

## A Rare Case of Late Recurrence in Pseudomyxoma Peritonei and Advanced Stage of Borderline Mucinous Ovarian Tumor

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### ABSTRACT

Pseudomyxoma peritonei (PMP) is characterized by mucinous ascites in the peritoneal cavity and might involve the omentum and peritoneum. The PMPs originating from the ovary are mostly caused by ruptured ovarian mature teratomas and mucinous ovarian carcinomas. The present case is a rare advanced mucinous borderline ovarian tumor and late recurrence in PMP in a 52-year-old menopausal woman. She presented with gradual abdominal enlargement and cystic abdominopelvic lesion with internal septa and ascites. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, lymphadenectomy, and appendectomy. Histopathologic examination revealed mucinous borderline tumors. About 5.5 years after the first surgery, she presented with abdominal bloating and a sonography report of peritoneal seeding in the abdomen and pelvis. Abdominal exploration showed gelatinous-mucinous ascites and disseminated peritoneal carcinomatosis. The final histopathologic evaluation indicated PMP. Although the recurrence of mucinous borderline tumors is in an average of two years, the present case had relapsed after 5.5 years as pseudomyxoma with borderline pathology.

**Keywords:** Mucinous borderline ovarian tumor, Ovarian neoplasm, Pseudomyxoma Peritonei



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### Introduction

Science is the continuous and systematic ac Epithelial ovarian tumors are mucinous tumors in 10-15% of the cases and most of the mucinous tumors are reported as benign (75%), borderline (10%), or invasive carcinomas (15%) (1). The mean age of patients with mucinous borderline ovarian tumor (MBTs) is 41 years, less than 10% of them are diagnosed as bilateral and 90% of all MBTs are stage I at presentation. Pseudomyxoma peritonei (PMP) is a borderline neoplasm and a rare clinical syndrome with an estimated incidence of 1–2 per million per year and it is characterized by an increasing aggregate of mucinous ascites and mucinous peritoneal implants. In most cases, PMP originates from the alimentary tract, especially from appendiceal mucinous adenocarcinoma. Ovarian origin of PMP is rare. In the

normal appendiceal histopathology, the origin is somewhere else. In this case report, we describe a rare case of late recurrence in PMP and an advanced stage of MBTs.

### Case Presentation

A 52-year-old menopausal woman with no previous medical problem presented with gradual abdominal enlargement during the last four months and abdominal pain in the last 20 days. The sonographic findings showed a cystic abdominopelvic lesion measuring 160 mm×152 mm×103 mm with internal septa and approximately 200 cc ascites.

In March 2014, she referred to Imam Hossein Hospital as a tertiary gynecology-oncology center. Abdominopelvic computed tomography (CT) revealed multiple cystic lesions in pelvis extended to the abdomen. The uterus was observed to be dilated and contained fluid. The endometrial biopsy indicated normal histopathology with little proliferation. Tumor markers were elevated, including CA19-9=69 (normal: <40), CEA=224 (normal: <5), and normal CA125.

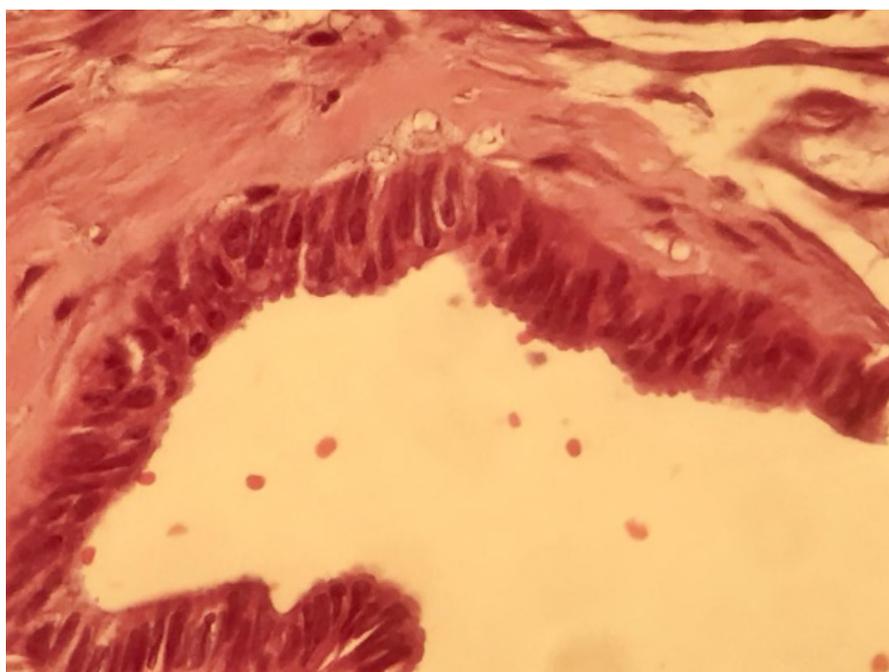
The findings of preoperative colonoscopy and gastroscopy were normal. The laparotomy with midline incision demonstrated multilocular cysts measured approximately 20 cm×17 cm×7 cm in the right adnexa involving multiple peritoneal surfaces, including diaphragmatic surfaces, anterior and posterior cul-de-sac, and gelatinous ascites. The gastrointestinal tract was detected to be normal. However, the intraoperative frozen section indicated MBTs. In addition, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, lymphadenectomy, and appendectomy were performed, which resulted in optimal debulking.

Mucinous borderline tumors with bilateral involvement of the ovary, omentum, and appendix were reported in the final histopathology examination (Figure 1). There was no invasive implant. However, muscularis propria and mesoappendix were diagnosed to be affected without the mucosal layer involvement. The one-year follow-up with ultrasonography and magnetic resonance imaging (MRI) was normal. The patient did not attend any further follow-up due to personal problems and the absence of symptoms.

About 5.5 years following the initial surgery, she returned to the hospital with abdominal bloating and an ultrasonography report indicating peritoneal seeding in the abdomen and pelvis including lesser sac, liver surface, and cul-de-sac. Supplementary MRI revealed PMP suggesting mucinous neoplastic lesion. Tumor markers elevated, namely CEA=550 (normal: <5) and CA19-9=520 (normal: <40) with normal CA125. No abnormality was detected in gastroscopy and colonoscopy.

The case was again discussed in a multidisciplinary session, the conclusion of which was conducting a biopsy of the omental lesions to confirm relapse. Diagnostic results of omental biopsy revealed a recurrent mucinous borderline tumor. Therefore, the patient became a candidate for a debulking operation in collaboration with the general surgery team. Abdominal exploration showed gelatinous-mucinous ascites and disseminated peritoneal carcinomatosis with implants widely spread over the peritoneum, intestinal mesentery, spleen, and diaphragm with severe dense and deep infiltration and adhesion into the stomach (Figures 2 and 3). Pelvic involvement was not noted.

Optimal debulking was not technically feasible. Nevertheless, a supracolic omentectomy was performed and she was discharged without any problem. The final histopathology examination demonstrated PMP and the seeding of mucinous neoplasm, which most probably is indicative of borderline mucinous neoplasm (Figure 4). According to the results of all examinations, the patient was prepared for systemic chemotherapy.



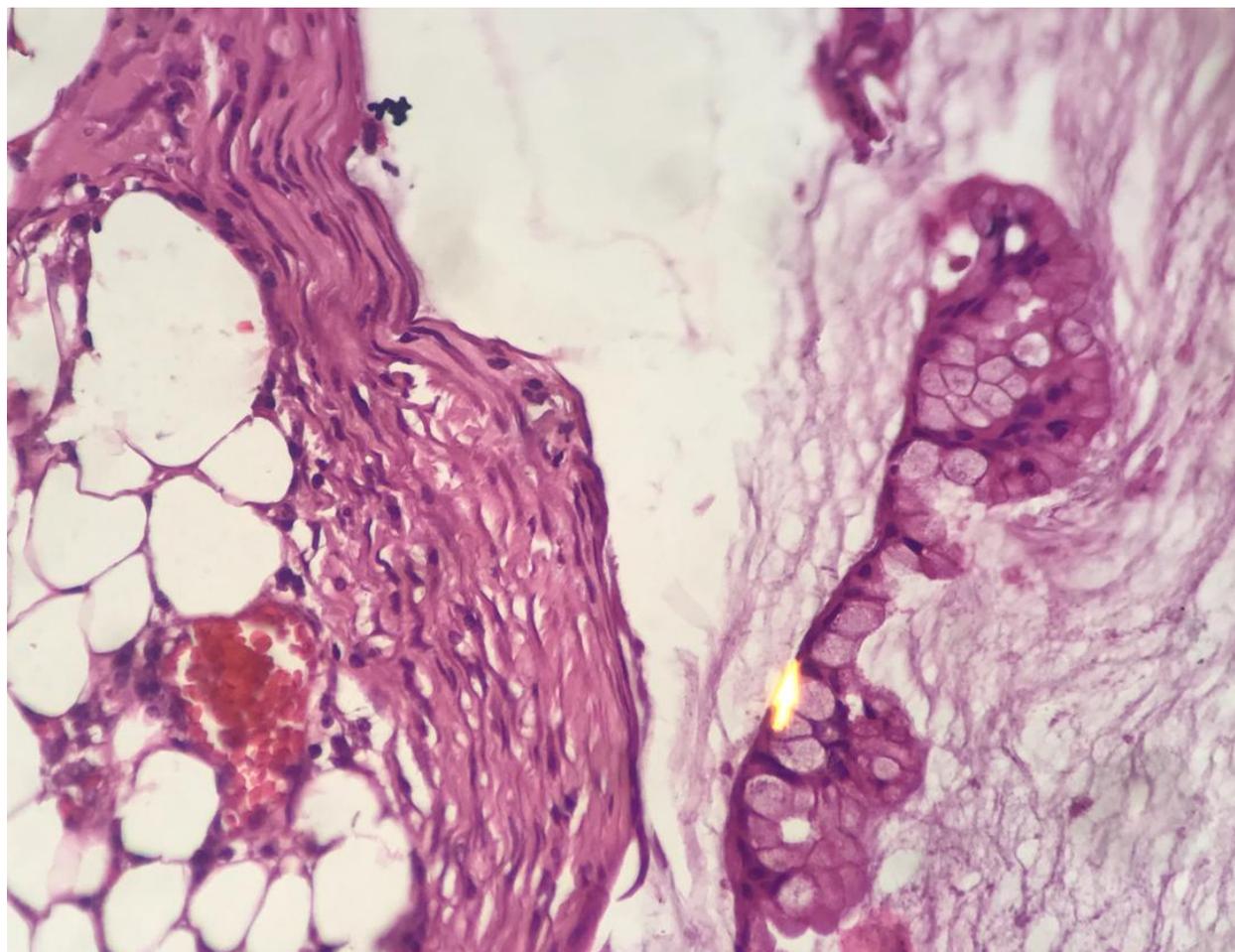
**Figure 1.** A single layer mucinous epithelium resembling intestinal-type cell lines, cyst wall with mild nuclear hyperchromasia, nuclear stratification and hyperchromasia, confirming tumor as a mucinous neoplasm with low malignancy potential or borderline type (H&E staining, ×400 magnification)



**Figure 2.** Involvement of intestine



**Figure 3.** Dense infiltration and adhesion of stomach and transverse colon



**Figure 4.** PMP due to ovarian borderline mucinous neoplasm. Dissecting extracellular mucin with fibrosis and neoplastic mucinous type epithelial cells (H&E staining,  $\times 200$  magnification)

## Literature Review

The literature review was based on the relevant research during 2000–2020 on SCOPUS, PubMed, UpToDate, Ovid, and clinical key databases using “PMP” and “mucinous borderline ovarian tumors” as keywords. To ensure that all potentially relevant papers were included, the reference studies of all retrieved articles were reviewed as well.

## Discussion

Approximately 40-50% of malignant mucinous tumors are categorized as borderline tumors (7). Intestinal mucinous borderline tumors constitute 85% of mucinous borderline ovarian tumors (MBTs) and mostly occur in the fourth to seventh decades of life (the mean age is 41 years). Less than 10% of these lesions are diagnosed as bilateral (4, 5). Intestinal mucinous borderline tumors show large multiloculated cysts with PMP and have a good prognosis.

The patient in the present study was 52 years old (older than the mean age in mucinous borderline tumors) and presented with abdominal distension,

abdominal pain, 16 cm abdominopelvic mass, and ascites in imaging. The ovarian involvement was diagnosed as bilateral. About 90% of all mucinous borderline tumors are stage I at the time of presentation and extra-ovarian involvement is diagnosed in other cases (13). The current case was in the advanced stage III at diagnosis time, which is uncommon.

The PMP is characterized by the presence of mucinous ascites in the peritoneal cavity. The clinical syndrome (1, 2) may entail mucinous ascites, peritoneal and omental nodules, and ovarian involvement (3). Moreover, it can relatively spare small bowel serosa. The annual incidence of PMP has been reported as 2 per million individuals (1) and is most prevalent in women of the age range of 50-70 years (3, 4).

Tumors of the appendix, colon, and ovary are suggested to be the most common origin of PMP (2-8). Lung, fallopian tube, uterus, urachus, common bile duct, pancreas, and stomach are mentioned as the other origins of PMP (9-14). The PMPs originating from the ovary mostly result from ruptured ovarian mature teratomas and mucinous ovarian carcinomas (4, 6).

It has been reported that 1/3 to 1/2 of women afflicted with PMP across the world represent synchronous ovarian and appendiceal mucinous tumors (7). In cases that PMP is related to synchronous ovarian and appendiceal mucinous tumors, it is not easy to assign a single organ as the primary site based on the pathological characteristics.

Distinguishing primary ovarian mucinous tumors from metastatic mucinous tumors requires taking several criteria into account, such as a primary ovarian neoplasm is indicated by large size (>10 cm), unilateral involvement, benign or borderline focus, an expansible pattern of invasion, a smooth surface and the lack of extra-ovarian disease, and a low grade and low stage at diagnosis. Smaller size, bilateral ovarian involvement, the involvement of ovarian surface, multiple nodules, and an infiltrative pattern of stromal invasion are the clear signs of a non-ovarian origin (11-14).

The recurrence in the present case was PMP still with borderline pathology. Abdominal distension due to the increasing aggregation of mucinous ascites and an ovarian mass is mentioned as the most frequent symptoms of PMP (2, 16, 17). The preoperative CA 19-9 level in patients with MBTs was more frequently elevated (57%), in comparison with CA 125 (15%) or CEA (8). An elevated level of serum CA19-9 and CEA are observed in most patients with PMP and is considered to be efficient for diagnosis and relapse following therapy (16). In the present case, CA19-9 and CEA were high in the first presentation. Furthermore, these markers augmented to a higher level in the recurrence time, though CA125 was normal.

Low-attenuation lesions or loculated ascites distributed all over the peritoneal cavity and peritoneal or omental nodules are known as the typical CT scan findings of PMP. These implants are often characterized by mass effects on the liver and spleen producing a scalloped appearance as the most characteristic feature of PMP in CT scan (18-20). According to the literature, the diagnostic accuracy rate for frozen section diagnosis is high for malignant and benign tumors, while diagnostic accuracy in BOTs remains low (9).

The complete staging procedure in postmenopausal women or women who do not want to preserve fertility consists of several steps, namely peritoneal washing, type I hysterectomy with bilateral salpingo-oophorectomy, multiple peritoneal biopsies, omentectomy, resecting visible metastases, and exploring the abdominal cavity. Appendectomy is strongly advised to rule out a synchronous or primary appendiceal neoplasm. Advanced-stage BOT (FIGO stage III or IV) has been reported to be accompanied by the involvement of the lymph node in about 25% of the patients (18). In most centers with PMP management experience, tumor debulking along with hyperthermic intraperitoneal chemotherapy (HIPEC) is

suggested regardless of chemotherapy in the adjuvant setting.

There is no evidence concerning the efficacy of chemotherapy in MBTs even in the patients of advanced stage (5) which is known as a chemo-resistant type of tumor. Taxane plus platinum, which is the standard systemic chemotherapy regimen for epithelial ovarian cancer, has limited efficiency in this type of ovarian cancer (10). Nonetheless, it is still prescribed as the standard regimen for MBTs. Furthermore, systemic chemotherapy has minimal advantages in PMP and is typically applied to patients with the advanced or relapsed disease (10).

Some recent studies have shown that the molecular biology of ovarian mucinous tumors is similar to gastrointestinal malignancies (10, 11). Prognosis in patients with MBTs depends on the stage of the disease and the appearance of PMP. The advanced stage as the major risk factor associated with recurrence and acellular intraperitoneal mucus seems to be a prognostic feature. Microinvasion is not considered a prognostic factor in mucinous tumors. Mucinous tumors and DNA aneuploidy are regarded as negative factors in patients aged over 75 years.

The recommended follow-up plan is three visits yearly for the first two years and one visit every six months during the next three to five years followed by annual examinations. Patients with MBTs experience relapse less frequently, compared to those with serous borderline ovarian tumors. However, the risk of an invasive relapse appears to be higher for MBTs if a relapse occurs (24). The recurrence rate is different between surgery types with 5%, 10-20%, and about 31% noted after radical surgery, fertility-preserving surgery, and cystectomy, respectively (21).

The mean time-lapse between surgery to recurrence is 26.4 months with a range of 13-50 months in the literature (25). In the current case, the relapse occurred after 5.5 years making it a rare case in this tumor type. There was no difference reported in the relapse rate between intestinal MBTs and endocervical MBTs. Although most of the recurrences are diagnosed to be borderline tumors, the relapse is invasive in 20-30% of the cases. Mucinous tumors are more likely to recur in invasive form than serous tumors. In most cases, an invasive recurrence is observed after five years. They are usually low-grade tumors and are rarely high grade. Relapse almost always is reported inside the ovary with 2% of the patients exhibiting extra-ovarian recurrence at stage I and about 20% at higher stages (21).

Most authors believe that patients with a recurrence of mucinous ovarian tumors have a poor prognosis. For the small group of patients with relapse, the best management approach has not been determined and the outcomes of reoperations have not been released until now. Although repeated surgery has been mentioned for MBTs relapse, the surgical approach has not been described.

No substantial difference in median survival was observed between patients with optimal and suboptimal secondary cytoreduction surgery. The poorer response to platinum-based chemotherapy of the mucinous pathology was argued to be the reason contributing to the poor prognosis of relapse (5). The median survival since the detection of relapse was about 10 months.

Some studies recommend that durable survival is feasible with complete debulking surgery and HIPEC for MBTs relapse. To date, no well-designed randomized clinical trial has addressed the efficacy of HIPEC combined with debulking surgery in a recurrence condition. In addition, HIPEC is an investigational modality with potential disadvantages and should only be prescribed in prospective randomized clinical trials.

## Conclusion

The MBTs making approximately 11% of BOTs are uncommon tumors among ovarian neoplasms. About 90% of the cases with these lesions represent in stage I. In other words, presentation in the advanced stages, as occurred in our patient, is rare. Recurrence of mucinous borderline tumor occurs on average within two years. However, the present patient experienced relapse after 5.5 years and its manifestation was pseudomyxoma with borderline pathology. The current case was rare due to the advanced stage of the mucinous borderline tumor at primary presentation and late relapse with PMP.

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## Conflict of Interest

Authors declared no conflict of interests.

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