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## Case Report

## Peritoneal well-differentiated papillary mesothelioma coexisting with endometrial adenocarcinoma mimicking peritoneal carcinomatosis: A case report

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## ABSTRACT

**Objective:** We present a rare case of well-differentiated papillary mesothelioma (WDPM) found incidentally in a 59-year-old woman with endometrial cancer.**Case report:** A 59-year-old nulliparous obese woman with a past history of hypertension and diabetes mellitus presented with postmenopausal bleeding for 11 months. Two months prior to this admission, an episode of massive vaginal bleeding lasting for a day was noticed by the patient. Hysteroscopy was performed after her visit to our outpatient department. Papillary tumors with active bleeding were found in the uterine cavity. Endometrial biopsy showed adenocarcinoma, endometrioid type characterized by papillary architecture lined by columnar cells with mild nuclear pleomorphism. The patient proceeded to magnetic resonance imaging (MRI), which demonstrated a 6.4 × 5.5 × 4.9 cm intrauterine mass. Her tumor marker levels were elevated (CA 125 87.8 IU/ml, CA19-9 160.54 IU/ml). The patient then underwent a staging surgery and final pathology revealed stage IA endometrial cancer. During surgery, multiple nodules were found in the peritoneum, initially considered as tumor metastasis and eventually proved to be WDPM.**Conclusion:** In conclusion, the simultaneous occurrence of WDPM with endometrial cancer is a rare entity. Although no standardized treatment has been established, WDPMs have a relatively favorable prognosis compared to malignant mesotheliomas.© 2020 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Well-differentiated papillary mesothelioma (WDPM) of the peritoneum is a rare variant of epithelioid mesothelioma, which most frequently occurs in women of reproductive age and is usually incidentally found during pelvic or abdominal surgery [1]. WDPM is normally asymptomatic and has low-grade malignant potential. The etiology and association with other malignancies are unclear and the patient is lacking a history of asbestos exposure [2]. The simultaneous occurrence of WDPM with endometrial cancer is rare with only 3 cases reported in the literature [3–5]. We present a case

of WDPM associated with endometrial cancer in a 59-year-old woman, initially considered as peritoneal metastasis.

## Case report

A 59-year-old nulliparous obese woman with a past history of hypertension and diabetes mellitus presented with postmenopausal bleeding for 11 months. With unknown BRCA status, she has no family history of cancer, nor did she ever expose to talc or asbestos. Her menarche was at 11 years old and menopause at 53 years old. She has no sexual exposure and did not take contraceptive pills.

Two months prior to this admission, an episode of massive vaginal bleeding lasting for a day was noticed by the patient. Otherwise, no abdominal pain, distension or increased urinary frequency was complained by the patient. There were no

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systemic symptoms such as weight loss, poor appetite, fever or chillness. Hysteroscopy was performed after her visit to our outpatient department. Papillary tumors with active bleeding were found in the uterine cavity (Fig. 1A). Endometrial biopsy showed adenocarcinoma, endometrioid type characterized by papillary architecture lined by columnar cells with mild nuclear pleomorphism. The solid area was less than 5%. Immunohistochemical stain showed ER (++), PR (++), p53 (–) and p16 (+/–). The patient proceeded to magnetic resonance imaging (MRI), which demonstrated a  $6.4 \times 5.5 \times 4.9$  cm intrauterine mass (Fig. 1B). Her tumor marker levels were elevated (CA 125 87.8 IU/ml, CA19-9 160.54 IU/ml).

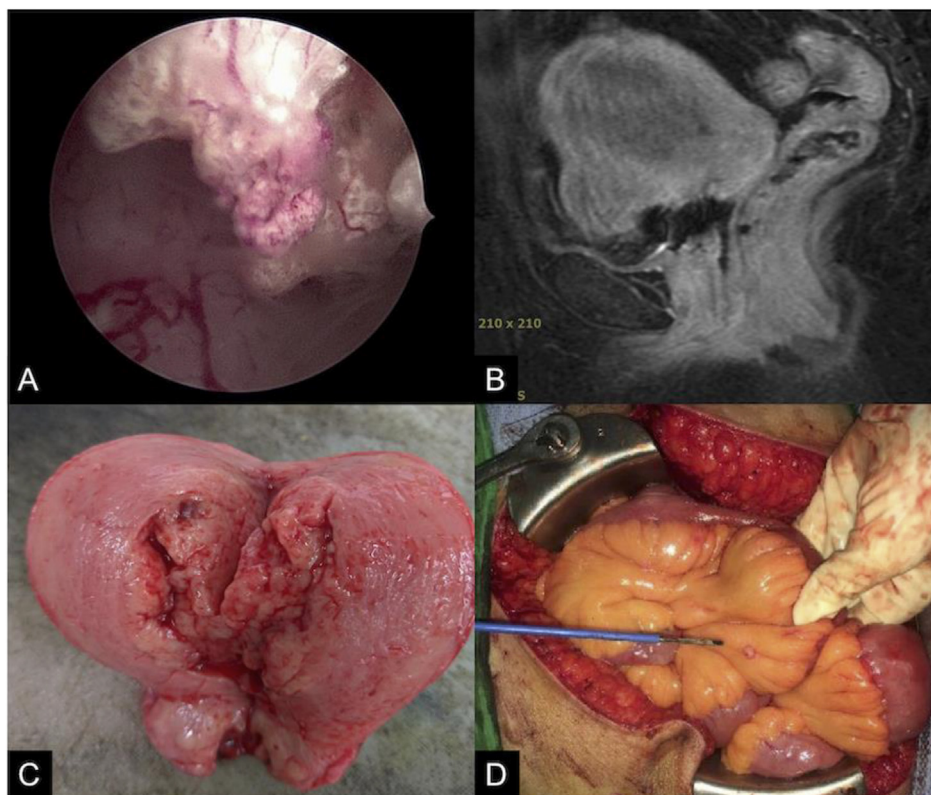
The patient then underwent a staging surgery including total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection, para-aortic lymph node dissection, and omentectomy. Intraoperative findings showed an enlarged uterus about  $8 \times 7$  cm in size with endometrial invasion about 3 cm in thickness and superficial invasion to the myometrium (Fig. 1C). Multiple white miliary nodules were found on the omentum, bladder, pouch of Douglas, lateral pelvic wall, and mesentery (Fig. 1D). Peritoneal carcinomatosis was suspected initially. However, the pathology revealed grade 1 endometrioid adenocarcinoma of the uterus, pT1bN0, and WDPM of omentum, bilateral ovaries, peritoneum of the bladder, the pouch of Douglas and lateral pelvic wall and mesentery (Fig. 2A and B). On immunohistochemical study, the endometrial tumors showed positive for ER and PR and negative for p53 and p16. The peritoneal tumor cells were positive for WT-1 (Fig. 2C) and Calretinin (Fig. 2D). No lymph nodes involvement was seen and no cancer cells in ascites. The patient's postoperative recovery was uneventful and she received adjuvant radiotherapy.

## Discussion

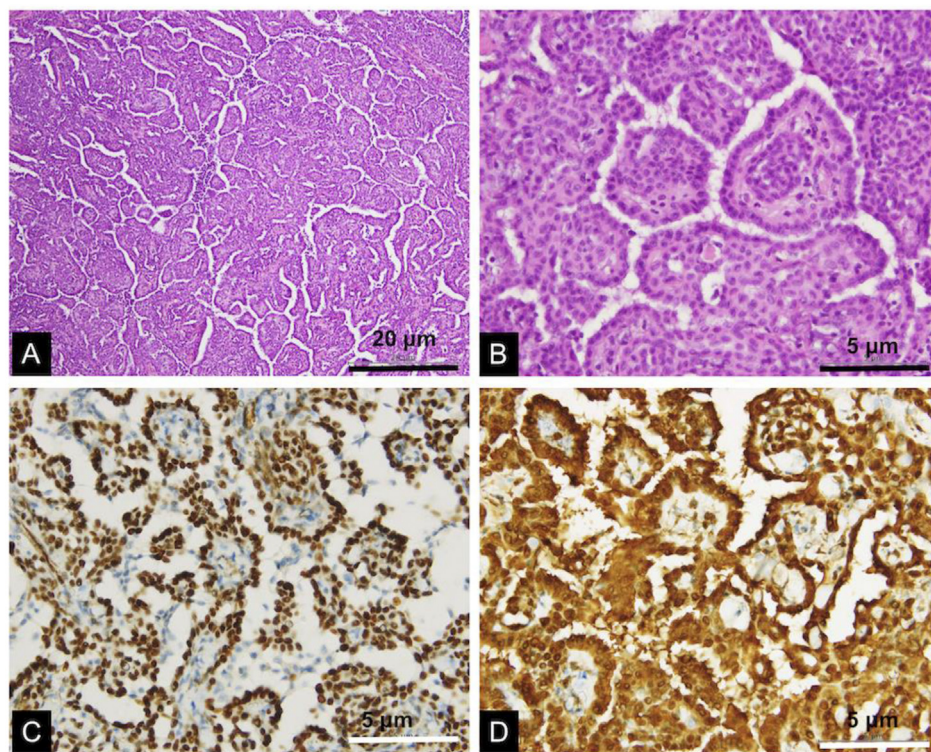
Mesothelioma is a rare tumor arising from the mesothelial cells. Besides the pleural cavity, it also involves the peritoneal cavity, pericardium or tunica vaginalis. Peritoneal mesothelioma can be divided into three pathological subtypes: malignant mesothelioma, cystic mesothelioma and well-differentiated papillary mesothelioma [6]. Different from malignant mesothelioma which is known to be related to asbestos exposure, the etiology of WDPM remains unclear. Previous abdominal surgeries, trauma, alcohol use, smoking history, and family history were considered to be the possible factors [7].

The clinical course of WDPM is indolent and rarely become malignant. Malpica et al. showed 26 cases with WDPM and most of the diagnoses were made incidentally during surgeries. Only two cases presented with symptoms, one with chronic pelvic pain and another with acute abdomen due to bleeding from one of the WDPM lesions which caused small hemoperitoneum [8]. In another study with 75 WDPM cases, there were only 4 peritoneal WDPM patients having clinical symptoms presented as acute or chronic abdominal pain [9]. Kim et al. reported 12 cases of peritoneal WDPM. Ten tumors were detected incidentally during surgery for other causes and only one patient had symptoms with abdominal discomfort [10].

The preoperative diagnosis of peritoneal WDPM is challenging. Computed Tomography (CT) findings may show peritoneal thickening, multiple peritoneal nodules, omental infiltration, and ascites. However, these findings are nonspecific nor sensitive due to most of the WDPMs are smaller than 1 cm and difficult to differentiate from other peritoneal implants [6]. MR imaging and positron emission tomography (PET) did not have superiority over the CT scan in the diagnosis for peritoneal WDPM [11,12].



**Fig. 1.** The image of hysteroscopy, magnetic resonance imaging (MRI), gross view of the uterus, and operative view. (A) Hysteroscopy showed papillary tumors in the uterine cavity. (B) Abdominal MRI T1 Sagittal view. (C) Gross view of the resected uterus. (D) A white nodule on the mesentery finally approved as well-differentiated papillary mesothelioma.



**Fig. 2.** The histology of well-differentiated papillary mesothelioma (WDPM). (A, B) The tumor histology showed by hematoxylin and eosin staining. The morphology of WDPM showed uniform epithelioid cells with moderately cellular and arranged in papillary morphology. No mitosis was seen. The immunohistochemistry was positive for WT-1 (C) and Calretinin (D). Scale bar = 5  $\mu$ m in (B, C, D), = 20  $\mu$ m in (A).

The differential diagnosis of WDPM includes tuberculous peritonitis, mesothelial hyperplasia, serous surface papillary carcinoma, malignant mesothelioma, or peritoneal carcinomatosis. Peritoneal WDPM does not have specific clinical and radiological characteristics. Therefore, diagnostic surgery and pathologic exam ensure a definite diagnosis. Histologically, the tumor exhibits well-developed papillary structures with fibroconnective tissue cores lined by a single layer of cuboidal mesothelial cells [8]. Immunohistochemical stains usually revealed positive for calretinin, AE1/AE3, D2-40, HBME, WT1, cytokeratin 5/6, cytokeratin 7, vimentin, PAS, EMA and PAX8 [9,10].

Most of WDPM was incidentally discovered during surgeries for other indications. Several associated malignancies have been reported including endometrioid ovarian cancer, endometrioid adenocarcinoma, rectal carcinoma, hepatocellular carcinoma, common bile duct carcinoma, uterine cervical carcinoma, and gastric gastrointestinal stromal tumor (GIST). In this study, the case presented as endometrial adenocarcinoma with peritoneal WDPM. Synchronous occurrence of WDPM with endometrial cancer is extraordinarily rare with only 3 reported cases [3–5].

Given the rarity of WDPM, there is no consensus regarding optimal treatments, particularly when it occurred in association with another primary cancer. In previous studies, some patients received complete tumor resection or debulking surgery [2,8,13]. Recurrence after surgical resection was rare even without adjuvant therapy. Medical treatments include chemotherapy, radiation therapy, immunotherapy, and sclerosing therapy. According to case series by Lee et al., the author suggested that if WDPM tumor is completely resectable, an excisional biopsy seems to be sufficient. If complete excision is not possible, platinum-based chemotherapy appears to be an option and close follow-up is recommended [14].

Regarding this case, after the treatment, we will monitor the WDPM by the CT image every 6 months or annually. As previously

mentioned, for the WDPM lesion larger than one centimeter, CT findings may show peritoneal thickening, multiple peritoneal nodules, omental infiltration, and ascites. Due to no specific image characteristics of WDPM, the difference between recurrent endometrial cancer and WDPMs lesion showed in the CT images is small. The laparoscopic diagnosis may be helped [15].

In conclusion, the simultaneous occurrence of WDPM with endometrial cancer is a rare entity. The peritoneal implants may be misinterpreted as tumor metastasis. The pathologic examination with immunohistochemical analysis is important to establish an accurate diagnosis.

#### Author contribution

YYC, PCL: acquisition, analysis, and interpretation of data, and drafting the manuscript. YHH: provide a pathological diagnosis. DCD: Study concept and design; acquisition, analysis, and interpretation of data; drafting and final approval of the manuscript.

#### Declaration of competing interest

The authors have no conflict of interest relevant to this article.

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