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Case Report

Concurrent Primary Peritoneal Low-Grade Serous Carcinoma and Endometrial High-Grade Serous Carcinoma

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Summary: A 64-yr-old postmenopausal woman with high-grade squamous intraepithelial lesion and atypical glandular cell of undetermined significance on her Pap test was found to have endometrial serous carcinoma (high grade) involving a polyp in a subsequent endometrial biopsy. She underwent hysterectomy and bilateral salpingo-oophorectomy with multiple biopsies of the peritoneum. Microscopic examination of the entirely submitted uterus showed no residual serous carcinoma. Multiple foci of low-grade serous tumor with extensive calcifications and psammoma bodies were identified on the surfaces of the left fallopian tube, ovaries, and biopsies of the peritoneum, consistent with peritoneal primary low-grade serous carcinoma. To our knowledge, this is the first reported case of low-grade serous carcinoma of the peritoneum with a concurrent (high-grade) serous carcinoma of the endometrium arising from an endometrial polyp. **Key Words:** Serous carcinoma of endometrium—Low-grade serous carcinoma of peritoneum—Endometrial polyp.

Histogenesis of primary peritoneal serous carcinoma is not clear and the most common theory hypothesizes that it originates from preexisting endosalpingiosis as their common origin is the Mullerian ductal system. Recently the fallopian tube, particularly the fimbrial end, has been proposed as a potential site of origin of some ovarian or peritoneal serous cancers. We encountered a case of low-grade serous carcinoma of the peritoneum with a concurrent (high-grade) serous carcinoma of the endometrium arising from an endometrial polyp. To our knowledge, this association has not been reported and we hope that this incident may shed some light on the etiology of primary peritoneal serous carcinoma.

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The authors declare no conflict of interest.

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CASE REPORT

A 64-yr-old G6P5014 postmenopausal woman presented for routine Pap test and well woman examination. Her family history was significant for endometrial cancer in her mother, endometrial cancer in one of her sisters at the age of 52, and liver cancer in her other sister. She had no complaint of vaginal bleeding. Her last menstrual period was in 1997. According to the patient her last Pap tests were reported normal. Her Pap test at this visit was significant for high-grade squamous intraepithelial lesion and atypical glandular cell of undetermined significance. Her subsequent cervical biopsy and endometrial biopsy demonstrated pleomorphic cells with high nuclear to cytoplasmic ratio and hyperchromatic nuclei (Figs. 1, 2). Mitotic figures were seen. By immunohistochemistry, the neoplastic cells were reactive for p16, ER, WT1, p53 (diffuse and strong nuclear staining), and low-molecular cytokeratin.

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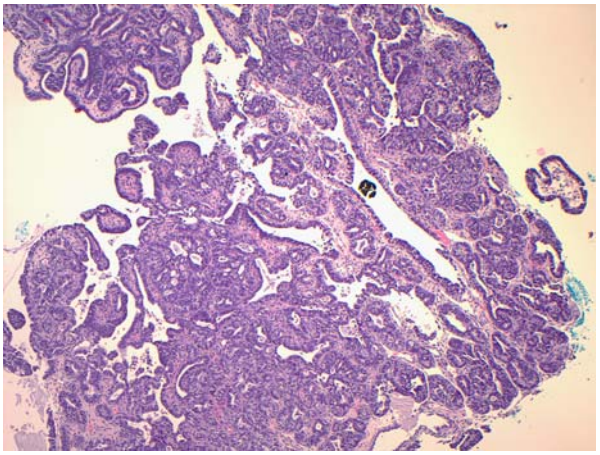

FIG. 1. Serous carcinoma in the endometrial polyp. Hematoxylin and eosin stain, original magnification: × 40.

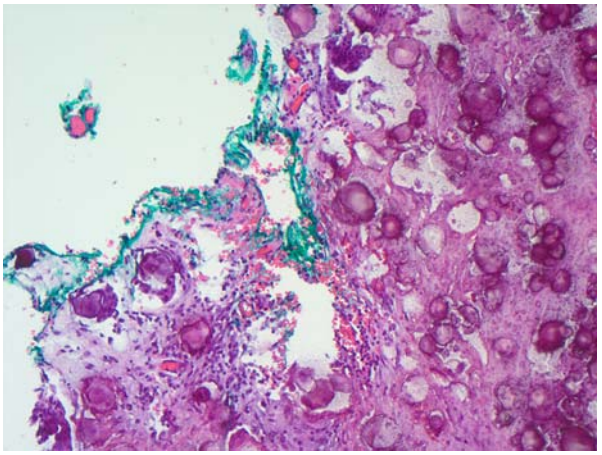

FIG. 3. Low-grade peritoneal serous carcinoma. Monomorphic cells associated with psammoma bodies are seen. Hematoxylin and eosin stain, original magnification: × 100.

Vimentin, CEA, and β-catenin were negative. The patient was diagnosed with uterine serous carcinoma and underwent hysterectomy, bilateral salpingo-oophorectomy, and staging.

On gross examination, the uterus was unremarkable except for a 2.2 × 1.4 × 0.9 cm leiomyoma in the posterior wall and an endometrial polyp. Bilateral ovaries and fallopian tubes had no discrete lesions. Anterior and posterior vaginal margins, omentum, left pericolic nodules, and lymph nodes from the pelvis, bilateral common iliacs, bilateral obturators, and para-aortic were also received.

No tumor was identified in the entirely submitted endometrium. There were multiple foci of low-grade peritoneal serous carcinoma with extensive calcifications and psammoma bodies on the surfaces of both of the ovaries and left fallopian tube (Figs. 3–5). The tumor in the pericolic nodules and omentum (Figs. 6–8) had identical cytomorphologic features. The same immunohistochemical stains performed on the endometrial carcinoma were performed on the peritoneal lesion. Peritoneal lesions were focally positive with vimentin. They were strongly and diffusely positive with CAM 5.2, low–molecular-weight cytokeratin, β-catenin, and ER (nuclear). They were negative with CEA.

All of the lymph nodes were negative for malignancy. A final diagnosis of primary peritoneal carcinoma, low grade, was established.

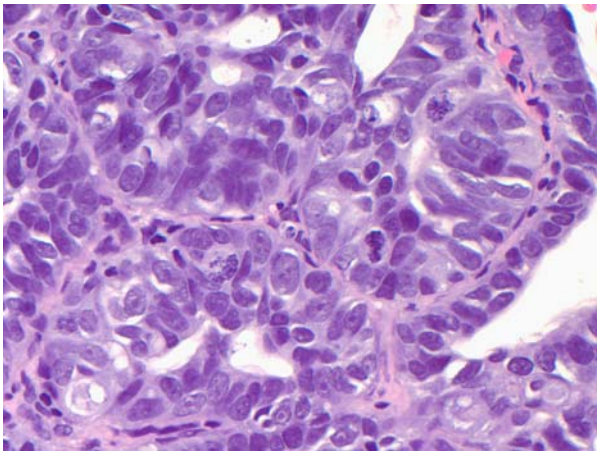

FIG. 2. High power of the tumor: malignant cells with high nuclear to cytoplasmic ratio, hyperchromatic nuclei, and prominent nucleoli. Multiple mitotic figures are seen. Hematoxylin and eosin stain, original magnification: × 400.

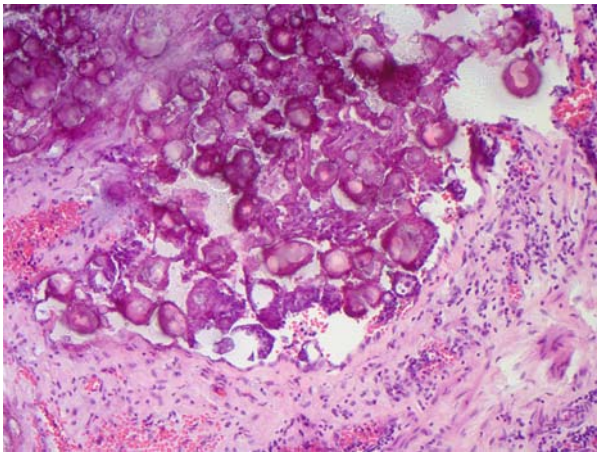

FIG. 4. Low-grade peritoneal serous carcinoma. Monomorphic cells associated with psammoma bodies are seen. Hematoxylin and eosin stain, original magnification: × 100.

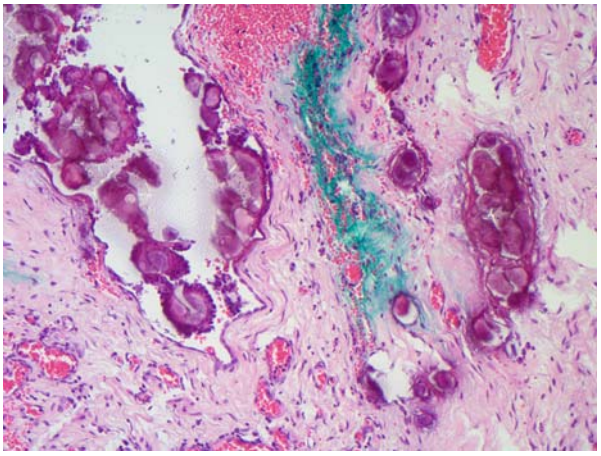

FIG. 5. Low-grade peritoneal serous carcinoma. Monomorphic cells associated with psammoma bodies are seen. Hematoxylin and eosin stain, original magnification: × 100.

The pelvic washing had sheets of mesothelial cells and psammoma bodies with rare groups of neoplastic cells with high nuclear to cytoplasmic ratio and hyperchromatic nuclei. These cells cytomorphologically were similar to the neoplastic cells of the peritoneal low-grade serous carcinoma. They were positive for ER and focally positive for p53.

After further review of the endometrial biopsy, it was deemed that the neoplastic cells were confined to an endometrial polyp (Figs. 9 and 10). Since the endometrium had been entirely submitted for microscopic evaluation and no invasive carcinoma was identified, we concluded that the serous carcinoma had been limited to the polyp.

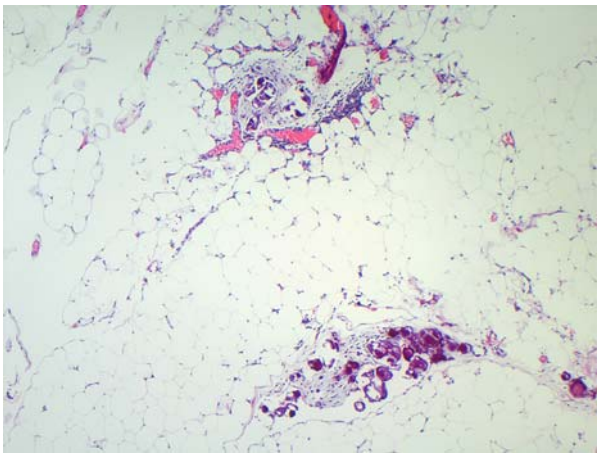

FIG. 6. The tumor in the omentum with identical cytomorphologic features; monomorphic cells with associated psammoma bodies. Hematoxylin and eosin stain, original magnification: × 40.

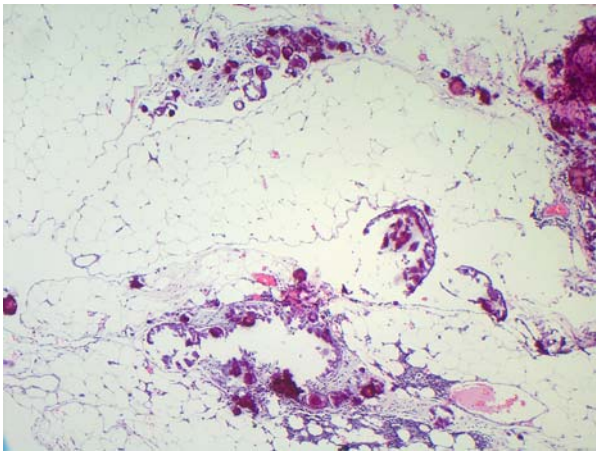

FIG. 7. The tumor in the omentum with identical cytomorphologic features; monomorphic cells with associated psammoma bodies. Hematoxylin and eosin stain, original magnification: × 40.

Endometrial and peritoneal lesions were evaluated for Kras and BRAF V600E/K/D mutations. Both lesions were negative for these mutations.

DISCUSSION

The prevalence of endometrial polyp in the general population is about 24%, although they are more common in postmenopausal woman (1–6). The literature suggests up to 8% risk of malignant transformation of an endometrial polyp, with the risk higher in postmenopausal women, especially if they present with bleeding and have large polyps (7–10). Interestingly, 12% to 34% of uteri containing endometrial carcinoma also contain polyps (11,12).

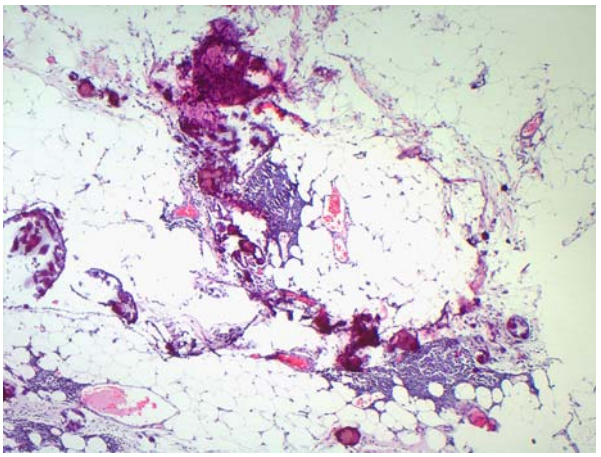

FIG. 8. The tumor in the omentum with identical cytomorphologic features; monomorphic cells with associated psammoma bodies. Hematoxylin and eosin stain, original magnification: × 40.

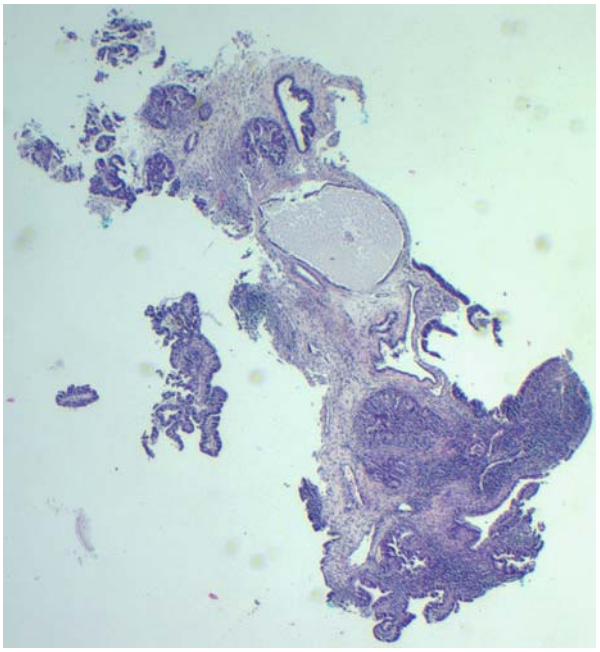

FIG. 9. Nests of malignant cells in an endometrial polyp with fibrotic stroma and cystic change of gland. Hematoxylin and eosin stain, original magnification: $\times 20$.

Many patients with adenocarcinoma in an endometrial polyp (8 of 9, 90% in 1 study) have adenocarcinoma or complex atypical hyperplasia of the nonpolyp endometrium, indicating a need for hysterectomy in most of these cases, particularly if the patient is postmenopausal (13,14). Although our patient had high-grade serous carcinoma in an endometrial polyp, she did not have any malignancy in the rest of endometrium or in the second endometrial polyp.

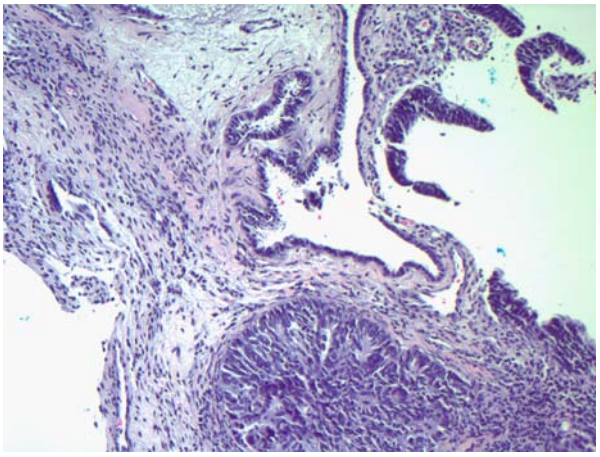

FIG. 10. Endometrial polyp with fibrotic stroma and multiple blood vessels with a large nest of malignant cells. Hematoxylin and eosin stain, original magnification: $\times 100$.

Although serous carcinoma of endometrium can metastasize extensively, the chance of the peritoneal tumor to be metastatic from the serous carcinoma involving endometrial polyp in our patient is unlikely, as the tumor cells on the serosal surface are low grade, whereas the endometrial carcinoma is high grade. The more typical association of serous carcinoma in a polyp is with high-grade serous carcinoma in the peritoneum (15). Patients with primary peritoneal serous carcinoma have a mean age of 50 to 65 yr (16–18). Abdominal pain and ascites are common presenting signs and symptoms (16).

The most commonly accepted criteria for peritoneal primary serous carcinoma are Gynecology Oncology Group criteria; which includes the following (i) the ovaries were either absent or normal in size; (ii) the involvement of the extraovarian sites was greater than the involvement of the surface of either ovary; (iii) an absence of a deep-seated invasive ovarian carcinoma or invasive disease in the ovarian cortical stroma with tumors that were $< 5 \times 5\,mm^2$; (iv) the histopathologic and cytologic characteristics of the tumors were similar to that for epithelial ovarian cancer (19).

On the basis of Gynecology Oncology Group criteria, as the ovaries in this patient were of normal size; the involvement of the extraovarian sites was greater than the involvement of the surface of either ovary; absence of a deep-seated invasive ovarian carcinoma and characteristic cytomorphology of the lesions, primary peritoneal serous carcinoma was diagnosed.

Endosalpingiosis in the peritoneum is commonly found concurrently with implants of serous borderline tumors of ovary that has metastatsized to the peritoneum (20). This finding has sparked the theory that primary peritoneal serous carcinoma may arise from preexisting endosalpingiosis (21). However, the histogenesis of this tumor remains undetermined. As the surface epithelium of the ovary, the peritoneum, and subjacent connective tissue all originate from coelomic epithelium and subcoelomic mesenchyme, which are derived embryologically from the Mullerian ductal system, it could be maintained that endosalpingiosis, serous borderline tumors, and even peritoneal serous carcinomas are derivatives of the secondary Mullerian system. Indeed, this has been one the most accepted theories, as these tumors are derived from cells that retain a potential for Mullerian differentiation, and could account for the simultaneous occurrence of these entities (20–24).

Recently the fallopian tube, particularly the fimbrial end, has been proposed as a potential site of origin of some ovarian or peritoneal serous cancers (25–27). It has been shown that intraluminal shedding of tumor cells in the fallopian tubes from serous carcinoma cases are common and a likely route of abdominal spread (28). Our patient had psammoma bodies in the endothelial lining of fallopian tube, but no associated epithelial cells or mucosal dysplasia was found.

Although our patient's uterus and adnexa were grossly normal, she had pericolic nodules described in the operative report as small (2 mm) white punctate lesions that were found to contain serous carcinoma.

The differential diagnosis of primary peritoneal serous carcinoma includes endometriosis, endosalpingiosis, adenomatoid tumor, florid mesothelial hyperplasia, papillary mesothelioma, primary ovarian papillary serous borderline tumor with implants, and primary peritoneal serous papillary carcinoma. Although the other entities can often be distinguished by morphology and architecture alone, immunohistochemistry may be useful in some instances. Calretinin can be used to distinguish mesothelial lesions.

Primary peritoneal serous carcinoma is currently treated similar to primary ovarian serous carcinoma with platinum-based chemotherapy (22). Our patient underwent radiation therapy followed with combination carbo/taxol chemotherapy.

We believe this is the first reported case of synchronous primary peritoneal low-grade serous carcinoma and a (high-grade) serous carcinoma of endometrium. Although this may be an incidental finding, it may also indicate a common histogenetic pathway for these tumors. Additional cases and further studies are required for the evaluation of this hypothesis.

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