What is your diagnosis?

A 34-year-old woman, P2L2, presented to the outpatient department with a one-month history of abdominal distension. It was sudden in onset, progressive, and associated with abdominal pain and heaviness, accompanied by backache. She reported irregular and frequent menstrual cycles for two years. A history of loss of appetite and constipation was also present. Abdominal examination revealed a grossly distended abdomen with a huge abdominopelvic mass corresponding to 30 weeks' size involving all quadrants of the abdomen, with no shifting dullness and fluid thrill. External genitalia, cervix and vagina appeared healthy. The same abdominopelvic mass was felt on vaginal examination with bilateral fornical and pouch of Douglas fullness; uterus could not be palpated separately. Ultrasound was suggestive of a large (26x25.3x14.7 cm) cystic lesion with septations and Doppler color flow, but the bilateral ovaries and uterus were not defined separately. Among tumor markers, CA-125 (339 U/mL) and lactate dehydrogenase (LDH) (1650 U/L) values were raised while carcinoembryonic antigen, alpha-fetoprotein (AFP), beta-hCG and CA19-9 levels were within normal limits. A contrast-enhanced magnetic resonance imaging study was ordered for mass characterization and reported a 28x25x18 cm large solid cystic mass in the right adnexa with solid areas, apparently a right ovarian neoplastic mass. In view of a high suspicion of ovarian malignancy, staging laparotomy was planned after thorough counseling of the patient and her husband. She had no desire for future fertility and was keen to undergo definitive surgery in a single session. A prior written consent was obtained for staging laparotomy, along with hysterectomy and contralateral oophorectomy, if intraoperative frozen section suggests epithelial ovarian malignancy.

Intraoperatively, straw-coloured ascites (≃800 cc) was noted. An approximately 30x30 cm large solid cystic mass was seen arising from the right ovary with an intact capsule and no surface excrescences. The mass was dissected from all attachements. It weight 5.8 kg (Figure 1A). The cut specimen contained 2.5 litres of hemorrhagic fluid with multiloculated cystic, solid and necrotic areas (Figure 1B). The frozen section was suggestive of serous cystadenocarcinoma. Therefore, complete cytoreductive surgery was performed (total abdominal hysterectomy, left salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy, and gastric arcade sparing omentectomy).

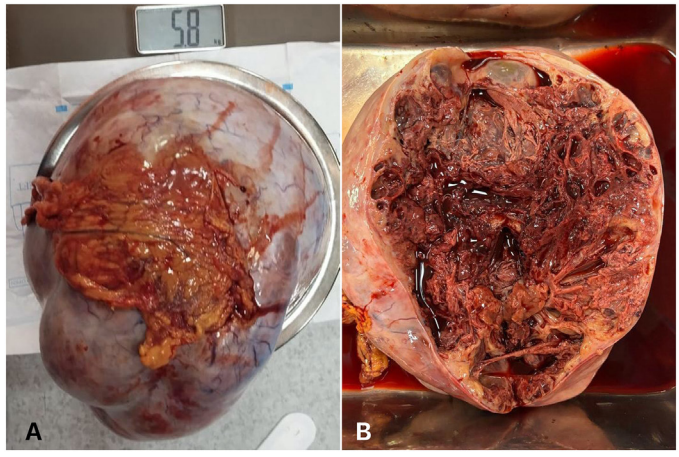

Figure 1. (A) Right ovarian mass weighing 5.8 kg; (B) The cut specimen containing 2.5 litres of hemorrhagic fluid with multiloculated cystic, solid and necrotic areas

Answer

The final histopathology report revealed the diagnosis of a Sertoli Leydig cell tumor (SLCT) FIGO stage 1A with calretinin focal positive, CD 56 focal positive, vimentin positive and PR focal positive (Figure 2).

Inhibin A and B levels were ordered after the final diagnosis, which were within normal limit (0.8 ng/L and <10 pg/L, respectively). A medical oncology opinion was sought, and she was planned for three monthly follow-ups with CA-125 measurements.

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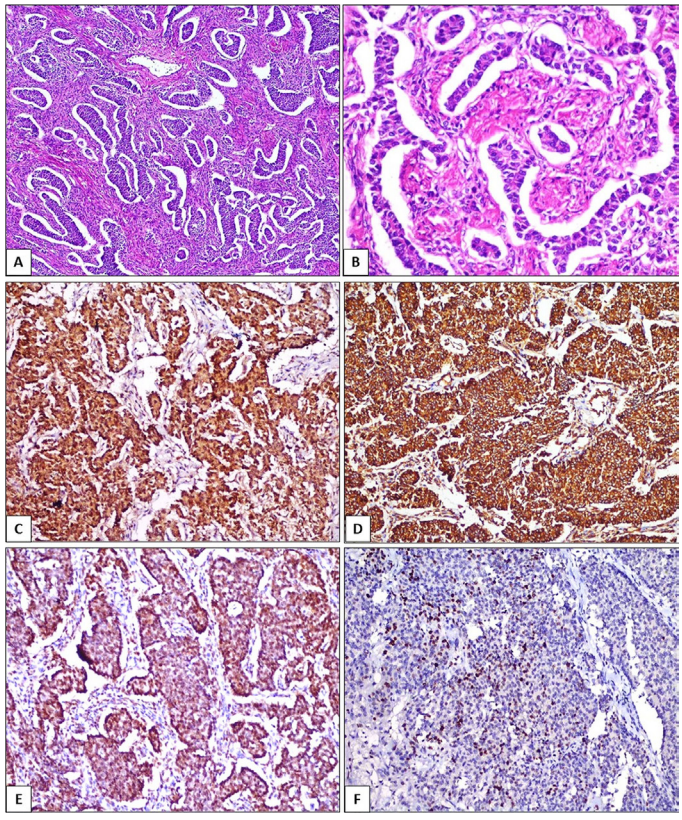

Figure 2. (A) Haematoxylin and eosin stained section shows Sertoli cells arranged in nests and tubules without significant nuclear atypia. Delicate fibrous stroma contains Leydig cells singly (Ax100); (B) Higher magnification shows irregular solid tubules, nests of Sertoli cells with mild cytological atypia and plump eo-sinophilic Leydig cells in within stroma (Bx200); (C) Immunohistochemistry (IHC) demonstrating positivity for Vimentin; (D) Immunopositive for calretinin; (E) Weak minimal positivity for WT-1; (F) IHC for Ki-67 shows mild mitotic activity

Postoperative CA-125 values were 9 U /mL and 5.50 U/mL at 3 months and 6 months, respectively. Currently, she is asymptomatic with no signs of radiological or biochemical recurrence.

SLCTs are a rare group of ovarian malignancies that contribute to <0.5% of all ovarian neoplasms (1). It occurs mostly in prepubertally or within the first three decades of life (2,3). It is the most common virilizing ovarian tumor. These tumors frequently produce sex steroid hormones, mostly androgens. Therefore, most of the patients present with overt virilization (amenorrhea, hirsutism, acne, hoarseness of voice, clitoromegaly, labial hypertrophy and psycho-sexual behavioral changes) (2-5). Rarely, patients may present with features of hyperestrogenism, i.e. precocious pseudopuberty, menometrorrhagia and postmenopausal bleeding (6). In the absence of hormonal manifestations, patients may present with non-specific mass symptoms like abdominal distension, pain, and heaviness (7). Hence, preoperative diagnosis may be challenging. The present case also had an atypical presentation with complaints of abdominal distension, pain and frequent menstrual cycles. The majority of SLCTs are unilateral and classified as stage I. In the literature, the largest size of SLCT documented was 24 cm, with an average size being 12-14 cm (7,8), whereas the mass in the present case was 30 cm and weighed 5.8 kg.

Grossly, SLCTs show solid, fleshy, yellow, and lobulated cut surfaces with focal cyst formation. Histologically, SLCTs are classified into five sub-types: well-differentiated, moderately-differentiated, poorly-differentiated, retiform, and those with heterologous elements (1). The degree of differentiation is based on Sertoli tubular differentiation, the proportion of Leydig cell component, and the quantity of primitive gonadal stroma. Sertoli and Leydig cells of SLCTs express inhibin, calretinin, SF1, and CD5. Molecular types of SLCT are: (a) DICER1- mutant; (b) FOXL2 c.402C>G (p.Cys134Trp)-mutant; and (c) DICER1/FOXL2-wildtype (9).

Inhibin-B is the most commonly used biomarker for the diagnosis of SLCTs. However, CA-125 has also been reported to be elevated in 42% of cases of sexcord stromal tumors and has a prognostic role in such cases. Patients with raised CA-125 had worse overall survival than those with normal values (10). Our patient had raised CA-125 and LDH levels with normal AFP, inhibin A and B levels. There are no specific imaging findings pertaining to SLCTs.

Surgery is the mainstay of treatment. Since the majority of these tumors are unilateral and affect young women, a fertility-sparing surgical approach is appropriate. For women with bilateral disease, advanced stage, or postmenopausal status, a complete cytoreductive procedure, including total abdominal hysterectomy and bilateral salpingo-oophorectomy should be performed (11). Lymphadenectomy may be omitted as these tumors rarely spread to lymph nodes (12). Complete cytoreductive surgery was performed in the present case as the frozen section was suggestive of serous cystadenocarcinoma and the patient was keen to undergo definitive surgery in a single operating session. The role of frozen section is limited in the accurate diagnosis of rare ovarian tumors, such as sex cord stromal tumors and germ cell tumors, as they can mimic epithelial ovarian tumors, which was what happened in our case (13).

The scarcity of data limits the understanding of the prognostic factors of the disease and the role of adjuvant therapy. However, the grade and stage of the disease seem to be important prognostic factors. Sigismondi et al. (14) reported an excellent five-year survival rate of 100% in grade 1 tumors, while it fell to 77.8% in grade 2 and 3 tumors. They also documented a high five-year survival rate of 92.3% when tumors were localized

to the ovary, but once they become metastatic, the prognosis worsens significantly, with a five-year survival of only 33.3%. This tumor type has a relapse rate of 0 to 33.3% and 95% of them relapse within 5 years. The prognosis is extremely poor in recurrent disease, with a salvage rate of less than 20% (15).

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