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Peritoneal Well-Differentiated Papillary Mesothelial Tumor (WDPMT): Case Report and Literature Review

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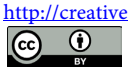

Abstract

The pathogenesis and biological behavior of well-differentiated papillary mesothelial tumors (WDPMT) are poorly understood. WDPMT can arise in both the pleura and the peritoneum. As its benign and malignant features are often ambiguous, establishing an optimal treatment strategy can be challenging. In this report on peritoneal WDPMT, we analyzed nine Japanese cases, including our own case involving a 70-year-old male, and eight additional cases identified through a literature review from 2002 to 2025. The patients' ages (median; range) were 47 years (range, 30 - 71 years), and 6 of the 9 patients were female. Almost all cases were incidentally detected and presented as multiple raised lesions on the abdominal peritoneum associated with ascites in six cases. Pathologically, the lesions retained BAP1expression and were considered unrelated to asbestos exposure. Treatment was variable: chemotherapy in 2, observation in 5, and no information in 2. All nine patients were alive at the time of reporting, with a median follow-up period of 8 months (range, 6 - 84 months). One case of late recurrence was reported in these cases.

Subject Areas

Oncology, Surgery & Surgical Specialties

Keywords

Well-Differentiated Papillary Mesothelial Tumor, Peritoneum, Inguinal Hernia, BAP1, Ascites

1. Introduction

A well-differentiated papillary mesothelial tumor (WDPMT) is a neoplastic mes-

othelial proliferation of low malignant potential that occurs in the pleural or peritoneal types; the peritoneum of young women is highly involved [1]. Benign and malignant characteristics of the tumor were noted. However, it is differentiated from ordinary invasive diffuse mesotheliomas, although morphological overlaps exist between the two tumors [2]. Pathology revealed a composite of branching papillae lined by a single layer of bland cuboidal mesothelial cells, for which immunostaining with BAP1 and MTAP was important for pathological diagnosis. Detection of CDKN2A using fluorescence *in situ* hybridization (FISH) can also be useful for differentiating benign from invasive tumors [3]. Clinically, malignancy should be considered when tissue invasion, such as fat, muscle, or ovarian stroma, is observed [1]. In addition, among peritoneal WDPMT, there are two morphologically identical but functionally distinct lesions: one is true WDPMT, probably benign, and the other is papillary mesothelioma *in situ* (MIS) from which invasive mesothelioma may arise [2 Churg]. Galateau-Salle *et al.* previously hypothesized that WDPMT consists of two morphologically identical lesions: true WDPMT and a form of mesothelioma *in situ* (MIS). Since peritoneal WDPMT shows slow progression, treatment is difficult, and no standard treatment has been established. In MIS cases, cytoreductive surgery followed by observation and/or heated intraperitoneal chemotherapy can be employed [4]. Currently, the pathogenesis and behavior of peritoneal WDPMT remain poorly understood, and the treatment of WDPMT (including MIS) may be challenging. We report a case in which a disseminated peritoneal lesion of WDPMT (not MIS) was incidentally found during surgery for inguinal hernia repair, leading to the diagnosis. We also collected eight similar peritoneal WDPMT cases in Japan for discussion and review purposes.

2. Case Report and Methods

Case: The patient was a 60-year-old male. Physical examination revealed a height of 163 cm and a weight of 58 kg. He had been previously healthy with no significant weight change for approximately 20 years. The patient is a pharmacist by profession and has no history of occupational or environmental asbestos exposure, including any secondary exposure via family members. He presented with the chief complaint of a right inguinal hernia and associated groin pain. The right groin area was swollen to approximately the size of a ping-pong ball in a standing position and could be easily reduced by hand. The pain was resolved in the supine position. Laboratory tests showed that the white blood cell count (WBC) and C-reactive protein (CRP) were both within normal limits, with no evidence of anemia. Tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9, were also within the normal range. Pre-operative computed tomography (CT) revealed grossly normal findings except for ascites (**Figure 1(A)**, **Figure 1(B)**), which was presumed to be related to recurrent bowel incarceration. On the CT images, the peritoneum appeared normal.

The patient wished to undergo surgery for an inguinal hernia as early as possi-

ble. In the operative findings, a moderate amount of turbid yellowish ascites was observed in the pouch of Douglas. In addition, numerous small nodules measuring approximately 0.5 - 1 cm were noted on the peritoneum and greater omentum, which were considered peritoneal dissemination of an uncertain malignant tumor (**Figure 2(A)**, **Figure 2(B)**). Ascitic fluid analysis was performed, showing negative cytology for malignancy and a negative culture result. Biochemical analysis of the fluid was not obtained. We performed hernia surgery with a Transabdominal Preperitoneal repair. Additionally, we aspirated as much ascites as possible and excised the peritoneum for pathological examination. The post-excised peritoneum was covered with a lightweight, three-dimensional mesh (3D MAX Light, BD) and then sutured using absorbable materials.

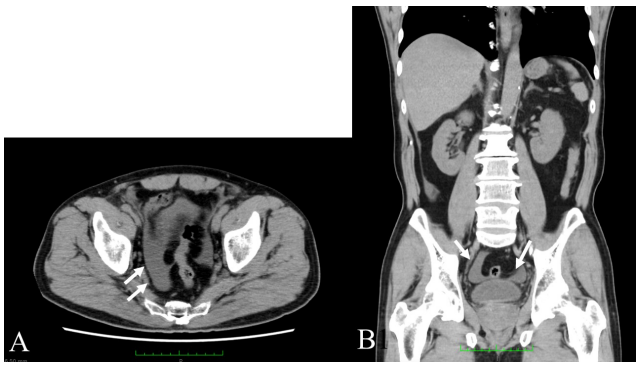

Figure 1. Pre-operative CT findings: Peritoneal and omental lesions are difficult to detect on imaging studies. Small amounts of ascites (arrows) are observed in the pelvic cavity. (A) Axial (B) coronal views.

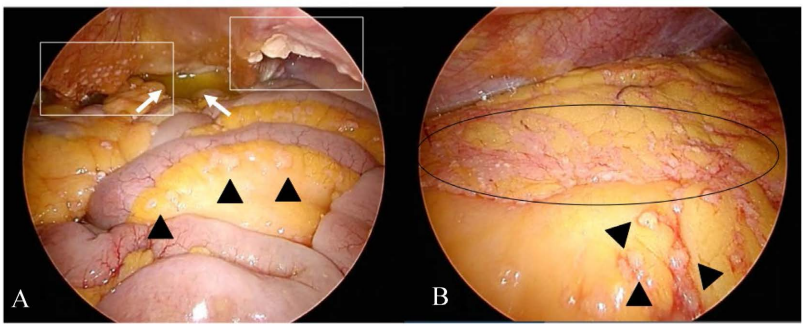

Figure 2. Surgical findings revealed a moderate volume of free fluid in the pouch of Douglas (white arrows) and numerous small nodules measuring approximately 0.5 - 1 cm were noted on the peritoneum (white squares) (A); intestinal mesentery (arrow heads) and the greater omentum (black circles) are also indicated (B). Lesions in the intestinal mesentery (arrow heads) are noted in both (A) and (B).

Pathological examination revealed a tumor with papillary architecture and an exophytic growth pattern, covered by a single layer of cells with scant atypia. The papillary structures contained fibrovascular cores and were sometimes associated with foamy macrophages. The covering cells retained BAP1, MTAP, D2-40 expressions, and calretinin, but negative for the carcinoma markers CEA, claudin-

4, TTF1, and napsin A. Clear stromal invasion was not identified by AE1/AE3 staining. Explicit diagnostic criteria for true WDPMT were met, including the strict absence of stromal invasion and preserved nuclear staining for BAP1 and MTAP. Fluorescence in situ hybridization (FISH) for *CDKN2A*/*p16* was not conducted, as the small size of the lesion precluded further molecular testing; however, the bland cytologic features and the absence of BAP1 loss provided sufficient evidence to exclude MIS. Pathologically, the diagnosis was highly consistent with that of a well-differentiated papillary mesothelial tumor (WDPMT) (**Figure 3**).

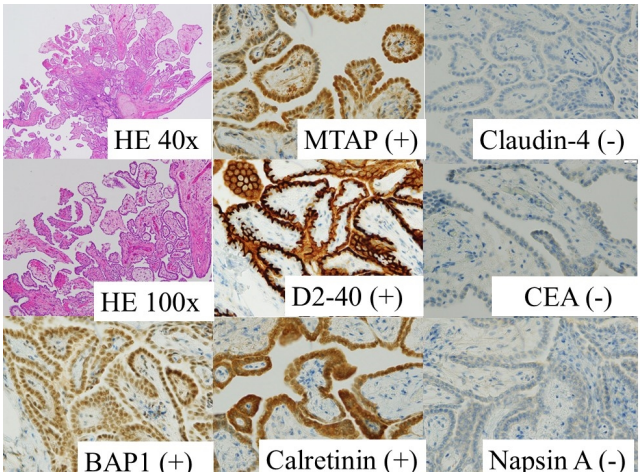

Figure 3. Pathological diagnosis: The peritoneal nodules biopsied exhibited a typical WDPMT pathology with papillary structures. Hematoxylin & Eosin (HE) stains are shown at a magnification of ×40 and ×100, respectively. All immunostaining figures (BAP1, MTAP, D2-40, and calretinin were positive, while claudin-4, CEA, and napsin A were negative) are at a magnification of ×400.

The postoperative course was uneventful, and the patient was discharged on postoperative day 2 and managed conservatively under observation. After a postoperative follow-up period of > 14 months, the patient remained stable with no evidence of increased ascites or other significant changes.

Methods: We searched the *Ichushi Web* (Japan Medical Abstracts Society) database (https://login.jamas.or.jp) for Japanese cases using the keyword, Well-differentiated Papillary Mesothelioma. We analyzed nine cases, with eight reported cases in Japan between 2002 and 2024 [5]-[12], and our own case was diagnosed in 2025 (**Table 1**).

3. Results

As summarized in **Table 1**, we analyzed nine peritoneal WDPMT cases in Japan (2002-2025), derived from eight reported cases and our own case. The patients' ages ranged from 30 to 71 years, with a median age of 47. Six of the 9 patients were female. Almost all the cases were incidentally identified. Abnormal lesions were noted in the omentum and ovary areas in two cases: in the peritoneum and uterus area in one case, peritoneum/omentum and intestinal mesentery in our case, and

in the peritoneum in the remaining cases. Because the greater omentum is a part of the peritoneum, a high probability of omental involvement is present when peritoneal lesions are identified. In our case, although both the parietal peritoneum and the greater omentum were involved, we referred to the location simply as "peritoneum." Although there were no specific imaging findings, the lesions were confirmed to be multiple raised lesions in the abdominal peritoneum. In addition, ascites was observed in six out of nine cases, and in those cases, multiple scattered granular nodules were found extensively throughout the peritoneal cavity. Pathologically, the lesions retained BAP1 expression and considered asbestos-unrelated. En bloc resection of the affected peritoneum (omentectomy) was performed in three cases, but macroscopic residual tumor was observed in five cases. Chemotherapy was administered to 1 of these 5 cases; in another case, FOLFOX6 was administered because the WDPMT was found incidentally during treatment for colon cancer. All nine patients were alive at the time of reporting, with a median (range) of 8 (6 - 84) months. Late recurrence in one case has been described [10], as described below.

Table 1. Reports of peritoneal disseminated WDPMT incidentally identified in Japan (2002-2025).

N	Ref	age/sex	Sites	Nodule size (mm)	Ascites	Surgical Tx	Chemo Tx	Outcome (month)
1	5	35/F	Omen ovary	NA	Yes	Yes	Yes	NA
2	6	37/F	perito, uterus	5.0 - 10	Yes	Yes	none	8
3	7	50/F	omen ovary	NA	Yes	Yes	NA	36
4	8	30/F	perito	NA	Yes	biopsy	NA	6
5	9	71/M	perito	5.0	No	biopsy	Yes*	8
6	10	58/F	perito	0.5	Yes	Yes	none	84**
7	11	44/M	perito	8.0	No	Excisional resection	none	7
8	12	47/F	perito	5.0	No	Excisional resection	none	18
9	This case	60/M	perito	5.0	Yes	biopsy	none	14

Footnotes: Abbreviations; omen = omentum, perito = peritoneum (Details of peritoneal dissemination is described in the text), Tx = treatment, NA = not available, * FOLFOX6 = administered for colon cancer associated with WDPMT ** This patient developed late relapse.

4. Discussion

Regarding WDPMTs across various sites, Sun *et al.* [13] summarized 75 of their own cases, along with 180 cases from the literature. Among these, 135 arose in the peritoneum, 37 in the pleura, and 28 in other sites. In peritoneal cases, the male-to-female ratio was 1:6, whereas a nearly equal ratio was noted in pleural cases. Offin *et al.* analyzed 54 patients with peritoneal WDPMTs and reported that most cases (94%, n = 51) were identified incidentally during surgical procedures performed for other indications, primarily malignancies [14]. Similarly, Sun *et al.* and Offin *et al.* both emphasized that peritoneal WDPMTs are usually discovered incidentally during surgery for unrelated conditions [13] [14]. Only a minority of

patients present with abdominal pain or ascites attributable to WDPMT [13]. Notably, our case was preceded by the detection of ascites on abdominal CT before diagnosis. According to Offin *et al.*, among patients with peritoneal WDPMTs, only two underwent surgical resection, and none received systemic therapy. The median overall survival was not reached (19 deaths among 54 patients) at a median follow-up of 4.5 years [14]. In our analysis of nine cases, all patients were alive at the time of reporting, suggesting that the prognosis of peritoneal WDPMT is generally excellent.

To evaluate the benign or malignant behavior of peritoneal WDPMT, it is critical to determine whether a lesion represents a true WDPMT or should instead be suspected as mesothelioma in situ (MIS), which has been proposed to be malignant [4]. Pathologically, WDPMT typically expresses traditional mesothelial markers, including BAP1, calretinin, MTAP, and D2-40. In addition, PAX8, often positive in ovarian and other gynecologic tumors, is frequently expressed in peritoneal WDPMT [13], although we did not test PAX8. In contrast, MIS, which is prone to malignant progression, is characterized by loss of BAP1 expression [15]. Galateau-Salle *et al.* reported that four of five peritoneal MIS cases presenting with ascites were considered to represent diffuse peritoneal malignancy, showing loss of BAP1 [4]. In our case with ascites, the retained BAP1 expression supported the diagnosis of WDPMT rather than MIS.

The primary treatment options for WDPMT include observation, surgical resection, and other modalities. In the present case, the treatment strategy for peritoneal WDPMT was based on its presumed low malignant potential despite dissemination within the peritoneal cavity. Complete surgical removal is challenging because the lesions are widespread on the peritoneal surface. More intensive treatments are typically reserved for cases of aggressive malignant peritoneal mesothelioma [16]. For invasive mesothelioma, regional treatments such as hyperthermic intraperitoneal chemotherapy (HIPEC) combined with cytoreductive surgery (CRS), as well as immunotherapy and targeted therapy, may be considered [17].

Long-term follow-up of WDPMT is essential because several reports have documented late recurrences or malignant progression. Burrig *et al.* [18] described a mesothelioma occurring 5 years after the initial diagnosis of WDPMT, and Washimi *et al.* [10] reported a case of invasive mesothelioma 7 years later. Costanzo *et al.* [19] documented metastatic mesothelioma that developed 13 years after diagnosis. Sun *et al.* [13] reported a case of progression to invasive mesothelioma after 15 years, and Galateau-Salle *et al.* [4] described two patients who developed invasive lethal mesothelioma 10 years after the initial diagnosis. It is reasonable to question whether some of these cases may have been misdiagnosed as peritoneal WDPMT rather than MIS. Conversely, Vitlarov *et al.* [20] described a patient with MIS who received no treatment and remained alive for 15 years after presentation. Collectively, these observations highlight the persistent uncertainty regarding the true benign versus malignant nature of WDPMT and lesions classified as MIS.

The management of disseminated WDPMT remains a clinical challenge, neces-

sitating a balance between preventing progression and avoiding the morbidity of aggressive surgery. In our case, the retention of BAP1 expression was a critical determinant in choosing an observational strategy. Unlike MIS, which is characterized by BAP1 loss and a high risk of progression to invasive disease, BAP1-retained WDPMT typically follows a benign course. We recommend serial cross-sectional imaging, CT scan, MRI, or abdominal ultrasoud every 6 to 12 months. Escalation to CRS/HIPEC should be strictly reserved for evidence of radiographic bulk or symptomatic transformation, as upfront cytoreduction in the absence of these factors has not demonstrated a clear survival advantage in this molecularly favorable subset.

5. Conclusion

Currently, no standardized or less invasive multidisciplinary treatment options are available for peritoneal WDPMT. Given the tumor's ambiguous biological behavior, ranging from benign to potentially malignant, further investigation is needed to establish widely accepted diagnostic criteria and treatment strategies.

Author Contribution

All authors have made substantial contributions to all the following: 1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content, 3) final approval of the version to be submitted.

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Highlights

- Peritoneal well-differentiated papillary mesothelial tumor (WDPMT) is incidentally detected multiple raised abdominal lesions, frequently associated with ascites.
- Extensive peritoneal dissemination is observed, yet a standard treatment has not been established.
- This article added 9 cases of Japan and literature review to suggest a standard approach to the treatment of the disease.

Ethical Statement

The study was conducted in accordance with the ethical standards of our affiliated institution and principles of the Declaration of Helsinki (revised 2013). Written informed consent was obtained from the patient for publication of this case and the accompanying images. This study was approved by the Institutional Review Board of our hospital.

Conflicts of Interest

The authors declare no conflicts of interest.

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