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Interval Cytoreductive Surgery for High Grade Ovarian Serous Cyst ADE- Nocarcinoma in the Third Trimester of Pregnancy - A Case Report and Literature Review.

Dr Kanika Gupta *[1], Dr Shubham Bidhuri [2], Dr Sanjeev Arora [3], Dr Subhrangsu Dasgupta [4], Dr Anita Sharma [5], Dr Meenu Walia [6]

Corresponding Author: Dr Kanika Gupta,

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Introduction

Adnexal masses occur in 2.4-5.8% of all pregnancies. Most of these masses are benign and their clinical significance is limited. However, ovarian cancer is diagnosed in 0.2 to 3.8 per 100000 preg- nancies.**[**1**]** Among ovarian malignancies in pregnancy, germ cell tumours, stromal tumours, and bor- derline tumours are the most common,**[**2**]** while the incidence of epithelial ovarian cancer is only 1:12,000-1:50,000 of pregnancies.**[**3**]** Routine obstetric ultrasound examinations often detect adnexal masses incidentally, typically in the first trimester. Most of these are asymptomatic or present with non-specific symptoms which easily overlap with pregnancy symptoms and regress spontaneously. The literature reports good oncologic and foetal outcomes in women treated for cancer during preg- nancy.**[**4**]** There is no evidence of adverse effects of pregnancy on the survival of women with ovarian cancer.**[**5**]** However treatment of pregnant women with adnexal cancer is difficult because numerous complications can occur, endangering both the mother and the developing foetus. A general recom- mendation is that patients considering pregnancy continuation should undergo cystectomy or ad- nexectomy followed by platinum-based chemotherapy and cytoreductive surgery after delivery, as surgery cannot be performed without residual disease during pregnancy. It is recommended that chemotherapy not be started until after the end of the 14th week of pregnancy.**[**6**]** Studies performed in pregnant patients undergoing chemotherapy have shown that paclitaxel and platinum salts can be safely administered during the second and third trimesters of pregnancy without increasing the risk of foetal malformation.**[**7**]**

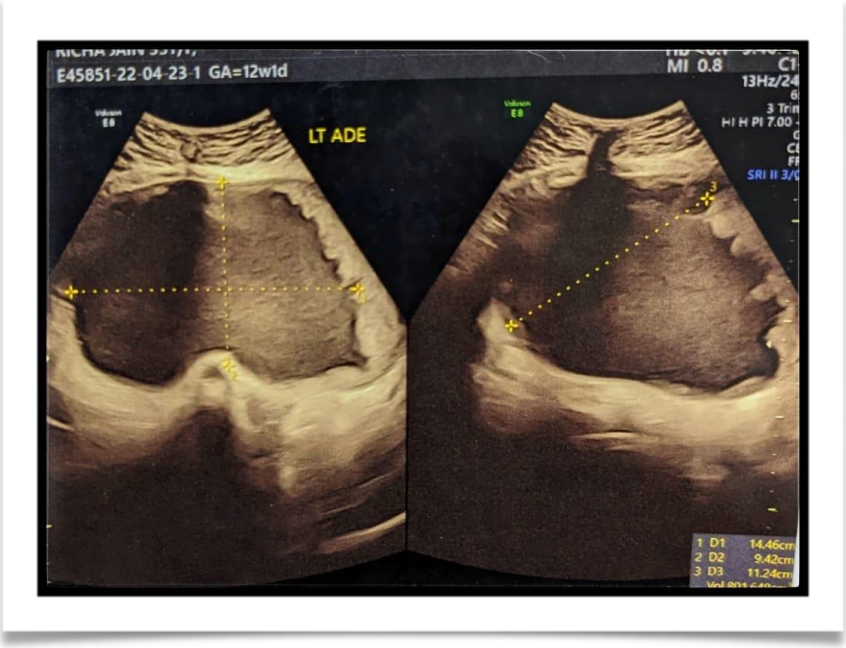
We present the case of a 35-year-old primigravida with high-grade serous cystadenocarcinoma dis- covered by the incidental finding of a solid cystic mass in the left adnexa during a routine obstetric ultrasound examination in the first trimester.

Case Presentation

A 35 yr old primigravida at 16 weeks + 3 days of gestation with singleton pregnancy was reported to the Hospital for medical oncology opinion. She had undergone laparotomy with excision of left tube-ovarian mass in view of a solid cystic mass of size 14x9x11cm in the left adnexa reported in routine early obstetric ultrasound and the same findings were confirmed in an MRI.(Image 1,2) Post-op histopathological studies revealed high-grade serous cystadenocarcinoma of the left ovary (pT1bNxMx) and left ovarian cyst fluid was found positive for malignant cells. Histopathology slides were reviewed at another centre and were reported as endometroid carcinoma, grade 2 of the left ovary.

After having a multidisciplinary discussion with the institutional tumour board including a gynaecological oncologist, medical oncologist, obstetrician, psychologist, and paediatrician to discuss which is the best therapeutic strategy in this particular case as the patient wanted to continue with the pregnancy. It was decided to offer adjuvant chemotherapy with carboplatin and paclitaxel fol- lowed by definitive surgery (consisting of total hysterectomy with bilateral adnexectomy, lymph node dissection, and omentectomy) along with cesarean section. The patient and her family mem- bers were explained the aggressive nature of the disease, prognosis and chances of recurrence and relapse. Side effects of chemotherapy and the risk of premature termination of pregnancy or terato- genic effects of chemotherapeutic drugs were explained. Detailed counselling of the patient and her family with the multidisciplinary staff was done and written informed consent was obtained for ini-tiation of chemotherapy with preservation of pregnancy. No gross fetal anomalies were documented at ultrasound examination before treatment. Weekly-based chemotherapy with carboplatin and pa- clitaxel was started and 5 cycles were given over a period of 3 months. The patient showed good tolerance to treatment with mild gastrointestinal and haematological toxicity observed in the last cycle of treatment. The pregnancy proceeded uneventfully and the patient had routine obstetric fol- low up and foetal growth was monitored with regular Doppler ultrasound.

After three weeks of the last chemotherapy, following an extensive conversation with the patient and her family, the decision was made to perform LSCS with full cytoreductive surgery as the pa- tient denied the option of fertility-preserving surgery. After adequate blood products were arranged, a lower uterine segment caesarean section was performed by the obstetrics team. A healthy baby girl weighing 1.9 kg was delivered with Apgar scores of 9 and 10 at 1 and 5 minutes, and she was sent to the paediatrician team. Placenta & membranes were delivered out and the uterus was closed. Radical hysterectomy with right salpingo-oophorectomy was done along with bilateral pelvic and para-aortic lymphadenectomy and omentectomy by the gynae oncology team. (Image3,4) Intraop- eratively no enlarged lymph nodes were found and the omentum appeared normal. Post op period was uneventful and the patient was discharged with a healthy baby on a postoperative day third and is currently on a follow-up. Postpartum follow-up was uneventful. After discussion with the medical oncologists breastfeeding the baby was avoided. The final histopathological diagnosis revealed no secondary tumour tissues in the uterus, with omentum showing no secondary deposits and all lymph nodes free of tumour. The placenta appeared normal at the time of delivery and showed no tumour at histology.



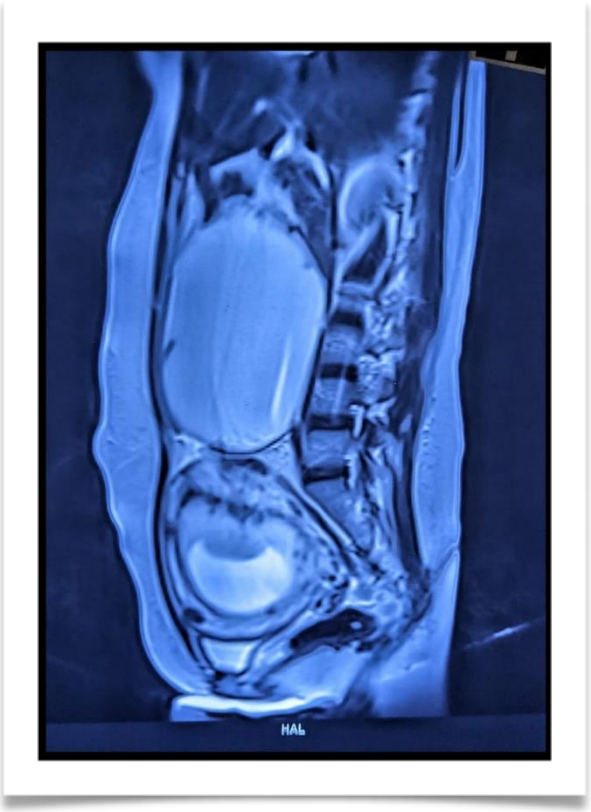
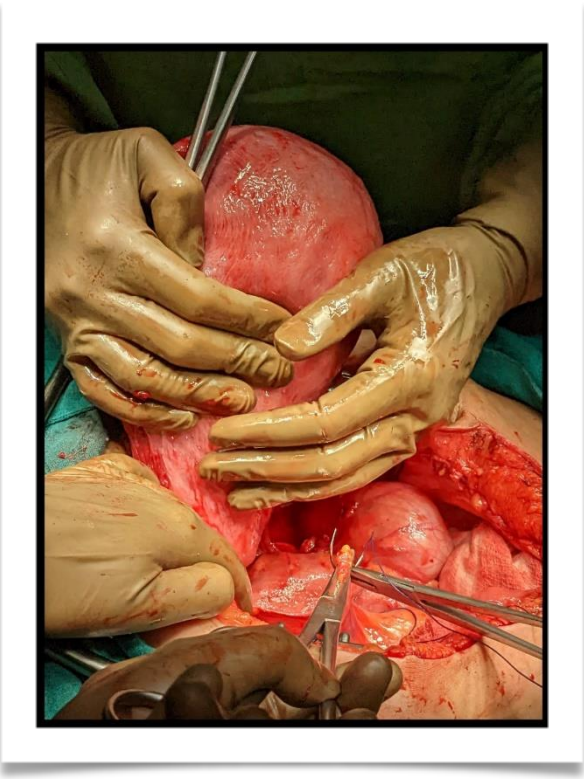


Image 1& 2: Ultrasound and MRI images of the abdominopelvic mass.



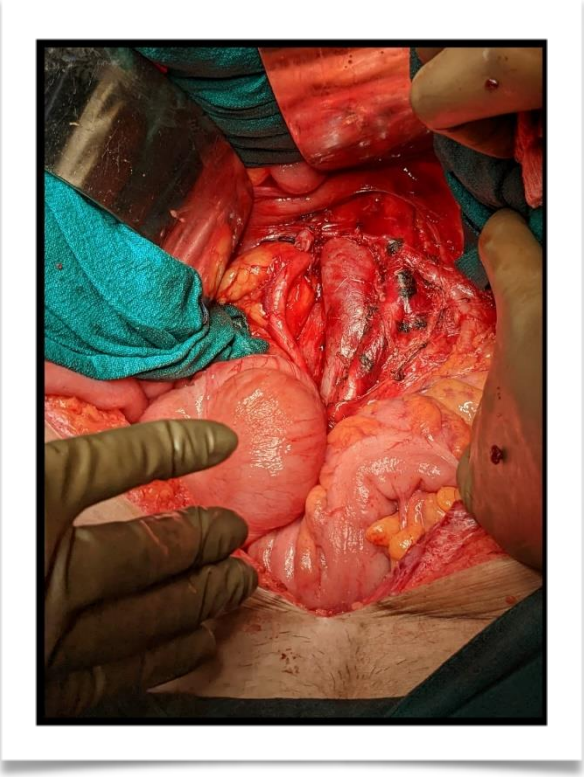


Image 3 & 4: Intraoperative dissection images

Discussion

In the second half of their reproductive years, women with low parity are more likely to develop primary ovarian cancer. Notably, the patient's age was 35. Although it is unclear whether ovarian cancer linked to pregnancy is on the rise,**[**8**]** it is possible that it is attributable to the rise in older pa- tients giving birth as a result of the recent delay in the onset of menopause. According to earlier studies, the majority of pregnant women with adnexal masses are asymptomatic, as was the case in this instance.**[**9**]** and the majority of masses are found unintentionally during routine ultrasonography or pelvic exams.**[**9**]** Epithelial ovarian cancer detection during pregnancy is a rare occurrence since occasionally the symptoms resemble normal pregnancy symptoms.

According to the Federation of Gynaecology and Obstetrics (FIGO), the surgical approach for ear- ly-stage ovarian cancer (stage I and II) consists of hysterectomy, bilateral adnexectomy, omentec- tomy, peritoneal biopsies, and lymphadenectomy. Complete cytoreduction may be impossible in the presence of the fetus and may pose unnecessary risks to both the mother and the fetus.1 A study by Garcia-Soto published in 2012 in the American Journal of Obstetrics and Gynaecology highlighted the importance of

comprehensive surgical staging for ovarian cancer at an apparently early stage, a total of 29% of cases were upstaged after comprehensive staging was performed.[10] Total abdominal hysterectomy and bilateral salpingo-oophorectomy are standard. Total omentectomy is also impor- tant because the supracolic omentum harbours subclinical metastases in 10-30% of cases.1 Early- stage apparent cancer is upgraded to stage IIIc if the nodal disease is confirmed. The finding of an invasive epithelial tumour apparently confined to the ovary warrants systematic bilateral pelvic lymphadenectomy and complete para-aortic lymphadenectomy extending to the left renal vein cephalad and gonadal vessels laterally.

Depending on the duration of pregnancy, abortion, early delivery, or neoadjuvant chemotherapy with preservation of pregnancy could be suggested after multidisciplinary consultation.[11] Initiation of chemotherapy during pregnancy is a possible strategy to improve maternal outcomes while pre- serving pregnancy and delaying delivery.[12] Chemotherapy is advised to start in the second trimester, when foetal organogenesis is complete, as there is a larger likelihood of congenital abnormalities between weeks 4 and 10 of gestation. Chemotherapy is not advised after 35 weeks of pregnancy because the foetal and maternal bone marrow need time to heal during the three weeks preceding delivery. It should reduce the baby's risk of bleeding, infection, or anaemia by preventing drug buildup in the foetus. Also, hematologic toxicity may lead to an increased risk of infection and bleeding complications during delivery.[13]

Cardonick and Iacobucci [14] reported that no fetal complications occurred in mothers receiving plat- inum-based chemotherapy. Several studies reported good oncologic and fetal outcomes with com- bination treatment with paclitaxel and carboplatin.[15] However, there are reports that the administra- tion of chemotherapy drugs in the second and third trimesters increases the risk of intrauterine growth restriction (IUGR) and contributes to the low birth weight of the child. Steroid cover should be taken into consideration when premature delivery is unavoidable.[16] The placenta should be histopathologically evaluated for metastases after delivery because some gynaecological malignan- cies are unusually associated with metastases in the child and placenta. Women must be counselled with regard to the administration of chemotherapy in pregnancy and should be advised of the neces- sary long-term follow-up of their children. In our case, with the continuation of pregnancy and chemotherapy during the second and third trimesters, complete cytoreduction along with a cesarean section was performed after 3 weeks of the last chemotherapy cycle.

Breastfeeding during cytotoxic chemotherapy has been discouraged in general. There are limited data about the feasibility of lactation after chemotherapy during pregnancy. Breastfeeding while re- ceiving

chemotherapy is contraindicated as neonatal leukopenia and thrombocytopenia have been reported in an infant receiving breast milk from his mother undergoing treatment with cyclophos- phamide.**[**17**]** Whether or not any chemotherapeutic agents will be excreted into the breast milk after this 3-week window depends on multiple factors, including concentration, half-life in the maternal plasma, lipid solubility, molecular size and ionization, protein binding, and the phase of breastfeed- ing itself. Stopenski Set al **[**18**]** reported that for patients in whom at least 3 weeks have passed be- tween chemotherapy during pregnancy and delivery, it was found to have no adverse effects on the children who were breastfed. However due to the paucity of literature and safety data regarding chemotherapy drugs and breastfeeding, after having a detailed discussion with a medical oncologist, the patient and her family, we decided to avoid breastfeeding the baby in our case.

Conclusion

There are currently no definite recommendations for the treatment of epithelial ovarian cancer dur- ing pregnancy in the literature. It is even more challenging to evaluate the real results of treatments due to the dearth of data in the literature. Case reports should unquestionably provide comprehen- sive details on clinicopathologic factors and treatment plans.

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