Case Report
A case of neoplastic granulosa cells in the fallopian tube, but no evidence of granulosa cell tumor

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Abstract: The discovery of displaced granulosa cells in the fallopian tube is concerning for a granulosa cell neoplasm and can lead to further surgical intervention. Discerning the risk of neoplasm can be challenging, even with immunohistochemical staining of CD56, a highly sensitive marker of granulosa cell neoplasm. A 48-year-old underwent an uncomplicated hysterectomy and bilateral salpingectomy for symptomatic fibroids and was found to have a small focus of granulosa cells staining positive for CD56 in her left fallopian tube. Post-operative imaging demonstrated a left adnexal mass. The patient underwent a left oophorectomy. Final pathology demonstrated a benign mucinous cystadenofibroma without evidence of granulosa cell neoplasm. Displaced granulosa cells require further pathologic and surgical evaluation, but do not always equate to neoplasm and should be managed accordingly.

Keywords: Granulosa cell neoplasm, CD56, ovarian cancer, adnexal mass

Introduction
Ovarian granulosa cells are sex cord derivatives that surround ovarian follicles to assist in their growth and development. They represent cells of stromal origin, specialized in steroid hormone production. Granulosa cell neoplasms are the most common sex cord-stromal tumors, constituting 2-4% of ovarian cancers, and have morphologic resemblance to non-neoplastic granulosa cells. This tumor is most commonly seen in post-menopausal women with a peak incidence between 50 and 55 years [1]. The initial management of adult granulosa cell tumors in women without childbearing desire is surgery, including hysterectomy and bilateral salpingo-oophorectomy [2]. Chemotherapy may be required for disease that has spread beyond the ovary or for recurrent disease.

Case
A 48-year-old premenopausal G1P1001 woman underwent a robotic-assisted total laparoscopic hysterectomy and bilateral salpingectomy for symptomatic fibroid uterus. The bilateral ovaries appeared normal at the time of surgery. The final pathology demonstrated a granulosa cell proliferation in the left fallopian tube. Several microscopic foci of granulosa cell clusters beneath the intact benign serous epithelium of the fallopian tube in the fimbriated end were identified (Figure 1). The classic morphology and positive inhibin immunohistochemical staining of the cells supported the diagnosis of the sex-cord nature of the displaced cells (Figure 2). Additionally, immunohistochemical staining for CD56, a marker seen in neoplastic granulosa cells, showed diffuse membranous positivity (Figure 3).

The patient was referred to gynecologic oncology for further evaluation. The pathology was reviewed at a separate institution and the findings as previously detailed were confirmed. The patient underwent an interval transvaginal sonogram approximately three months after her surgery for evaluation of the ovaries, which revealed an enlarged multicocular, multi-septated left ovary, measuring 5.7 × 4.2 × 3.8 cm and containing a partially solid component with abnormally increased blood flow. The sonographic findings were read as highly concerning for granulosa cell tumor by an expert in gynecolog-
The granulosa cell tumor that wasn’t

Figure 1. Multifocal granulosa cell proliferation beneath the intact benign serous epithelium of the fallopian tube in the fimbriated end (H&E-stained slides, A: 100×, B: 200×, C: 400×).

Figure 2. Inhibin-positive granulosa cells.

Figure 3. CD56-positive granulosa cells.

The patient proceeded to a laparoscopic left oophorectomy with intraoperative consultation with frozen section evaluation and a plan for right oophorectomy and surgical staging if the pathology was consistent with neoplasm. Intraoperative findings included an enlarged left cystic ovary, a nodular appearing left uterosacral ligament, and a normal appearing right ovary. Intraoperative pathology of the left ovary suggested a mucinous cystadenofibroma and a hemorrhagic corpus luteum. Biopsies of the right ovary, the left uterosacral ligament and left pelvic peritoneum were obtained and negative for malignancy. Final pathology of the complete left ovary revealed no evidence of a granulosa cell tumor.

Discussion

A limited number of previous cases have been reported of displaced granulosa cells in ovarian stroma, vascular channels, and the fallopian tubes [3-6]. Proposed methods of displacement include traumatic versus ovulatory mechanisms. McCluggage and Young [4] suggest traumatic displacement during the surgical specimen dissection or in the laboratory processing of the specimen, and argue against true displacement of granulosa cells. Duncan [3] supports a theory of displacement through ovulation first proposed by Vydianath [6] given proliferation of granulosa cells in the stroma of the fimbria without crushed morphology. The ovarian pathology sample in those cases also demonstrated multiple corpora lutea and cystic follicles indicating active follicular development. The case presented here demonstrated minute foci of granulosa cells below intact benign serous epithelium of the fallopian tube in the fimbriated end with classic granulosa morphology and positive inhibin staining, making the possibility of traumatic displacement
The granulosa cell tumor that wasn’t

during dissection or laboratory specimen processing quite unlikely. This patient was on cycle day 21 of 30 when she underwent the initial surgery where the displaced cells were discovered, suggesting she was past her ovulation window. The location of the cells below an intact layer of tubal serous epithelium raises the question if migration occurred during an earlier ovulatory cycle or even earlier during embryologic development and raises further investigation.

The prior cases reported by Duncan [3] and Vydianath [6] were initially concerning for metastatic granulosa cell tumors with migration of cells into the fallopian tubes. In these reported case, however, the granulosa cells in question were negative for CD56, a finding supportive of their benign nature. CD56 is a neuroendocrine marker or neural cell adhesion molecule that is widely regarded as a highly sensitive marker of neuroendocrine neoplasms. McCluggage [7] and Katu [8] have investigated the ability of CD56 to differentiate between benign and malignant granulosa cells and demonstrated high sensitivity as a marker in diagnosing sex cord neoplasms. Katu [8] found 100% CD56-positivity in granulosa cell tumors (n=32) compared with none of the 47 normal ovarian follicles. McCluggage [7] reported similar results, but also found positive CD56 staining in three non-neoplastic pregnancy-related proliferation of granulosa cells questioning if hormonal status, or exogenous hormonal treatment, may affect the expression of this marker. Given that a positive CD56 is not necessarily equal to malignancy in nature, further investigation is required to understand this and the impact that positive expression has on clinical decision making.

In the case presented here, incidentally found granulosa cells with a positive CD56 marker in a patient with a left adnexal mass prompted a second surgical procedure for treatment and staging of a presumed granulosa cell neoplasm. Intraoperative pathologic evaluation enabled real time diagnosis of a benign condition that afforded highly-desired preservation of unilateral ovarian function in the patient. Future cases of incidentally found displaced granulosa cells, including with CD56-positive staining, warrant comprehensive decision making prior to definitive intervention.

Disclosure of conflict of interest

None.

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References