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 apha fetoprotein levels were elevated. Magnetic resonance imaging was suggestive of ovarian tumors, possibly germ cell tumor. Bilateral salpingo-oophorectomy was performed and histopathology showed features of Sertoli Leydig cell tumor 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 Sertloli 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.

Introduction

Sertoli Leydig cell tumors are rare ovarian neoplasms, accounting for less than one percent of ovarian tumors and commonly occurring unilaterally, in second to third decade.[1,2] They present with masculinizing features due to excessive testosterone secretion.[2] Bilateral occurrence of Sertoli Leydig cell tumor is rarely reported.[3] Occurrence of this tumor with pregnancy is rarer and there is, to the best of our knowledge, only a single case report describing a unilateral tumor of 0.6 cm diameter in a pregnant female.[4]

We present a unique case of bilateral adnexal masses in a primigravida, which turned out to be Seroli Leydig cell tumor on histopathology. The tumor was discovered incidentally in the patient, who displayed no features of virilization. After surgical removal of both the adnexae, chemotherapy was administered. The patient is now on close follow up.

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 period 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 adenexal 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. Anteriorly these masses were indenting on 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 ascietic fluid was negative for malignant cells. The hematological, bio- chemical and other investigations of the patient are summarized in Tables 1 and 2. Other laboratory tests including sex hormone binding globulin, 17 β estradiol, were within normal limits. Staging laparotomy was planned and frozen section of the right adnexal mass was suggestive of malignancy. Bilateral salpingo-oophorectomy was performed. Per operatively, both the ovaries were enlarged. However, the capsular surface was intact. No lymphadenopathy or metastatic deposits were noted. Thus, the tumor was assigned FIGO Stage 1B. The uterus was found to be of 14 weeks size and was handled as gently as possible. Post-operative course was uneventful and there were no contractions or undue bleeding per vaginum. Ultrasound revealed single living fetus, with fetal cardiac activity present. The patient was discharged on fourth post-operative day.

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 breech. 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 calretinin and inhibin. CK-7, CK-20 and AFP were negative. A diagnosis of Sertoli-Leydig cell tumor with intermediate to poor differenti-

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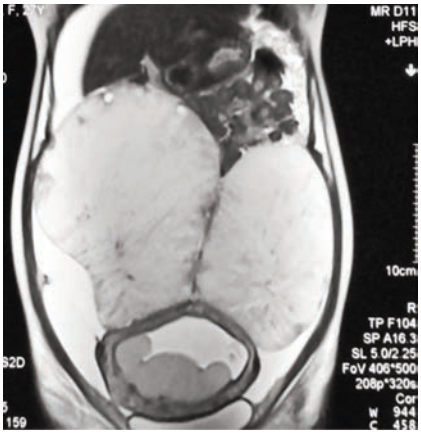

Figure 1. Magnetic resonance imaging showed large well defined bilateral abdomino-pelvic adenexal masses, 20×16×15 cm (R), 18×12×11 cm (L); extending into the abdomen and superiorly indenting liver/gall bladder on right side and small bowel loops on left side. The radiological impression was that these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

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.[1] 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.[5] 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.[2,5] 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

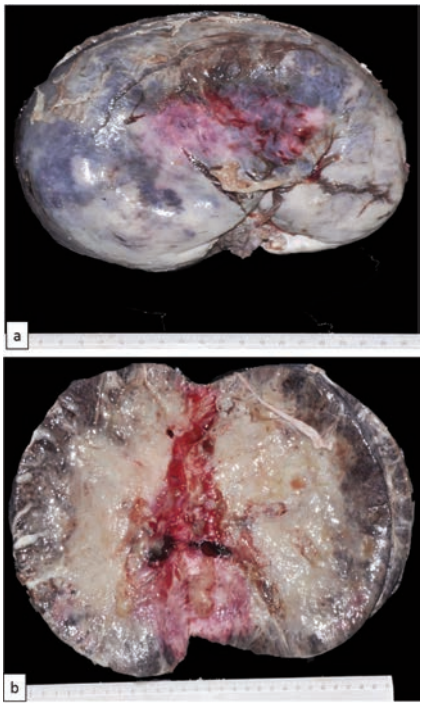

Figure 2. Outer surface of the ovarian masses was smooth, without capsular breech (a); cut surface showed solid areas with foci of hemorrhage (b).

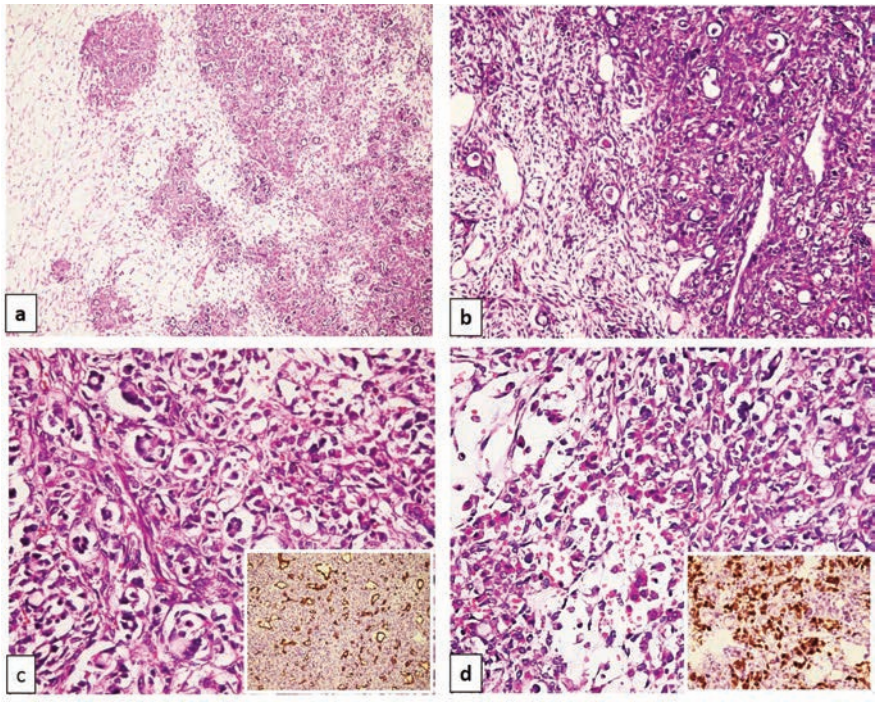

Figure 3. The tumor showed (a) hypercellular areas separated by loose hypocellular stroma (2×); b) Lobules of Sertoli cells separated by myxoid stroma containing spindle cells (10×); c) Sertoli cells arranged in the form of cords, hollow and solid tubules, some of which contained eosinophilic secretions (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.

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 mU/L	0.3-4.5 mU/L
17 β 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.

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

age of the patient, stage of the tumor, presence of rupture and degree of differentiation. Adjuvant therapy is warranted for stage 1 tumors with poor differentiation, containing mesenchymal heterologous elements, or ruptured tumors with intermediate differentiation.[2] Due to the presence of high risk factor (intermediate to poor differentiation of tumor on morphology), the patient was planned for four courses of combination chemotherapy regimen which included bleomycin, etoposide and cisplatin, at three week interval.[6] However, she aborted during second cycle of chemotherapy. The patient reported white discharge per vaginum along with bleeding. Ultrasonographic evaluation could not detect fetal cardiac activity. Nevertheless, the chemotherapy regimen was not discontinued. The patient received third and fourth cycles of chemotherapy also after interval of three weeks each, as scheduled. She is on close follow up with ultrasonographic evaluation of abdomen and pelvis along with serial monitoring of serum inhibin and testosterone levels, every three months, to detect any tumor recurrence.[7] 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.[8] 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.[2,7,8]

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 Sertloli 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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