Gynecology & Obstetrics
ISSN: 2161-0932

Gonzalez et al., Gynecol Obstet 2013, 3:5
DOI: 10.4172/2161-0932.1000179

Case Report Open Access

Ovarian Serous Borderline Tumor Identified in Endometrial Biopsy: A Case Report

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Abstract

Endometrial biopsies are useful for evaluating endometrial disease, but the presence of non-endometrial, non-cervical tissue is rare and is typically restricted to metastasis to the endometrial cavity. We report, for the first time, a case of an endometrial biopsy seeded with serous cells in a young patient with a known history of a serous borderline tumor of the ovary. Given the patient's diagnosis of an ovarian serous borderline tumor, the most likely explanation for the presence of serous cells in her endometrial biopsy is transit via the fallopian tube into the endometrial cavity. The morphologic and IHC profile of the cells from the endometrial biopsy were consistent with that of the ovarian tumor counterpart. The impact of this finding on tumor prognosis cannot be determined, and follow-up should be observed.

Keywords: Metastasis; Serous Borderline Tumor; Endometrium; Ovary

Introduction

While there are various indications for endometrial biopsy, a common objective in this setting is detection of hyperplasia and malignancy of the endometrium. Cervical tissue is commonly present in endometrial biopsy due to the anatomic relationship of the organs, but detecting tissue from other organs is uncommon and is usually caused by metastasis of a frankly malignant neoplasm [1,2]. Though the phenomenon of synchronous primary ovarian and endometrial tumors is well-known in the literature [1,2] and while endometrial biopsy is indicated in the setting of estrogen-secreting ovarian tumors given the increased risk of endometrial hyperplasia and malignancy [3], nevertheless, this does not lend evidence to the use of endometrial biopsy as an effective screening tool for ovarian neoplasms.

Immunohistochemistry (IHC) may prove useful in the distinction of metastatic versus synchronous primary ovarian and uterine serous carcinomas. WT1 is infrequently expressed in endometrial serous carcinomas (20-30% of cases) in comparison to the common expression (70-80% of cases) in ovarian, tubal and primary peritoneal counterparts [4,5]. Additionally, ER, IMP3, P53 and P16 have been reported to be expressed in ~92% of ovarian serous carcinomas compared to 30%, 85%, 64% and 76% of uterine serous carcinomas, respectively with the ER expression showed statistical significant difference [4]. Gene expression profiling proved to be useful in discriminating ovarian from uterine serous carcinomas [6]. Plasminogen activator inhibitor (PAI-2) is highly overexpressed in ovarian serous when compared to uterine serous carcinoma. On the other hand, HER2 is the most overexpressed gene in uterine serous when compared to ovarian serous counterpart [6].

We report a case of incidental identification of a patient's known ovarian serous borderline tumor on an endometrial biopsy, which to our knowledge has not yet been reported in the literature.

Case Report

Clinical history

A 31-year-old female with polycystic ovarian syndrome and primary infertility presented for surgical management of a 5.5 cm ovarian tumor that was diagnosed as a serous borderline tumor without surface involvement. Peritoneal washing performed at the time of surgery was positive for cells consistent with her serous tumor (pT1c by American Joint Committee on Cancer criteria [7]. The patient returned to clinic three months after her ovarian surgery, complaining of irregular vaginal bleeding postoperatively. Endometrial biopsy done during her clinic visit showed simple hyperplasia without atypia. The patient was treated with metformin for polycystic ovarian syndrome and had resumption of normal menstruation. Eleven months after being diagnosed with endometrial hyperplasia, the patient returned for a follow-up endometrial biopsy. Trans-abdominal and transvaginal ultrasound performed at time of endometrial biopsy was interpreted as showing "thickened endometrium consistent with luteal phase." Microscopic examination was negative for endometrial hyperplasia but was remarkable for the presence of cells resembling those of the patient's ovarian tumor.

Pathologic findings

The ovarian serous borderline tumor demonstrated neoplastic serous cells lining the surfaces of fibrous cores, with occasional small tufts and tight clusters of cells (Figure 1A). Areas of invasion were not detected after extensive sampling. The patient's most recent endometrial biopsy consisted predominantly of non-hyperplastic proliferative-pattern endometrium. At one edge of the hematoxylin and eosin-stained slide were small clusters of serous cells forming micropapillary formations similar to those observed in the peritoneal washing (Figure 1B). The cells displayed an increased nuclear:cytoplasmic ratio and condensed chromatin, but no mitotic figures were present. Reactive histiocytes (positive for CD68 IHC stain) surrounded the serous cells. By IHC, the serous cells identified in the endometrial biopsy were positive for Estrogen Receptor (ER) and WT1, and negative for calretinin; the same pattern of staining was observed retrospectively on IHC evaluation of tissue from the patient's ovarian primary (Figure

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Received October 07, 2013; **Accepted** October 29, 2013; **Published** October 31, 2013

Citation: Gonzalez RS, Chamberlain BK, Giannico G, Fadare O, Crispens MA, et al. (2013) Ovarian Serous Borderline Tumor Identified in Endometrial Biopsy: A Case Report. Gynecol Obstet 3: 179 doi:10.4172/2161-0932.1000179

1C-F). Similar clusters were observed microscopically in the fluid from the peritoneal washing (Figure 1G).

Discussion

Tissue of non-cervical, non-uterine origin is not typically encountered on endometrial biopsy. The uterus is a rare site for metastasis of malignancies from other organs, with most instances targeting the myometrium [8-10]. The most common metastasis to endometrial structures is lobular mammary carcinoma metastasizing to tamoxifen-associated endometrial polyps, though metastases from other sites have been reported, including metastasis of frankly malignant ovarian neoplasmsa [8-10].

Borderline tumors of the ovary, while not malignant in the traditional sense, have a propensity to shed malignant epithelial cells into the peritoneal cavity, leading to ascites and peritoneal implants [8-11]. Their presence in the relatively difficult-to-access endometrial cavity, however, is extraordinarily unusual and has not been previously reported. Despite the fact that the fallopian tubes were not available for histopathologic examination in this case, the most likely point of access seems to be the fallopian tubes, with the serous cells traveling the length of the tube(s) as would an ovum following ovulation. Other methods of spread, such as hematogenous, are unlikely given that the tumor otherwise fulfilled the criteria for a serous borderline tumor, not a carcinoma. The possibility of the endometrial biopsy penetrating the uterine wall and partially sampling the uterine serosa, or attached tissues containing tumor, should also be entertained and excluded in such cases through communication with the clinician.

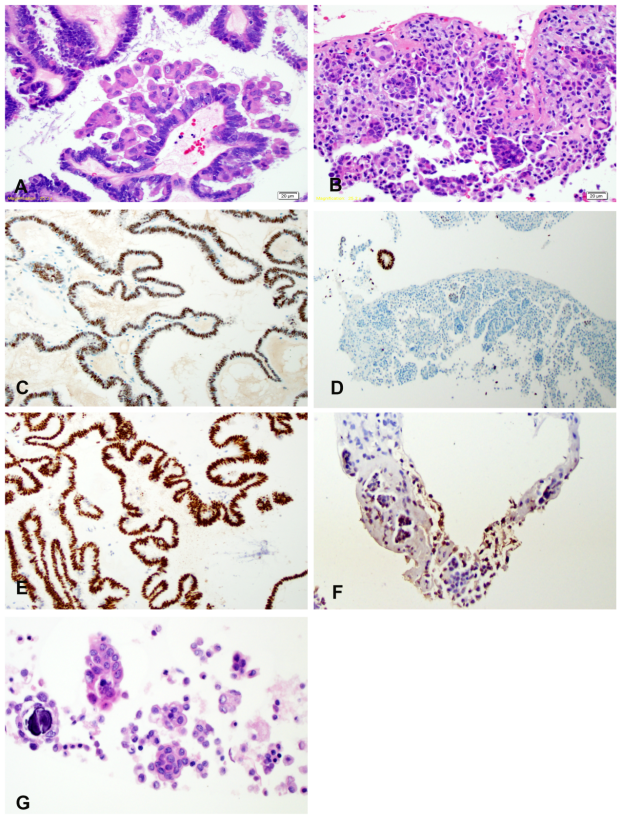

Figure 1: Ovarian serous borderline tumor identified in endometrial biopsy. A) The patient's primary ovarian borderline tumor was serous in nature. B) Tissue from the patient's endometrial biopsy consisted of proliferative-pattern endometrium seeded with serous borderline tumor. Positive expression of estrogen receptor by IHC was detected in cells from the ovarian primary (C), as well as those detected in the endometrial biopsy (D). Serous cells from both ovarian and endometrial sites similarly expressed WT1 protein (E and F, respectively). Tumor cells had been previously detected on pelvic washing fluid (G; cell block)

In determining whether the cells detected on endometrial biopsy were indeed from the patient's ovarian serous borderline tumor, we took care to exclude the possibility of contamination from another specimen. A review of the day's cases revealed no serous neoplasms or other malignancies that formed small, tight clusters of serous-like cells. This suggested that the cells were unlikely to have been introduced after the biopsy procedure.

IHC analysis of the cells in the endometrial biopsy and the patient's original serous borderline tumor revealed an identical staining pattern. These findings, in conjunction with the background of reactive histiocytes, gave further evidence that the cells originated from the patient's ovarian tumor.

Consideration was given to the possibility of the patient harboring a metachronous primary serous lesion of the endometrium. However, this scenario in our case was felt unlikely for several reasons. First, the patient was 31 years old, whereas serous carcinoma of the endometrium is typically seen in patients older than 65 [12]. Additionally, the cells appeared relatively bland and without frank anaplasia or mitotic figures, in contrast to those seen in most serous endometrial carcinomas [13]. The IHC pattern of staining, with positivity for ER and WT1, also favored ovarian over uterine origin [4,5]. Finally, the patient's ultrasound at time of biopsy was interpreted as benign, without any suspicion of a malignant process.

As a result, given the clinical and IHC findings, the patient's prior ovarian serous borderline tumor was considered by far the most likely origin of the cells in her endometrial biopsy. While the detection of borderline serous ovarian cells on endometrial biopsy may at first seem an incidental finding, it does have potential implications. Had this patient's ovarian tumor somehow gone undetected previously, the finding of these cells might have prompted a search for their origin. Additionally, appearance of a tissue reaction to the serous cells implies that they may have been trying to actively implant, rather than simply represent detached cells in the endometrial cavity. The implications on the prognosis of this patient cannot be determined at this time, and follow up should be observed. If other instances of borderline tumor cells within the endometrium can be identified and the patient outcomes followed, the effect of this finding on prognosis may become more clearly understood.

Conflict of Interest

All authors of the manuscript do not have a direct financial relation with any commercial identity that might lead to a conflict of interest for any of the authors.

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