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Case report

Well-differentiated papillary mesothelioma of the peritoneum: a borderline mesothelioma

Report of two cases and review of literature

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Summary. Well-differentiated papillary mesothelioma (WDPM) is considered to be a distinct subtype of peritoneal mesothelioma. Although the WDPM is usually qualified as benign, the natural history of this lesion has not been clearly established. This report relates to two WDPMs which were found incidentally. In a 51-year-old man the WDPM developed over a period of 5 years into a typically malignant diffuse mesothelioma. Thus, although the WDPM morphologically lacks signs of malignancy, it should be regarded as a borderline mesothelioma.

Key words: Mesothelioma – Pathology – Ultrastructure – Peritoneum

Introduction

The well-differentiated papillary mesothelioma (WDPM) has been recorded as a rare but distinct entity in the AFIP fascicle of tumours of serous surfaces (McCaughey et al. 1985). The WDPMs reported to date (Babera and Rubino 1957; Foyle et al. 1981; Goepel 1981; Hanrahan 1963; McCaughey 1985; McCaughey et al. 1985; Rhind and Wright 1939; Roggli et al. 1987; Wells 1935) usually had a benign clinical course, but long-term follow-up was performed in only a few cases (Foyle et al. 1981; Goepel 1981; McCaughey 1985; Roggli et al. 1987). We report a case of WDPM with malignant behaviour that exhibited histological and cytological patterns suggestive of a benign mesothelial tumour at the time of its incidental discovery. Furthermore, the ultrastructural, histochemical and immunocytochemical findings of two WDPMs are presented.

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Case reports

Case 1

Several small grey papules were found on the omentum and the parietal peritoneum in a 53-year-old man during the resection of an aneurysm of the abdominal aorta. A series of biopsies were taken for frozen sections.

Under the light microscope, the lesions presented a characteristic WDPM with multiple, rather coarse papillae lined by a single layer of flat to cuboidal cells (Fig. 1). A slight cellular atypia was seen with single hyperchromatic nuclei which were even increased in size (Fig. 1). In some areas the cytoplasm contains granular PAS-positive substances, which were were not found after treatment with diastase. After staining with alcian blue (pH 2.5) the apical cytoplasmic membranes were outlined, but this was not resistant to hyaluronidase.

Under the electron microscope, the plump coarse papillae were covered with polygonal cells which have multiple slender microvilli.

Case 2

During a laparotomy for of a sliding hernia with torsion of the stomach, multiple whitish-grey papules were found on the surface of the omentum and the parietal layer of the peritoneum in a 51-year-old otherwise healthy man. A series of biopsy specimens were taken.

Under the light microscope, the lesions presented likewise a characteristic WDPM (Fig. 2). In contrast to the above-mentioned case 1, however, no signs of atypia were recorded.

One and 2 years later, abdominal paracentesis was performed because of recurrent ascites. The aspirated viscid fluid contained numerous single or clustered cells and some of these demonstrated moderate signs of atypia.

The patient died 5 years after the diagnosis of WDPM. At autopsy, the viscera were encased by nodular and diffuse tumour proliferations, resulting in complete obliteration of the peritoneal cavity (Fig. 3). The tumour extended to the left side of the diaphragm and had invaded the adjacent pericardium. A final massive embolism of tumour cell masses to the pulmonary arteries, disturbances of the small and large bowel and cachexia contributed to the patient's death. The tumour cell embolism was attributable to an extensive invasion into veins of the retroperitoneum and the anterior abdominal wall.

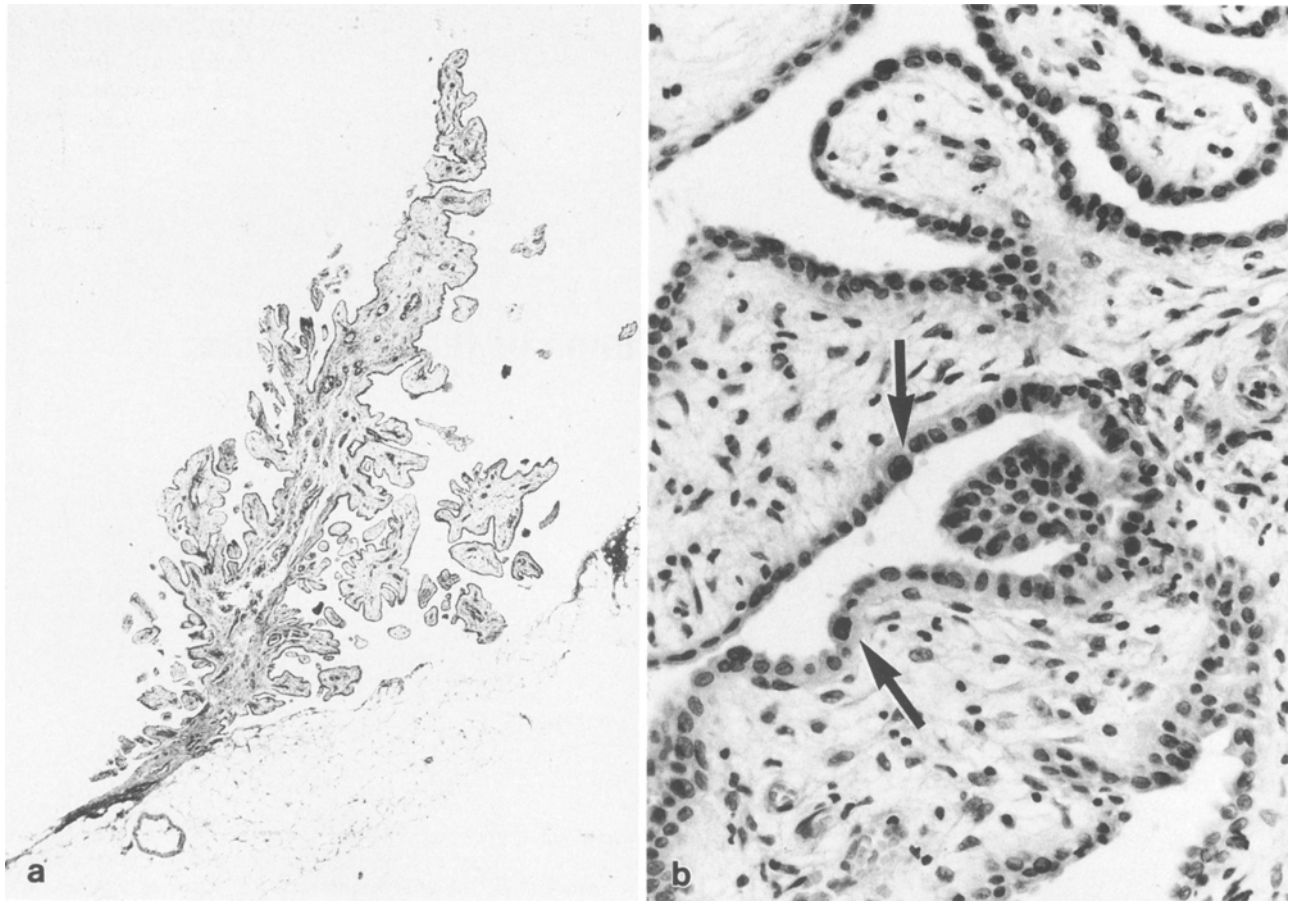
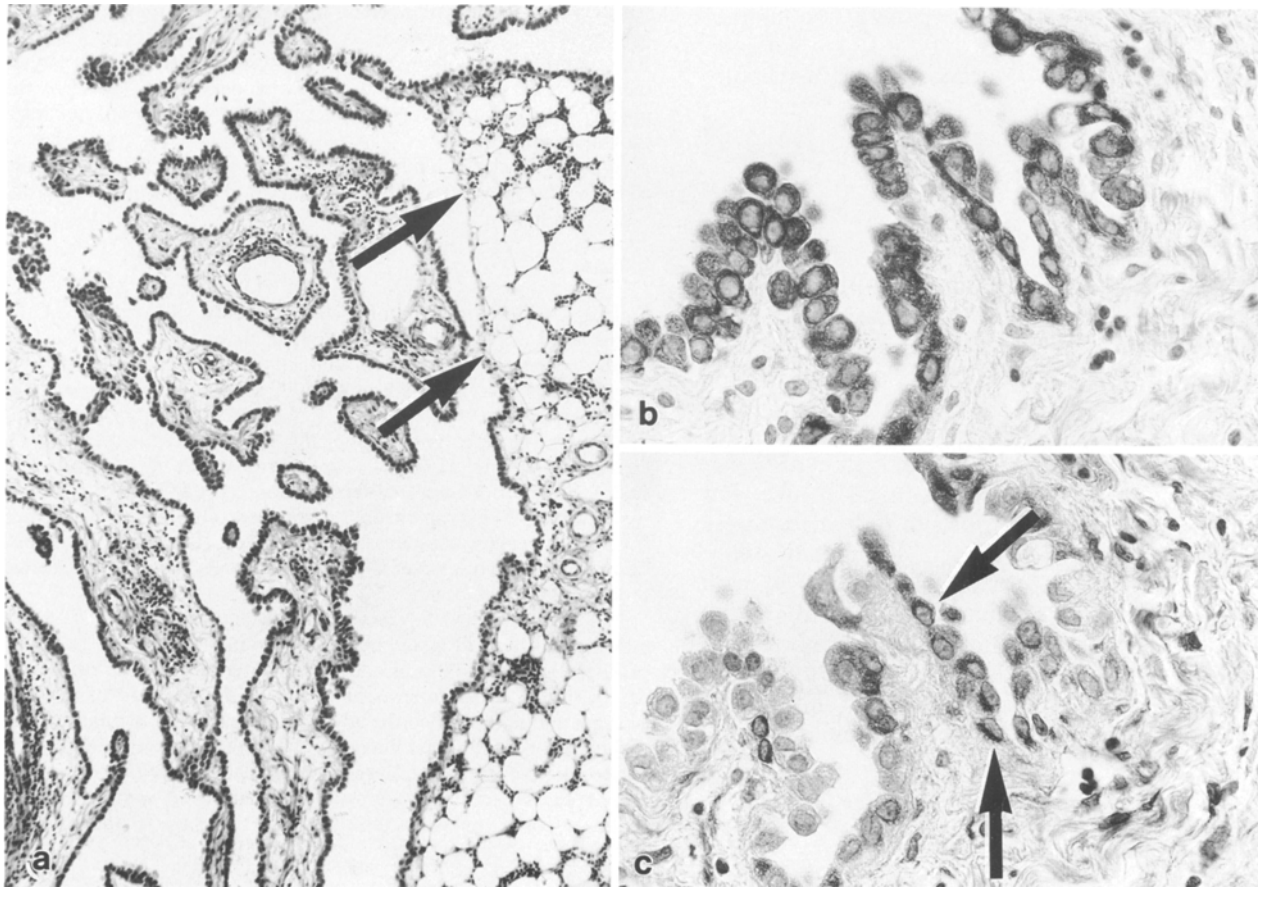


Fig. 1. a Well-differentiated papillary mesothelioma (WDPM) of the peritoneum (case 1) with coarse and slender papillae. H & E, ×18. **b** Coarse papillae lined by mesothelial cells with slight anisonucleosis and hyperchromatic nuclei in places (*arrows*). H & E, ×180



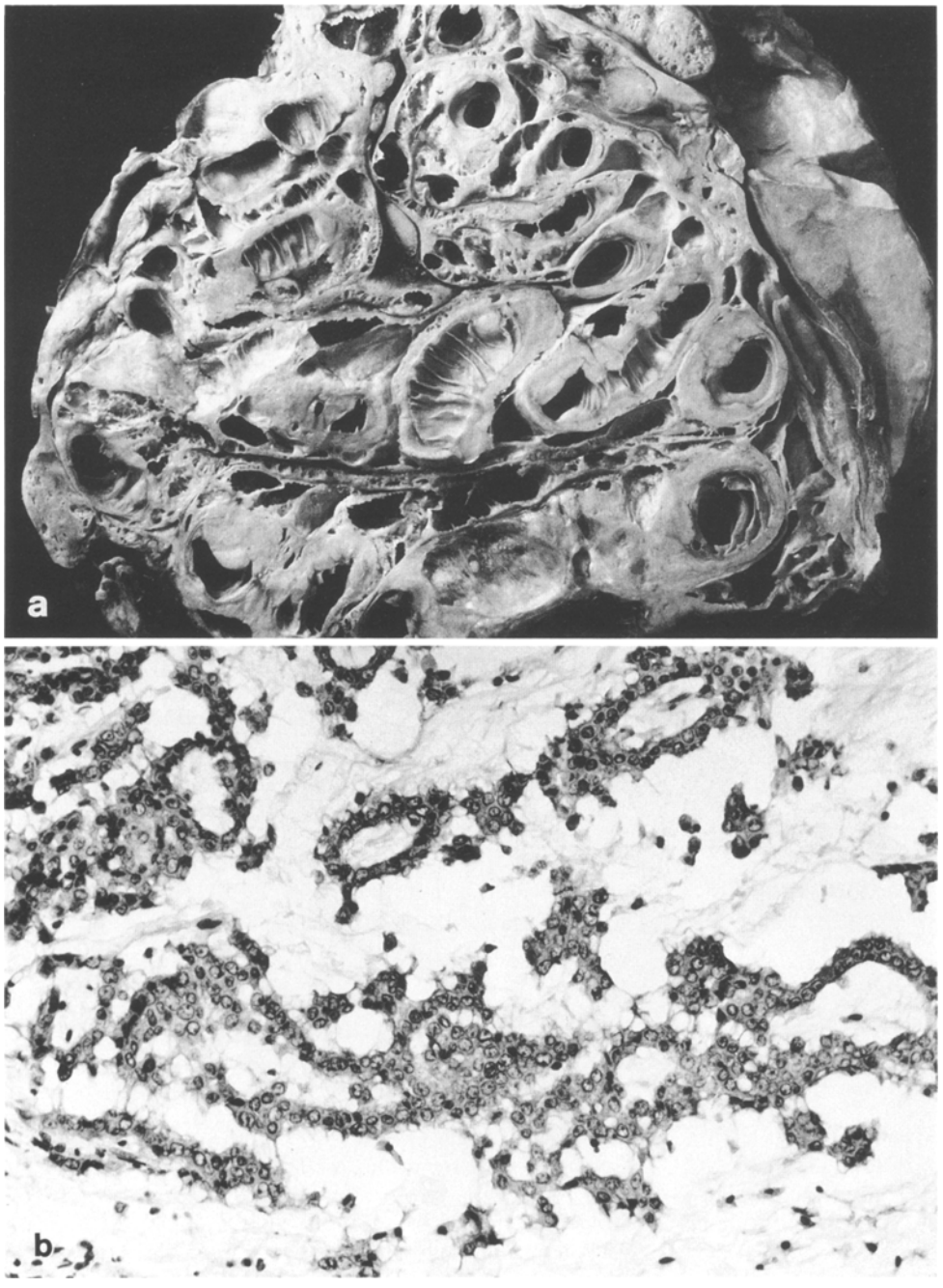


Fig. 3. a Frontal section through the abdominal viscera showing extensive encasement of the small bowel by masses of the malignant diffuse mesothelioma. **b** Small, solid nests and tubular proliferations of the malignant diffuse mesothelioma of epithelial type, demonstrating moderate nuclear atypia. H & E, ×160

Histologically, the tumour was composed of tubular and tubulo-papillary proliferations consistent with a malignant diffuse mesothelioma (MDM) of epithelial type (Fig. 3). In comparison with the initial WDPM there was a manifest change in the histological patterns and signs of atypia were frequently recorded. All morphological findings relating to the WDPM and the MDM, including immunocytochemistry and transmission electron microscopy, are summarized in Table 1.

No asbestos bodies could be identified in the lung tissue by means of microfiltration after chemical digestion (Bignon et al. 1974).

Fig. 2. a Well-differentiated papillary mesothelioma of the peritoneum (case 2) which evolved into a typical malignant mesothelioma (compare with Fig. 1). Small area with flattened surface cells, probably non-neoplastic mesothelial cells (*arrows*). H & E, ×85. **b**, **c** Surface cellular lining of WDPM expressing both cytokeratin (**b**) and vimentin (**c**, *arrows*) as seen in adjacent sections. Indirect immunoperoxidase, hemalaun counterstain, ×350

Discussion

The WDPM is a rare type of peritoneal mesothelioma which has not been described in the pleural cavity. Typically, it is an incidental finding in the peritoneum of females (Foyle et al. 1981; Goepel 1981; McCaughey 1985; McCaughey et al. 1985), although the patient may

Table 1. Morphological characteristics of a well-differentiated papillary mesothelioma that developed into a malignant diffuse mesothelioma of epithelial type over a period of 5 years

	Well-differentiated papillary mesothelioma	Malignant diffuse mesothelioma
Pattern	Coarse papillae	Tubulo-papillary
Nuclear area[a] ($n=50$; $\bar{x}\pm SD$)	$318\pm91\ \mu m^2$ $P\leq0.001$	$405\pm129\ \mu m^2$ $P\leq0.001$
Nuclear atypia	No	Moderate
Immunocytochemistry		
HEA 125[b-d], CEA[c, e]	–	–
EMA[c, f]	Focal	Intense
Cytokeratin[c, g]	+	+
Vimentin[c, h]	Focal	–
Electron microscopy[i]	Tonofilaments, desmosomes, moderate quantity of perinuclear arranged organelles, slender long microvilli	Prominent intermediate filaments, prominent rough endoplasmatic reticulum, other organelles scarce, short plump microvilli

[a] Measured with a Kontron MOP-Videoplan
[b] See Möller et al. (1986)
[c] Indirect immunoperoxidase
[d] Human epithelial antigen 125 (source: Camon, Wiesbaden, FRG)
[e] Carcinoma embryonal antigen (source: Behring, Marburg, FRG)
[f] Epithelial membrane antigen (source: Dakopatts, Copenhagen, Denmark)
[g] Cytokeratin (source: Dakopatts, Copenhagen, Denmark)
[h] Vimentin (source: Dakopatts, Copenhagen, Denmark)
[i] See Bürrig (1988) for methods

Table 2. Review of reported cases of well-differentiated papillary mesothelioma of the peritoneum

Author(s)	Sex	Follow-up (years)	Comment
Wells	M	–	Post-mortem finding
Rhind and Wright	M	2	Alive
Babera and Rubino	M	1	Alive
Hanrahan	F	5	Alive
Foyle et al.	F	1	Alive
	F	29	Deceased, tubulo-papillary MDM, psammoma bodies
	F	1	Alive
	F	–	–
	F	7	Deceased, no details reported
	F	14	Alive
Goepel	M	6	Alive
	F	10	Alive
	M	6	Alive
	F	1	Alive
	M	–	–
	F	1	Deceased, breast cancer, no necropsy
McCaughey	F	29	Alive
Roggli et al.	–	13	Recurrent well-differentiated papillary mesothelioma after 11 years
Reported case 1	M	0.5	Alive
Reported case 2	M	5	Deceased, tubulo-papillary MDM

MDM, Malignant diffuse mesothelioma

present with abdominal pain or ascites. None of the reported tumours have been asbestos related. They are generally grey to white, firm, single or multiple papillary lesions which usually involve the peritoneum of the omentum, mesentery, or stomach (Foyle et al. 1981; Goepel 1981).

Under the light microscope, the WDPM exhibits a characteristically uniform, papillary pattern. The papillae are often coarse or branching and are covered by a single layer of uniform mesothelial cells (McCaughey et al. 1985) that closely resemble reactive non-neoplastic mesothelium and lack any signs of cellular atypia. As with reactive mesothelial hyperplasia or MDM (Blobel et al. 1985; Bolen et al. 1986), the cells of WDPM possess a complex cytoskeleton of intermediate filaments, including both cytokeratin and vimentin. Furthermore, the profiles of other immunocytochemical and histochemical markers are consistent with a mesothelioma (Table 1).

In the peritoneal cavity of women, differentiation of papillary mesothelioma from papillary serous carcinoma – originating from either the ovary or the peritoneum itself (McCaughey et al. 1985) – may be difficult, especially because some WDPMs have reportedly been associated with psammoma bodies (Foyle et al. 1981). However, through immunocytochemistry antibodies such as human epithelial antigen (HEA 125) or carcinoembryonal antigen or Leu M1 (Bollinger et al. 1989; Möller et al. 1986; Pfaltz et al. 1987) provide useful markers for differentiating between tumours of mesothelial or epithelial nature.

The WDPM clearly differs from the classical diffuse peritoneal mesothelioma by having a rather good prognosis. The solitary tumours appear to be uniformly benign; even multifocal tumours are reported to follow a benign course for up to 28 years (McCaughey 1985). However, only a small number of cases with complete follow-up have been reported in the literature (Table 2). The present cases reported met all morphological criteria for a WDPM; nevertheless, one of these has had a slow but malignant course and progressed into a typical MDM. Malignant mesotheliomas resembling mesothelial hyperplasia at their initial phase have also been reported from the pleural cavity (Hellström et al. 1977;

Klima and Györkey 1977). Thus, in cases of WDPM, pathologists should be aware of the probably biological borderline behaviour of such morphologically benign-looking tumours.

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Note added in proof

Since this paper was submitted, a clinicopathological study of WDPM has been published by Daya and McCaughey (Cancer 65:292–296, 1990) which adds 13 new cases with follow-up information to those previously reported. Two patients in this series died, 2 and 7 years after the diagnosis of WDPM, under circumstances that may be related to the effects of the tumour. However, autopsy was not performed in these cases.