Bilateral Sertoli-Leydig cell tumor in a primigravida: a rare case

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Abstract

We present a unique case of incidentally discovered bilateral Sertoli Leydig cell tumour in a primigravida who displayed no features of virilization. The alpha fetoprotein levels were elevated. Magnetic resonance imaging was suggestive of ovarian tumour, possibly germ cell tumour. Bilateral salpingo-oophorectomy was performed and histopathology showed features of Sertoli Leydig cell tumour with intermediate to poor differentiation. Immunohistochemistry was positive for calretinin and inhibin, while cytokeratin was negative. Four courses of bleomycin-, etoposide- and cisplatin-based chemotherapy regimen was started, but the patient aborted while receiving the second cycle of chemotherapy. She received the remaining two cycles of chemotherapy and is now on close follow up with monitoring of serum inhibin levels to detect any tumor recurrence. Bilateral Sertoli Leydig cell tumor has not been reported previously in a pregnant female. The aim of this article is to describe the clinical, radiological and pathological features and management of this rare entity.

Case Report

A 27-year-old primigravida presented with abdominal pain and distension for 3 months, and vomiting for 2 weeks. She was found to have bilateral adnexal masses on routine ultrasound examination at 16 weeks of gestation. On palpation, these masses were mobile, non-tender, soft to firm in consistency and had smooth surface. The lower border could not be made out. These masses were felt apart from uterus which was around twelve weeks size. There was moderate ascites. Both the ovaries were enlarged and replaced by well-defined hypoechoic lesions. There was another anechoic, cystic lesion measuring 5.8×5.3 cm in left ovary which had increased vascularity on color Doppler. Alpha fetoprotein (AFP) levels were elevated (27.05 μg/L) while lactate dehydrogenase (LDH) (190.70U/L) and CA 125 (4.78 U/mL) levels were normal. Magnetic resonance imaging (MRI) showed large well-defined bilateral abdomino-pelvic adnexal masses, measuring 20×16×15 cm (R), 18×12×11 cm (L); extending into the abdomen and superiorly indenting liver/gall bladder on right side and small bowel loops on left side. These lesions were indenting the parietal wall without any infiltration and posteriorly they were indenting on right kidney and vessels in root of mesentery. The radiological impression was that these masses were neoplastic, likely to be germ cell tumor (Figure 1). There was no evidence of any metastatic deposits on whole body MRI examination. The chest X-ray was normal. There was moderate ascites. Cytological examination of ascitic fluid was negative for malignant cells. The patient was discharged on post-operative day.

Histopathology

Microscopically, the tumor showed areas of hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells having hypercellular areas showed Sertoli cells 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Pathology

Grossly, right and left ovarian masses measured 21×19×11 cm and 19×17×9 cm respectively. Outer surface was smooth, without any capsular breach. The cut surface of both the masses showed solid areas with greyish white appearance and foci of hemorrhage (Figure 2). Microscopically, the tumor showed areas of variable cellularity. The hypercellular areas were separated by loose hypocellular stroma containing Leydig cells. Occasional scattered cells had signet ring cell morphology. The hypercellular areas showed Sertoli cells having round to oval and angular nuclei, some with prominent nucleoli. Few Sertoli cells were spindle shaped. The Sertoli cells were arranged in the form of masses and nests, forming lobular pattern, as well as in the form of hollow and solid tubules and cords. Some tubules contained eosinophilic secretions (Figure 3). Large areas of hemorrhage and necrosis were also present. No heterologous elements were identified. The tumor cells were negative for PAS-AB and Mucicarmine. Immunohistochemistry showed positivity for alpha fetoprotein, CK-7, CK-20 and inhibin. The patient was discharged on fourth post-operative day.
ation was made. Both Fallopian tubes were free of tumor.

**Discussion**

Sertoli Leydig cell tumor, a type of sex cord stromal tumor is an unusual ovarian neoplasm which accounts for less than one percent of ovarian tumors. Majority of these tumors are diagnosed in young women of reproductive age group (second and third decade) and are unilateral. Clinical signs and symptoms can be ascribed to the pressure symptoms arising from the presence of abdomino-pelvic mass and/or excessive production of androgen and rarely, estrogen. Patients generally present with signs and symptoms of virilization due to excessive testosterone production like oligomenorrhea followed by amenorrhea, loss of female secondary sexual characteristics with atrophy of breasts and loss of normal bodily contours, flaring up of acne, clitoromegaly, deepening of voice, hirsutism and temporal baldness. Excessive estrogen production may result in precocious puberty, abnormal vaginal bleeding, menstrual irregularities, generalized edema, weight gain, endometrial hyperplasia, endometrial polyps and endometrial carcinoma. Features of masculinization were absent in this case. Instead, the patient had secondary amenorrhea due to pregnancy. Serum testosterone and dehydroepiandrosterone levels were also within normal range. This can be explained by aromatization of androgens to estrogen by placenta. Due to bilaterality of the tumor and the presence of signet ring cells on histopathology, a differential diagnosis of metastatic carcinoma was considered. However on immunohistochemistry, the tumor cells were found to be positive for inhibin and calretinin and negative for cytokeratin, which clinched the diagnosis of Sertoli Leydig cell tumor.

The prognosis of these rare tumors depends on the stage and degree of differentiation. Tumors in advanced stage have poor prognosis with 100% mortality. The survival rates in tumors diagnosed in stage I is associated with the degree of differentiation. In a large series, 11% of tumors with intermediate differentiation and 59% of tumors with poor differentiation behaved in a malignant fashion with ten year survival rates of 87% and 41% respectively. Other factors which adversely influence prognosis include high mitotic profile, presence of heterologous elements, retiform component and tumor rupture. The factors to be kept in mind while deciding the treatment are

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**Figure 1.** Magnetic resonance imaging showed large well defined bilateral abdomino-pelvic adenexal masses, 20×16×15 cm (R), 18×12×11 cm (L); extending into the abdomen and superiorly indenting liver/gall bladder on right side and small bowel loops on left side. The radiological impression was that these masses were neoplastic, likely to be germ cell tumor.

**Figure 2.** Outer surface of the ovarian masses was smooth, without capsular breech (a); cut surface showed solid areas with foci of hemorrhage (b).

**Figure 3.** The tumor showed (a) hypercellular areas separated by loose hypocellular stroma (2×); b) Lobules of Sertoli cells separated by myxoid stroma containing spindle cells (10×); c) Sertoli cells arranged in the form of cords, hollow and solid tubules, some of which contained eosinophilic secretions (20×). Inset showing Sertoli cells staining positive for Inhibin on IHC; d) Leydig cells scattered in the hypocellular stroma (40×). Inset showing tumor cells staining positive for Calretinin on IHC.
age of the patient, stage of the tumor, presence of rupture and degree of differentiation. Adjuvant therapy is warranted for stage I tumors with poor differentiation, containing mesenchymal heterologous elements, or ruptured tumors with intermediate differentiation. Due to the presence of high risk factor (intermediate to poor differentiation of tumor morphology), the patient was planned for chemotherapy also after interval of three weeks each, as scheduled. She is on close follow-up with occurrence of serum inhibin and testosterone levels, every three months, to detect any tumor recurrence. Post treatment follow-up should be done every three months during the first year, every four months during the second year, every six months during the third year, and annually thereafter for lifetime. Sertoli-Leydig cell tumors generally recur within 36 months. However, recurrences as late as 35 years have also been reported. Therefore, lifelong follow-up is recommended. Recurrences are confined to the pelvis and abdomen, although distant metastatic deposits in bones, lung and lymph nodes have also been reported.

Conclusions

Herein, we have described the clinical, radiological and pathological features of a rare gynecological tumor in a primigravida, along with its management. To the best of our knowledge, bilateral Sertoli Leydig cell tumor has not been reported previously in a pregnant female. Such a rare phenomenon should alert the clinician to the possibility of rare ovarian tumor while evaluating abdomino-pelvic masses in women of reproductive age group.

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Table 1. Hematological, biochemical and other investigations of the patient.

| Test                        | Patient’s values | Normal values |
|-----------------------------|------------------|---------------|
| Hemoglobin                  | 10 gm%           | 11-14 gm%     |
| Total leucocyte count       | 11,800/µL        | 4000-11,000/µL|
| Platelets                   | 4.3 lac/µL       | 1.5-4 lac/µL  |
| Prothrombin time index      | 86%              | >80%          |
| Serum testosterone          | 0.4 ng/mL        | 0.2-2.98 nmol/L|
| Serum dehydroepiandrosterone| 6.6 nmol/L       | 4.5-34 nmol/L |
| Thyroid stimulating hormone | 2.8 m U/L        | 0.3-4.5 m U/L |
| 17ß estradiol               | 125 pg/mL        | 112-143 pg/mL |
| Sex hormone binding globulin| 42               | 18-114 n mol/L|
| Alpha fetoprotein           | 27.05 µg/L       | <15 µg/L      |
| Lactate dehydrogenase       | 190.70 U/L       | 100-190 U/L   |
| CA 125                      | 4.78 U/mL        | 0-35 U/mL     |
| CA 19.9                     | 3.5 U/mL         | 0-37 U/mL     |
| Carcinoembryonic antigen    | 0.2 µg/L         | 0-3.4 µg/L    |

Table 2. Hematological, microbiology and radiological investigations of the patient.

| Test                        | Patient’s values | Normal values |
|-----------------------------|------------------|---------------|
| Rh blood group              | B negative       |               |
| Indirect Coomb’s test       | Negative         |               |
| Urine routine microscopy    | Normal           |               |
| Urine culture and sensitivity| Sterile         |               |
| HIV , HBsAG, VDRL           | Not reactive     |               |
| Hemoglobin electrophoresis  | Normal           |               |
| Chest X-Ray and electrocardiogram| Normal      |               |