar or identical to any grade of PSOC (1). The present case satisfied these criteria in that the microscopic features of the peritoneum-based tumor were indistinguishable from those of PSOC and the bilateral ovaries were normal in size and shape, without any pathologic abnormalities.

Histologically, MPM has an almost identical appearance to that of PSPC and PSOC. MPM is chemotherapy- and radiotherapy-resistant (12), whereas these treatment modalities can significantly improve patient survival in cases of PSPC and PSOC. Therefore, making an accurate diagnosis among these tumor types is very important. Immunohistochemical staining can assist in distinguishing MPM from PSPC and PSOC. Specifically, positive markers for mesothelioma calretinin, podoplanin and D2-40 are best for diagnostic purposes (13-15). In addition, the frequent expression of estrogen receptors in PSPC and PSOC, but not in mesothelioma, suggests that this marker is very useful for discriminating between these malignancies (16). No morphologic features can provide a reliable distinction between PSPC and metastatic peritoneal carcinomatosis; diagnosis of the latter relies on identification of the primary tumor, usually in the salpinx or endometrium and less frequently in the breast, gastrointestinal tract, lungs or thyroid gland (17).

The standard treatment for PSPC is similar to that for PSOC, which includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy and radical debulking followed by platinum-based combination chemotherapy. Maximal cytoreduction is the primary goal of these procedures, and excision of all visible implants is the hallmark of cytoreductive efforts. However, this may not be the case for localized forms of PSPC. Retrospectively, considering the extent of the tumor in our patient, colectomy alone appeared to be sufficient for treating the disease and also allowed for preservation of the ovaries for continued production of hormones. Due to its rarity, the optimal treatment strategy for localized PSPC remains to be determined; additional case reports are required to determine the appropriate therapy for PSPC without peritoneal dissemination.

In summary, we considered the present case to be worth reporting due to its unusual clinical presentation in which the carcinoma spread, namely, as a localized mass without peritoneal dissemination or distant metastasis. Awareness of this unusual presentation of PSPC should make future diagnoses more straightforward, thus leading to more precise management.

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

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