



## Case Report

# Pseudomyxoma peritonei with endometrial mucinous carcinoma and appendicular mucinous tumor: An unusual association



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## ABSTRACT

The association between pseudomyxoma peritonei and appendicular or ovarian mucinous tumors is usually reported in the literature, while the association with endometrial carcinoma is exceptional. Although there has been always a continuous debate regarding its primary origin, tumors of the appendix and ovary remain the most common primary sites for this disease. The association of pseudomyxoma peritonei with two primaries from endometrial mucinous adenocarcinoma and appendicular mucinous tumor is very rare. So, we report this case to raise awareness among clinicians about this rare tumor association.

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## 1. Introduction

Pseudomyxoma peritonei (PMP) is an uncommon disease entity accounting for one to two per million per year [1]. It affects females three to four times more than males [2].

PMP is characterized by diffusely spread collection of gelatinous material into the intra-abdominal cavity along with scattered mucinous implants over peritoneal surfaces and omentum with variable cellularity [3]. Ronnett et al. [4] classified PMP into low-grade disseminated peritoneal adenomucinosis associating, high-grade peritoneal mucinous carcinomatosis, and peritoneal mucinous carcinomatosis with intermediate or discordant features. The origin of PMP is still controversial; mucinous tumors of the appendix,

ovary, and gastrointestinal tract are the most common association [4–6].

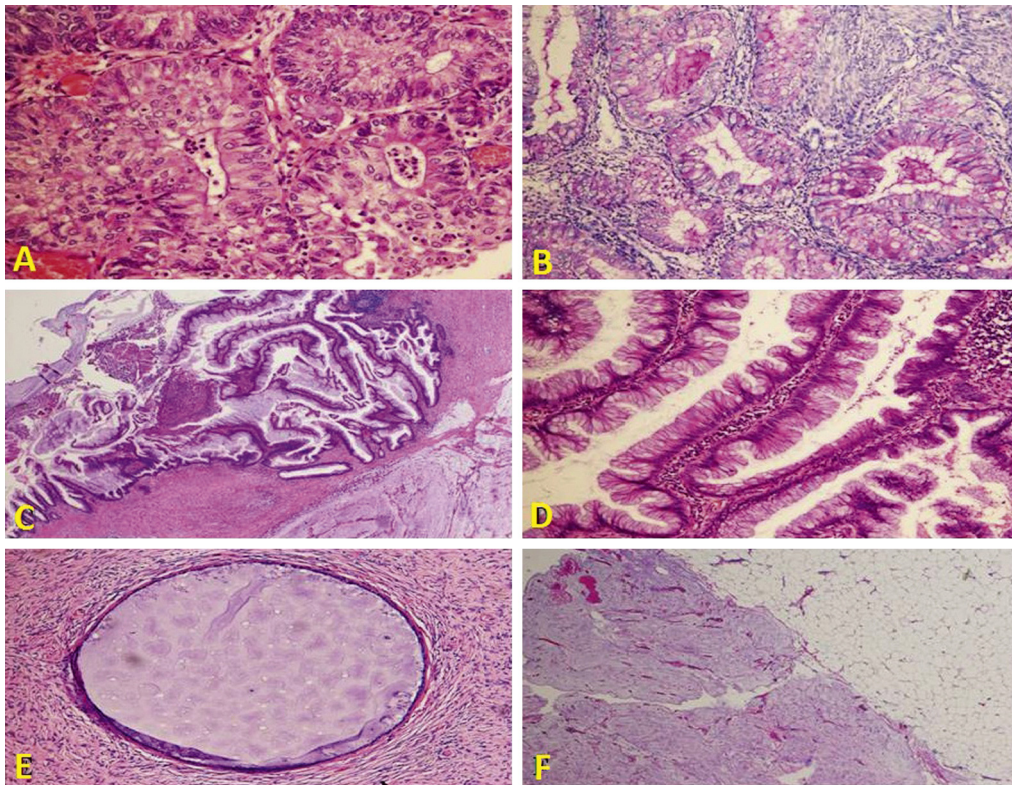
PMP is not commonly encountered in our clinical practice, and to our knowledge, primary appendiceal mucinous tumors associated with primary endometrial mucinous carcinoma have been reported rarely in the medical literature. We are reporting a case of a female patient presented with PMP associated with mucinous borderline tumor of the appendix and an infiltrating mucinous endometrial carcinoma, to raise awareness among clinicians about this rare tumor association.

## 2. Case report

A 56-year-old postmenopausal woman presented with a history of recent uterine bleeding. Her medical history was significant for morbid obesity and hypertension. On admission, her vital signs were stable. A physical examination revealed fullness in the lower abdomen. The computed tomography of the abdomen revealed a mildly

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**Fig. 1.** (A) Endometrial mucinous carcinoma showing complex glandular structures with back-to-back arrangement [hematoxylin and eosin (H&E), 200 $\times$ ]; (B) endometrial mucinous carcinoma showing positive staining to periodic acid-Schiff before and after digestion (periodic acid-Schiff–diastase, 200 $\times$ ); (C) appendicular tumor composed of confluent papillary structures displaying a circumferential growth pattern all over the appendiceal lining mucosa (H&E, 100 $\times$ ); (D) appendicular tumor, high-power view showing bland-looking tumor cells (H&E, 200 $\times$ ); (E) small benign-looking mucin-filled cyst within the ovarian stroma (H&E, 200 $\times$ ); and (F) omentum revealed noninvasive acellular mucin pools bisecting fat lobules (H&E, 200 $\times$ ).

enlarged uterus; otherwise, there were no specific changes. No ascites or pelvic lymphadenopathy was noticed. An endometrial biopsy was obtained that was diagnosed as complex endometrial hyperplasia with atypia highly suspicious of malignancy.

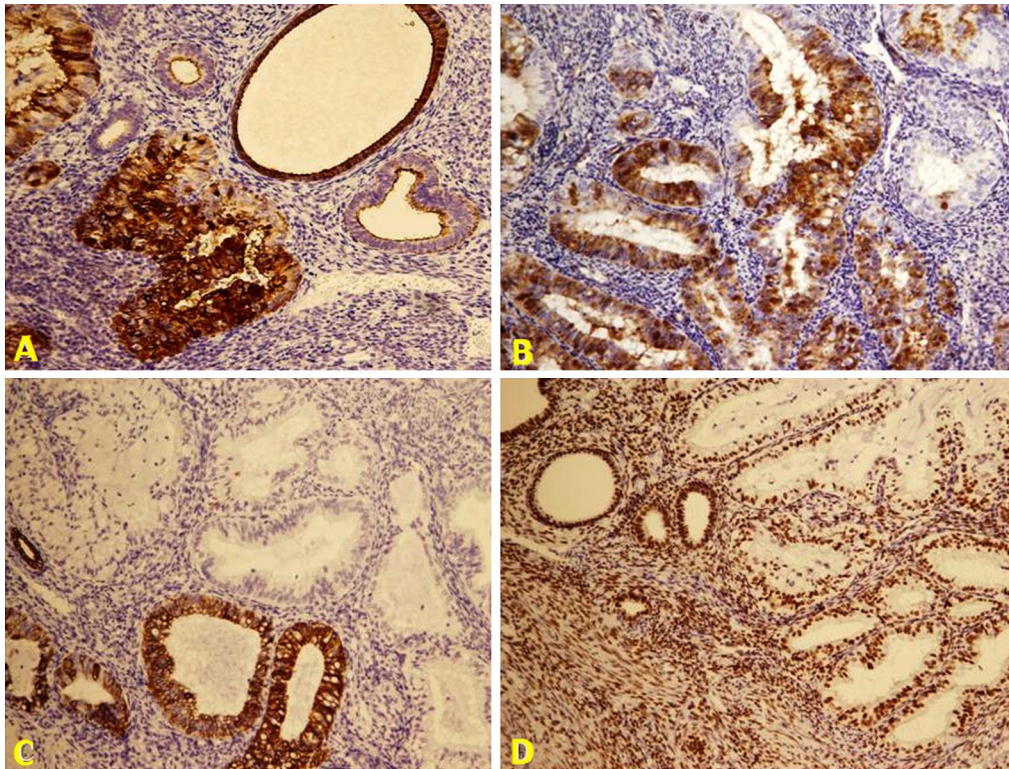
An explorative laparotomy was performed; the uterine cervix was found to be distended with a small tumor. An appendicular mass was identified, measured 4 cm in length. Lobular infiltrate on the omental surface was identified, as well as mild peritoneal collection. An aggressive surgical debulking of the appendix and radical hysterectomy with bilateral salpingo-oophorectomy were performed. Due to suspected malignancy, surgical staging was completed by omentectomy, while no enlarged lymph nodes were detected. Peritoneal fluid was collected.

The specimen received in the pathology laboratory consisted of transabdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and appendectomy. The uterus with attached cervix weighed 250 g and measured 13 cm  $\times$  6 cm  $\times$  5 cm. The serosal surfaces are unremarkable. The endometrial cavity measured 6 cm  $\times$  3 cm  $\times$  2 cm, and contained a friable, papillary, fungating, tan-colored tumor mass. The tumor was originating from the fundus. The tumor measured 4 cm  $\times$  2.5 cm  $\times$  0.5 cm, and invaded the inner half of the

myometrium (1.5/3.5 cm), reaching 0.5 cm close to the superior serosal surface. The right and left ovaries, and the attached Fallopian tubes showed unremarkable outer and cut surfaces, except for a 1-cm cyst in the left ovary. A piece of thickened omentum with mucoid outer surface was sent (weighing 600 g and measuring 25 cm  $\times$  18 cm  $\times$  2 cm). The appendix and attached mesoappendix measured 4 cm  $\times$  3.5 cm  $\times$  2.5 cm. A mucoid irregular mass measured 4 cm  $\times$  3 cm  $\times$  1 cm, and was attached to the serosal surface of the appendicular tip. The appendix lumen is filled with mucoid materials, and a perforation area is present near the appendiceal tip measuring 0.5 cm.

A microscopic examination of the uterine specimen revealed a malignant tumor composed of a complex glandular structure showing focal cystically dilated spaces with branching intraluminal papillae. The tumor cells are mucin-secreting tall columnar cells having round nuclei showing a mild degree of atypia. The glandular lumina are loaded with mucin and heavy neutrophilic infiltrate (Fig. 1A). The intracytoplasmic and intraluminal secretions were proved by periodic acid-Schiff and periodic acid-Schiff–diastase stains (Fig. 1B). The tumor was superficially invading the myometrium and lower uterine segment. There was no lymph–vascular space involvement. The lower uterine segment, cervix, and omentum were free





**Fig. 2.** Immunohistochemical study of endometrial carcinoma showing: (A) strong positive immunostaining to cancer antigen 125 [immunohistochemistry (IHC), 100 $\times$ ], (B) strong nucleocytoplasmic staining to Wilms tumor-1 (IHC, 100 $\times$ ), (C) negative immunoreactivity of tumor cells to cytokeratin 7 in contrast to positive normal glands (IHC, 100 $\times$ ), and (D) strong nuclear staining of tumor cells as well as stromal cells to antibody to estrogen receptor (IHC, 100 $\times$ ).

of disease. No lymph nodes were identified. Sections from the appendix showed a mucinous tumor displaying a circumferential growth pattern in the appendiceal mucosa with variable papillary architecture. The tumor cells were tall columnar, and contained abundant cytoplasmic mucin and two layers of stratified hyperchromatic nuclei in basal location showing minimal cytological atypia. Extracellular mucin pools bypassing the muscularis mucosa to the serosa of the appendix are seen. Chronic inflammatory cells are seen (Fig. 1C and D). The surgical-resection margins were clear. No endometriosis was identified. Both ovaries and tubes were unremarkable, except for a mucous cyst 1 cm in diameter lined by flattened epithelium and is full of mucin in the left one (Fig. 1E). An examination of the omentum revealed noninvasive a cellular mucin pools bisecting fat lobules (Fig. 1F).

The immunohistochemical staining for endometrial carcinoma showed positive immunoreactivity of tumor cells to cancer antigen 125 (CA125), Wilms tumor-1 (WT-1), and estrogen receptor (ER) confirming an endometrioid origin, whereas caudal-type homeobox 2 (CDX2), cytokeratin 7 (CK7), and cytokeratin 20 (CK20) were negative excluding gastrointestinal origin (Fig. 2).

By contrast, the appendiceal tumor showed positive immunoreaction to CK20 and CDX2 confirming gastrointestinal origin, while CK7, WT-1, CA125, and ER were negative excluding an endometrioid origin (Fig. 3).

The case was diagnosed as disseminating peritoneal adenomucinosis associated with borderline mucinous

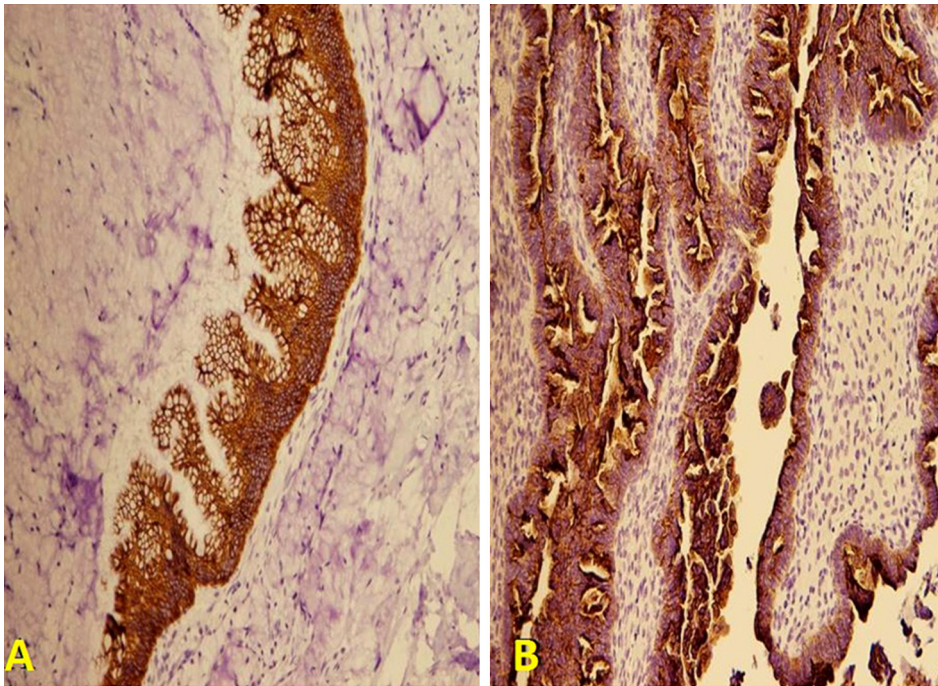
appendicular tumor and mucinous endometrial carcinoma, grade 1 and stage 1A (according to the International Federation of Gynecology and Obstetrics staging system [7]).

Following surgery and diagnosis, the patient was treated by intraperitoneal chemotherapy. The patient was doing well for 2 months after surgery with no signs of disease recurrence. The patient will be followed up every 3 months with annual chest radiograph.

### 3. Discussion

Clinically, most cases of PMP are detected during the performance of laparoscopy or laparotomy for cases suspected to be appendicitis, peritonitis, or ovarian tumors [8–10]. There has always been a continuous debate regarding the primary origin of PMP, especially in female patients. Most of the opinions in the literature regarding the origin of PMP support appendicular origin in about 94% of cases in males and females [8–15]. The synchronous existence of mucinous appendicular tumors and ovarian tumors, particularly borderline mucinous tumors, is well documented. Molecular genetics and immunohistochemical studies support the opinions that the ovarian tumor in such cases usually represents a metastatic deposit from an appendicular primary [16,17].

By contrast, the coexistence of PMP with appendicular tumor and endometrial pathology as endometrioma, or endometrial adenocarcinoma, was exceptional [18,19].



**Fig. 3.** Immunohistochemical study of appendiceal mucinous tumor showed (A) strong positive cytoplasmic immunoreactivity to cytokeratin 20 (immunohistochemistry, 200 $\times$ ), and (B) strong positive immunoreactivity to caudal-type homeobox 2 in cytoplasm and luminal border (immunohistochemistry, 200 $\times$ ).

To the best of our knowledge, only one case was reported previously by Kalogiannidis et al. [19]. The reported case was of a 49-year-old female who was presented with postmenopausal bleeding. Total abdominal hysterectomy with bilateral salpingo-oophorectomy and appendectomy was done to the patient. The histopathological examination revealed an endometrioid endometrial adenocarcinoma associated with mucinous cystadenoma of the appendix [19].

We are reporting a case of a female patient presented with PMP associated with a well-differentiated mucinous borderline tumor of the appendix and an infiltrating mucinous endometrial carcinoma.

Our case was presented with uterine bleeding, and a physical examination revealed fullness in the lower abdomen. The computed tomography of the abdomen revealed a mildly enlarged uterus; otherwise, no specific changes were found. Upon laparotomy, cervical and appendicular masses were detected, and so transabdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and appendectomy was performed.

The histopathologic studies revealed that the patient had borderline mucinous appendicular tumor, as well as mucinous endometrial adenocarcinoma. Due to the presence of two mucinous tumors with different histological grades, the most likely explanation was either a multifocal mucinous carcinoma or a primary mucinous tumor of the appendix metastasizing to the endometrium and omentum, or otherwise simultaneously developed tumors. Surprisingly, the immunohistochemical studies of both tumors revealed that the appendicular tumor was positive CK20 and CDX2 confirming gastrointestinal origin,

while CK7, WT-1, CA125, and ER were negative excluding an endometrioid origin. By contrast, the endometrial carcinoma showed positivity to CA125, WT-1, and ER, and negativity to CDX2 and CK20, which prove that the endometrial and appendicular mucinous tumors were two independent primary neoplasms, and PMP probably was the result of rupture of the appendicular neoplasm seeding the peritoneum.

In most cases, a pre- or intraoperative diagnosis is rarely achieved, and patients frequently require a second operation for definitive therapy. Once diagnosed, the traditional treatment for a mucinous cystadenocarcinoma of the appendix has been surgery in the form of a right hemicolectomy, and aggressive debulking is added if found associated with pseudomyxoma peritonei (intra-abdominal metastasis), which is seen in up to 50% of patients. We report a case of a mucinous cystadenocarcinoma of the appendix, which presented as a mass in the right iliac fossa, and the problems encountered during surgery.

Our case is the second case in the literature representing the combination or coexistence between appendicular mucinous tumor and endometrial carcinoma. The mechanism underlying this unusual association is still obscure.

In cases presented with PMP, clinicians usually focus on appendiceal mucinous tumors and ovarian pathological structures; we presented this case to raise awareness among gynecologists about this additional pathological association, such as endometrial carcinoma. In such cases, the diagnostic and therapeutic approach needs to be multidisciplinary, and general surgeons should be involved so as the optimal approach of appendicular pathology is ensured.



## Conflicts of interest

No conflict of interest.

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