Bilateral Ovarian Capillary Hemangioma with Stromal Luteinization and Hyperandrogenism

Richard Sheng Poe Huang, Michael Covinsky, and Songlin Zhang

Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, USA.

Abstract. A 77-year-old female presented to the outpatient clinic with a six-month history of left lower quadrant abdominal fullness and pressure. Serum levels included free testosterone 3.8 pg/mL (normal 0-1.8 pg/mL) and testosterone 259 ng/dL (normal 3-41 ng/dL). Magnetic resonance imaging of the pelvis showed bilateral small ovarian cystic masses with marked, progressive enhancement, and restriction of diffusion. Laparoscopic bilateral salpingo-oophorectomy was performed and showed left and right ovarian hemorrhagic masses measuring 2.1 cm and 0.6 cm respectively. The histology showed benign vascular lesions composed of small capillary vessels with a rim of luteinized stromal cells. The luteinized cells were strongly positive for inhibin A. The endothelial cells were negative for estrogen receptor and progesterone receptor. To our knowledge, this is the first reported case of bilateral ovarian hemangioma with stromal luteinization and hyperandrogenism.

Introduction

Hemangiomas are benign vascular tumors and are rarely found in the ovaries. Indeed, only approximately 50 cases have been reported in the literature [1-4]. It is possible that some cases may not be recognized or recorded, but all investigators consider ovarian hemangiomas rare. In most patients, ovarian hemangioma is an incidental finding during operation or autopsy, but some patients present with abdominal pain associated with torsion, abdominal enlargement due to the mass effect, or ascites [3,5-6]. The lesions are usually unilateral, but rarely present with bilateral or diffuse disease [7]. Very few cases of ovarian hemangiomas have shown stromal luteinization [6,8-12], and this phenomenon has been only occasionally associated with hyperandrogenism [8,12]. Here, we report a case of bilateral ovarian hemangiomas with stromal luteinization and hyperandrogenism.

Case Report

A 77-year-old female (grAVIDA 3, para 3) presented to the gynecology outpatient clinic with a six-month history of left lower quadrant abdominal fullness and pressure. She rated the pain as 5 out of 10 and described the pain as intermittent and non-radiating. The patient denied weight changes, fever, chills, vomiting, male-pattern hair growth, hair loss, and vaginal discharge. Her medical history was significant for a hysterectomy performed 40 years previously and a left breast cyst removal 30 years previously. She had no history of hormone replacement therapy. A pelvic exam demonstrated a normal clitoris and a two-centimeter vaginal polyp at 11 o’clock. The cervical cytology was negative for intraepithelial lesions or malignancy. The vaginal polyp was benign. Complete blood counts and serum chemistries were within normal limits. The serum hormonal levels were free testosterone 3.8 pg/mL (normal 0-1.8 pg/mL), and testosterone 259 ng/dL (normal 3-41 ng/dL).

Chest X-ray and bilateral mammographic examination demonstrated no abnormalities. A trans-vaginal ultrasound examination demonstrated a hyper-echoic left pelvic mass measuring 2.8 x 2.7 x 2.4 cm. Magnetic resonance imaging of the pelvis showed bilateral small ovarian cystic masses with marked, progressive enhancement, and restriction of diffusion. Mural nodularity and enhancing septations were noted in the left ovary. Computed tomography scanning of the abdomen and pelvis demonstrated diffuse lamellate-type calcification of the left ovary and a small area of focal calcification of the right ovary.

Laparoscopic bilateral salpingo-oophorectomy was performed. Intraoperative frozen section consultation revealed no evidence of epithelial malignancy. Grossly, the left ovary measured 4.3 x 3.8 x 1.0 cm with tan-pink bosselated serosal surface and some capsular adhesions. The cut sections revealed a variegated pink-red focally hemorrhagic mass measuring 2.1 x 2.0 x 1.5 cm. The right ovary measured 3.0 x 2.0 x 1.0 cm with some serosal adhesions. A small hemorrhagic mass was noted measuring 0.6 cm.
The histopathology revealed benign vascular lesions composed of numerous capillary vessels with a rim of surrounding luteinized ovarian stromal cells (Figure 1A). This finding was present in both the left and right ovaries. The endothelial lining cells showed no nuclear atypia or any mitoses. The luteinized stromal cells had abundant granular cytoplasm, and some had clear vacuolated cytoplasm (Figure 1B and 1C). No teratoma or epithelial tumors were found. The endothelial cells were negative for estrogen receptor (ER) and progesterone receptor (PR). The luteinized stromal cells were strongly positive for Inhibin A, and had no PAS-D resistant cytoplasmic crystals (Figure 1D).

**Discussion**

Even though the ovary is very rich in vasculature, ovarian hemangiomas are very rare, with only 50 reported cases [1]. Small ovarian hemangiomas may be difficult to distinguish from the dilated hilar vessels. A true hemangioma should have minimal amounts of ovarian stroma and form a reasonably circumscribed mass. Ovarian hemangiomas can occur at any age. Most ovarian hemangiomas are cavernous type, and some are mixed cavernous-capillary or pure capillary type [11]. Other types of ovarian vascular lesions also have been reported in the literature, such as epithelioid hemangioendothelioma [13] and infantile hemangioendothelioma [14]. Ovarian hemangiomas are usually incidental findings, but some may mimic ovarian carcinoma presenting with an adnexal mass, elevated CA-125, and ascites [6,15,16]. Ovarian hemangiomas may occur synchronously with ovarian serous papillary carcinoma [17]. Some authors believe that hyperestrogenism resulting from stromal luteinization is the inciting event in the development of ovarian hemangiomas [9,11], based on the fact that estrogen has a growth-stimulatory effect on vasculatures. Miliars et al [11] found that endothelial cells were positive for ER and PR in their case; however, endothelial cells were negative for both ER and PR in our case and in other reports [8].

*Figure 1. The ovarian mass is composed of a proliferation of capillary vessels with bland-appearing endothelial cells (A, H&E, 40X). A rim of luteinized ovarian stromal cells is noted with abundant eosinophilic granular cytoplasm or clear and vacuolated cytoplasm (B, H&E, 40X; C, H&E, 100X). These cells are strongly positive for inhibin A (D, Inhibin A, 20X).*
Ovarian hemangiomas may have associated stromal luteinization [6-12], and different hypotheses have been proposed for the pathogenesis of stromal luteinization. One hypothesis is the mechanical theory, in which it is thought that the tumor behaves like an enlarged follicle with pressure on the adjacent tissue, inducing the development of thecal cells [6]. Another hypothesis is that stroma-stimulating substances secreted by neoplastic endothelial cells cause the stromal luteinization [6]. Like other reported cases, our case showed a layer of stromal luteinization surrounding the capillary hemangioma. There was minimal or no intrallesional stromal luteinization, which is consistent with the mechanical hypothesis. It is well established that human chorionic gonadotropin may also induce stromal luteinization. In our patient’s lesions, there is no morphological evidence of intermediate trophoblast or syncytiotrophoblast, further supporting the mechanical hypothesis.

Gucer hypothesized that ovarian hemangiomas initiate stromal luteinization and can lead to hyperandrogenism and hyperestrogenism [8]. It is well known that luteinized stromal cells produce androgens that can be converted to estrogen in the adipose tissue. This can result in both hyperandrogenism and hyperestrogenism. In our patient, both the free and total testosterone levels were high at 3.8 pg/mL and 259 ng/dL, respectively. Only rare reported cases of ovarian hemangiomas have had hyperandrogenism [8,12]. Our patient had no male hormonal manifestation when presented at outpatient clinic, but the other two patients in the literature presented with male pattern receding front hairline, endometrial carcinoma, and virilization [8,12].

To our knowledge, this is the first reported case of bilateral ovarian capillary hemangioma with stromal luteinization and hyperandrogenism. While the relationship between ovarian hemangiomas and stromal luteinization remains unclear, our case provides some evidence to support the hypothesis that mechanical force may be the inciting event in the development of stromal luteinization. Ovarian hemangioma with elevated male hormones may mimic ovarian sex-cord stromal tumors such as Leydig cell tumor, and it may mimic ovarian epithelial carcinoma when serum CA-125 is significantly high.

References