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Colorectal Cancer Treatment During Pregnancy

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Abstract

Colorectal cancer (CRC) impacts about 1 in 13,000 pregnancies in the United States. Although chemotherapy is generally avoided in pregnant patients due to a concern for adverse effects to the fetus, there are situations where the benefits outweigh the potential risks. In this article, we discuss a unique patient case of a 36-year-old woman diagnosed with CRC while pregnant. She received chemotherapy during her second and third trimesters and delivered a healthy baby at 34 weeks. Specific information about oncologic therapies for colorectal cancer in the setting of pregnancy is discussed. Additionally, this article highlights considerations around CRC diagnosis and cancer treatment during pregnancy.

CASE STUDY

A 36-year-old female with a past medical history including multiple sclerosis (MS), seizure disorder, and prior pregnancy with intrauterine fetal demise (IUFD) at 20 weeks presented to her obstetrics (OB) provider with a new pregnancy. Her active medications included lamotrigine for seizures and ocrelizumab for MS. Additionally, she had a vagus nerve stimulator (VNS) implanted for seizure disorder management. Obstetrics planned to monitor her closely due to her prior fetal loss, seizure disorder, and potential need for medication management. She underwent noninvasive prenatal testing (NIPT) at 10 weeks, which demonstrated abnormalities on almost every chromosome. This was suggestive of a maternal complication such as malignancy, as this would be considered incompatible with life if it were a fetal issue. She was subsequently referred to maternal-fetal medicine (MFM) for further evaluation.

On initial evaluation with MFM, the patient denied signs and symptoms associated with potential malignancy, including weight loss, abdominal pain, or bleeding with bowel movements. She did not have changes in bowel habits, night sweats, or a family history of colon cancer. However, laboratory results demonstrated elevated tumor markers, including carcinoembryonic

antigen (CEA) and cancer antigen 19-9 (CA 19-9). A hepatic ultrasound (US) was performed and revealed multiple hepatic lesions. Her case was reviewed in a multidisciplinary conference and additional imaging was recommended for further assessment. Due to her VNS, she was not able to undergo MRI; therefore, a CT scan of the abdomen was performed after a risk-benefit discussion. The CT scan showed a primary colon cancer with metastatic disease to the liver.

Colorectal cancer (CRC) is the third most common cancer diagnosed in women across the United States (Siegel et al., 2026). The incidence of CRC is increasing in younger adults, and the age at which women are becoming pregnant is delayed (Fidler et al., 2017; Salani et al., 2014; Siegel et al., 2026). Currently, it is estimated that 1 in 13,000 pregnancies will be affected by CRC; however, this incidence is expected to increase given delayed childbearing and more cases of early-onset CRC (Rogers et al., 2016; Salani et al., 2014). Another recent article documented the incidence rate of gestational CRC to be 0.002% (Ge et al., 2025). A systematic review found the median age at CRC diagnosis in pregnant patients to be 32 years. The majority of diagnoses were during the second and third trimesters, and metastatic disease at diagnosis was identified in 48% of patients. Factors leading to CRC in pregnancy may include hormone fluctuations, an increase in growth factors, and changes in the mother's immune system (Pellino et al., 2017).

Regarding imaging and further workup for diagnosis, the teratogenic effects of ionizing radiation need to be considered. Imaging modality choice requires a multidisciplinary discussion to determine which method will provide the needed staging information with the least radiation exposure. Ultrasound (US) and MRI are preferred during all trimesters since there is no ionizing radiation exposure to the fetus. CT imaging of the abdomen is considered contraindicated during pregnancy due to ionizing radiation exposure. However, US is not as sensitive for CRC, and both US and MRI can require additional diagnostic imaging with CT imaging if inconclusive. Colonoscopy can be considered; however, the risks of pressure on the placenta, exposure to teratogenic medications, and fetal injury from hypoxia or hypotension must be acknowledged and discussed (Petruzzelli et al., 2020; Sorouri et al., 2023).

CANCER TREATMENT PRINCIPLES DURING PREGNANCY

The treatment of cancer in pregnant patients must consider the location of the tumor, cancer stage, symptoms on presentation and associated urgency, gestational age of the fetus, the mother's wishes, and assessment of quality of life (Walsh & Fazio, 1998). The use of anticancer therapy in pregnancy comes with many challenges that involve balancing the effectiveness of treatment with maternal and fetal safety, along with ethical considerations. The treatment team must consider various factors, including drug exposure to the fetus, teratogenicity, pharmacokinetic and pharmacodynamic changes in the mother, and timing of treatment. It is crucial to employ multidisciplinary discussions with the patient and family when making treatment decisions due to the complexity of these cases (Rogers et al., 2016; Sorouri et al., 2023). A clinical practice guideline was previously developed discussing general principles of cancer in pregnancy (Peccatori et al., 2013).

Physiologic changes that occur within the mother during pregnancy include enhanced renal and hepatic function, increased volume of distribution, changes in gastric motility, and decreased protein binding (Esposito et al., 2016; Rogers et al., 2016; Wiebe & Sipila, 1994). These changes may impact drug metabolism, distribution, and clearance, and in turn, maternal and fetal drug exposure (Esposito et al., 2016; Rogers et al., 2016; Ngu & Ngan, 2016). The placenta is also instrumental in fetal exposure to medications. Placental passage of drugs is dependent upon numerous medication factors, including molecular weight, protein binding, lipid solubility, and ionization constant. Unfortunately, many drugs, including chemotherapy agents, have characteristics that allow fetal exposure, although usually in reduced concentrations compared to the mother. Lastly, the rate of metabolism and excretion in the placenta and placental transporters also impact fetal exposure (Esposito

et al., 2016; Sorouri et al., 2023; Syme et al., 2004). In general, standard dosing based on the mother's actual body weight is recommended (Ngu & Ngan, 2016; Wolters et al., 2021).

Teratogenicity of chemotherapy is based on minimal data of case reports and animal studies since these patients are routinely excluded from clinical trials; the data also vary based on the agent and gestational age. It is recommended to avoid chemotherapy administration during the first trimester as this is when the fetus is developing. Risks of administration during this time include congenital malformations, organ impairment, and spontaneous abortion (Boere et al., 2017; Cardonick & Iacobucci, 2004; Silverstein et al., 2020). During the second and third trimesters, the limited data do not show significant teratogenicity; however, possible risks include prematurity and intrauterine growth restriction (Amant et al., 2012a; Cardonick & Iacobucci, 2004; Esposito et al., 2016). Additionally, the available data have shown that the administration of chemotherapy during pregnancy has not had an impact on neurological, psychological, cognitive, or general development (Avilés & Neri, 2001; Amant et al., 2012a, 2012b; Cardonick et al., 2015; Hahn et al., 2006; Korakiti et al., 2020). However, prematurity may have independent implications on different aspects of development (Amant et al., 2015; Sorouri et al., 2023).

Additionally, chemotherapy administration should be coordinated with delivery to avoid cytopenias in the mother and fetus at the time of delivery, to help prevent increased risk of bleeding from thrombocytopenia or infection from leukopenia or neutropenia (Leslie et al., 2005; Ngu & Ngan, 2016). A general recommendation is to cease chemotherapy treatment after the 35th week of gestation (Cardonick & Iacobucci, 2004; Esposito et al., 2016). Lactation and breastfeeding must also be considered postpartum with multidisciplinary discussion surrounding the safety and feasibility of each chemotherapy agent (Sorouri et al., 2023).

Regarding other treatment modalities, surgery can be performed during pregnancy with the beginning of the second trimester being the most favorable timeframe to balance the risk of miscarriage early in the pregnancy with the size of the fetus during later stages of pregnancy. Overall, surgery carries the risk of preterm labor; however, advances in maternal-fetal monitoring and anesthesiology allow for surgeons to carry out procedures more safely. Radiation should generally be avoided during pregnancy; however, it may be used depending on the location of the cancer (Moran et al., 2007; Pellino et al., 2017; Sorouri et al., 2023).

COLORECTAL CANCER TREATMENT DURING PREGNANCY

Patient case reports and case series documenting the treatment of CRC in pregnancy are available (Amarjothi et al., 2019; Cao et al., 2020; Cardonick et al., 2010; Cirillo et al., 2012; Dogan et al., 2013; Gensheimer et al., 2009; Jeppesen & Østerlind, 2011; Kanate et al., 2009; Kocián et al., 2019; Kraljević et al., 2014; Makoshi et al., 2015). Yet, considering these publications, data and experience are still limited, especially concerning treatment consensus and long-term outcomes.

Colorectal cancer symptoms can mirror common pregnancy symptoms, including fatigue, abdominal pain and bloating, bowel changes, nausea and vomiting, decreased appetite, and rectal bleeding (Morice et al., 2012; Pellino et al., 2017). Therefore, the diagnosis of CRC in pregnant patients is often delayed, and the cancer may be more advanced at presentation leading to emergent surgery or prompt hospitalization. However, it has been documented that survival is comparable to patients who are not pregnant (Kocián et al., 2019; Pellino et al., 2017).

In patients with resectable disease at diagnosis, a surgical approach is recommended if feasible based on gestational age, especially in patients presenting with acute symptoms such as obstruction (Pellino et al., 2017; Sorouri et al., 2023; Walsh & Fazio, 1998). However, patients with advanced disease will likely need systemic anticancer therapy, which should be initiated as quickly as possible.

Systemic anticancer therapy in CRC commonly includes fluoropyrimidines, such as fluorouracil and capecitabine. Fluoropyrimidines have low molecular weights with minimal to moderate protein binding, and therefore will likely undergo placental transfer (National Toxicology Program [NTP], 2013; Rogers et al., 2016). There are many reports of fluorouracil administration in pregnant patients. When given in the first trimester, 31%

of the cases had major malformations compared with 1% in the second or third trimesters. All patients with CRC received fluorouracil in the second or third trimesters and no congenital abnormalities were seen (Kocián et al., 2019; NTP, 2013). Additionally, no significant long-term effects were reported. There is currently a lack of data supporting the use of capecitabine in pregnancy, so fluorouracil is preferred. It is unknown if fluoropyrimidines are present in breast milk; therefore, it is not recommended to breastfeed during treatment (Johnson et al., 2020).

Oxaliplatin is a platinum chemotherapy commonly used in CRC in combination with fluoropyrimidines and is also thought to cross the placenta. In some of the CRC case reports mentioned previously, fluorouracil was given in combination with oxaliplatin (FOLFOX regimen) in the second or third trimesters. Again, no congenital malformations or developmental deficits were seen; however, height and weight were mentioned to be in a lower percentile for a few children, and one child had hypothyroidism (Cardonick et al., 2010; Dogan et al., 2013; Gensheimer et al., 2009; Jeppesen & Østerlind, 2011; Kanate et al., 2009; Kocián et al., 2019; Kraljević et al., 2014; Makoshi et al., 2015; Pellino et al., 2017; Rogers et al., 2016). Oxaliplatin is present in breast milk, and therefore, it is not recommended to breastfeed during oxaliplatin treatment and for 3 months after the last dose (Krutsch et al., 2023).

Irinotecan, a topoisomerase I inhibitor, is another chemotherapy agent commonly used in combination with fluoropyrimidines in CRC. Fetal exposure is likely; however, human data are limited to a few case reports that administered fluorouracil and irinotecan, FOLFIRI, in the second or third trimesters. One report noted intrauterine growth restriction at birth but no congenital malformations. Given the lack of data with irinotecan at this time, it may be preferred to avoid this agent (Cirillo et al., 2012; Rogers et al., 2016). Irinotecan and its metabolites are present in breast milk, and therefore, it is not recommended to breastfeed during irinotecan treatment and for 7 days after the last dose (Pharmacia & Upjohn Co, 2024).

In addition to traditional chemotherapy agents, monoclonal antibody drugs may pass through the placenta; however, fetal data are currently limited (Lambertini et al., 2015). Vascular endothelial growth factor (*VEGF*), human epidermal growth factor receptor 2 (*HER2*), and epidermal growth factor receptor (*EGFR*) can all be involved in CRC growth, and therefore are potential monoclonal antibody targets. Each of these regulators also plays a key role in embryogenesis as well as placental and fetal development, so agents that aim to inhibit these growth factors are not recommended during pregnancy (Demir et al., 2007; Silverstein et al., 2020). One meta-analysis reported oligohydramnios/anhydramnios when fetuses were exposed to trastuzumab (Herceptin), a HER2-directed agent, during the second and third trimesters (Zagouri et al., 2013). There are no human reports currently available describing the use of VEGF or EGFR monoclonal antibodies in pregnancy (Rogers et al., 2016).

There are also minimal data regarding the use of immunotherapy in pregnancy with only a few case reports published (Burotto et al., 2018; Menzer et al., 2018; Xu et al., 2019). Use is generally discouraged due to the concern for maintaining maternal-fetal tolerance (Guleria & Sayegh, 2007; Silverstein et al., 2020; Sorouri et al., 2023).

Babies exposed to chemotherapy in utero should have long-term monitoring for adverse outcomes including secondary malignancies and various developmental issues. Additional monitoring may be necessary based on the specific chemotherapy administered. For example, babies exposed to platinum agents in utero should be assessed for auditory complications during infancy and childhood (Cardonick & Iacobucci, 2004; Sorouri et al., 2023). As stated previously, due to the risk of chemotherapy agents being present in lactation, patients are advised to not breastfeed while on chemotherapy.

CASE STUDY CONTINUED

The patient's CRC treatment plan was created by a multidisciplinary team including MFM, medical oncology, gastroenterology, interventional radiology, surgical oncology, pharmacy, and neurology. The medical oncology team recommended the FOLFOX chemotherapy regimen and had an in-depth discussion with the patient regarding the risks and benefits of administering chemotherapy during pregnancy. The medical

oncology team also coordinated with interventional radiology for chemotherapy port placement and the needed sedation for the procedure. Maternal-fetal medicine planned for weekly fetal monitoring including a non-stress test. The patient started FOLFOX at 28 weeks and 6 days gestation and was scheduled to receive 4 cycles prior to planned induced delivery at the 37th week. This timing aimed to allow for a treatment break prior to induction to prevent delivery during count nadir. Additionally, the goal was to optimize neonatal growth while avoiding significant delays in cancer treatment.

The patient went into spontaneous labor at 34 weeks on Cycle 4, Day 1 of FOLFOX and was admitted to her local hospital with the 46-hour fluorouracil infusion pump still active. The patient delivered a healthy baby girl via vaginal delivery who stayed in the neonatal intensive care unit for 12 days. There was no indication that chemotherapy precipitated labor. The patient had restaging imaging after delivery, which demonstrated stability of her CRC. She resumed treatment with FOLFOX after delivery with the addition of panitumumab (Vectibix). She chose not to breastfeed due to the potential risks of chemotherapy being present in her breast milk.

Additionally, a hepatic artery infusion (HAI) pump was surgically placed after Cycle 9 of FOLFOX and her systemic chemotherapy regimen was changed to FOLFIRI + panitumumab due to ongoing neuropathy. From there, she underwent a partial hepatectomy after 4 cycles of FOLFIRI + panitumumab and then continued HAI pump therapy. The patient had a laparoscopic colectomy about a year after delivery and coordinated timing of surgery around her daughter's first birthday party.

DISCUSSION

With the incidence of CRC increasing in young adults and the trend toward delayed childbearing, it is probable that the incidence of CRC during pregnancy may increase. Unfortunately, CRC in young adults is usually more aggressive, which makes it difficult to delay treatment in the case of pregnancy. This patient case highlights a unique cancer diagnosis and the many considerations of treating cancer during pregnancy including the safety of diagnostic tests and chemotherapy.

This patient had no symptoms indicative of CRC and was instead diagnosed during her pregnancy workup with NIPT. Noninvasive prenatal testing has been widely used since 2020 to identify fetal abnormalities during pregnancy but has also incidentally detected maternal malignancies (Turriff et al., 2024). With the increased use of this testing, it is possible that cancers may be diagnosed in earlier stages before symptoms develop and may result in more patients undergoing cancer treatment while pregnant. This diagnostic avenue may be described more frequently as testing uncovers unanticipated maternal health issues.

The FOLFOX chemotherapy regimen was chosen due to the available literature deeming this to be the best option in treating advanced or metastatic CRC during pregnancy. In non-pregnant patients with newly diagnosed advanced or metastatic colorectal cancer, FOLFOX is one of the standard first-line chemotherapy regimen options. Non-pregnant patients will often receive a targeted agent in combination with first-line chemotherapy, such as a VEGF or EGFR inhibitor; however, these targeted agents have not been deemed safe in pregnant patients.

Next-generation sequencing is a recommended practice within advanced or metastatic cancer guidelines to assess for targetable genomic alterations that may guide treatment decisions (Chakravarty et al., 2022). Next-generation sequencing would be appropriate to perform in pregnant patients as well; however, the agents targeting the mutations would need to be individually evaluated for safety in pregnancy.

The patient was able to deliver her baby without complication, and no congenital malformations nor developmental deficits were observed. While induction was planned for the 37th week to allow for adequate blood cell count recovery, the patient went into labor while her chemotherapy was actively infusing during the 34th week. This highlights the need for flexibility in these complex cases where each step in the treatment plan may not progress as intended. No complications occurred with the timing of birth in this patient. This article adds additional data demonstrating FOLFOX can be given safely in pregnant patients after a thorough discussion of risks and benefits.

Furthermore, this case emphasizes the need for collaboration across numerous disciplines to ensure the safety of the mother and fetus and optimal cancer outcomes. Each member of the team played a vital role and added their expertise to a complicated patient case. It is important for oncology providers to recognize how to care for this emerging population. Advanced practitioners are crucial to ensure optimal outcomes.

While published data exist in treating pregnant patients with CRC, formal guidance is crucial to better inform these complex cases. Additionally, long-term follow-up of babies exposed to chemotherapy in utero into childhood and adulthood is warranted. ●

Disclosure

Ms. Green has served on the speakers bureau for AstraZeneca. Dr. Hatch has received consulting fees from Intera Oncology.

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