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Clinicopathological Characteristics of Well-differentiated Papillary Mesothelioma of The Peritoneum: A Single-institutional Experience of 12 Cases

MOONSIK KIM[1] and HYUN-SOO KIM[2]

[1]*Department of Pathology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea*
[2]*Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*

Abstract. *Background/Aim: Well-differentiated papillary mesothelioma (WDPM) is histologically characterized by papillary architecture with fibrovascular cores, lined by bland mesothelial cells. We recently experienced a case of WDPM associated with multiple peritoneal inclusion cysts, which prompted us to initiate a comprehensive review of previously diagnosed WDPM cases. Materials and Methods: The clinicopathological characteristics and immunophenotype of 12 cases of peritoneal WDPM were investigated using a review of electronic medical records, pathological examination, and immunostaining. Results: The patients' ages ranged from 23 to 75 years. No patient had endometriosis or a previous history of asbestos exposure. Ten tumors were detected incidentally during surgery for other causes. Most tumors appeared as a small, single nodule on the peritoneal surface, but in three cases, WDPM presented as multiple lesions. All but one patient had no symptoms. All the patients examined are still well without postoperative recurrence. Histologically, all cases demonstrated typical papillary architecture with fibrovascular cores. The mesothelial cells lining the papillae consisted mostly of single row of cells, although areas of proliferation to multiple layers were observed in a few cases. Their nuclei appeared bland, but two cases exhibited mild nuclear atypia and prominent nucleoli. Immunostaining revealed that the mesothelial cells were positive for D2-40, cytokeratin 5/6, cytokeratin 7, and Wilms' tumor 1. Conclusion: We herein demonstrated the clinicopathological characteristics of peritoneal WDPMs. WDPM has distinct pathological features. Although all cases we examined were uneventful after surgery, further surveillance is recommended since the biological behavior of WDPM is still uncertain.*

Correspondence to: Hyun-Soo Kim, Department of Pathology, and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81, Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea. E-mail: hyunsookim16@gmail.com

Key Words: Peritoneum, well-differentiated papillary mesothelioma, peritoneal inclusion cyst, immunohistochemistry, case series.

Mesothelial lesions can be categorized into reactive mesothelial proliferation, malignant mesothelioma, and other forms of less aggressive mesothelial tumors (1-3). Well-differentiated mesothelial papilloma (WDPM) is a rare tumor that usually occurs in the peritoneum (4-6). Less frequently, it also arises from the pleura, pericardium, and *tunica vaginalis*/testis (7-9). Most cases of WDPM are incidentally detected as a small, single nodule during surgery for other causes. WDPM can also present as multiple lesions involving the pleural or peritoneal surfaces (10, 11). WDPM typically shows an indolent clinical course (12); however, a few cases of recurrent WDPM have been reported (13). Some previous studies have documented that WDPM should be considered a tumor of uncertain malignant potential (13, 14). Histologically, WDPM shows papillary structures lined by bland-looking, single-layered mesothelial cells. However, more complex papillary architectures containing multilayered mesothelial cells are occasionally observed (15).

We recently experienced a very rare case of peritoneal WDPM associated with multiple peritoneal inclusion cysts, which initiated a thorough review of WDPM cases previously diagnosed at our Institution. In this study, we describe their clinicopathological characteristics and immunophenotype. Comprehensive clinicopathological analyses of WDPM involving the peritoneum or omentum may expand our knowledge regarding WDPM.

Materials and Methods

Patient selection. This study was reviewed and approved by the Institutional Review Board at the Severance Hospital (no. 4-2018-0921). The cases were extracted from computerized files of surgical

pathology diagnoses. A thorough search of archived surgical pathology cases was performed using the key words "peritoneum," "mesothelioma," "papillary mesothelioma," "well-differentiated papillary mesothelioma," and "peritoneal inclusion cyst." From January 2005 to September 2018, 12 patients were diagnosed as having peritoneal WDPM. The clinical details that were extracted from the electronic medical record included age and sex of the patients, greatest dimension of tumor, multiplicity, clinical presentation, coexisting disease, association with endometriosis, asbestos exposure, and tumor recurrence.

Pathological examination. The resected tissue was initially examined by pathologists before fixation in 10% neutral-buffered formalin. After fixation for 12–24 h, the tissues were examined macroscopically and sectioned. After processing with an automatic tissue processor (Peloris II; Leica Microsystems, Wetzlar, Germany), the sections were embedded in paraffin blocks. Four-micrometer-thick slices were cut from each formalin-fixed, paraffin-embedded tissue block and stained with hematoxylin and eosin stain using an automatic staining instrument (Ventana Symphony System; Ventana Medical Systems, Tucson, AZ, USA). After staining, the slides were covered with a glass coverslip and sent to two independent pathologists specialized in gynecological oncology. They examined all available hematoxylin and eosin-stained slides using light microscopy (BX43 System Microscope; Olympus, Tokyo, Japan), made definite pathological diagnoses, and chose the most representative slide for immunostaining. The pathological characteristics that were analyzed included architectural pattern (papillary, tubular, and glandular), cell shape (columnar, cuboidal, and flat), degree of nuclear atypia, mitotic activity, conspicuous nucleoli, presence of psammomatous calcification, stromal morphology, and associated lesion.

Immunohistochemistry. The formalin-fixed, paraffin-embedded slices were deparaffinized and rehydrated with xylene and alcohol solutions. Immunostaining was performed using automatic immunostaining instruments [Ventana Benchmark XT automated staining system (Ventana Medical Systems) or Dako Omnis (Dako, Agilent Technologies, Carpinteria, CA, USA)] according to the manufacturer's recommendations (16-22). Antigen retrieval was performed using Cell Conditioning Solution (Ventana Medical Systems) or EnVision FLEX Target Retrieval Solution, High pH (Dako). The slices were incubated with primary antibodies against calretinin (polyclonal, 1:100; Cell Marque, Rocklin, CA, USA), cytokeratin 5/cytokeratin 6 (CK5/6; clone D5/16 B4, 1:200, Dako), CK7 (clone OV-TL 12/30, 1:100; Dako), D2-40 (clone D2-40, 1:50, Dako), epithelial membrane antigen (EMA; clone E29, 1:200; Dako), Ki-67 (clone MB-1, 1:150; Dako), p53 (clone DO7, 1:300; Novocastra, Leica Biosystems, Newcastle Ltd., Newcastle upon Tyne, UK), paired box 8 (PAX8; polyclonal, 1:50; Cell Marque), and Wilms' tumor 1 (WT1; clone 6F-H2, 1:200; Cell Marque). After chromogenic visualization using an ultraView Universal DAB Detection Kit (Ventana Medical Systems) or EnVision FLEX /HRP (Dako), slices were counterstained with hematoxylin. Appropriate positive controls were stained concurrently to validate the staining method. Negative controls were prepared by substituting nonimmune serum for the primary antibody. No staining was detected in the negative controls.

For calretinin immunostaining, staining with a moderate-to-strong intensity in the cytoplasm was interpreted as positive expression. For CK5/6, CK7, D2-40, and EMA immunostaining, staining with a moderate-to-strong intensity in the cell membrane was interpreted as positive expression. For PAX8 and WT1 immunostaining, staining with a moderate-to-strong intensity in the nuclei was interpreted as positive expression. p53 immunostaining was interpreted as mutation pattern (all or no nuclear staining) or wild-type pattern (weak-to-moderate and patchy nuclear staining) (22-25). Positive staining was considered diffuse when at least 50% of tumor cells were immunoreactive and focal when fewer than 50% of the cells were stained.

Results

Representative case presentation. A 65-year-old Korean woman presented with abdominal discomfort. She had a history of antihypertensive medication for 8 years and sparganosis of the breast 3 years previously. Abdominopelvic computed tomographic scan revealed a huge pelvic mass, measuring 13.0 cm along the greatest dimension. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed on the clinical impression of large uterine leiomyoma. Intraoperatively, multiloculated cystic masses filled with serous fluid were observed. There were also small, multiple nodules involving the surfaces of the masses. Histologically, the cystic masses consisted of multiple peritoneal inclusion cysts (Figure 1A). On their surfaces, multiple WDPMs displayed typical papillary architecture containing fibrovascular cores (Figure 1B). The greatest dimension of papillae ranged from 0.1 to 0.5 cm. Also noted were some areas showing tubuloglandular (Figure 1C) or adenomatoid tumor-like (Figure 1D) growth pattern and a transition between peritoneal inclusion cyst and WDPM (Figure 1E). The mesothelial cells lining the papillary architectures were cuboidal in shape. Although the majority of the lining cells possessed bland-looking nuclei, mild nuclear atypia and conspicuous nucleoli were identified in areas exhibiting higher cellularity or more complex papillary architectures (Figure 1F). No mitotic figure was observed. The stroma consisted of fibrous connective tissue with focal edematous and myxoid change (Figure 1G). No stromal invasion was seen. In one case, there were some areas of mixed inflammatory infiltrate in the stroma (Figure 1H). Immunostaining revealed that the mesothelial cells lining the papillary architectures were positive for WT1, D2-40, CK7, and PAX8, but negative for CK5/6. EMA expression was very weak and focal. Ki-67 labeling index was approximately 3-4%. In addition to the peritoneal inclusion cysts and WDPMs, the hysterectomy specimen showed incidental atypical hyperplasia/endometrioid intraepithelial neoplasia in the endometrium and small, multiple leiomyomas in the myometrium. The patient's postoperative course was uneventful without any complication. Currently, there is no clinical or radiological evidence of tumor recurrence at 6 months postoperatively.

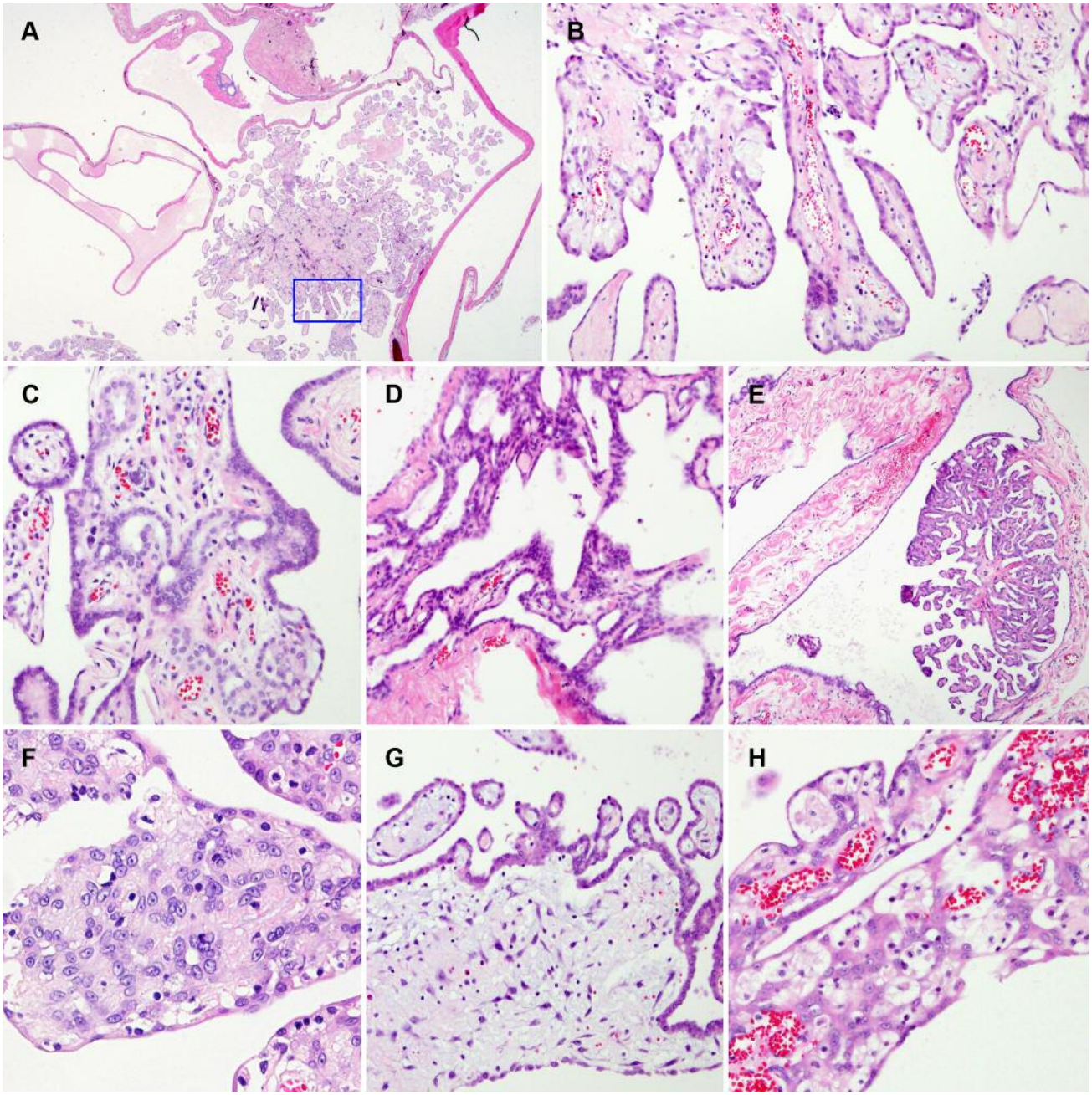

Figure 1. *Histopathological findings of the representative case described in the text. A: Overview of well-differentiated papillary mesothelioma (WDPM) in the peritoneum associated with peritoneal inclusion cyst. B: Higher magnification of the area highlighted in A, showing typical papillary architectures with fibrovascular cores. C: Areas showing tubuloglandular pattern. D: Areas showing adenomatoid tumor-like features. E: A transition between WDPM and the lining epithelium of peritoneal inclusion cyst. F: Mild nuclear atypia with conspicuous nucleoli. G: Myxoid stroma and mild inflammatory infiltrate. H: Mixed infiltration of acute and chronic inflammatory cells. Hematoxylin and eosin stain. Original magnification: A: 12.5×; B-D: 100×; E: 40×; F: 200×; G: 100×; H: 200×.*

Clinical characteristics of 12 WDPM cases. Eleven additional WDPM cases were diagnosed at our Institution between January 2005 and September 2018. Table I summarizes the clinical characteristics of 12 cases of peritoneal WDPM. The patients' ages ranged from 23 to 75 years (median=64 years). Seven (58.3%) patients were women, and the remaining five (41.7%) were men. None (0/12, 0%) of the patients had a previous history of asbestos exposure. None (0/7, 0%) of the

Table I. *Clinical characteristics of well-differentiated papillary mesothelioma of the peritoneum.*

Case	Gender	Age (years)	Location	Size (cm)	Multiplicity	Clinical presentation	Endometriosis	Asbestos exposure	Recurrence
1	Woman	62	Peritoneum	0.4	No	Incidental finding during surgery for cecal carcinoma	No	No	No
2	Woman	66	Peritoneum	0.4	No	Incidental finding during surgery for uterine leiomyoma	No	No	No
3	Man	53	Omentum	0.3-0.5	Yes	Incidental finding during surgery for hepatocellular carcinoma	Not applicable	No	No
4	Woman	23	Omentum	3.0	No	Incidental 3.0-cm-sized mass on computed tomographic scan	No	No	No
5	Woman	52	Omentum	0.3	No	Incidental finding during surgery for gastric GIST	No	No	No
6	Woman	75	Pelvic peritoneum	0.7	No	Incidental finding during surgery for uterine cervical carcinoma	No	No	No
7	Man	63	Omentum	0.5	No	Incidental finding during surgery for common bile duct carcinoma	Not applicable	No	No
8	Man	74	Peritoneum	0.3	No	Incidental finding during surgery for gastric carcinoma	Not applicable	No	No
9	Man	74	Peritoneum	0.1-0.2	Yes	Incidental finding during surgery for gastric carcinoma	Not applicable	No	No
10	Man	46	Peritoneum	0.4	No	Incidental finding during surgery for hepatocellular carcinoma	Not applicable	No	No
11	Woman	71	Peritoneum	0.5	No	Incidental finding during surgery for colorectal carcinoma	No	No	No
12	Woman	65	Pelvic peritoneum	0.1-0.5	Yes	Abdominal discomfort and a 13.0-cm-sized mass on computed tomographic scan	No	No	No

GIST: Gastrointestinal stromal tumor.

women had endometriosis. In all 12 cases, the tumors involved the abdominal or pelvic peritoneum. In 10 (83.3%) cases, the tumors were incidentally detected during surgery for other causes: two cases with gastric carcinoma, two with colorectal carcinoma, two with hepatocellular carcinoma, one with common bile duct carcinoma, one with uterine cervical carcinoma, one with gastric gastrointestinal stromal tumor (GIST), and one case with uterine leiomyoma. The remaining two (16.7%) patients underwent surgery for WDPMs that were suspected preoperatively as small intestinal GIST (3.0 cm) and uterine leiomyoma (13.0 cm), respectively; they were diagnosed as having WDPMs postoperatively. The size of WDPM ranged from 0.1 to 3.0 cm. Most of the tumors appeared as a small nodule on the peritoneal surface, measuring less than 1.0 cm along the greatest dimension. Nine (75.0%) tumors presented as a single mass, whereas in the remaining three (25.0%) cases, WDPM presented as multiple nodules on the peritoneal surface. Two WDPMs, the one initially presenting as a small intestinal GIST and the other case associated with multiple peritoneal inclusion cysts, had intratumoral cystic component. These tumors appeared larger than the other tumors in imaging studies. All but one patient had no symptoms; the only patient whose tumor was associated with multiple peritoneal inclusion cysts complained of abdominal discomfort.

Pathological characteristics of 12 WDPM cases. Table II summarizes the pathological characteristics of 12 WDPM cases. Histologically, all (12/12, 100.0%) cases demonstrated typical papillary architectures (Figure 2A) with fibrovascular cores lined by bland-looking mesothelial cells (Figure 2B). No submesothelial stromal invasion was identified in any case. In three (25.0%) cases, focal tubuloglandular growth pattern was noted in the stroma (Figure 2C), but no desmoplastic stromal reaction was associated. The mesothelial cells lining the papillae or tubuloglandular lumina consisted mostly of single row of cells, although some areas of proliferation to multiple layers were observed in a few cases (Figure 2D). Mesothelial cells were predominantly cuboidal in shape. Four (33.3%) tumors exhibited columnar cells with subnuclear vacuoles, and seven (58.3%) had hyalinized stroma lined by attenuated mesothelial cells (Figure 2E). The nuclei of the mesothelial cells appeared bland, with generally rounded ends and an even chromatin distribution. Nuclear membranes were smooth, and no hyperchromasia was noted. Two (16.7%) cases exhibited a few areas with mild nuclear atypia and variation in cell size (Figure 2F). There was no mitotic figure in the mesothelial cells. The stroma consisted predominantly of fibrous connective tissue, but relatively edematous, hypocellular foci were often observed in 10 (83.3%) cases

Table II. *Pathological characteristics of well-differentiated papillary mesothelioma of the peritoneum.*

Case	Architectural pattern	Cell type	Nuclear atypia	Mitosis	Conspicuous nucleoli	Psammomatous calcification	Stroma	Associated lesion
1	Papillary	Cuboidal, columnar	No	No	No	No	Fibrous (mostly), edematous (partially)	No
2	Papillary	Flat (mostly), cuboidal (partially)	No	No	No	No	Fibrous (mostly), myxoid (partially)	No
3	Papillary	Cuboidal, flat	No	No	No	No	Fibrous (mostly), edematous (partially)	No
4	Papillary, tubuloglandular	Cuboidal, columnar	Mild	No	No	No	Fibrous (mostly), edematous, inflammatory (partially)	No
5	Papillary	Cuboidal, columnar	No	No	No	No	Fibrous (mostly), edematous (partially)	No
6	Papillary (mostly), tubuloglandular (partially)	Cuboidal, columnar	No	No	No	No	Fibrous (mostly), myxoid, edematous (partially)	No
7	Papillary	Cuboidal (mostly), flat (partially)	No	No	No	No	Fibrous (mostly), myxoid, edematous (partially)	No
8	Papillary	Cuboidal (mostly), flat (partially)	No	No	No	No	Fibrous (mostly), edematous (partially)	No
9	Papillary	Flat (mostly), cuboidal (partially)	No	No	No	No	Fibrous	No
10	Papillary	Cuboidal (mostly), flat (partially)	No	No	No	No	Fibrous (mostly), no edematous (partially)	
11	Papillary	Cuboidal, flat	No	No	No	No	Fibrous (mostly), myxoid, edematous (partially)	No
12	Papillary (mostly), tubuloglandular (partially)	Cuboidal	Mild	No	Focal	No	Fibrous (mostly), myxoid, edematous, inflammatory (partially)	Multiple peritoneal inclusion cysts

Table III. *Immunostaining results of well-differentiated papillary mesothelioma of the peritoneum.*

Expression status	Cytokeratin 5/6	D2-40	Wilms' tumor 1	Cytokeratin 7	Calretinin	Paired box 8	Epithelial membrane antigen
Diffusely positive	9/12 (75.0%)	8/8 (100.0%)	7/10 (70.0%)	4/4 (100.0%)	3/3 (100.0%)	2/7 (28.6%)	0/2 (0%)
Focally positive	2/12 (16.7%)	0/8 (0%)	2/10 (20.0%)	0/4 (0%)	0/3 (0%)	0/7 (0%)	2/2 (100.0%)
Negative	1/12 (8.3%)	0/8 (0%)	1/10 (10.0%)	0/4 (0%)	0/3 (0%)	5/7 (71.4%)	0/2 (0%)

(Figure 2G). Five (41.7%) cases demonstrated myxoid change in the stroma (Figure 2H).

Immunostaining results of 12 WDPM cases. Table III summarizes the immunostaining results. The number of cases examined using the different antibodies varied. All eight cases examined for D2-40 showed diffuse and strong, membranous immunoreactivity (Figure 3A). Out of the 12 cases examined, 11 (91.7%) cases showed membranous CK5/6 immunopositivity (Figure 3B), nine with diffuse and strong expression, and the remaining two with focal and weak expression. All four cases examined for CK7 expression showed diffuse and strong staining in the membrane (Figure 3C). Seven out of 10 tumors were diffusely positive for WT1 (Figure 3D), and two tumors displayed focal and weak staining. Both cases assessed for EMA demonstrated focal and very weak expression (Figure 3E). Ki-67 labeling index was less than 1% in most (9/12, 75.0%) cases (Figure 3F). Two WDPMs showed strong nuclear immunoreactivity for PAX8 (case 4 and 13; Figure 3G); in both cases, adjacent peritoneal lining mesothelial cells also reacted for PAX8.

Discussion

In this study, we comprehensively analyzed the clinicopathological characteristics of 12 peritoneal WDPM cases diagnosed at a single institution. The patients were aged 23-75 years. The age range was similar to that recorded in

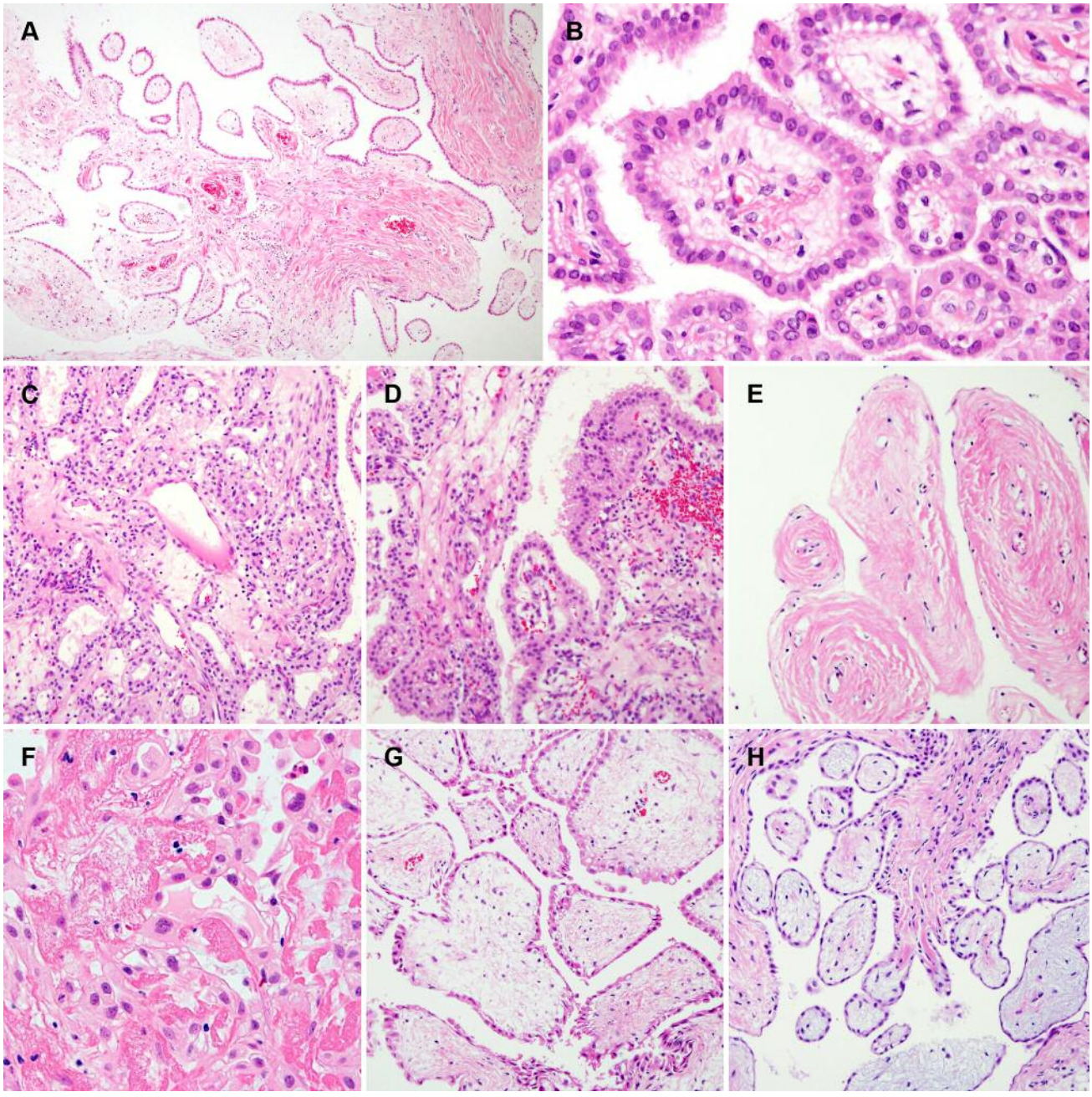

Figure 2. *Histopathological findings of well-differentiated papillary mesothelioma of the peritoneum. A: Papillary architectures containing fibrovascular stromal cores. B: Single-layered, cuboidal mesothelial cells without significant nuclear atypia. C: Tubuloglandular growth pattern. D: Multilayered mesothelial cell proliferation. E: Densely hyalinized stromal cores lined by flattened mesothelial cells. F: Areas showing mild nuclear atypia, conspicuous nucleoli, nuclear membrane irregularities, and slight variation in nuclear size. G: Edematous stroma. H: Fibrous and myxoid stroma. Hematoxylin and eosin staining. Original magnification: A: 40×; B: 200×; C-E: 100×; F: 200×; G, H: 100×.*

previous studies (12, 15, 26). WDPM is known to frequently occur in the peritoneum of young women (14). However, we did not observe any predilection for women. Given that our case series consisted only of WDPMs arising from the peritoneum and did not include those of the pleura or *tunica vaginalis* origin, the incidence of WDPM in men might have been underestimated. Although a few previous studies have suggested the possible association of WDPM with endometriosis (10), seven women had no evidence of peritoneal endometriosis. None of the patients had a history

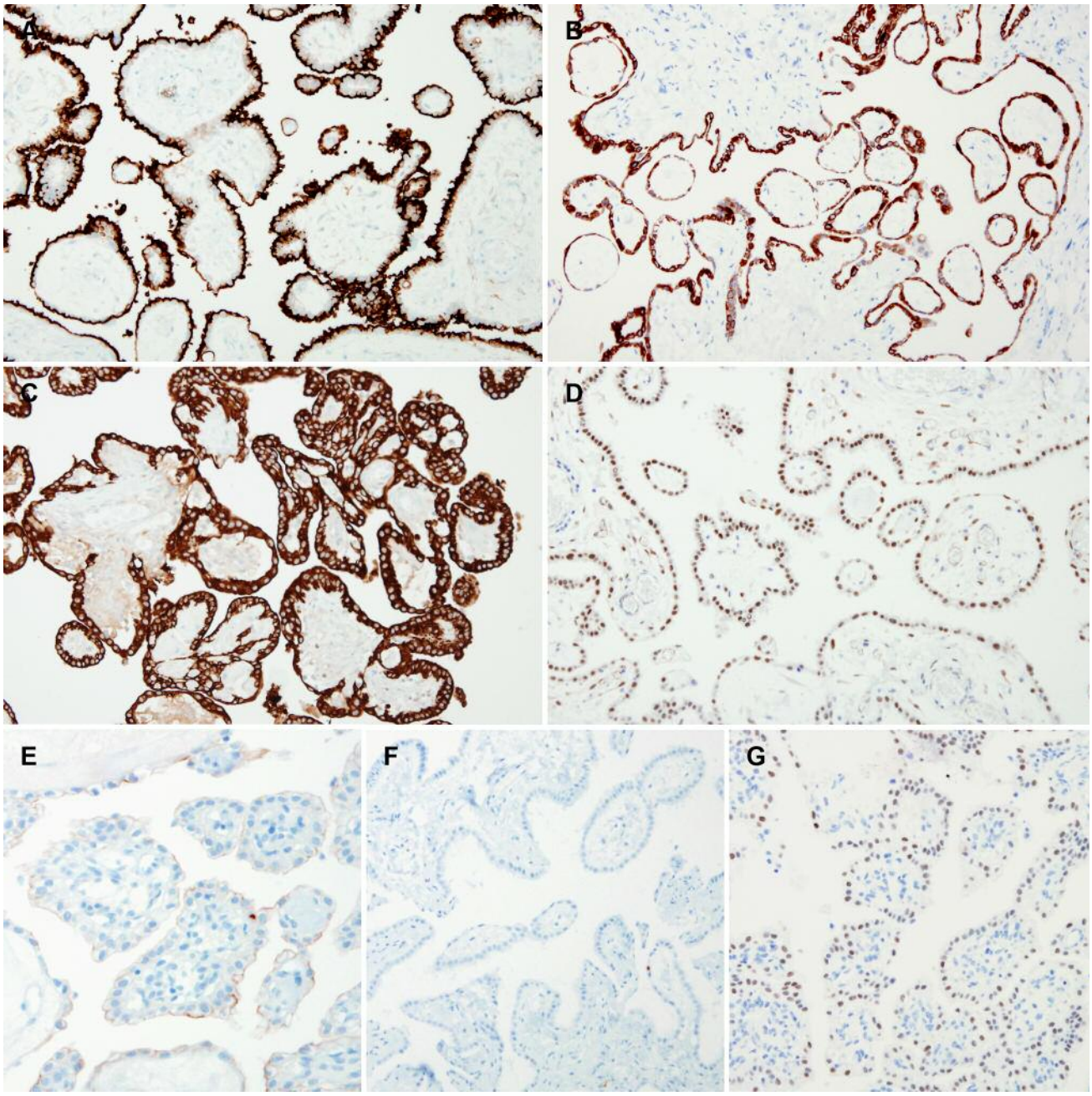

Figure 3. *Immunohistochemical staining results of well-differentiated papillary mesothelioma of the peritoneum. A–C: Strong membranous immunoreactivities for D2-40 (A), cytokeratin 5/6 (B) and cytokeratin 7 (C). D: Strong nuclear immunoreactivity for Wilms' tumor 1. E: Focal and faint membranous immunoreactivity for epithelial membrane antigen. F: Low (less than 1%) Ki-67 labeling index. G: Strong nuclear expression for paired box 8. Polymer method. Original magnification: A-D: 100×; E: 200×; F, G, 100×.*

of asbestos exposure; this finding is further supported by the fact that our case series did not include pleural WDPM, which is more likely to be associated with asbestos exposure (27). Similarly to a previous study (12), most tumors were detected incidentally as small, single, or multiple nodules during surgery for a wide variety of unrelated diseases. All but one patient did not have any symptoms. In fact, in the only patient who complained of abdominal discomfort, it is likely that the multiple peritoneal inclusion cysts rather than WDPM itself caused the symptom, given that the major portion of the mass

consisted of multiple peritoneal inclusion cysts. All the patients examined are currently well without postoperative recurrence, reflecting the indolent nature of the tumor.

Histologically, all tumors exhibited well-developed papillary structures lined by bland-looking mesothelial cells, a feature characteristic of WDPM. Even though the mesothelial cells were mostly single layered, in a few cases, focal multilayering and mild nuclear atypia were observed in areas with higher cellularity or more complex papillary architecture. However, these findings imply a reactive change rather than aggressive biological behavior because moderate-to-severe nuclear pleomorphism, mitotic figure, and stromal invasion were not identified in any case examined. In addition to papillary structures, three tumors showed focal tubuloglandular growth pattern. These were larger than the other tumors, ranging from 0.7-3.0 cm along the greatest dimension.

A few previous studies have reported composite tumors consisting of WDPM and peritoneal inclusion cyst or adenomatoid tumor (15, 26, 28). Malpica *et al*. reported a case of WDPM associated with peritoneal inclusion cyst (15). Chen *et al*. also reported three cases of WDPM with intimate association with multiple cystic mesothelioma (14). In the most recent of our case series, WDPM coexisted with multiple peritoneal inclusion cysts. The transition between WDPM and peritoneal inclusion cysts was noted, and PAX8 expression was positive for both lesions, raising the possibility that WDPM is closely linked with multiple peritoneal inclusion cyst and shares common histogenesis during development. Focal adenomatoid tumor-like foci were even observed in this case. However, the adenomatoid tumor-like component was very focal and contiguous with the typical WDPM component. Therefore, it is considered the result of complex invagination of tubuloglandular architecture rather than representing the true composite features of WDPM and adenomatoid tumor.

Immunohistochemical staining revealed that WDPMs were positive for D2-40 (100.0%), CK5/6 (91.7%), CK7 (100.0%), WT1 (90.0%), and calretinin (100.0%). EMA immunoreactivity was observed in both examined cases, and the expression was very focal and considerably weaker than that of malignant epithelioid mesothelioma, which uniformly expresses EMA (29). Xing *et al*. reported PAX8 expression in 20 (60.6%) out of 33 WDPMs examined (30). In contrast, we observed PAX8 immunoreactivity in two (28.6%) out of the seven cases examined. Interestingly, both tumors with positive PAX8 expression demonstrated a more complex papillary architecture and were larger than the other tumors. PAX8 is a member of the paired box family of transcription factors, which is essential to the development of the Wolffian duct and the Mullerian system (31). Based on our observation, we raise the possibility that PAX8-positive WDPMs have a different pathogenesis from PAX8-negative WDPMs. However, a comparative genetic analysis is necessary to reach a firm conclusion on the association of PAX8 expression and WDPM development.

The differential diagnoses of WDPM include reactive mesothelial hyperplasia and malignant mesothelioma (15). Even though both WDPM and reactive mesothelial hyperplasia can show papillary structures, tubuloglandular formation, lack of stromal invasion, and uniform simple papillae lined by a single layer of mesothelial cells, reactive mesothelial hyperplasia is usually associated with diffuse and moderate-to-severe mixed inflammatory infiltrate in the submesothelial connective tissue. In this study, only one case showed patchy mixed inflammatory infiltrate. Endometriosis, which is also usually associated with reactive mesothelial hyperplasia (32), was not identified in our case series. The major diagnostic challenge lies in the distinction of WDPM from malignant mesothelioma. Thorough sampling is necessary to ensure that there is no evidence of stromal invasion. Additionally, bulky tumor masses with the presence of stromal invasion, severe nuclear pleomorphism, and frequent mitotic figures should warrant the diagnosis of malignant mesothelioma (1-3). In fact, Churg *et al*. reported 13 cases of peritoneal WDPM with invasive foci (13). They stated that the invasive patterns ranged from simple, bland-appearing glands invading the stalks of the papillae to solid foci of invasive tumor of higher nuclear grade than that of the original WDPM. However, based on a tendency for multifocality and recurrence, these lesions should be separated from typical WDPM and considered a distinct clinical entity. The authors suggested that these lesions be called WDPM with invasive foci to alert clinicians to the possibility of recurrence (13). In difficult cases, immunostaining can be helpful. Malignant mesothelioma is positive for EMA and negative for epithelial cell adhesion molecule (1), whereas WDPM is negative for EMA (15, 26).

In summary, we demonstrated the clinicopathological characteristics of WDPM with peritoneal origin. All WDPM cases demonstrated typical papillary structures lined by single or multilayered, bland-appearing mesothelial cells without evidence of nuclear atypia or stromal invasion. WDPM is a rare mesothelial tumor and its biological behavior is still uncertain. Therefore, although all cases examined were uneventful after surgery, further surveillance is recommended for patients.

Conflicts of Interest

None of the Authors have any conflicts of interest to declare regarding this study.

Authors' Contributions

All Authors were responsible for substantial contributions to the conception and design of the study, acquisition of data, analysis and

interpretation of the data, as well as drafting the manuscript, revising the manuscript critically for important intellectual content, and providing final approval of the version to be published.

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