Case Report

Colorectal cancer during pregnancy in a Sudanese female

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Abstract:

We report a new case of uncommon but not rare condition of colorectal cancer during pregnancy in 33 years old Sudanese female at her 16th weeks of gestation presented with bloody diarrhea and intermittent left side abdominal pain. Initially she was diagnosed as a case of dysentery which was treated by antibiotics. Condition was diagnosed by colonoscopy and histopathology as colonic cancer, located in the sigmoid colon 50 cm from anal verge.

A review of literature found that 276 cases of colon cancer associated with pregnancy have been reported. Pregnancy affects the clinical presentation, evaluation, therapy, and prognosis of colon cancer. Patients usually present with misdiagnosed symptoms. Diagnostic delays often lead to the tragic demise of a young woman from a potentially curable disease and of an otherwise viable fetus. This delay in diagnosis is a major contributing factor to the poor prognosis associated with this disease. Synchronous colon cancer during pregnancy presents a diagnostic and therapeutic challenge for clinicians because there are no generally accepted guidelines regarding diagnosis or treatment.

This article reviews this uncommon condition with a focus on the features of colon cancer in pregnancy to facilitate earlier diagnosis, to modify investigations, to optimize the therapy, and to improve the maternal and fetal outcomes.

Keywords: Colorectal cancer; Pregnancy; CEA, FOLFOX

The reported incidence of cancer during pregnancy is between 0.002% [1] and 0.1%[2]. Although we are aware that there were few cases reported worldwide, this is the first case of colorectal cancer during pregnancy to be reported in Sudan. Approximately 276 cases of colon cancer associated with pregnancy have been reported in the literature[3].

Colorectal cancer during pregnancy is very rare because most cases of colorectal cancer occur in patients 50 years of age or older[4]. Younger patients who develop colorectal cancer during pregnancy tend to have an advanced stage of disease at the time of initial assessment due to a delay in the diagnosis. A delay in diagnosis during pregnancy associated with gastrointestinal changes is a common feature, and metastatic spread, bowel obstruction and subsequent perforation are more prevalent during pregnancy[2].

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Case report:

A 33-years-old Sudanese pregnant female, gravid V, Para I + III, presented to our surgical department referred from Niala Hospital in southern Dar-four, during her 16th week of gestation, complaining of bloody diarrhoea for more than six months, bleeding was minimal in amount, bright red in colour associated with intermittent passage of mucus and vague left lower abdominal pain during defecation that was relieved by passage of motion. The condition was concomitant with evidence of abortion. The treating doctor attributed her symptoms to dysentery, for which she received antibiotics but without improvement. Three months later she got pregnant again, this led her to re-consult a doctor, who performed colonoscopy due to the persistence of bleeding, and reported the

presence of circumferential mass about 3 cm in diameter and 50 cm from the anal verge, a biopsy was taken for histopathological examination. The patient appeared to our clinic with the inconclusive histopathological result that mentioned the presence of villous tumour. There was no family history of colorectal cancer. On clinical examination, the patient was slightly pale with a haemoglobin level of 10 g/dl and a 16th week intrauterine pregnancy. There was no dental cyst, jaw oseteoma, retinal pigmentosa or desmoid tumour in the abdominal wall. The fundal level was corresponding to date. There was no other abnormality. Other laboratory investigations carcinoembryonic antigen (CEA), liver function test, and renal function tests all were within normal range. Abdomenopelvic ultrasound scan revealed no abnormality or signs of dissemination to liver, adjacent organs or regional lymph nodes. To help to determine the extent and exact location of the tumour, a possibility to perform a computed tomography (CT) scan was discussed with radiologist who did not agree to the idea, this is because of the high radiation dose that might affect the pregnancy. The case was discussed with obstetrician and gynecologist who excluded the need for termination of pregnancy prior to surgery.

During hospital stay she started to develop features of subacute bouts of intestinal obstruction. Therefore, at 18th week of gestation, operation was performed through midline laparotomy, the tumour was found to be confined to the mid portion of sigmoid colon. On examination of abdominal organs, there was no obvious metastasis. Then intra operative decision was made to perform partial sigmoidectomy and primary end-to-end anastamosis instead of total sigmoidectomy as the gravid uterus was close to area of anastomosis, the anastomosis was 7 cm below the tumor. The patient recovered uneventfully. The resected specimen was sent for hitopathological examination, which macroscopically showed a tumour measuring 5 cm in length and 7 cm in circumference, and microscopically showed moderately differentiated mucin secreting adenocarcinoma penetrating the muscularis propria, this is staged as Duke's B2, the lymph nodes showed reactive changes and the resection margins were free of tumour. For further management, the case was discussed with oncologist who initiated FOLFOX regimen of chemotherapy at the beginning of the 3rd trimester. Patient did not report back to us following referral to the oncologist and the fate of pregnancy after chemotherapy is not known to us. It should be mentioned that fiberoptic sigmoidoscopy was suggested to the patient but was not performed for different reasons.

Discussion:

The key to an early diagnosis of colorectal cancer includes a complete history and thorough physical examination[5,6]. However, the symptoms of colorectal cancer are nonspecific, including abdominal pain, nausea, vomiting, constipation and rectal bleeding, that can be confused with the symptoms of normal pregnancy[6,7]. The physicians should be alert to the rare possibility of colorectal cancer in pregnancy and must rule it out from the cases of persistent abdominal discomfort associated with vomiting and constipation[7].

There are no guidelines for surgical management based on the gestational age of the fetus at the time of tumour diagnosis[8].

The serum carcinoembryonic antigen (CEA) levels are normal or marginally elevated in a normal pregnancy[9- 12]. The CEA levels should therefore be measured and used in the same way as in non-pregnant patients[9]. Although the CEA level is not useful as a screening test for colon cancer because its low sensitivity and low specificity, preoperative testing is useful in determining the prognosis and for providing a baseline for comparison with postoperative levels. After an apparently complete colon cancer resection, the serum CEA level almost always returns to normal; failure for this level to normalize after surgery indicates a probable incomplete resection[11]. In contrast in our patient the CEA level

preoperatively was normal (1.30 ng/ml, normal reference < 3.4 ng/ml).
The carcinogenesis of colorectal cancer is not fully understood. The hypothesis that oestrogen (ER) and progesterone receptors (PgR) may be involved in the pathogenesis of colorectal cancer during pregnancy has been studied. Several studies have reported the presence of ERs in colon cancer[13-15].
Some families have higher frequency of colorectal cancer due to familial adenomatous polyposis (FAP), hereditary non-polyposis colon cancer (HNPCC) or other familial colon cancer which is essentially a diagnosis of exclusion of the first two conditions. FAP is responsible for 1% of all colorectal cancers. It is characterized by multiple colorectal adenomas and typical extra-colonic stigmata as shown in table 1[16].

Table 1: Extra-colonic manifestations of FAP

• Hamartomatous polyps in the stomach • Adenomas of the duodenum • Dental cysts • Osteomas of the jaw	• Retinal pigmentation • Epidermoid cysts • Desmoid tumours, usually in the abdomen

While HNPCC is responsible for 3% to 5% of all colonic cancers[16,17]. Given our patient's age at diagnosis (33 years), consideration of HNPCC at this time is prudent[18]. Patients with strong family history of colorectal cancer are likely to have HNPCC if they fit the Amsterdam criteria, as shown in table 2[16].

Table 2: Amsterdam criteria for clinical diagnosis of HNPCC.

• Three or more family members with colorectal cancer • Colorectal cancer in two generations	• One or more affected before the age of 45 • Exclusion of familial adenomatous polyposis (FAP)

Our patient was not fitting the characteristics and extra-colonic stigmata of FAP or Amsterdam criterion of HNPCC. Also have no other familial colonic cancer.
Most patients eventually develop liver metastases[19].
Abdominal CT imaging for staging of cancer is contraindicated in pregnancy due to radiation teratogenicity, particularly in the first trimester[20,21]. An abdominal ultrasound is an alternative to abdominal CT imaging in pregnant patients; this is useful in evaluating the presence of hepatic metastasis and has a sensitivity of 75% for detecting macro-metastatic lesions[22,23]. Magnetic resonance imaging (MRI) appears to be safer than CT in pregnancy, although experience in using MRI is limited[24].
Bernstein et al[8], in their study demonstrated that all of the patients with colorectal cancer in pregnancy presented with Dukes class B or greater disease. This is comparable to our patients' stages as found to be Dukes class B2.
Aster- Coller (modified Duke's classification) seen on table 3[25].

Table 3: Aster- Coller (modified Duke's classification)

Aster- Coller (modified Duke's classification)		5yr survival (%)
A	Limited to mucosa	100
B1	Into MP, no nodes	67
B2	Through MP, no nodes	54
C1	Into MP, nodes	43
C2	Through MPa, nodes	22
D	Metastases	0

MP= muscularis propria.

Surgical management and prognosis are primarily determined by the extent of local disease and presence of hepatic metastases. Surgery and adjuvant chemotherapy are common treatments for patients with stage III disease[26].
When cancer diagnosed in a pregnant woman, life saving chemotherapy for the mother poses life-threatening concerns for the developing fetus. Depending on the type of cancer and the stage at diagnosis, chemotherapy cannot

necessarily be delayed until after delivery. Safe uses of chemotherapy especially during the second and third trimester after organogenesis is complete have been reported, and pregnant women with cancer accept therapy without definite neonatal harm[27-29].

FOLFOX regimen is a widely used for treatment of colorectal cancer. It involves two chemotherapy drugs, oxaloplatin and flurouracil (5FU). They are given with a vitamin called folinic acid (leucovorin), which makes 5FU more effective[30]. The use of adjuvant 5-FU administration has been demonstrated to increase the colorectal cancer survival rate by 5% to 10% [31,32].

Survival differs markedly, and clinicians must tailor patient-specific strategies[26]. Pregnant women with colorectal cancer generally have a poor prognosis. In one study by Chan et al of patients with colorectal cancer during pregnancy 56% died by the time the cases were reported in the literature. Most died within 1year of being diagnosed, and the median survival for the group was less than 5 months. One patient survived for 3.5 years after bowel resection but had multiple recurrences[5].

No patient with colorectal cancer in pregnancy reported in the literature has survived longer than five years[3].

Conclusion:

Patients with colon cancer during pregnancy usually have a very poor prognosis. The most appropriate treatment should be performed as soon as possible whenever a diagnosis of colon cancer during pregnancy is suspected or established. Arguably, colon cancer should be diagnosed expeditiously during pregnancy because of frequent obstetric clinic visits.

The choice of therapy of colon cancer during pregnancy is influenced to a large extent by the tumour operability and the timing of delivery or termination. One has to balance the risk of prematurity/abortion and that of tumour progression. Therefore, a multidisciplinary approach required, including surgeons, obstetricians, anesthetists and oncologists.

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