

Mucinous cystadenoma of the ovary with stromal luteinization and hyperestrinism in a post-menopausal female

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Summary

Rare cases of virilization caused by ovarian tumors with functioning stroma have been reported, typically during pregnancy. The authors report a case of a post-menopausal 60-year-old woman who presented with breast tenderness and vaginal bleeding and was found to have an 18.4-cm adnexal mass by imaging. Cystectomy revealed a benign mucinous cystadenoma with stromal luteinization associated with elevated estradiol levels and features of hyperestrinism. Due to the high clinical suspicion of a malignancy, a total abdominal hysterectomy with bilateral salpingo-oophorectomy and appendectomy was performed. These hormonally induced changes must be recognized to avoid misinterpretation of a malignancy.

Key words: Mucinous cystadenoma; Stromal luteinization; Hyperestrinism; Post-menopausal.

Introduction

Sertoli–Leydig cell tumors and stromal Leydig tumors are well-known ovarian tumors associated with clinical virilization [1, 2]. Granulosa cell tumors and thecomas are also known as estrogen producing ovarian tumors [1, 2]. As imaging characteristics of each tumor have been reported, some typical cases can be correctly diagnosed before surgery. However, other types of ovarian tumors can have stromal cells that show hormonal activity such as luteinization, or contain Leydig cells [1]. The authors report a benign mucinous cystadenoma with stromal luteinization in a post-menopausal 60-year-old female with features of hyperestrinism.

Case Report

A 60-year-old woman presented with complaints of bilateral breast tenderness of two months duration followed by vaginal bleeding. She also noted small caliber stool, frequent urination, and increase in abdominal girth. On physical examination, abdominal palpation revealed a mass below her umbilicus that was mobile and non-tender. Laboratory data showed normal CA-125 and inhibin levels with elevated estradiol at 45 pg/mL (normal ≤ 31 pg/mL). Pelvic ultrasound revealed a large cystic right adnexal mass measuring 18.4 \times 14.2 \times 8.9 cm with central septations. The uterus was found to have a thickened endometrial stripe of 1.9 cm. A subsequent abdominal CT scan confirmed the findings. Endometrial biopsy was attempted but only scant tissue was obtained due to cervical stenosis.

Exploratory laparotomy revealed the large cystic mass was arising from the right ovary. The right adnexal mass was sent for intraoperative consultation weighing 1,217 grams and measuring 19.5 cm in greatest dimension. Frozen section analysis favored a

mucinous cystadenoma. However, the surgeon was concerned for a malignancy and a total abdominal hysterectomy with bilateral salpingo-oophorectomy and an appendectomy was performed.

The resected right ovarian mass was multiloculated and cystic with rare yellow speckling. The cyst contained thin mucinous fluid. No solid areas or papillary excrescences were identified. Microscopically, the cyst was lined by a single layer of tall columnar, non-ciliated cells with basally situated nuclei and abundant intracellular mucin. Within the stroma of the cyst wall underlying the mucinous epithelium was a prominent layer of polygonal cells with abundant eosinophilic cytoplasm, typically resembling

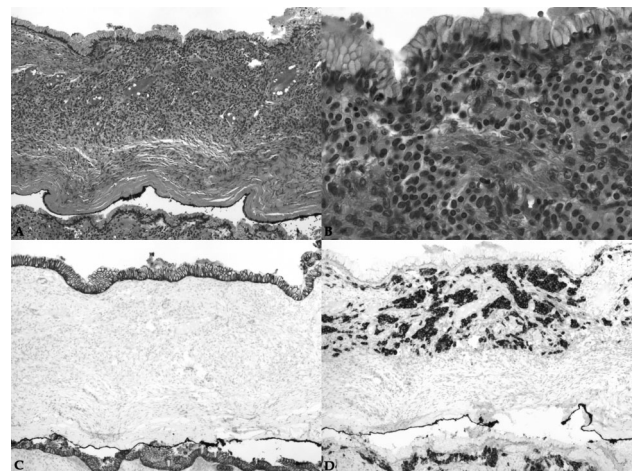


Figure 1. — Benign mucinous cystadenoma with A) medium- and B) high-power views showing numerous foci of hyperplastic Leydig cells in the cyst wall ($\times 100$ and $\times 400$, H&E stain), which are B) negative for pancytokeratin (mucinous epithelium is positive) ($\times 100$) and strongly positive for inhibin ($\times 100$).

Revised manuscript accepted for publication November 23, 2017

luteinized stromal cells or Leydig cells (Figures 1A-B).

Immunohistochemically, the luteinized stromal cells were strongly positive for inhibin and negative for pancytokeratin (Figures 1C-D). The combination of the morphological features and immunohistochemical findings were consistent with a mucinous cystadenoma with ovarian stromal luteinization.

The hysterectomy specimen revealed atrophic endometrium with adenomyosis and a 4.0 cm benign endometrial polyp. The appendix was unremarkable. Four weeks after the operation, she denied breast tenderness, vaginal bleeding or discharge, as well as problems with her bowel or bladder habits.

Discussion

Benign ovarian mucinous cystadenoma is one of the most common benign ovarian neoplasms comprising 10-15% of all benign ovarian tumors and roughly 80% of all primary ovarian mucinous neoplasms [2, 3]. Typically, they are thin-walled, uni- or multiloculated cystic neoplasms ranging in size from a few centimeters to >30 cm (mean 10-18 cm) [2, 3]. These tumors have been reported in a wide age range from premenarchal to postmenopausal women, but typically between 20-40 years of age [3]. Due to the large size, patients may present with an abdominal/pelvic mass accompanied by pain, as well as urinary symptoms due to ureteral obstruction or bowel obstruction with abdominal compartment syndrome [2, 3]. On occasion, cases have been reported to have an association with estrogenic or androgenic effects due to luteinization of the stromal cells or Leydig cell hyperplasia within the cyst wall which have been hypothesized to produce these hormones [2, 4]. Rare case reports have been reported in young pregnant women with hormonally induced changes such as virilization and intrauterine growth retardation secondary to stromal luteinization [4-8].

In the present case, the patient suffered from bilateral breast tenderness followed by vaginal bleeding with a thickened endometrial stripe for two-months duration likely due to an elevated estradiol level and estrogen effect. Because of the stromal luteinization or Leydig cell hyperplasia, one might have expected clinical signs of virilization, which were absent in the present patient, but when present, often correlate with the histopathologic findings and resolve after removal of the ovarian tumor [6].

Histologically, the luteinized cells or Leydig cells are polygonal which contain abundant clear to eosinophilic cytoplasm with a centrally placed nucleus and small nucleolus. The cells are often arranged in a diffuse or sheeted pattern, but may also grow in cords and nests [2]. Immunohistochemically, they are positive for sex cord-stromal markers, such as inhibin, and negative for

pancytokeratin, similar to our case [2]. Under-recognizing the occurrence of stromal luteinization may lead to a misdiagnosis of an invasive epithelial component of a primary ovarian neoplasm or metastatic carcinoma. The bland cytologic features and the differences in immunoprofile, would help to distinguish these entities.

In summary, the authors report a case of a benign mucinous cystadenoma with stromal luteinization in a postmenopausal woman with hyperestrinism which was clinically concerning for malignancy. Clinicians should be aware that patients with clinical symptoms of hyperestrinism and/or virilization may be secondary to a benign hormonally active ovarian neoplasm and not necessarily a malignancy.

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