

CASE REPORT

A rare case of pseudomyxoma peritonei caused by borderline mucinous tumor arising from primary mature cystic ovarian teratoma

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Abstract

Pseudomyxoma peritonei (PMP) is a rare clinical syndrome characterized by diffuse intraperitoneal mucinous spread originating from mucinous neoplasms. The most common cause of PMP is a mucinous epithelial tumor of the appendix, but may also develop from other abdominal organs such as the ovaries, colon, and pancreas. Here, we describe the case of a patient with a prior history of appendectomy, in whom the appendix was easily excluded as the primary site of PMP. Previous studies have reported that only 3–8% of ovarian mucinous tumors may arise from mature cystic teratoma. In addition, borderline ovarian malignancies from mature cystic teratoma are not common, and the occurrence of PMPs from these borderline ovarian mucinous tumors is very rare. We report a rare case of PMP with clinicopathological features between PMP and borderline mucinous tumors arising in a mature cystic teratoma of the ovary.

Keywords

Pseudomyxoma peritonei; Ovarian neoplasm; Adenocarcinoma; Mucinous

1. Introduction

Pseudomyxoma peritonei (PMP) is a rare clinical syndrome characterized by diffuse intraperitoneal mucinous spread originating from mucinous neoplasms, with most cases involving appendiceal mucinous epithelial neoplasms [1]. PMP can also originate from other organs in the abdomen, such as the ovaries but has a rare incidence. Ovarian involvement in PMP is almost always due to metastatic spread from an appendiceal tumor [2]. Ovarian mucinous neoplasms and mature cystic teratomas are extremely rare sources of PMPs. Irrespective of the tumor source, these tumors can easily rupture, spread mucinous materials into the abdomen, and accumulate in the peritoneal cavity. Here, we report a rare case of PMP with clinicopathological features to explain the association between PMP and borderline mucinous tumors arising in a mature cystic teratoma of the ovary.

2. Case report

A 49-year-old woman (gravida 2, parity 2) presented to our hospital's gynecology department on 08 July 2019, with abdominal distension for 3 months as her main complaint. She had a history of appendectomy and left salpingo-oophorectomy about 20 years ago due to appendicitis and a mature cystic teratoma, respectively. Physical examination revealed a palpable mass in the lower abdomen. Transvaginal ultrasound identified a multiseptated cyst of approximately 20 cm with a solid portion in the right ovary and abundant cul-de-sac fluid col-

lection. Both positron emission tomography and abdominal-pelvic computed tomography (CT) suggested the possibility of an immature teratoma with peritoneal carcinomatosis and ascites. No anomalies were observed on colonoscopy and esophagogastroduodenoscopy. Tumor marker analysis showed an elevation in carcinoembryonic antigen (CEA) to 172.77 ng/mL (normal range: <8 ng/mL), while both cancer antigen 125 (CA125, level: 33 U/mL, normal range: 0–35 U/mL) and CA19-9 (level: <2 U/mL, normal range: 0–37 U/mL) were within the normal range.

Laparotomy was performed through a high midline skin incision. PMP was identified due to large amounts of mucin found to grossly spread throughout her abdominal wall and fill her entire peritoneal cavity. Intraperitoneal mucin and fluid were collected, and cytology was performed. A large ruptured right ovarian mass of approximately 10 cm in diameter containing gelatinous fluid was also found and suspected to be a cystic teratoma containing fat, hair and bone tissues. The appendix and left adnexa were absent due to the prior appendectomy and left salpingo-oophorectomy. The right fallopian tube and uterus were grossly unremarkable. Based on these findings, the patients underwent right salpingo-oophorectomy with total hysterectomy, peritonectomy including both para-colic gutters, para-aortic area, and cul-de-sac. As the omentum was also suspected of seeding mucin, an infra-colic omentectomy was also performed. No gross lesions were left since all visible lesions were removed and cytoreduced.

The final histopathologic result was confirmed approximately 10 days after surgery. Cytological examination of the

peritoneal fluids found no malignant cells. Gross examination showed a previously ruptured multilocular ovarian cyst measuring $23.0 \times 17.0 \times 10.0$ cm in size and weighing 730 g. The inner surface of the cyst was filled with yellowish sebaceous material, multiple hairs, teeth, and mucoid material (Fig. 1). On the cut surface, the tumor was partially cystic and solid. The solid portion (about 20% of the total tumor volume) exhibited a whitish-yellow to light brown heterogeneous cut surface with bone.



FIGURE 1. Gross findings of the right salpingo-oophorectomy specimen. The inner surface of the ruptured multilocular ovarian cyst is filled with partly mucinous (left side) and partly hairy (right side) sebaceous material.

Microscopic examination of the ovarian tumor revealed a biphasic tumor composed of a mature cystic teratoma and mucinous tumor. The teratomatous elements consisted of epidermal tissues, thyroid and fat tissues, and tracheobronchial epithelium with cartilages (Fig. 2). Extensive sampling of the resected specimen did not show the presence of any immature or invasive carcinomatous tissues. The mucinous component was lined with intestinal-type mucinous epithelium of low-grade dysplasia and areas of cribriform architecture but without obvious stromal invasion, which was consistent with mucinous borderline ovarian tumor (Fig. 2). Immunohistochemical staining of the mucinous component revealed positive expression of cytokeratin (CK) 7, CK20, MUC5AC and CDX2, suggesting that the mucinous component originated from the intestinal epithelium of the teratomatous component. Histopathological biopsy of the omentum showed multifocal acellular mucus deposits surrounded by fibrosis, consistent with grade 0 pseudomyxoma peritonei (Fig. 3). In addition, histopathological biopsy of the peritoneum suggested non-invasive peritoneal implants of mucinous borderline tumors of the ovary with mucin pools, clinically suggestive of PMP.

After the surgery, the patient had a successful recovery, did not undergo additional treatment (*e.g.*, chemotherapy or others), and was followed up for 6 months thereafter. Her serum CEA level returned to normal within 1 year, while her CA125 level, which was initially close to the upper limit, reduced from 33 U/mL to 7 U/mL. After two and a half years, the patient remained asymptomatic with normal tumor markers level, and successive abdominopelvic CT scans showed no

sign of tumor recurrence. A follow-up examination is planned for about 10 years after surgery for recurrence assessment.

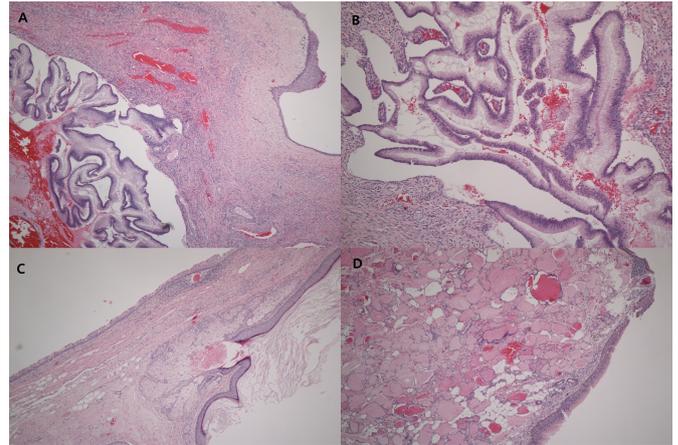


FIGURE 2. Histologic findings of the right ovarian tumor. A. A biphasic tumor with mucinous (left side) and teratomatous portions (right side) is seen (magnification: $40\times$). B. The mucinous portion is composed of an intestinal-type tall columnar epithelium with stratification and hyperchromasia, with focal cribriform architecture ($100\times$). C. The teratomatous portion shows epidermal lining with skin appendages and respiratory mucosa. ($40\times$). D. Mature benign thyroid tissue can be seen in the teratomatous portion ($40\times$).

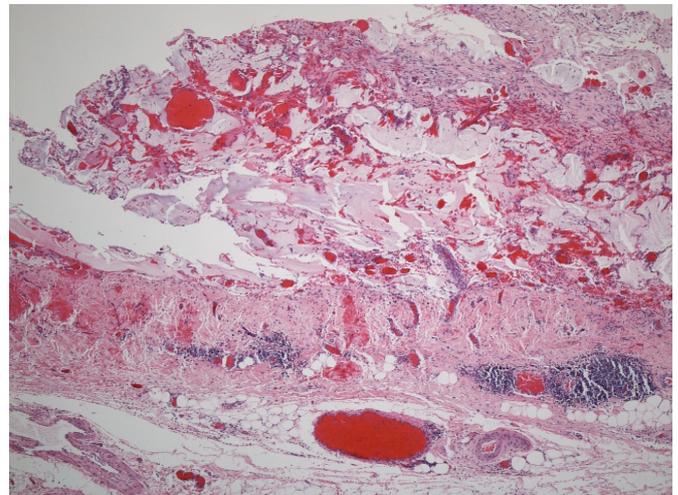


FIGURE 3. Histologic findings of the omentum. The omentum is covered with acellular mucinous material surrounded by fibrosis (magnification: $40\times$).

3. Discussion

PMP is a very rare disease in which a ruptured mucinous neoplasm progressively produces mucin that gradually accumulates in the abdominal cavity, leading to abdominal distension and is characteristically called “jelly belly”. It has an estimated annual incidence of 1–2 cases per million [3]. Continued accumulation of mucin fluid can lead to intestinal obstruction and may be life-threatening [2]. PMP is most commonly derived

from appendiceal epithelial tumors. In rare cases, it can be caused by benign or malignant tumors originating in various organs such as the ovaries, colon, and pancreas. PMP is not a histological term and is grossly confirmed perioperatively by the presence of mucin-filled ascites in the abdominal cavity can be grossly confirmed. The causative tumor is diagnosed by histological examination via hematoxylin and eosin (H&E) staining.

According to the World Health Organization (WHO), primary ovarian mucinous tumors can be classified into benign (mucinous cystadenoma and mucinous adenofibroma), borderline (mucinous borderline tumor) and malignant (mucinous carcinoma) [4]. In addition, teratoma-derived ovarian tumors can be classified by terminology based on appendiceal or lower gastrointestinal morphology and immunophenotype. According to this system, the histological classification of the ovarian tumor was a low-grade mucinous neoplasm arising in a teratoma.

PMPs can be sometimes difficult and confusing to characterize as their histological classification criteria may vary. Among them, the commonly used classification does not depend on the origin of the tumor, and divides the cells into disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinomatosis (PMCA), and the intermediate category containing tumors with inconsistencies or discordant features (PMCA-I/D), according to whether the cells are benign, borderline, or malignant [5]. Most recently, the 2016 Peritoneal Surface Oncology Group International criteria classified PMP into 4 distinct categories: grade 0 (acellular mucin (AC)), grade 1 (low-grade mucinous carcinoma peritonei (LGMC)), grade 2 (high-grade mucinous carcinoma peritonei (HGMC)), and grade 3 (high-grade mucinous carcinoma peritonei with signet-ring cells (HGMC-S)) [3, 6]. Based on this histological diagnosis, treatment directions, such as hyperthermic intraperitoneal chemotherapy (HIPEC) or intravenous chemotherapy, are decided.

Although the origin of the PMP is confirmed via immunohistochemistry (IHC), morphological indicators may also provide some hints about its origin perioperatively, especially in this case when the mass was confirmed in the ovary. Considering that tumors arising from the ovaries can be considered as the second leading cause for PMP, cases of non-appendiceal ovarian tumors may have the following characteristics: (1) normal appendix morphology; (2) no evidence of appendiceal rupture or metastasis to other organs, and; (3) ovarian epithelium exhibits characteristics of benign or borderline malignancies [7].

In this case, the origin of PMP was confirmed by IHC. It is well known that CK7/CK20 expression is useful for differentiating appendiceal but also colorectal origin from none intestinal origin [7]. However, since approximately 50% of appendiceal carcinomas show CK7 positivity, CK7/CK20 expression is not an absolute indicator for determining the origin [7, 8]. The reliability of this marker is particularly low in cases of ovarian mature cystic teratoma, a rare cause of PMP because the cyst itself can produce the intestinal cell type. Therefore, in addition to CK7 and CK20, MUC5AC, CDX2, Ki67, SATB2 and CA125 are also used [9]. Further, since all these markers can be found in mucinous cysts arising from

ovarian mature cystic teratomas, it is not easy to distinguish the origin of teratomas solely by IHC. Therefore, preoperative clinical symptoms and intraoperative findings also have a significant impact on the diagnosis of PMP. Additionally, when operating on a patient with PMP, it is necessary to perform an appendectomy to confirm the histology of the appendix, even if the appendix appears grossly normal [3].

Ovarian mucinous neoplasms account for 10–15% of all ovarian neoplasms. Approximately 80% of these cases are benign mucinous cystadenomas, and the majority of the remaining cases are mucinous borderline neoplasms. Most metastatic mucinous carcinomas originate from the gastrointestinal tract [10, 11]. Primary ovarian mucinous neoplasms are predominantly grossly unilateral, have a smooth external surface and are without surface involvement. Conversely, if the neoplasm is bilateral with surface involvement or a cyst not confined to the ovary is found, a high possibility of metastasis from the gastrointestinal tract should be considered [12, 13]. Usually, mucinous carcinoma originating from the ovary rarely presents with gross PMP, and when PMP is seen, it is considered to occur almost exclusively as a result of ovarian metastasis of the appendiceal primary.

Abdominal-pelvic CT is a good diagnostic modality to assess the appendix, adnexa and gastrointestinal tract but cannot be used to accurately predict PMP. Therefore, PMP is clinically diagnosed during surgery. The treatment for PMP is decided after histopathologic confirmation of the final biopsy specimen following cytoreductive surgery and, if necessary, HIPEC is given [14]. Complete cytoreductive surgery is known to have the greatest effect on the prognosis of PMP, with a 5-year overall survival rate of 85% [14]. However, the extent to which HIPEC alone affects the prognosis of PMP remains unclear. HIPEC appears to benefit in the case of malignant cell types; however, it is highly possible that HIPEC may also have no significant benefit on benign or borderline cells [15]. Examination of serum tumor markers, including CEA, CA 125 and CA 19-9, may help to assess the aggressiveness of the disease and the risk of recurrence after surgery [16]. For this reported case, considering that the tumor was a low-grade mucinous neoplasm arising from a teratoma derived from the ovarian dermoid cyst and her serum tumor marker levels were maintained within the normal range during regular follow-up examinations, postoperative HIPEC was not performed.

Despite being a very rare disease, PMPs caused by mucinous neoplasms arising from primary ovarian teratomas have previously been reported. Prior reports indicated that only 3–8% of ovarian mucinous tumors arise from mature cystic teratomas, and the subtypes of these mucinous tumors can be benign, borderline or adenocarcinoma [8]. In this reported case, the patient had a clear history of prior appendectomy, which allowed us to easily rule out the appendix as the primary site of PMP. In addition, preoperative colonoscopy and gastroscopy confirmed that the stomach and large intestine were not the primary sites of mucinous ovarian cysts and PMPs. Thus, based on surgical findings, histopathological examination and immunohistochemistry, the patient was finally diagnosed with PMP originating from borderline mucinous neoplasms arising from mature cystic teratomas.

AUTHOR CONTRIBUTIONS

SJL—performed the research study and took the pictures; JMR—collected data and wrote the manuscript; YYJ—wrote the manuscript; YSC—designed the research. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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