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SHORT COMMUNICATION

# Administration of oxaliplatin to a pregnant woman with rectal cancer

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**Abstract**
*Purpose* The platinum agent oxaliplatin could be useful in treatment of cancer in pregnant women, but it is fetotoxic in rats and its effect on the human fetus is unknown.
*Methods* Oxaliplatin was administered to a 25-year-old pregnant woman with metastatic rectal cancer from 20 to 30 weeks gestational age as part of the mFOLFOX-6 regimen.
*Results* The patient gave birth to a healthy girl at 33 weeks gestational age. At follow-up, the 3-year-old child had achieved all appropriate growth and developmental milestones.
*Discussion* Oxaliplatin is a component of several modern chemotherapy regimens. This report demonstrates the administration of oxaliplatin in the second and third trimesters of pregnancy without apparent fetal harm.

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## Introduction

Oxaliplatin is an antineoplastic agent approved by the FDA in 2004 for use in metastatic colon cancer. It is a third-generation platinum analog which appears to act on tumor cells by forming DNA adducts [5]. Oxaliplatin has activity against cancers that are resistant to the first- and second-generation platinum compounds cisplatin and carboplatin [5]. The use of other platinum agents in pregnancy has been associated with reports of intrauterine growth retardation, fetal demise, newborn hearing loss, and fetal ventriculomegaly [2]. The effect of oxaliplatin in human pregnancy is unknown, but administration of oxaliplatin to pregnant rats sometimes caused fetal loss and affected fetal growth [3]. Like other platinum agents, the FDA classifies oxaliplatin as pregnancy category D, indicating that there is risk of fetal harm but benefits of use in pregnancy may sometimes outweigh this risk [3]. The authors are not aware of any reports of oxaliplatin use in pregnancy. We report here a case of a 25-year-old pregnant woman with metastatic rectal cancer who we treated with a regimen containing oxaliplatin without apparent fetal harm.

## Case report

A 25-year-old woman presented at an estimated gestational age (EGA) of 12 weeks with rectal bleeding. She underwent colonoscopy and was found to have a malignant tumor in the upper third of the rectum. She underwent surgical resection with a partial proctectomy and colectomy and a resultant colostomy and Hartman's pouch. Intraoperatively, she

was found to have a solitary liver lesion that was completely resected. Pathology revealed a $3 \times 3 \times 1.5$ cm moderately differentiated adenocarcinoma that completely infiltrated the wall of the rectum including the serosa and adjacent mesocolon. She had a group of six matted lymph nodes resected, of which two were involved with tumor. Surgical margins were negative. Vascular and perineural invasion were identified within the specimen. The resected liver mass measured 1 cm, was consistent with metastatic moderately differentiated adenocarcinoma and had negative resection margins. Her cancer stage by AJCC TNM classification was T4N1M1.

The patient sought medical oncology consultation regarding adjuvant chemotherapy at 17 weeks gestation. The patient was counseled regarding possible pregnancy termination, but she wished to maintain the pregnancy. At the time of her initial visit, her CEA was noted to be elevated at 21.7 ng/mL, indicating probable metastatic disease despite the prior resection of her liver metastatic lesion. Due to her high risk of tumor recurrence, and after maternal–fetal medicine consultation, adjuvant chemotherapy with the modified FOLFOX-6 regimen was recommended, consisting of 2-h infusion of oxaliplatin 85 mg/m$^2$ and leucovorin (LV) 400 mg/m$^2$, 5-fluorouracil (5-FU) 400 mg/m$^2$ bolus, and 5-FU 2400 mg/m$^2$ 46 h infusion. After discussion with the patient, chemotherapy was delayed until 20 weeks of gestation to balance possible teratogenic effects on the fetus with cancer treatment effectiveness. A Level II fetal ultrasound performed at 19 weeks EGA identified no fetal abnormalities.

At 20 weeks EGA, biweekly FOLFOX chemotherapy was initiated. At 30 weeks EGA, the patient's treatment course was complicated by an episode of intractable nausea and vomiting, concerning for bowel obstruction. A CT scan performed during that episode revealed no evidence of obstruction, and her symptoms were presumed to be due to chemotherapeutic toxicity. The CT scan demonstrated multiple hypodense liver lesions consistent with metastatic disease. There was a 1.1 cm lesion in segment III, a 1.8 cm lesion in segment IVa and a large 5.8 cm $\times$ 4 cm multinodular lesion in segment VII. At that time the patient had received six biweekly courses of mFOLFOX-6. Her CEA level had fallen from 39.4 to 15.5 mg/mL during chemotherapy, indicating a probable treatment response. Despite this, chemotherapy was discontinued due to the probable toxicity.

Due to cervical progression, at 33.6 weeks gestational age the patient underwent induction of labor and had vaginal delivery of a normal infant girl of birth weight 5 lbs, 6 oz with Apgar scores of 8 at 1 min and 8 at 5 min. Four weeks following delivery, the patient resumed chemotherapy consisting of 5-FU/LV and irinotecan (FOLFIRI) with bevacizumab. Following 16 biweekly treatments with FOLFIRI with bevacizumab, she had disease stabilization/minor response. CT scans continued to demonstrate stable disease within the liver and a PET scan indicated no 2-[$^{18}$F] fluoro-2-deoxy-D-glucose uptake in the metastatic liver lesions or evidence of any extrahepatic disease. A repeat colonoscopy was also normal at that time. The patient then underwent resection of the three hepatic lesions without complications and was rendered free of known disease.

Nine months after her liver resection, she underwent takedown of her colostomy. One year after her liver resection she remained free of disease. The patient's daughter is now 3.5 years old. She has undergone routine pediatric evaluations and hearing testing and has no deficits. She is at the 60th percentile for height and the 45th percentile for weight.

## Discussion

In this patient, the possible benefit of chemotherapy had to be balanced against the potential risk of fetal death, growth retardation, and teratogenesis from its use. Colorectal cancer with isolated liver metastases is generally treated with curative intent. Chemotherapy with 5-FU/LV following resection of liver metastases has been shown to improve 5-year disease-free survival compared to resection alone [4]. The addition of oxaliplatin would be expected to further improve outcomes given the success of the FOLFOX regimen in stage II–IV colorectal cancer [1], though a benefit has not yet been proven in the setting of resected liver metastases. At least 53 cases of 5-FU use during human pregnancy have been reported [2], but to the authors' knowledge there have been no reports of oxaliplatin administration in pregnancy.

The greatest teratogenic risk occurs in weeks 2–8 post-conception [2]. After organogenesis is complete at around 8 weeks post-conception, risk to organs such as the eyes and CNS continues and is thought to decrease after the first trimester [2]. Therefore, as in our patient, chemotherapy intended to avoid fetal harm is generally delayed until after the first trimester [2, 6]. Similar to previous reports with other selected chemotherapeutic agents [6], we demonstrated administration of oxaliplatin during the second and third trimesters of pregnancy without apparent fetal harm.

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