



Colon Cancer during Pregnancy: A Report of Two Cases

Dobrokhotova Y¹, Danelian S² and Borovkova E^{1*}

¹Department of Obstetrics and Gynecology, Russian National Research Medical University, Russia

²Department of Obstetrics and Gynecology, City Clinical Hospital No. 40, Russia

Abstract

Background: Colorectal Cancer (CRC) is exceedingly rare in pregnancy, estimated to occur in 1 in 13000 pregnancies. CRC symptoms such as abdominal pain, constipation, nausea, and vomiting are usually attributed to the physiological changes of pregnancy.

Case Presentation: A 30-year-old woman at 23-24 weeks of gestation presented with abdominal discomfort, constipation, and bloody rectal discharge. A 34-year-old woman at 27-28 weeks of gestation delivered to the emergency room with the episode of unconsciousness and involuntary urination. Both patients underwent the MRI examination without contrast. MRI scanning showed a formation of the sigmoid colon without obstruction and a cystic-solid formation of the right ovary (in the first patient) and formations of the frontal-parietal lobe, multiple hepatic metastases, and the tumour of the ampullary rectum with stenosis (in the second patient). The diagnosis of the sigmoid and rectal adenocarcinoma was estimated in both women via performing the colonoscopy with biopsy. After the neoadjuvant chemotherapy with FOLFOX was done, doctors performed surgical operations as follows: the laparotomy, caesarean section, panhysterectomy, hemicolectomy with descendo-rectal anastomosis, and pelvic lymphodectomy for the first patient (performed on 33 gestation week due to increase of the size of metastasis in ovary); caesarean section for the second patient (performed on the 33 gestation week of pregnancy due to the fetal stress). The second patient deceased 5 months after delivery.

The first patient four weeks postoperatively, we continue the course of adjuvant chemotherapy with XELOX. Five months later PET/CT revealed a single metastasis in the liver and multiple metastases in the lungs. Two line chemotherapy (FOLFIRI+) was administered. Six months revealed a reactivation of tumour progression and a STIVARGA therapy was started.

Conclusion: The most common colorectal cancer symptoms can usually be masked by those developing due to the physiological changes during the pregnancy. That hardens the diagnosis of CRC in pregnant patients. The management tactics are similar in pregnant and non-pregnant patients, but there are some special considerations for securing fetal safety.

Keywords: Colorectal cancer; Pregnancy; Chemotherapy

Introduction

Colorectal Cancer (CRC) is exceedingly rare in pregnancy, estimated to occur in 1 in 13000 pregnancies. CRC symptoms such as abdominal pain, constipation, nausea and vomiting are usually attributed to the physiological changes of pregnancy [1].

However, constipation and rectal bleeding are also one of the earliest symptoms of colorectal cancer. The initial symptoms overlap with expected physiological changes in pregnancy and can easily be dismissed.

Case Presentation

Case 1

A 30-year-old G3P0 at 23-24 weeks gestation presented to the in-patient room with abdominal discomfort, constipation, and bloody rectal discharge. She had a history of constipation for 19 weeks of gestation. She denied any family history and chronic disease. Her vital signs and labs results were normal.

An abdominal ultrasound revealed a 94 mm formation behind the uterus (Figure 1). MRI of the abdomen without contrast showing the formation of the sigmoid colon without obstruction and cystic-solid formation of the right ovary (Figure 2 and 3).

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*Correspondence:

Ekaterina Borovkova, Department of Obstetrics and Gynecology, Russian National Research Medical University, Moscow, Akademika Pilyugina Street 14-2-295, Russia, Tel: +7-9037855793;

E-mail: katyanikitina@mail.ru

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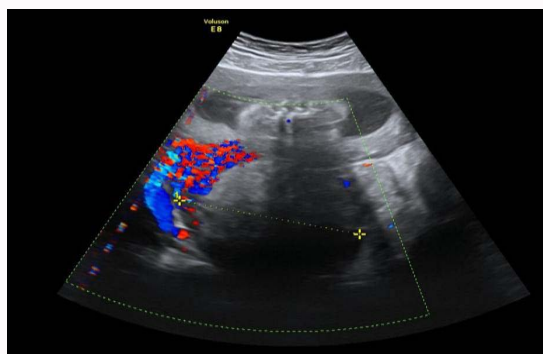


Figure 1: Abdominal ultrasound with Color Doppler.

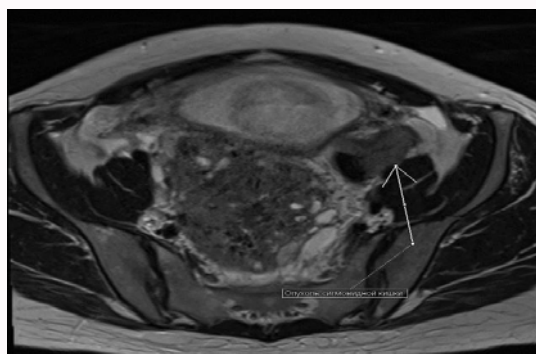


Figure 3: MRI of abdomen without contrast: sigmoid colon formation.

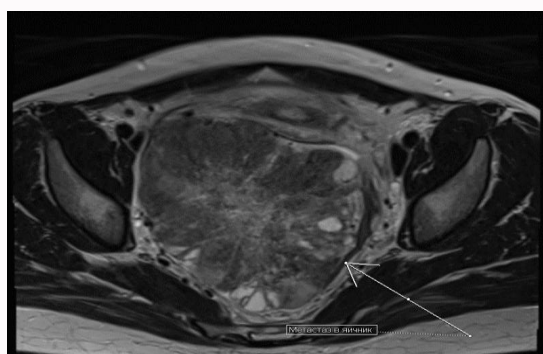


Figure 2: MRI of abdomen without contrast: right ovary formation.

The patient underwent a colonoscopy with biopsy. Colonoscopy revealed a nodular stricture partially narrowing the sigmoid lumen with a length of 5 cm.

According to histological and immunohistochemical studies, adenocarcinoma was diagnosed, cT3-4 NX M1.

Oncomarkers were as follows: CEA-56.5 ng/L, HE-4-48.3 pmol/L, CA72-429.1 IU/ml, AFP-85 ng/ml, CA-125-64.8 IU/ml, CA19.9-26.4 IU/ml.

After a discussion regarding the risks and benefits of treatment, the patient began neoadjuvant chemotherapy with 5-Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX). First course performed on 26 weeks pregnancy, second on 28-29 and the third on 30-31 weeks of gestation.

Control MRI at 30-31 weeks of gestation revealed a decrease in the size of the sigmoid colon tumor and an increase in the size of metastasis in the right ovary.

A course of the antenatal steroid was done, and at 33 weeks of gestation were performed a laparotomy, cesarean section, panhysterectomy, hemicolectomy with descendo-rectal anastomosis, and pelvic lymphodissection.

Histology examination revealed a sigmoid colon adenocarcinoma (T3N0M1a) with adipose tissue and its mesentery invasion without serosal invasion. Tumor emboli were presented in lymphatic vessels of the sigmoid colon in the tumor growth zone. Examination of 46 lymph nodes (sigmoid colon mesentery and mesorectal fiber, iliac obturator nodes on both sides) detected no tumor metastases. A distant CRC metastasis that invades the uterine wall was found in the right ovary. Also was revealed an incomplete morphological

regression of tumors in the intestine and ovary due to chemotherapy. No tumor growth was detected in the edges of the rectum and mesentery samples.

Molecular genetics study of the finished histological material (postoperative) from August 2019: KRAS-positive; BRAF and HER2/neu, PD-L1 and MSI-negative.

Four weeks postoperatively, we continue the course of adjuvant chemotherapy with XELOX. After the third course, she presents presented polyneuropathy.

Thoracic and abdominal cavities and pelvic CT scan (06.2018), and PET/CT (09.2018) indicated no distant metastasis.

Five months after delivery (11.2018) the patient completed 9 courses of chemotherapy with the XELOX scheme. Complications: polyneuropathy 3 grade, thrombocytopenia 2 grade.

Thoracic and abdominal cavities and pelvic CT scan with contrast (Dec 2018) -normal. The patient began monotherapy with the Xeloda since December 2018 to April 2019. We detected the increase of Carcinoembryonic Antigen (CEA) concentration in March 2019.

PET/CT 04.2019-revealed a single metastasis in the liver and multiple metastases in the lungs. Two line chemotherapy (FOLFIRI+) was administered. In May 2019 the patient has developed an adhesive bowel obstruction. The last chemotherapy course was complicated by 3-4-grade neutropenia and thrombocytopenia.

Control PET/CT (Jul 2019) revealed a reactivation of tumor progression. Were observed multiple small foci with high metabolic activity in the lungs, single metastasis with high metabolic activity in the liver S8 segment, and local metabolic activity increase in the liver S4 segment.

A contrast-enhanced MRI scan of the abdominal cavity revealed (Jul 2019) new metastatic foci in liver S8 and S5 segments.

In August 2019 was started a Stivarga therapy.

MRI scan of the abdominal cavity on October 2019 indicated negative dynamics of the disease course (enlarged and multiplied secondary metastases in liver and lungs).

Now the patient is stabile and undergoes a 4th course of the Stivarga therapy.

Case 2

A 34-year-old G1P0 at 27-28 weeks of gestation presented to an emergency room with a reference to the episode of loss of consciousness and involuntary urination. On admission, APACHE

II evaluation was performed, the patient scored 10 points. Vitals on admission were as follows: temperature 36.7°C, pulse 98 beats per minute, and blood pressure 105/60 mmHg. Height 150 cm, weight 43.5 kg, BMI 19. Patient labs on admission included a white blood cell count $9.6 \times 10^9/L$, hemoglobin 83 g/L, hematocrit 23.5%, mean corpuscular volume 87 μm^3 .

The patient had a history of constipation, abdominal discomfort, and bloody rectal discharge since the 8 weeks of gestation. Since the 12 weeks of gestation, she had complained about periodical diarrhea to 5 to 10 times per day. A consultation with gastroenterologists allowed us to suppose an irritable bowel syndrome. Abdominal ultrasound on 13 weeks pregnancy revealed no signs of pathology. The patient gained 2.5 kg since the beginning of the pregnancy.

In the emergency department, an abdominal ultrasound revealed hepatomegaly and multiple hepatic metastases. MRI without contrast showed formations of the frontal-parietal lobe of the brain, and the tumor of the ampullary rectum with stenosis.

Due to no clinical improvement after 4 days of conservative treatment, the patient underwent a colonoscopy. Colonoscopy revealed a stricture partially narrowing the rectal lumen. According to histological and immunohistochemical studies, adenocarcinoma was diagnosed (cT4NXM1).

After stabilization of her vital status, we began neoadjuvant chemotherapy with 5-Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX). We had performed two courses on 29 weeks and 31-32 weeks of pregnancy.

On the 33 weeks, the pregnancy urgency cesarean section had performed due to fetal distress.

By hospital day 47 (8 days after delivery), the patient was discharged to continue outpatient treatment. She had three neoadjuvant chemotherapy courses with 5-Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX). The patient deceased five months after delivery.

Discussion

Colon cancer does not present differently in pregnant patients, however, most of its symptoms may be similar to physiological. Pregnancy is a period in which women regularly consult a doctor and have physical exams, blood analysis, and ultrasound examinations. This allows early diagnosis. Unfortunately, it is possible not always [2].

Our second patient had a long history of chronic constipation and diarrhea and presented with worsening of her vital status. The delay in diagnosis worsened the prognosis for the patient.

Abdominal ultrasound has a low sensitivity in detecting metastases and nodal involvement because of the enlarged uterus. Endorectal ultrasound can be used safely during pregnancy for local staging of CRC, tumor infiltration into the vagina. The preference method in pregnancy is MRI. Based on the recommendations of the American Radiological Society in 2013, the use of MRI is safe in all three trimesters of pregnancy. The use of a contrast agent is not recommended during pregnancy. Thoracic CT can be used for detecting pulmonary metastases. CRC may be diagnosed by endoscopy and confirmed with a biopsy. Rectosigmoidoscopy is safe during pregnancy [3,4].

The only potentially curative treatment of CRC is radical surgery. Before the 20th week of gestation, resection should be performed. After 20th weeks, in the non-acute setting, it is usually advisable to wait until the end of pregnancy and then perform surgery. In rectal cancer, cesarean section is recommended, in colon cancer, vaginal delivery remains a possibility [5].

Chemotherapeutic regimens used in CRC are 5-fluorouracil and oxaliplatin-based. The treatment must be stopped three weeks before delivery to decrease the risk of myelosuppression of the fetus and mother.

Survival for pregnant CRC patients is similar to non-pregnant with the same stage. However, a pregnant patient is more often diagnosed with advanced disease. The INCIP workgroup report an overall 2-year survival of 65% for CRC in pregnancy [1,5].

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