

A case of microscopic granulosa cell tumor with marked hyperestrogenism diagnosed and treated by laparoscopic intraoperative venous blood sampling

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Summary

Among other causes of hyperestrogenism, granulosa cell tumors (GCT) can be the cause of excessive estrogen production. However, localizing the source of hyperestrogenism preoperatively can be difficult when the tumor is minuscule. The authors describe herein a case of microscopic GCT associated with postmenopausal vaginal bleeding and marked breast enlargement. Extensive work-up included endocrinological tests, pelvic ultrasound, computed tomography, and magnetic resonance imaging, without direct localization of the source of hyperandrogenism. Persistently high plasma estradiol prompted an explorative laparoscopy. Intraoperative selective ovarian venous sampling revealed a 13-fold higher estradiol concentration in the left ovarian veins. Based on these findings, a left salpingo-oophorectomy was performed, but failed to identify estrogen-producing lesions on frozen sections. The detailed histological and immunohistological examination confirmed the diagnosis of a GCT of 5 mm in diameter, postoperatively. Exploratory laparoscopy with intraoperative selective blood sampling of the ovarian veins is a useful approach in patients without accurate preoperative localization of diminutive estrogen-producing tumors of the ovaries.

Key words: Microscopic granulosa cell tumor; Laparoscopy; Selective venous sampling.

Introduction

Clinical signs in postmenopausal women of hyperestrogenism, such as vaginal bleeding and breast enlargement, with rapid onset of symptoms and markedly elevated serum levels of estradiol strongly suggest the presence of an estrogen-secreting tumor. The correct surgical approach to remove such tumors depends on their accurate localization. Usually, imaging procedures help to identify the tumor preoperatively. However, localizing the source of hyperestrogenism preoperatively can be difficult when the tumor is small.

The authors report herein a postmenopausal woman with hyperestrogenism associated with microscopic granulosa cell tumor (GCT), which failed to be preoperatively detected due to diminutive tumor size but was successfully excised during explorative laparoscopy after selective ovarian vein sampling.

Case Report

A 58-year-old menopausal gravida 0 para 0 woman was referred to this clinic for evaluation of vaginal bleeding and marked breast enlargement and tenderness, which had appeared six months earlier. Her menopause occurred at 53 years of age and

she did not take any medication that had estrogenic side-effects. Her medical history included hypertension and type II diabetes mellitus. At gynecological examination, multiple uterine myomas were palpated without adnexal masses. Pelvic ultrasound and magnetic resonance imaging revealed multiple uterine leiomyomas, endometrial thickness was 14 mm, and normal ovaries without evidence of tumor or cyst. Endometrial biopsy revealed simple endometrial hyperplasia without atypia. Laboratory investigations revealed an extremely elevated serum estradiol level of 713 pg/ml. FSH and LH concentrations were premenopausal (FSH level of 2.02 mIU/ml and LH level of 5.74 mIU/ml). The concentrations of progesterone (0.3 ng/ml) and testosterone (0.37 ng/ml) were normal.

An exploratory laparoscopy was performed. Macroscopically both ovaries seemed to be normal (Figure 1). Selective sampling of the ovarian veins was performed intraoperatively, giving clear evidence of an estrogen-producing tumor of the left ovary: the left ovarian venous estradiol concentration was 5,320 pg/ml. In contrast, the serum estradiol level from the right ovarian vein was 398 pg/ml. Consequently, left salpingo-oophorectomy was carried out during the same surgical procedure, but failed to identify estrogen-producing lesions on frozen sections.

The patient's postoperative course was uneventful. Serum levels of estradiol decreased markedly after the operation. The detailed histological and immunohistological examination confirmed the diagnosis of a GCT of 5 mm in diameter with grooved nuclei and Call Exner bodies (Figure 2). Twenty months after surgery the patient is without evidence of recurrence. The patient gave her consent for the case report to be published.

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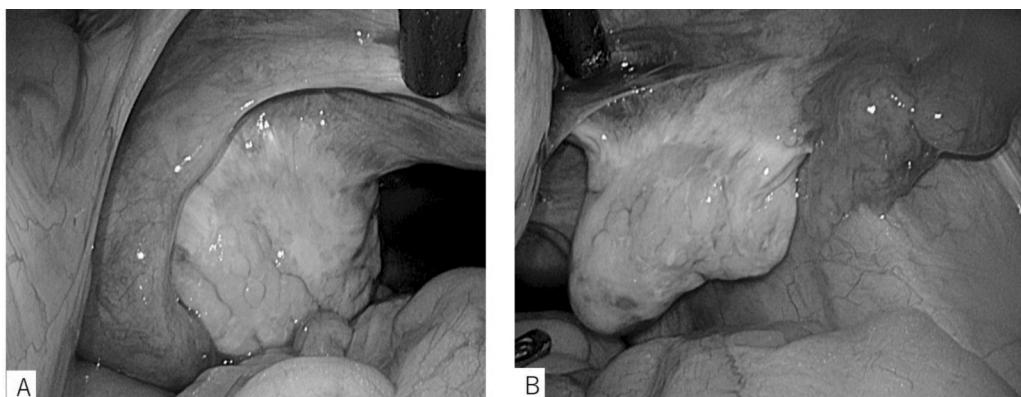


Figure 1. — Macroscopically both ovaries (A: left ovary, B: right ovary) appear to be normal.

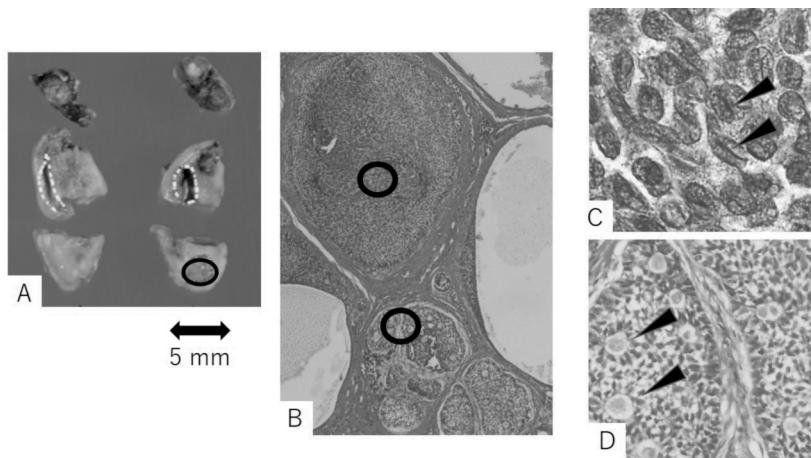


Figure 2. — The tumor is 5 mm in diameter (A). With Hematoxylin-Eosin staining (B), longitudinal nuclear grooves (C), and Call-Exter bodies (D) are demonstrated.

Discussion

GCTs are derived from the granulosa cells and hormonally active neoplasms secreting high levels of estrogen. Symptoms related to hyperestrogenism occur at all ages. Postmenopausal bleeding is the most common finding in the postmenopausal age group. Breast enlargement and tenderness occurs secondary to estrogen action. Around 25–50% cases are associated with endometrial hyperplasia and endometrial cancer is seen in 5–13% cases [1]. Detection of high estrogen production requires identification of the exact anatomic location of the hormone-producing tissue, before performing a surgical procedure to remove the pathological tissue. GCTs are usually >10 cm in size (73.5%) but can vary from a small nonpalpable lesion to large masses (3–24 cm) [2]. Localizing the source of excessive hormone secretion preoperatively can be difficult when the tumor is small as in the present case.

In the literature, two alternative diagnostic approaches for androgen-secreting tumors of the ovary have been reported: preoperative selective venous blood sampling by catheterization of the ovarian veins or intraoperative selective blood sampling in combination with a rapid hormone assay.

Selective venous catheterization has been recommended as an accurate method for the diagnosis and localization of hormone-secreting ovarian and adrenal tumors [3, 4]. However, diagnostic specificity of this technique is often disappointing even in experienced hands, and in some cases pre-operative venous sampling was attempted but not achieved [5]. Moreover, this procedure carries the risks of invasive and may cause complications including systemic reaction to the contrast agent, hematomasis [6]. Due to these reasons, the present authors chose to perform a laparoscopy and selectively obtained blood samples from the ovarian veins for immediate laboratory investigation, which gave them clear evidence of an estrogen-producing tumor of the affected ovary, and pathological examination of the removed ovary confirmed the presence of the GCT.

In conclusion, gynecologists may be faced with diagnostic pitfalls when confronted with patients with severe excess estrogen production which cannot be identified preoperatively due to the diminutive size. In such cases, exploratory laparoscopy with ovarian venous sampling might be correct in order to establish the histological nature of the neoplasm with a chance of removing the entire lesion.

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