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Metastatic colon adenocarcinoma in pregnancy

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Abstract:

Colon cancer in pregnancy is rare. Symptoms are nonspecific; hence, patients are often diagnosed at an advanced stage with poor prognosis. We present a 40-year-old multigravid who had recurrent severe abdominal pain. She underwent surgeries at 9 and 21 weeks age of gestation with an initial assessment of ovarian malignancy. Further workup showed metastatic adenocarcinoma to the pelvis with colonic primary. Chemotherapy was subsequently deferred due to COVID-19 infection. She eventually developed partial gut obstruction and underwent bowel diversion with intraoperative fetal monitoring at 31 weeks age of gestation. Although the fetus developed growth restriction, the pregnancy was successfully carried to term with a good outcome. Palliative chemotherapy was started postpartum and she completed eight cycles. Unfortunately, she succumbed to death after 1 year due to pulmonary metastases. Despite challenges in diagnosis and management, this case shows that it is possible to have a good outcome in a pregnancy complicated by advanced-stage colon cancer.

Keywords:

Carcinoma in pregnancy, metastatic colon adenocarcinoma, surgery in pregnancy

Introduction

Cancer in pregnancy has an incidence of 1 case per 1000 pregnancies.^[1] Among these, colorectal cancer is rare with an incidence of 1 in 13,000 pregnancies or 0.008%.^[2] Less than 300 cases are reported in the literature.^[1] Ovarian metastasis is associated with poor prognosis, occurring in 25% of pregnant patients but only in 3%–8% among nonpregnant females.^[2]

Known risk factors for colorectal cancer include family history, age, and ethnicity.^[1] A history of chronic inflammatory bowel disease also predisposes to a higher risk of developing colorectal cancer.^[3] Other possible risk factors that are modifiable include high-animal fat and low-fiber diet, sedentary lifestyle, drinking alcohol, obesity, and smoking.^[3] Although risk factors are usually present among these

patients, particularly those diagnosed at a younger age, there have also been reports of its occurrence among pregnant patients without risk factors.^[2]

Symptoms during pregnancy are nonspecific and include abdominal pain, nausea, vomiting, and altered bowel movements. Consequently, late diagnosis is common.^[1] Difficulties in differentiating a primary ovarian versus colonic neoplasm as seen in this case further add delay in diagnosis. This suggests that colon cancer during pregnancy in this population (pregnant patients with colorectal cancer without risk factors) might be attributed to predisposing factors, highlighting a potential difference from colon cancer occurrence in the general population.

Management of colon cancer in pregnancy is dependent on several factors which include age of gestation, tumor location, and stage.^[2] The approach to management is challenging since a balance between maternal and fetal

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well-being must always be considered. Here, we present a case of metastatic colorectal cancer initially diagnosed as primary ovarian malignancy in pregnancy that was successfully carried to term despite obstacles in diagnosis and management.

Case Report

Our patient is JA, a 40-year-old, multigravid, who consulted at a local hospital at 9 weeks and 4 days age of gestation due to abdominal pain. She was managed as a case of ovarian new growth in complication and underwent emergency exploratory laparotomy, left salpingo-oophorectomy, and right tubal ligation. The surgeon's intraoperative findings include an enlarged left ovary measuring 10 cm × 10 cm with a 5 cm point of rupture extruding "brain-like" material; a grossly normal right ovary, bilateral fallopian tubes, and abdominal organs. Histopathology of the left ovary showed endometrioid adenocarcinoma, FIGO Grade 2 with intestinal metaplasia, initially. She was advised to transfer to a tertiary hospital but was not immediately able to comply due to financial constraints.

At 20 weeks age of gestation, she started experiencing a decreased caliber of stool, followed by episodes of severe abdominal pain, hence admission to our institution. Transabdominal ultrasound showed an irregular, multilocular-solid ovarian mass measuring 11.6 cm × 11.4 cm × 5 cm with consideration of a malignant ovarian new growth, right, secondary to probable tumor progression [Figure 1]. Abdominal magnetic resonance imaging (MRI) likewise showed a large complex right abdominopelvic mass occupying the right hemiabdomen and pelvis [Figure 2]. No other abdominal masses were noted. Preoperative serum CA-125 was 3.4 times elevated. She subsequently underwent exploratory laparotomy, adhesiolysis, enterolysis, right salpingo-oophorectomy, and biopsy of omentum, umbilical, and mesenteric implants at 21 weeks

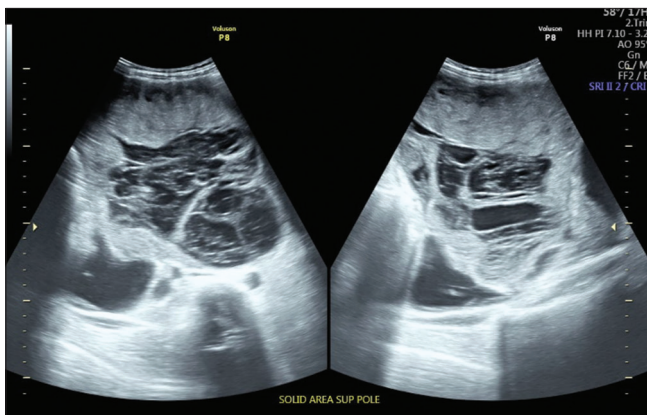


Figure 1: Transabdominal ultrasound at 21 2/7 weeks showing an abdominal mass measuring 11.6 cm × 11.4 cm × 5 cm, with a consideration of ovarian new growth, malignant

and 5 days age of gestation. Intravenous isoxsuprine was given for tocolysis. Intraoperatively, the right ovary was converted into a predominantly solid and necrotic mass measuring 20.0 cm × 16.0 cm × 8.0 cm [Figure 5], which was adherent to the right pelvic sidewall, cul-de-sac, appendix, and part of the transverse colon superiorly. The right ovary was inadvertently ruptured during adhesiolysis. There was a 2.0 cm × 2.0 cm residual tumor adherent to the ileum as well as multiple subcentimeter implants on the anterior surface of the uterus, bilateral pelvic peritoneum, omentum, and mesentery of the small and large intestines [Figure 4]. A palpable 6 cm × 4 cm intraluminal mass was noted at the sigmoid colon to which the left posterolateral aspect of the corpus was adherent [Figure 3].

Serum carcinoembryonic antigen (CEA) was requested postoperatively which was 19 times elevated. Proctosigmoidoscopy revealed a circumferential friable mass 15 cm from the anal verge, a biopsy of which showed adenocarcinoma of the colon.

Review of slides and immunohistochemical studies from her surgery showed adenocarcinoma with mucinous differentiation involving the left ovary and right paratubal soft tissue, which cannot rule out metastasis from a colonic primary [Figure 6].

This finding does not coincide with the initial reading of the ovary as the primary malignancy. Histopathology and immunohistochemistry (CK7 negative and CK20 positive for neoplastic cells with patchy staining in neoplastic cells) of specimens from her second surgery showed metastatic adenocarcinoma from a nongynecologic primary involving the right ovary, right fallopian tube, omentum, and umbilical implant [Figure 7]. These findings have thus shifted the diagnosis and caused additional dilemmas in the management of our patient.

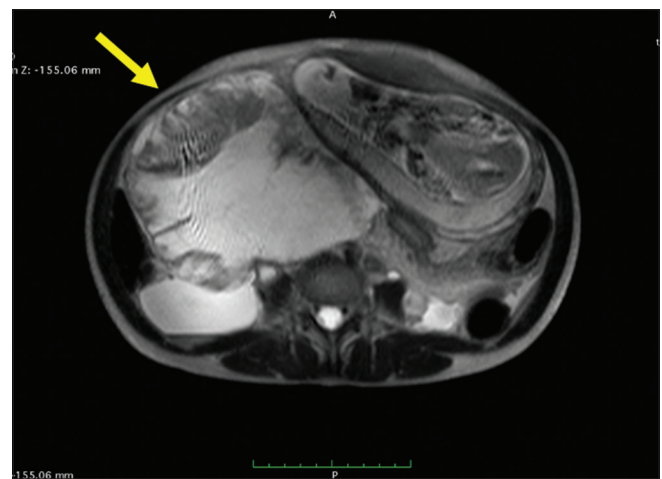


Figure 2: Magnetic resonance imaging done at 21 5/7 weeks of gestation showing the presence of multiloculated cystic masses (arrow) predominantly occupying the right hemiabdomen and pelvis

A multidisciplinary conference involving colorectal surgery, medical oncology, neonatology, and obstetric anesthesia was done with a consensus of doing the chemotherapy with folinic acid, fluorouracil, and oxaliplatin (FOLFOX) every 2 weeks for at least 2 cycles before scheduled abdominal delivery with bowel diversion at 34 weeks after completion of steroids for fetal lung maturation. Possible complications and benefits were well explained and understood by the patient. Unfortunately, she contracted COVID-19 infection with persistently positive nasopharyngeal.

Chemotherapy is indicated for Stage II colorectal cancers and beyond.^[2] It is generally avoided during the first trimester due to risks of teratogenicity but may be administered in the second and third trimesters.^[4] 5-fluorouracil (5-FU), capecitabine, and oxaliplatin are commonly used chemotherapeutic agents.^[5] Recent studies identified capecitabine plus oxaliplatin (CAPEOX) and folinic acid, fluorouracil, and oxaliplatin (FOLFOX) regimen as the first-line chemotherapy in patients with Stage IV colorectal cancer.

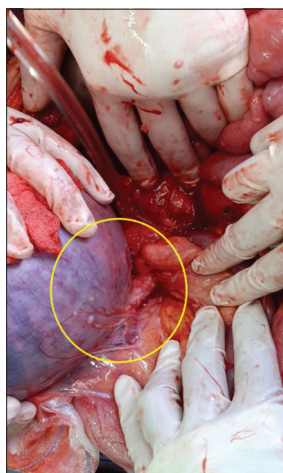


Figure 3: Part of the left posterolateral aspect of the corpus was adherent to the sigmoid, where there seemed to be 6 cm x 4 cm firm mass (encircled) within its lumen

This is considered as palliative management for patients either during pregnancy or the postpartum period.

Her prenatal course was followed up closely. A congenital anomaly scan at 22 weeks age of gestation showed no gross structural anomalies. Fetal surveillance was done every 2 to 3 weeks to monitor fetal growth. At 27 weeks, fetal growth restriction was noted, which was associated with poor maternal weight gain. Fetal growth monitoring with Doppler velocimetry was done, and oral nutritional supplements were started as advised by the nutrition clinic.

At 31 weeks age of gestation, she experienced severe, colicky, graded 10/10 abdominal pain, hence admission for preterm labor and possible partial gut obstruction. Abdominal X-ray showed ileus with a markedly dilated transverse colon measuring 9.8 cm wide with few gas-filled dilated small bowel loops and rectal gas.

The plan of the Colorectal Surgery Service was to proceed with bowel diversion due to the risk of bowel perforation. At this point, the sonographic estimated fetal weight was 1228 g, which was at the <3rd percentile for age by Hadlock. Delivery was considered to administer standard treatment for the patient's underlying malignancy. Should the surgery and delivery be carried out, however, chemotherapy would have to be delayed until 2 to 3 weeks postpartum. The delay will not help improve maternal survival. Neonatal survival is also doubtful with 50% neonatal mortality rate for the fetus' current weight and age at our institution. Taking these factors into consideration, the co-managing services as well as the patient have all agreed to proceed with bowel diversion, defer delivery, and bring the pregnancy as close to term as possible.

She underwent mini-laparotomy with total loop colostomy under epidural anesthesia. Magnesium sulfate infusion was given for neuroprotection as well as isoxsuprine for tocolysis. Steroids for fetal lung

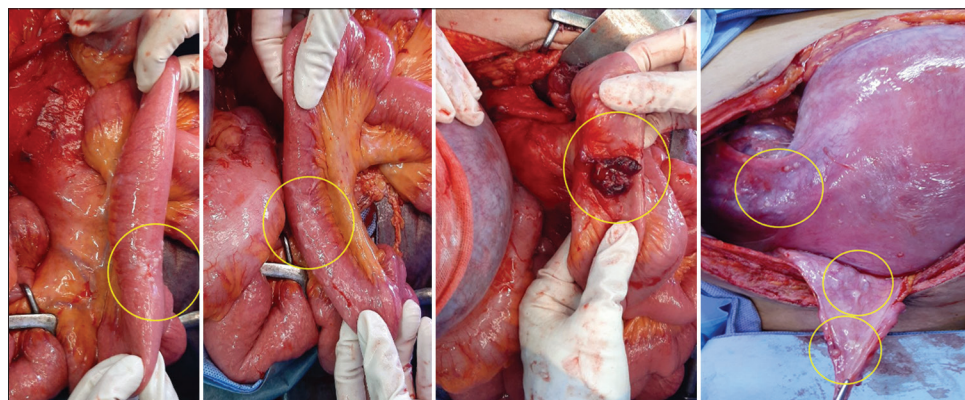


Figure 4: Intraoperative findings of multiple subcentimeter implants (encircled) noted on mesentery of the small and large intestines, omentum, bilateral pelvic peritoneum and uterus

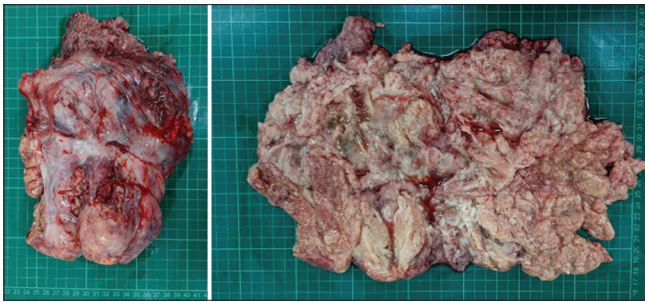


Figure 5: The right ovary was converted into a predominantly solid, necrotic mass, measuring 20.0 cm × 16.0 cm × 8.0 cm. The picture on the right is a cut section

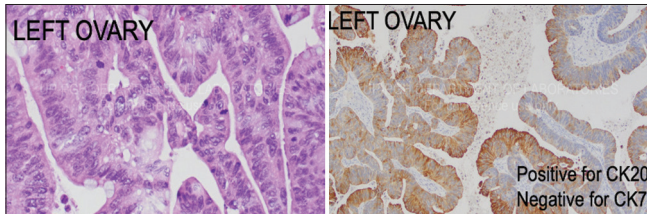


Figure 6: Shown is the high power view of the left ovary revealing adenocarcinoma with mucinous differentiation, which cannot rule out metastasis from a colonic primary. Immunohistochemistry results revealed CK7 negative for neoplastic and CK20 positive, patchy staining in neoplastic cells. Immunohistomorphologic features are supportive of metastatic adenocarcinoma, likely of the colorectal primary site

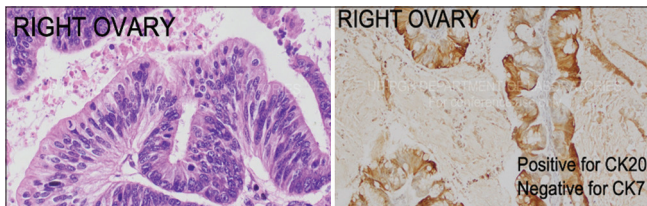


Figure 7: High power view of the histopathology of the right ovary showed metastatic adenocarcinoma from nongynecologic primary. Immunohistochemistry results for both ovaries revealed CK7 negative for neoplastic cells and CK20 positive, patchy staining in neoplastic cells. Immunohistomorphologic features are supportive of metastatic adenocarcinoma, likely of the colorectal primary site

maturity had been completed before the procedure. Intraoperatively, fetal heart rate was monitored intermittently every 5 min using handheld Doppler with no episodes of bradycardia noted. The preoperative nonstress test was reactive. Immediately postoperatively, she had mild uterine contractions with a category 1 trace for which isoxsuprine drip was titrated accordingly. She was subsequently discharged after control of preterm labor.

The patient was readmitted at 37 weeks age of gestation for induction of labor. She delivered vaginally to a baby boy, 1900 g, 37 weeks by pediatric aging, small for gestational age, with an APGAR score of 9 remaining 9. Before discharge, a chest and abdominal computed tomography (CT) scan with triple contrast was done as baseline imaging before chemotherapy which was unremarkable. Systemic chemotherapy was started 3 weeks postpartum using the CAPEOX

regimen. Repeat chest and abdominal CT scans showed a significant decrease in the size of the rectosigmoid mass from 17.8 cm to 5.9 cm. Serum CEA also decreased from 94.1 to 16.54 ng/mL. Unfortunately, there was a development of pulmonary metastasis. She eventually succumbed to death 1 year after giving birth. She had a total of eight cycles of systemic chemotherapy given every 3 weeks. Her baby is now 2 years old and with normal neurodevelopmental milestones.

Discussion

The pathogenesis of colon cancer in pregnancy is not clear, but literature suggests that increased levels of estrogen and progesterone related to pregnancy stimulate the growth of colorectal cancer with their receptors.^[2] Other factors implicated in the progression of colon cancer in pregnancy include steroid hormones, abnormalities in TP53 protein, and cyclooxygenase 2 enzyme levels. However, evidence on the role of these factors is conflicting.^[2,6]

Diagnosing metastatic colon cancer to the ovary poses challenges, particularly in determining whether secondary tumors are primary or metastatic deposits of the index tumor.^[7] Synchronous tumors are observed in approximately 2%–7% of patients, most commonly ovarian and lung or ovarian and colon.^[8] On the other hand, women with colorectal cancer exhibit an ovarian metastasis rate of 3.4%.^[8] As in the case presented in this report, it can be difficult to determine whether the second tumor is a primary or metastatic deposit of the index tumor. Several case series have documented cases of primary colorectal cancer coexisting with primary ovarian tumors. According to previous research, the incidence of cancer in other organs in females with ovarian cancer is 2.8%, with the most common combinations being ovarian cancer and lung cancer or ovarian cancer and colon cancer. Furthermore, women with colorectal cancer have an ovarian metastasis rate of 3.4%.^[8]

Our patient underwent a series of surgeries during her pregnancy. The first was at 9 weeks age of gestation due to an ovarian tumor in complication for which unilateral salpingo-oophorectomy with contralateral tubal ligation. This was followed by the removal of the contralateral adnexa at 21 weeks secondary to tumor progression. Challenges in detecting colon cancer as the index tumor led to delayed diagnosis and definitive management.

Colonoscopy has the additional advantage of providing tissue diagnosis through biopsy. However, pregnancy is considered a relative contraindication to this procedure due to theoretical risks of placental abruption, teratogenicity from endoscopic medications, and fetal risk of hypoxia.^[9] Nevertheless, it may be safely carried

out during the second trimester particularly if there is a high suspicion for the disease.^[10]

Immunohistochemistry is employed to distinguish between primary and secondary ovarian cancer, with primary ovarian cancer cells expressing cytokeratin (CK7) but not CK20, whereas colorectal tumors express CK7 but not CK20.^[8]

CT scan is the standard imaging modality for clinical staging, but MRI is preferred during pregnancy to avoid fetal exposure to ionizing radiation. Serum CEA levels, a strong prognostic marker for colon cancer, are not typically elevated during pregnancy;^[2] however, elevated levels were observed in the index patient.^[2]

The approach to treatment involves taking into consideration the stage, gestational age, and need for surgery.^[2] Patients with localized disease may undergo resection with wide margins. In cases of ovarian involvement with peritoneal implants indicating distant metastasis, systemic chemotherapy is necessary. Palliative techniques such as bypass or colostomy may alleviate potential complications such as bowel obstruction, perforation, and bleeding in advanced tumors.^[2,4,6]

Surgery is generally deferred until the second trimester due to increased miscarriage risk earlier.^[2] It may be performed if diagnosed before 20 weeks age of gestation; however, late diagnosis during pregnancy is common. Beyond 20 weeks, surgery may be delayed until the age of gestation with an acceptable neonatal survival.^[2] If performed after 24 weeks, continuous fetal monitoring should be done along with preparations for possible emergent delivery.^[2]

The mode of delivery is based on obstetric indications, with the role of cesarean delivery being controversial.^[11] When cesarean section is performed, however, cancer surgery may be done simultaneously. For the presented case, abdominal delivery at 34 weeks was initially considered but was changed due to bowel obstruction, requiring bowel diversion earlier in gestation. Intermittent fetal monitoring was done intraoperatively on the premise that emergency cesarean section would be performed in the event of fetal distress.

Systemic chemotherapy is the primary treatment for peritoneal metastases.^[4,6] Chemotherapy is indicated for Stage II colorectal cancers and beyond as adjuvant treatment or palliative in late stages.^[2] It is generally avoided during the first trimester due to risks of teratogenicity but may be administered in the second and third trimesters.^[4] In the general population, 5-FU, capecitabine, and oxaliplatin are commonly

used chemotherapeutic agents.^[5] Recent studies identified CAPEOX and folinic acid, fluorouracil, and oxaliplatin (FOLFOX) regimen as the first-line chemotherapy in patients with Stage IV colorectal cancer.^[6]

Despite risks associated with chemotherapy, both the FOLFOX and CAPEOX regimens have shown similar efficacy in the general population.^[6] Few studies on the use of 5-FU and oxaliplatin in pregnancy show that they are relatively safe to use albeit with a small risk of teratogenic effects and intrauterine growth restriction.^[11] There are limited data on the use of capecitabine in pregnancy.^[5] In our patient, the initial chemotherapeutic regimen planned during pregnancy was FOLFOX but was deferred due to gut obstruction. Postpartum, CAPEOX was given instead since it was more readily available for use as outpatient basis. Theoretically, outcomes would not have been changed since both regimens are acceptable first-line treatments.

Timing of administration of chemotherapy is also important in relation to timing of delivery. Treatment must be stopped 2–3 weeks before delivery to allow time for the placenta to clear active metabolites from the fetus.^[4] Furthermore, there is a maternal risk for myelosuppression if treatment is given near delivery or surgery.^[4] Unfortunately, our patient contracted mild symptoms of COVID-19 after diagnosis of colon cancer. The persistently positive nasopharyngeal swab result despite clinical recovery from COVID-19 was most probably due to her immunocompromised state. She was already near term and had room for only one cycle of chemotherapy by the time she had a negative swab. It was the opinion of the medical oncology service to defer chemotherapy postpartum since one cycle would not be significant to improve maternal survival.

Aside from the risk for preterm delivery, the fetus was also at risk for growth restriction owing to poor maternal nutrition which could be further aggravated by chemotherapy. Despite metastasis, however, fetal risk is small since placental metastasis is rarely observed.^[4]

Pregnancy does not affect the prognosis of colorectal cancer, hence is comparable to that of the general population.^[4] In a study by Kocian *et al.* involving advanced colorectal cancer in pregnancy, the overall survival was 48.6% and 20.8% at 1 and 2 years, respectively, for Stage IV disease. However, it was not specified whether improved survival was attributable to surgery or chemotherapy.

Our patient was thoroughly informed about her circumstances and actively participated in the decision-making process regarding her treatment.

Postpartum, she was advised to refrain from breastfeeding on initiation of chemotherapy due to potential excretion through breastmilk,^[2] hence she was advised to seek breastmilk donors. Close follow-up to monitor cancer progression, nutritional buildup, and emotional support from relatives were also emphasized.

Surveillance protocols include follow-up visits with a clinical examination, serum CEA, chest and abdominal CT, and colonoscopy. Follow-up visits are typically scheduled every 3 to 6 months for the first 2 years then 6 to 12 months thereafter.^[6] After eight cycles of chemotherapy, there was a significant decrease in the size of the rectosigmoid mass from 17.8 cm to 5.9 cm and a decline in CEA from 94.1 to 16.54 ng/mL. However, she subsequently developed pulmonary metastases and succumbed to death after 1 year.

Summary

Colon cancer in pregnancy presents with nonspecific symptoms, posing challenges for diagnosis and treatment. Missed diagnoses can have severe consequences for both the mother and fetus, necessitating a high index of suspicion in pregnant women with symptoms like rectal bleeding, abdominal pain, or bowel habit changes. Early diagnostic tests are crucial for improved prognosis. Surgery is typically safe in the early second trimester for localized disease, but late diagnoses are common, requiring surgery once fetal age ensures neonatal survival. Palliative surgery may be necessary in metastatic cases to prevent complications like intestinal obstruction. Systemic chemotherapy is preferably administered in the second trimester due to teratogenic risks, but treatment must cease 2 to 3 weeks before delivery to mitigate maternal and fetal risks.

Individualized management, supported by a multidisciplinary approach, is essential. Delayed diagnosis in our patient led to delayed palliative management, although bowel diversion was successfully performed with intraoperative fetal monitoring. Given the limited benefit of chemotherapy near term, it was deferred postpartum. Despite poor maternal prognosis with metastatic colorectal cancer, this case demonstrates successful pregnancy outcomes with good neonatal results.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their

images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authorship contributions

Deverly Rina V. Reyes, MD, FPOGS - Involved in the conceptualization, methodology, data curation, writing of the original draft, review and editing.

Mario Philip R. Festin, MD, MSc, MHPed, FPOGS - Involved in conceptualization, methodology, review and editing of the draft.

Jemimah T. Cartagena - Lim, MD, FPOGS, FPSMFM - Involved in conceptualization, methodology, review and editing of the draft.

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Conflicts of interest

There are no conflicts of interest.

References

- Ivanov T, Tsvetkov T, Dimitrov B, Karamanliev M, Khan A, Deliski T: A case report. *J Biomed Clin Res* 2018; p. 155-7.
- Resnik R, Lockwood C, Moore T, Greene M, Copel J, Silver R: Creasy and Resnik 's Maternal-Fetal Medicine, Principles and Practice. 8th ed. Philadelphia, 2019: 1019 -1020.
- Frydenberg H, Harsem NK, Ofigsbø Å, Skoglund H, Brændengen M, Kaasa S, *et al.* Chemotherapy during pregnancy for advanced colon cancer: A case report. *Clin Colorectal Cancer* 2020;19:141-4.
- Kocián P, de Haan J, Cardonick EH, Uzan C, Lok CA, Fruscio R, *et al.* Management and outcome of colorectal cancer during pregnancy: Report of 41 cases. *Acta Chir Belg* 2019;119:166-75.
- Liu F, Yang L, Wu Y, Li C, Zhao J, Keranmu A, *et al.* CapOX as neoadjuvant chemotherapy for locally advanced operable colon cancer patients: A prospective single-arm phase II trial. *Chin J Cancer Res* 2016;28:589-97.
- Saif MW. Management of colorectal cancer in pregnancy: A multimodality approach. *Clin Colorectal Cancer* 2005;5:247-56.
- Mason MH 3rd, Kovalcik PJ. Ovarian metastases from colon carcinoma. *J Surg Oncol* 1981;17:33-8.
- Nofal M, Al Awaysheh MM, Yousef AJ. Synchronous colonic and ovarian tumors: A case report. *Am J Case Rep* 2019;20:655-8.
- Cappell MS. Colon cancer during pregnancy. *Gastroenterol Clin North Am* 2003;32:341-83.
- Cappell MS, Fox SR, Gorrepati N. Safety and efficacy of colonoscopy during pregnancy: An analysis of pregnancy outcome in 20 patients. *J Reprod Med* 2010;55:115-23.
- Walsh C, Fazio VW. Cancer of the colon, rectum, and anus during pregnancy. The surgeon's perspective. *Gastroenterol Clin North Am* 1998;27:257-67.