Clinical Case Report

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Advanced gastrointestinal carcinoma with massive ascites and hydrothorax during pregnancy

A case report and review of the literature

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Abstract

Rationale: Gastrointestinal carcinoma is rare during pregnancy. It is usually diagnosed at an advanced stage because special gastrointestinal symptoms are generally overlooked during pregnancy, and there are many limitations and contraindications for using diagnostic tools during pregnancy.

Patient concerns: We present a case of a 29-year-old patient with 27 weeks and 5 days of gestation due to massive ascites and hydrothorax.

Diagnoses: The patient was diagnosed with an advanced gastrointestinal cancer. Pathological report showed poorly differentiated tumor with the signet ring cell component.

Interventions: Caesarean section was performed. At the same time, an abdominal exploration showed that the omentum was like biscuits . There were extensive and firm intestinal adhesions, and many tumor lesions were found on the surface of greater curvature of stomach, spleen, intestine, peritoneum, ascending colon and descending colon.

Outcomes: Gastrointestinal surgeon was invited during operation, and palliative gastrectomy was not performed because of extensive metastases. The patient died 30 days after caesarean section.

Lessons: This study present a case with advanced gastrointestinal cancer during pregnancy. We suggest that endoscopic exam is recommended if the patient is highly suspicious.

Abbreviations: CA = carbohydrate antigen, CT = computed tomography, HP = *Helicobacter pylori*, OGTT = oral glucose tolerance test.

Keywords: ascites, gastrointestinal carcinoma, hydrothorax, pregnancy

1. Introduction

Pregnancy-associated gastric cancer is extremely rare, accounting for only 0.025% to 0.1% of all pregnancies.[1] The major inducing factors include increased *Helicobacter pylori* (HP) infection,[2–4] specific host susceptibility (genetic alterations of the inflammatory mediators to HP), environmental influence, and so on. Most cases of pregnancy-associated gastric cancer are diagnosed at an advanced stage because special gastrointestinal symptoms are generally overlooked during pregnancy, and there are many limitations and contraindications for using diagnostic tools during pregnancy.[5,6] Because these diagnostic tests may complicate pregnancy and compromise the fetus, so most cases of pregnancy-associated gastric cancer lose the optimal timing of early diagnosis and treatment. Survival rates in cases of gastrointestinal cancer are strictly associated with the early diagnosis. The maternal prognosis was extremely poor, with 1 and 2-year survival rates of 18.0% and 15.1%, respectively,[1] Because no standardized treatment has been established due to its rarity, delayed diagnosis and limited treatment options.

In the present work, we reported a case of a 29-year-old patient, who was diagnosed with an advanced gastrointestinal cancer. At the time of admission, she was 27 weeks and 5 days pregnancy, and the patient died 30 days after cesarean section.

2. Case report

A 29-year-old female patient, gravida 1, para 0, was transferred to our Department of Obstetrics due to massive ascites and hydrothorax from ultrasonographic examination on April 28, 2017. At the time of admission, she was 27 weeks and 5 days pregnant with a 20-day history of slight abdominal distension and could not lie down for at least 3 days because of severe abdominal distension and dyspnea. She received regular prenatal care during pregnancy and was diagnosed as gestational diabetes

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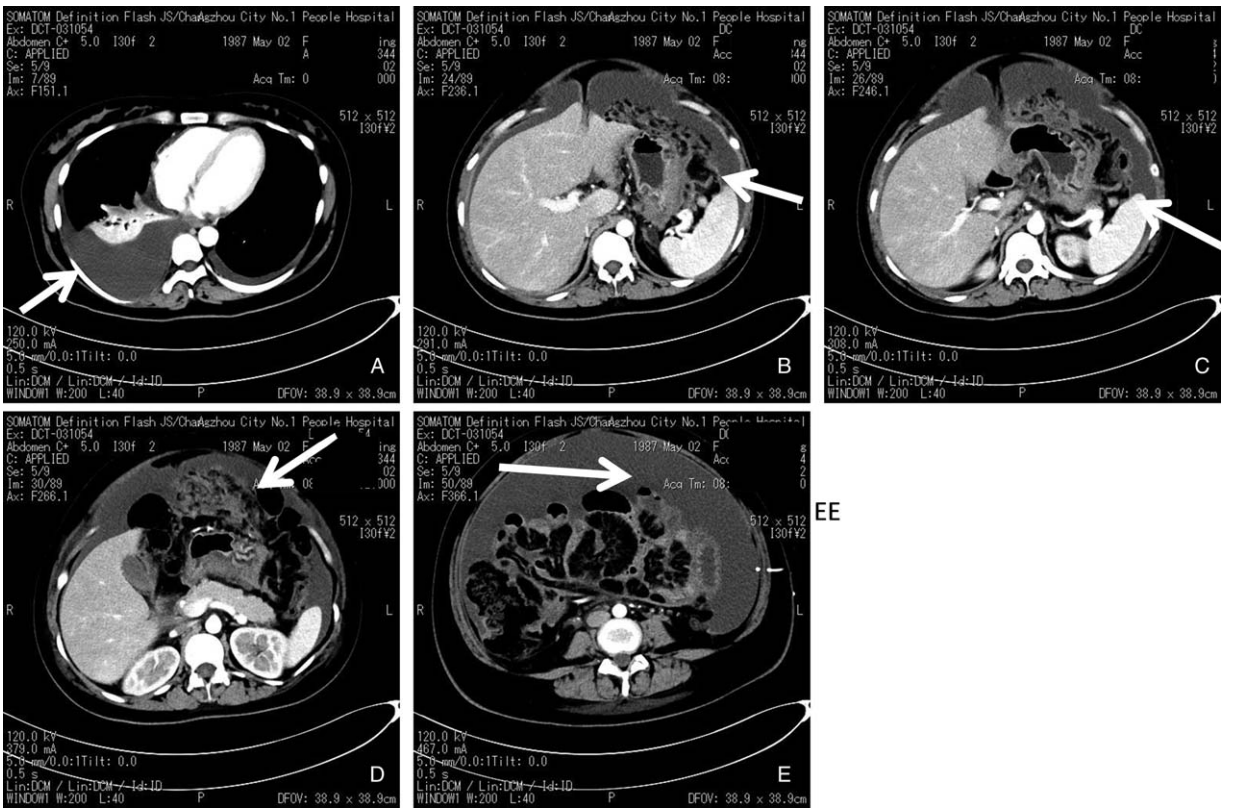

Figure 1. Computed tomography scan on admission. (A) Pleural effusion coupling with right pulmonary atelectasis; (B) gastric wall thickness; (C) enlarged lymph node; (D) cake-like omentum; (E) massive ascites.

mellitus 2 weeks ago by 75-g oral glucose tolerance test (OGTT) (4.59–13.9–12.8 mmol/L). She denied any family history of malignancy.

After admission, she was afebrile on examination, with a heart rate of 126 bpm and blood pressure of 141/85 mm Hg. The physical examination showed a gravid uterus at around 27 weeks of gestation, severe fullness in the flanks, and no epigastric tenderness or mass was found. Laboratory testing revealed hemoglobin of 9.1 mg/L, white blood count of 16.68×10^9, and platelets of 578×10^9. Biochemistry test showed natrium of 128.2 mmol/L, Chlorine of 94.6 mmol/L, and albumin of 30.4 g/L. Analysis of tumor markers indicated carbohydrate antigen (CA) 125 of 284.5 U/mL, CA19–9 >1000 U/mL, alpha-fetoprotein 157.9 ng/mL, and human epididymis protein 4 48.52 pmol/L, and her fecal occult blood test was positive. A thoracic and abdominal computed tomography (CT) scan showed pleural effusion coupling with right pulmonary atelectasis, massive ascites, thickened gastric wall of greater curvature, cake-like greater omentum, and enlarged mesentery lymph node (Fig. 1).

One day after admission, an abdominal tube was established to drain off the ascites (1000–2000 mL/d) to relieve her dyspnea and tachypnea due to abdominal distention. Cytological evaluation reported no abnormal cells. Based on above-mentioned evidence, the patient was suspicious of advanced gastrointestinal adenocarcinoma. After discussing the patient's condition with her family members and herself, the patient was administered with antibiotics and dexamethasone for fetal lung maturity, and meanwhile, supportive treatment was also provided. At 28 weeks and 4 days of gestation, the general condition of the patient became worse, cesarean section was performed on May 4, and the birth weight of the baby was 1000 g. The Apgar score was 5 and 6 at first and fifth minutes, respectively. The infant was admitted to the neonatal intensive care unit for prematurity.

At the same time, an abdominal exploration showed that the omentum was like biscuits (Fig. 2). There were extensive and firm intestinal adhesions, and many tumor lesions were found on the surface of greater curvature of stomach, spleen, intestine, peritoneum, ascending colon, and descending colon. There was no obvious lesion in liver, gallbladder, and pancreas. The surfaces of the uterus, fallopian tube, and both ovaries were normal at view. Gastrointestinal surgeon was invited during operation, and palliative gastrectomy was not performed because of extensive metastases.

Biopsy was conducted, and gastric tube was kept for gastrointestinal decompression. Pathological report showed poorly differentiated tumor with the signet ring cell component (Fig. 3). Immunohistochemical staining showed following findings: CK 7(+), CK 20(−), CK 5/6(+), Cdx-2(+), Villin(+), WT1(−), D2–40(−), CA125(−), and CA19–9(+). A chest tube drainage was established to relieve her dyspnea because more and more pleural effusion was found 4 days after cesarean section. Then the patient was transferred to the Oncology Department for chemotherapy. However, she suffered from intestinal obstruction without any anus exhaust and defecation, and palliative-supportive treatment was given. The patient's condition continuously deteriorated, and she died 30 days after cesarean on June 3. This study was approved by the Ethics Committee of Soochow University. The patient's husband agreed to authorize us to share the figures and the experiences during the treatment procedure in our department. Informed consent was obtained.

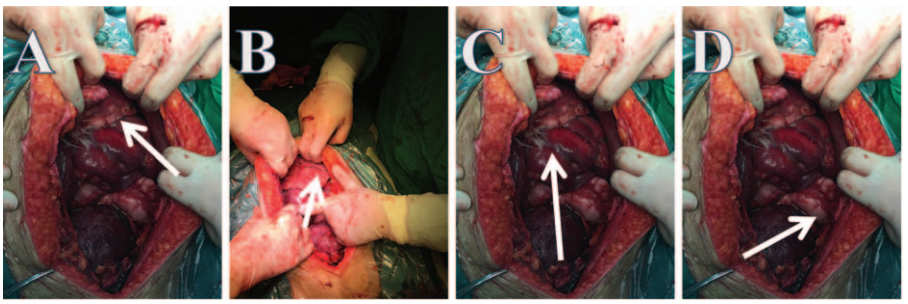

Figure 2. Abdominal exploration during operation. (A) lesion from greater curvature; (B) cake-like thickening omenta; (C) extensive intestinal adhesion; (D) lesion from intestines.

2.1. Symptoms and diagnosis

The most common symptoms of gastrointestinal cancer include epigastric pain, nausea and/or vomiting, nonspecific dyspepsia, dysphagia, anorexia, weight loss, and melena.[7] Except for weight loss and melena, all of these symptoms are common during pregnancy and will not draw any attention to both doctors and patients. Some of the patients have no obvious signs and symptoms. The initial diagnosis of gastric carcinoma is often delayed because up to 80% of patients are asymptomatic during the early stages of gastric cancer.[8] Nausea and vomiting are encountered in 75% of pregnancies, and the morning sickness of pregnancy usually occurs during the morning, but may continue during the day. The onset of nausea and vomiting usually occurs at the sixth week of gestation and may last up to 16 to 20 weeks. If the nausea and vomiting arising from hyperemesis generally continue to the 20th week of gestation, the clinicians must pay attention to symptoms. Hersh et al[9] have reported a case of hyperemesis gravidarum due to gastric cancer masquerading as preeclampsia. Distant metastatic features, including abdominal distention due to ascites, a palpable mass, and jaundice, are identified in some patients.[7] Although the patient had a 20-day history of abdominal distension, she did not tell the clinician her situation when she visited the doctor for 75-g OGTT 2 weeks ago. There are some rare symptoms, such as low back pain and bilateral erythematous breast hypertrophy, mimicking primary inflammatory breast carcinoma reported by Mandato et al,[10] Sister Mary Joseph's nodule reported by Ioannidis, and pericardial tamponade reported by Bacic et al.[11,12]

If gastrointestinal cancer in pregnant women is suspected, endoscopy is recommended for biopsy and pathological examination. However, CT is sometimes refused because the patients are worried about the radiation-induced damage, especially in the first trimester. Magnetic resonance imaging is considered relatively safe, because it avoids exposure of the mother and fetus to ionizing radiation and often does not require intravenous contrast material during pregnancy.

2.2. Treatment

The management of pregnancy-associated gastrointestinal cancer is dependent on the gestational age, and also the stage of the gastric cancer. At the same time, the patient's desire for a child and belief in the local district are also important factors in choosing the optimal treatment. If the diagnosis of gastrointestinal cancer is defined and it is in the early stage, operation is an optimum treatment. Nonobstetric surgical procedures during pregnancy should not be delayed if this will affect maternal health and outcome. The American College of Obstetrics and Gynecology recommends that a pregnant woman should never be denied indicated surgery, regardless of trimester.[13] If an operable gastric cancer is diagnosed before 22 weeks of gestation, surgery is recommended after termination of the pregnancy by induced abortion; at 22 to 27 weeks of gestation, induced premature delivery or careful monitoring is recommended, followed by surgery; at 28 weeks of gestation and beyond, surgery can be performed after delivery.[1] There are 2 operational methods, including open gastrectomy and laparoscopic approach.[14] Laparoscopic approach can reduce postoperative pain killer use and manipulation of the uterus during surgery, but it is difficult because of the enlarged uterus, and it has another potential risk, such as carbon dioxide absorption. Traditional open gastrectomy causes greater trauma and requires extended operation time. Although evidence from randomized controlled trials is missing, anesthesia during pregnancy has been

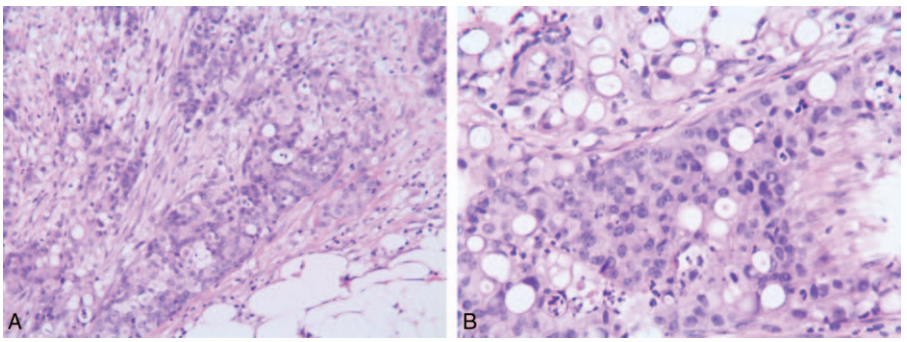

Figure 3. Pathological report showed poorly differentiated tumor with the signet ring cell component. (A) hematoxylin-eosin ×200; (B) hematoxylin-eosin ×400.

well-documented as safe for most open or minimally invasive operative procedures.[8,15]

In inoperable cases, chemotherapy is the first choice. Chemotherapeutic agents used in cancer treatment may cross the placenta and adversely affect embryogenesis by impairing cell division. Exposure to such medication after the first trimester of pregnancy has not been linked to increased risk of abnormality, but it is associated with increased risk of stillbirth, intrauterine growth restriction, and fetal toxicities.[16–18] During the first trimester, there are approximately 10% to 20% of infants with major malformations when exposed to cytotoxic agents. This might be attributed to the fact that the fetus is especially vulnerable when exposed during organogenesis, especially in 2 to 8 weeks after conception.[19] Exposure to chemotherapy during the second and third trimesters increases the risk of low birth weight because of delivery at lower gestational age and intrauterine growth restriction. Before chemotherapy treatment, careful counseling about the safety of several chemotherapeutic agents during gestation should be given to the patient, the patient's desire should be respected, and informed content should be obtained. The commonly used chemotherapy regime includes OLFOX (5-fluorouracil, oxaliplatin, and leucovorin) and FOLFIRI (5-fluorouracil, irinotecan, and folinic acid).[20] Another management includes targeted therapy, angiogenesis inhibitors, and epidermal growth factor receptor inhibitors. Because pregnancy-associated gastrointestinal cancer is rare, the experience is limited, leading to the poor long-term treatment effects and outcomes.

Except for operation and chemotherapy, radiotherapy is another treatment for gastrointestinal cancer. However, radiation exposure during pregnancy, particularly during organogenesis, is contraindicated, because it is associated with embryonic or fetal death, malformation, and growth retardation.[21] Therefore, radiotherapy is generally abandoned during pregnancy.

2.3. Prognosis

A recent study has shown that most pregnancy-associated gastric cancer was diagnosed at advanced stage, consequently resulting in a poorer prognosis compared with age-matched control groups.[22] The reasons could be attributed to aspects as follows. First, diagnosis is delayed, because it is difficult to identify whether a common symptom is induced by pregnancy or triggered by gastric cancer. In addition, noninvasive test, such as tumor marker, is not specific, whereas invasive examinations, including endoscopy and CT, are often refused due to potential damage to the fetus. As a result, most pregnancy-associated cancers are detected at an advanced stage or inoperable state. Second, the treatment is usually conflicting, because the safety of the fetus and the treatment of the mother have to be both considered. Hormonal changes during pregnancy can adversely affect gastric cancer.[14] The management of choice is associated with survival rate. It has been reported that the survival time of patients who underwent gastrectomy is 32.5 months (interquartile range [IQR] 21.8–76.0 months) compared with 6.2 months (IQR 1.0–7.0 months) for those who received palliative chemotherapy, and 2.1 months (IQR 1.0–13.5 months) for those who were given best supportive care only.[7] Our patient missed the optimal opportunity for the best possible surgical outcome. After cesarean section, she suffered from bowel obstruction. Although palliative-supportive care was provided, the patient died 30 days after cesarean section.

3. Discussion

Symptoms of gastrointestinal carcinoma are always neglected during pregnancy. One reason is that symptoms, such as nausea, vomiting, or abdominal discomfort, are generally overlooked during pregnancy, and the other reason is that the initial symptoms are nonspecific to cancer. Surgery is an optimum option if an early diagnosis is achieved. However, most cases are detected at an advanced stage, leading to limited choice of treatment. Mortality rate of gastrointestinal carcinoma remains high, especially for patients younger than 30 years, because hormonal stimulation and pregnancy in young women may accelerate the growth of gastric cancer. Pregnancy is characterized by specific biological and hormonal changes that can adversely affect gastric cancer.[23,24] For example, immunosuppression, elevated estrogen, and increased blood circulation during pregnancy render the mother susceptible to the rapid growth of tumors.[25] Our patient was just 29 years old, and she died quickly after diagnosis.

4. Conclusions

Taken together, both physicians and patients should not neglect the possibility of gastrointestinal cancer during pregnancy. Endoscopic examination is recommended if the patient is highly suspicious. A multidisciplinary team consisting of a gastrointestinal surgeon, oncologist, obstetrician, and neonatologist are important in deciding the optimal treatment. At the same time, maternal desires should be also taken into consideration. It is flexible to deal with gastrointestinal cancer during pregnancy depending on gestational age and the stage of the gastric cancer. Laparoscopic gastrectomy or open gastrectomy followed by chemotherapy might be a safe option for pregnancy-associated gastric cancer, although the long-term effects of this regimen remain largely unexplored.

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