A rare case of endometriosis to clear cell ovarian carcinoma: a case report

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ABSTRACT

Clear cell carcinoma of ovary is a rare tumour with a very low incidence in pregnancy. It is attributed to develop from an existing background of endometriosis. There are very few case reports of the above combination tumours in pregnancy. It is a very aggressive tumour with a worse prognosis and low survival rate because of its peculiar chemo resistant nature. Early detection and effective treatment are the best approach. The treatment options for advanced stages are still under research.

Keywords: Aggressive, Chemo resistant, Clear cell carcinoma, Endometriosis, Low survival, Rare, Worse prognosis

INTRODUCTION

Incidence of ovarian masses detected during pregnancy is between 0.1% and 2%.
Majority of them are cystic in nature and incidence of ovarian malignancy in pregnancy is between 1:10,000 and 1:50,000 with a higher prevalence for dysgerminomas and malignant teratomas.

Clear cell carcinomas arise from a back ground of ovarian endometriosis with an incidence of 0.8% with its occurrence in pregnancy being extremely rare. It is a subtype of epithelial ovarian cancer with a general incidence of 3.7-12.1%. Majority are diagnosed at FIGO Stage I and present as a large pelvic mass with size ranging from 3 to 20 cm. Bilaterality is rare with frequent complications like thromboembolism and hypercalcemia. Histologically, it is characterised by clear cells in solid/tubular or glandular pattern and hob nailing. The treatment consists of staging laparotomy followed by combination (platinum and paclitaxel) chemotherapy, but advanced stages are found to be chemo resistant. Therefore, the recurrence rate is found to be high and survival rate is low and as such it is a highly aggressive tumour.

CASE REPORT

A 31-year-old primi gravida at 30 weeks 4 days gestation who was a booked case in an outside hospital was referred to Travancore Medical College, Kollam as a case of IUGR, abnormal Doppler, oligohydramnios, placenta previa, breech presentation with a right adnexal cyst. On detailed enquiry into her pre conceptional and antenatal period, it was found that she conceived after ovulation induction and was a k/c/o ovarian endometriosis diagnosed with right ovarian cyst since 2013 and was advised cystectomy for the same, but was reluctant to undergo surgery. Therefore, as a part of infertility treatment she underwent multiple cycles of ovulation induction. First and second trimesters were uneventful and the scans were corresponding with an evident right...
adnexal endometriotic cyst of size 5x5 cm. At 29 weeks on her growth scan she was detected to have placenta previa, with growth corresponding to 27 weeks and AFI of 3-4 cm. So, she was admitted and was given supportive treatment with intravenous fluids for correction of oligohydramnios, betamethasone injection for foetal lung maturity repeat scan after 5 days also showed AFI of 3-4 cm and was referred to our hospital.
On obstetric USG and doppler assessment from our hospital at 30 weeks 4 days showed IUGR of 2 weeks disparity, high resistance flow in umbilical artery and a large cystic area in right adnexa measuring 8.5x6 cm containing focal solid areas (Figure 1) with minimal peripheral vascularity (Figure 2) and oligo hydramnios (AFI: 3-4 cm). MRI done showed complex right adnexal cyst measuring 8x8 cm with eccentric smooth solid components (Figure 3). Solid areas showing diffusion restriction with low ADC values (Figure 4). Tumour markers were normal. In view of her complaints of decreased foetal movements and non-reassuring NST, she was taken up for Emergency LSCS. A preterm live male baby of weight 1.315 kg was delivered as breech with good cry.

Figure 6: Gross specimen showed fragments of ovarian mass showing solid and cystic neoplasm, cyst wall is thick, yellowish white with fleshy nodules and solid papillary areas measuring 3.5x3.5 cm with tiny papillary projections.

Intra op findings were right ovarian endometriotic cyst 6x6 cm partly solid and cystic in nature with cyst wall ruptured and sealed off by omentum (Figure 5). Multiple endometriotic deposits on the posterior surface of uterus and peritoneum. No free fluid seen, peritoneal washings were taken and right salpingo-oophorectomy was done. Specimens were sent for cytology and histopathology. Intra op and post op periods were uneventful. Patient was discharged on 5th post op day. Histopathology report came as clear cell carcinoma of right ovary and cytology was negative. Gross specimen showed fragments of ovarian mass showing solid and cystic neoplasm, cyst wall is thick, yellowish white with fleshy nodules and solid papillary areas measuring 3.5x3.5 cm with tiny papillary projections (Figure 6). Microscopy showing neoplasm composed of tubule cystic spaces lined by tumour cells with clear cytoplasm, high grade nuclear features and nuclear hob nailing. Stroma shows dense lymphoplasmacytic infiltrate (Figure 7). Adjacent endometriotic foci seen. It was staged as FIGO stage Ic2 since tumour was limited to one ovary and capsule was ruptured before surgery. After the histopathology report she underwent a staging laparotomy followed by total abdominal hysterectomy with bilateral salpingo oophorectomy and at present is on third cycle of postoperative adjuvant chemotherapy with carboplatin and paclitaxel.

Figure 7: Microscopy showing neoplasm composed of tubule cystic spaces lined by tumour cells with clear cytoplasm, high grade nuclear features and nuclear hob nailing. Stroma shows dense lymphoplasmacytic infiltrate.

DISCUSSION

Long standing endometriosis can turn into either clear cell carcinoma or endometrioid carcinoma of ovary with an incidence of 0.8%. Clear cell carcinoma is a subtype of epithelial ovarian cancers. Nishida et al reported that malignant change occurred in 0.7% of ovarian endometriosis. Early diagnosis at an early stage can improve the survival rate. MRI during pregnancy is an important modality for the diagnosis.

The staging for clear cell carcinoma follows the same FIGO 2018 staging of ovarian, fallopian tube and peritoneal cancers which is a surgical staging. The origin of these tumors is thought to be from the distal end of
fallopian tube. Ovarian epithelial tumours are believed to originate from cortical inclusions of mullerian epithelium or from endometriosis.

The incidence of ovarian clear cell carcinomas is estimated to be less than 5% and majority present at stage I of the disease. Behbakht et al, in his study found 60% patients in stage I and 11% in stage II disease. Nishino et al reported out of 20 patients, 90% were in stage I/II with 12 in stage Ic, one in Iia and five in Iic.9 Kennedy et al reported 60% of cases were in stage I/II.9 Skirnisdottir et al, found that 64% patients belong to stage Ic and Iic.10 Similarly, Jennison et al in his study reported 59% patients in early stage of ovarian clear cell carcinomas.11

Besides our case there were 8 reported cases of pregnancy associated ovarian clear cell carcinoma which are as follows:

The definite diagnosis of ovarian clear cell carcinoma can be made by histological analysis of the ovarian cyst obtained by either frozen section or routine post op histopathology showing the characteristic clear cells and hob nailing pattern (Figure 7).

IHC shows CK7 positivity, CD 20 negativity, ER/PR and WT1 negativity. For preoperative diagnosis the imaging modalities may be helpful which can indicate a malignant change in ovarian cyst - USG and MRI (Figure 1, Figure 3). The presence of solid areas, complex nature, bilaterality, increased vascularity with low RI, papillary pattern, multilocularity and ascites may be suggestive of malignant nature. Tumour markers for epithelial ovarian cancers namely CA -125, CEA will be elevated but is of limited value in pregnancy. Normally the tumour markers peak in first trimester and returns to normal in second trimester.

The prognosis mainly depends upon the stage of cancer at the time of diagnosis, histological type, histological grade and the maximum diameter of residual disease after cyto reductive surgery. Stage I/II disease and low-grade disease has good prognosis. The foetal prognosis can be sub optimal due to intrauterine hemodynamic alterations causing reduced uterine and placental blood flow and immunological changes leading to the development of IUGR and stillbirth.

The treatment of ovarian clear cell carcinoma is similar to other malignant epithelial ovarian tumours with stage-based treatment regime. Stage I a/b grade 1 and 2 - Surgical staging followed by extra facial hysterectomy with BSO. For stage I a/b grade 3, stage I c and stage II - surgical staging with adjuvant chemotherapy (3-6 cycles of carboplatin and paclitaxel). For advanced stages- III and IV primary cyto reductive surgery followed by adjuvant chemotherapy or neo adjuvant chemotherapy followed by interval cyto reduction is done as per EORTC and CHORUS trials. However, in pregnancy surgical treatment result in increased risk of miscarriage in first trimester and preterm labour in third trimester. Hence, second trimester is considered ideal for surgery. Chemotherapy in pregnancy in contraindicated in view of embryo toxicity, congenital malformations such as gastroschises, skeletal anomalies, IUGR, reduced brain growth, dilatation of cerebral ventricles and intra uterine death associated with carboplatin.

The survival rate following surgery for ovarian clear cell carcinoma is higher for stage I and II. This is in accordance with Kennedy et al where survival rates for stage I and II were similar to other EOC while stage III (26%) and IV (0%) have a dismal outcome. Sugiyma et al reported a low response rate (11.1%) with platinum based chemotherapy. Goff et al reported that patients with stage III had a shorter survival rate. The poor

<table>
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<th>No.</th>
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response rates to platinum based regimens is attributed to chemo resistance developed as a result of decreased drug accumulation, increased detoxification, low proliferation rate of tumour and increase in DNA repair. No other chemotherapeutic agent is found to be effective in clinical studies.

CONCLUSION

Due to the low incidence rate of ovarian clear cell carcinoma, it is treated similar to other EOC. Chemo resistance is observed in advanced stages and therefore advanced stages have guarded prognosis with very low survival rates. Maternal outcome in advanced stages is very dismal.

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REFERENCES
