Well-differentiated papillary mesothelioma complicating endometrial carcinoma: A case report

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Summary

We present a case of well-differentiated papillary mesothelioma discovered during staging surgery for endometrial carcinoma in a 50-year-old postmenopausal woman.

In case of simultaneous well-differentiated papillary mesothelioma (WDPM) and endometrial carcinoma, the surgeon may be mistaken by considering peritoneal implants as tumor metastasis. This situation may result in overtreatment of the patient. Thus a thorough pathologic examination of the specimens taking care not to miss any areas of invasion, and utilizing immunohistochemical analysis when necessary are important to avoid such mistakes. To our knowledge this is the first report of the simultaneous occurrence of endometrial carcinoma in conjunction with diffuse WDPM of the peritoneum.

Key words: Well-differentiated papillary mesothelioma; Endometrial carcinoma.

Introduction

Mesotheliomas originating from the peritoneal surface of the abdomen are rare neoplasms, which account for approximately one-third of all mesotheliomas [1]. Well-differentiated papillary mesothelioma (WDPM) constitutes less than half of peritoneal mesotheliomas. The macroscopic and microscopic appearance of this tumor may resent diagnostic problems. However it is important to differentiate this subtype from malignant mesotheliomas due to differences in epidemiology, treatment and prognosis [2].

These peritoneal tumors are often discovered incidentally during surgery for other reasons. An association between asbestos exposure and WDPM has not been definitely established, unlike the conclusive link between asbestos and malignant mesothelioma [2, 3]. Endometrial cancer is the most frequent cancer of the female genital tract, and it is known that once the disease is outside the uterus the recurrence rate peaks from 7% to 43% [4].

A case of WDPM discovered during staging surgery for endometrial carcinoma is presented. To our knowledge this is the first report of the simultaneous occurrence of an endometrial carcinoma in conjunction with diffuse WDPM of the peritoneum.

Case Report

A 50-year-old gravida 0, para 0, postmenopausal woman presented to our clinic with the complaint of vaginal bleeding, abdominal pain and a sense of bloating. She did not have a history of asbestos exposure. Pelvic examination revealed an enlarged uterus, but no cervical pathology was noted. Transvaginal ultrasonography showed a thickened endometrial lining measuring 29.3 mm. An abdominal-pelvic computerized tomography scan showed a hypodense lesion filling the entire endometrial cavity, with no abdominal lymphadenopathy. Physical examination, colonoscopic studies and chest X-ray were unremarkable. Routine laboratory studies were within normal limits except for serum tumor marker Ca-125, which was elevated to 83 U/ml. With the diagnosis of well-differentiated endometrial adenocarcinoma after fractional curettage, staging laparatomy was performed where peritoneal cytology was obtained and the abdomen explored. There was no ascites, but multiple implants of lesions 2 cm in maximum diameter were observed diffusely over the peritoneum, fallopian tubes, uterus, left ovary, Morrison's pouch, and sigmoid colon. These implants, which seemed to be carcinoma metastases, were resected and sent for frozen section analysis where they were reported to be adenocarcinoma metastases. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymph node dissection were performed. The final pathology was reported to be a grade 2 endometrial adenoacanthoma, concurrent with a WDPM of the peritoneum.

Histopathological examination of the uterus revealed complex budding and branching irregular glands in the endometrium. Tumor cells showed nuclear pleomorphism, hyperchromatism and prominent nuclei. The tumoral invasion was limited to half of the myometrium, but the endometrial cavity was filled with tumor, which showed cervical extension. Nests of benign squamous cells were observed between the malignant glandular component (adenoacanthoma) (Figure 1). No metastases in the regional lymph nodes were detected and lymphovascular space invasion was absent.

Microscopic examination of the peritoneum and the mentioned implants revealed a different tumor from endometrial carcinoma. The tumor consisted of papillary or partial tubu-

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Fig. 1

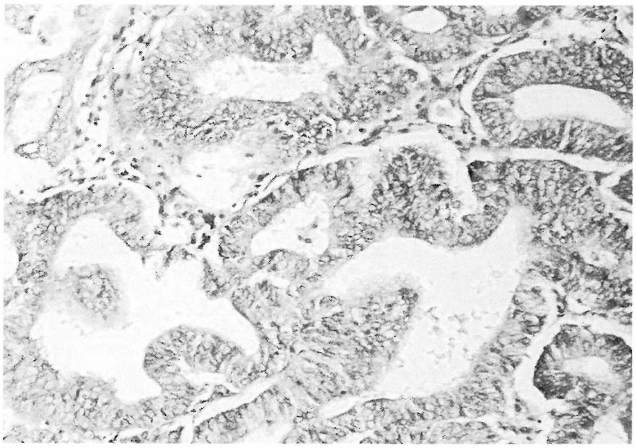

Fig. 2

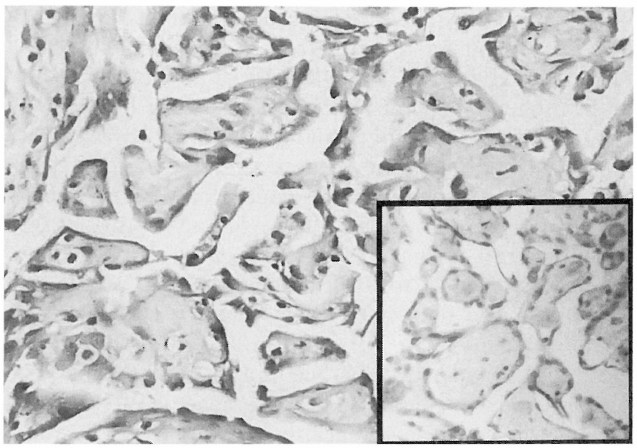

Fig. 3

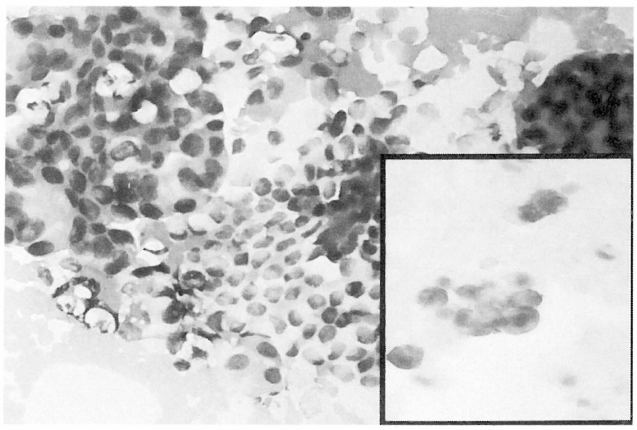

Figure 1. — Moderately well-differentiated adenocarcinoma of the endometrium (H&E x 200).
Figure 2. — WDPM characterized by fibrovascular papillae lined by uniform mesothelial cells (H&E x 200) Inset: Neoplastic mesothelial cells show strong reactivity for cytokeratins (IHC, cytokeratins, x 200).
Figure 3. — Cytologic examination of peritoneal washings. Cohesive cluster of tumor cells and some papillary clusters (H&E x 200) Inset: Immunoreactivity for calretinin in the membranes of tumor cells (IHC, calretinin x 200).

lopapillary structures. A single layer of cuboidal or columnar cells with bland cytological features lined the papilla and tubules. The tumor cells were small and uniform and showed no mitotic features. Slight cytological atypia was observed in some of the cells. No tumoral invasion in adipose or stromal tissue was detected. Immunohistochemical staining showed that the lining cells were strongly positive for cytokeratin and calretinin (Figure 2). Tumor cells showed a positive glycogen reaction with periodic acid schiff.

On cytological examination of peritoneal fluid, many papillary clusters and scattered cells were observed. At first glance, they resembled well-differentiated papillary carcinoma of ovary. The cells had abundant polygonal cytoplasm, and showed clearly outlined borders. The nuclei were centrally located, round or oval and uniform in size. There were no mitoses or hyperchromasia. Immunocytologically these cells were stained strongly positive for cytokeratin and calretinin (Figure 3).

The postoperative course was uncomplicated; the patient was discharged on postoperative day 7, and scheduled for external pelvic radiotherapy to counter the high risk of recurrence of endometrial carcinoma.

Discussion

WDPM must be differentiated from primary peritoneal carcinomatosis and peritoneal metastasis from ovarian or endometrial adenocarcinoma as in our case [3]. In most cases these entities can be readily distinguished microscopically. The features supporting a diagnosis of WDPM are absence of multilayering, cell stratification, cytologic atypia and mitotic activity [5]. Nevertheless in equivocal cases, immunoreactivity for CEA and CD15, and other glycoproteins such as Ber-EP4, TAG-72, and MOC-31, is useful in supporting a diagnosis of adenocarcinoma [6]. Furthermore, cells lining the papillary structures of WDPM are consistently immunoreactive for mesothelium-associated markers like calretinin, and HBME-1, as was true in our case [7].

The slight elevation of Ca-125 to 83 U/ml in our case was most likely secondary to either endometrial carcinoma or WDPM as it regressed to normal values postoperatively. Ca-125 is a well-known tumor marker for ovarian cancer, but the antigen may also be detected in reactive mesothelial cells. However, to our knowledge there has been only one case of WDPM reported in the literature with a simultaneous elevation of Ca-125 value and that was a pregnant patient [2].

Diffuse peritoneal malignant mesothelioma can also be confused with WDPM in that well-differentiated papillary elements are also prominent in malignant mesothelioma. However, cytologically, in most cases of diffuse malignant mesothelioma a few or occasionally many cells show nuclear and cytoplasmic abnormalities such as abnormal mitosis, large nucleoli and pleomorphism. [8-10]. Furthermore, WDPM usually occurs in the peritoneum, shows a female preponderance and its course is

usually benign. All these features are different than those of diffuse malignant mesothelioma. Accordingly, it seems that causative factors of WDPM are different from those of diffuse malignant mesothelioma [5]. Although WDPM usually follows a benign course, there are some cases reported in the literature with an aggressive course [3]. Despite the generally benign course of WDPM, long-term follow-up is needed due to the possibility of an unrecognized diffusely invasive component, and the potency of WDPM to dedifferentiate to true cancer [3, 11]. In view of the available data there is no beneficial effect of chemotherapy or radiotherapy unless there is a clear clinical indication that the tumor is progressing [5].

In case of the simultaneous appearance of WDPM and endometrial carcinoma, the surgeon may be mistaken by considering peritoneal implants as tumor metastasis. This situation may result in overtreatment of the patient. Thus, a thorough pathologic examination of the specimens taking care not to miss any areas of invasion, and utilizing immunohistochemical analysis when necessary are important to avoid such mistakes.

References

[1] McCaughey W.T.E.: "Papillary peritoneal neoplasms in females". *Pathol. Ann.,* 1985, *2*, 387.

[2] Hoekman K., Tognon G., Risse E.K.J., Bloemsma C.A., Vermorken J.B.: "Well-differentiated papillary mesothelioma of the peritoneum: a separate entity". *Eur. J. Cancer,* 1996, *32*, 255.

[3] Butnor K.J., Sporn T.A., Hammar S.P., Roggli V.L.: "Well-differentiated papillary mesothelioma". *Am. J. Surg. Pathol.,* 2001, *25* (10), 1304.

[4] DiSaia P.J., Creasman W.T.: "Clinical gynecologic oncology, Adenocarcinoma of the uterus". In: DiSaia P.J., Creasman W.T. (eds.), "Clinical Gynecologic Oncology", St. Louis, Mosby Inc., 2002, 153.

[5] Daya D., McCaughey W.T.: "Well-differentiated papillary mesothelioma of the peritoneum: a clinicopathologic study of 22 cases". *Cancer,* 1990, *65*, 292.

[6] Ordonez N.G.: "The immunohistochemical diagnosis of epithelial mesothelioma". *Hum. Pathol.,* 1999, *30*, 313.

[7] Goepel J.R.: "Benign papillary mesothelioma of peritoneum: a histological, histochemical and ultrastructural study of six cases". *Histopathology*, 1981, *5,* 21.

[8] Battifora H., McCaughey W.T.E.: "Diffuse malignant mesothelioma". In: Atlas of Tumor Pathology. Series, fascicle 15. Washington DC, Armed Forces Institute of Pathology, 1995, 17.

[9] Khoury N., Raju U., Crissman J.D., Zarbo R.J., Greenawald K.A.: "A comparative immunohistochemical study of peritoneal and ovarian serous tumors, and mesothelioma". *Hum. Pathol.,* 1990, *21,* 811.

[10] Koss L.G.: "Diagnostic cytology and its histopathologic bases, effusions in the presence of cancer". In: Koss L.G. (ed.). "Diagnostic Cytology and its Histopathologic Bases". Philadelphia, JB Lippincott, 1992, 1116.

[11] Burrig K.F., Pfitzer P., Hort W.: "Well-differentiated papillary mesothelioma of the peritoneum: a borderline mesothelioma". Virchows Archiv. Pathol. Anat., 1990, 417.

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