

Gastric cancer in pregnancy: A case report

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Abstract. Gastric cancer during pregnancy is uncommon but associated with a high maternal mortality rate. Symptoms are often non-specific, leading to delayed diagnosis due to pregnancy-related limitations in diagnostic approaches. The present report describes the case of a 35-year-old pregnant patient diagnosed with advanced gastric cancer. Although supportive therapies were administered, the condition of the patient deteriorated and they ultimately passed away shortly thereafter. The report highlights how early detection is vital for improving outcomes, underscoring the importance of prompt evaluation of maternal symptoms and targeted diagnostic examinations. Moreover, treatment strategies should be tailored according to the cancer stage and the developmental stage of the fetus. Notably, metastatic sites of gastric cancer during pregnancy can include the placenta, ovaries, lungs, bones and breasts, with fetal metastasis posing a notable clinical concern.

Introduction

Gastric cancer is one of the most common cancers, with specific geographical, ethnic and socioeconomic differences in incidence. These disparities are associated with key risk factors: High-incidence regions like Eastern Asia correlate with prevalent *Helicobacter pylori* infection and high-salt dietary patterns; ethnically, certain populations exhibit genetic susceptibility to gastric mucosal damage; socioeconomically, low-status groups face elevated risk due to limited access to screening and higher exposure to risk factors such as smoking and alcohol consumption (1). A total of >70% of gastric cancer cases occur in developing countries and most patients come from Eastern Asia (1). Furthermore, the age-standardized

incidence rate of gastric cancer is 13.0 per 100,000 in male and 6.1 per 100,000 in female patients (2).

Pregnancy-associated gastric cancer is defined as a diagnosis of gastric cancer during pregnancy or ≤ 1 year after delivery, and it is estimated to complicate 0.026-0.1% of all pregnancies (3). Gastric cancer detected during pregnancy is usually diagnosed in advanced stages with a poor maternal and fetal prognosis (4). Most cases of pregnancy-associated gastric cancer are diagnosed at an advanced stage as special gastrointestinal symptoms are generally overlooked during pregnancy, and there are several limitations and contraindications for using diagnostic tools during pregnancy. Current treatment adopts a multidisciplinary approach balancing maternal and fetal interests (5). Surgical resection is the primary curative option, though resectability is limited by late diagnosis. Chemotherapy is considered for advanced cases in the second/third trimesters (agents like 5-fluorouracil), while radiotherapy is avoided due to teratogenicity (3). Survival rates in cases of gastrointestinal cancer are strictly associated with the early diagnosis. The maternal prognosis is poor, with 1- and 2-year survival rates of 18.0 and 15.1%, respectively (6).

The present report describes a case of a 35-year-old female patient, who was diagnosed with an advanced gastrointestinal cancer. At the time of admission, the patient was 18 weeks pregnant. The patient died 1 month after onset of the disease.

Case report

A 35-year-old female patient (gravida 2, para 1) presented for *in vitro* fertilization and embryo transfer due to tubal obstruction. During routine prenatal checkups in May 2019 at the Affiliated Heping Hospital of Changzhi Medical College (Shanxi, China) the patient reported lower abdominal fullness, without cervical shortening, vaginal bleeding, fluid discharge or uterine contractions noted 1 month prior to admission. The patient was initially diagnosed with threatened abortion and treated with 10 mg dydrogesterone twice daily; however, the medication was discontinued after 2 weeks due to a lack of clinical improvement.

A total of 2 weeks before admission to the Affiliated Heping Hospital of Changzhi Medical College, the patient developed progressive nausea, abdominal distension and anorexia. Up to this time, the patient had undergone three ultrasound examinations: i) A scan at 6 weeks of gestation confirming an intrauterine pregnancy, with clear visualization of the fetal heartbeat and fetal pole; ii) a nuchal translucency

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ultrasound; and iii) an ultrasound performed due to lower abdominal bloating (original images not available). None of these examinations revealed the presence of ascites. However, 1 week before admission, the abdominal distension notably worsened, leading to an ultrasound that revealed substantial ascites (data not shown). Paracentesis was performed, draining 1,000 ml ascitic fluid for analysis. Despite this intervention, the abdominal pain and distension worsened 5 days later, prompting transfer to Peking University First Hospital, Beijing, China.

The local pathology report of the ascitic fluid showed a predominance of mesothelial cells, along with scattered lymphocytes, neutrophils and atypical cells (data not shown). Moreover, non-enhanced pelvic MRI at the local hospital revealed nodular thickening of the peritoneum, raising concerns about tumor metastasis or peritoneal tuberculosis, along with notable ascites showing fluid stratification (Fig. 1A and B). Due to limitations in diagnostic and treatment options at the local facility, the patient was referred to Peking University First Hospital for further management.

Since the onset of symptoms, the patient experienced anorexia, mental fatigue, oliguria, constipation and an 8 kg weight loss. The medical history of the patient included severe anemia in 2003, which was diagnosed as M3 leukemia following a bone marrow aspiration. After undergoing chemotherapy, the patient remained in remission without recurrence. The patient denied any history of tuberculosis or other malignancy. In June 2003, the patient delivered a healthy female infant via spontaneous vaginal delivery. The patient and family had not undergone any screening or examination for *Helicobacter pylori* (*H. pylori*) previously, and the family history was negative for genetic disorders, cancers or infectious diseases.

On physical examination, the patient presented with abdominal distension, dullness on percussion, an abdominal circumference of 104 cm, an indistinct uterine fundus and a fetal heart rate of 150 bpm. Laboratory investigations revealed a normal hemoglobin level (136 g/l) (ref. 115-150 g/l) but notable ketosis (+4) (ref. negative) on urinalysis. Biochemical tests showed an albumin level of 35.5 g/l (ref. 35-50 g/l). Notably, tumor markers were elevated, including α -fetoprotein at 36.74 ng/ml (ref. ≤ 10 ng/ml), cancer antigen 15-3 at 17.49 U/ml (ref. ≤ 30 U/ml), cancer antigen 72-4 at 14.64 U/ml (ref. ≤ 6.9 U/ml), cancer antigen 19-9 at $>1,000$ U/ml (ref. ≤ 37 U/ml), cancer antigen 125 at 1,040 U/ml (ref. ≤ 35 U/ml), carcinoembryonic antigen at 180.30 ng/ml (ref. ≤ 5 ng/ml) and neuron-specific enolase at 11.51 ng/ml (ref. ≤ 16.3 ng/ml). Tests for tuberculosis were negative. Obstetric ultrasound confirmed an intrauterine pregnancy with a viable fetus and showed a large amount of free fluid in the pelvic and abdominal cavities, ~ 90 mm in depth and with no abnormalities in the bilateral adnexa. Abdominal ultrasound further showed thickened greater omentum, notable ascites with a maximum depth of ~ 93 mm (Fig. 1C and D).

After abdominal paracentesis and tube placement, the patient experienced an improvement in symptoms, and the aspirated ascitic fluid was sent for further analysis. Supportive therapies, including intravenous nutrition, fluid replenishment and ketone reduction, were also initiated. During ultrasound-guided paracentesis, a gastric mass was noted,

raising suspicion for gastric cancer. Yellow ascitic fluid was drained. Subsequent abdominal CT with contrast enhancement revealed a mass at the greater curvature of the gastro-pyloric junction, highly suspicious for malignancy, with alterations in the peritoneum and omentum, suggesting metastatic seeding (Fig. 2A and B).

The patient was informed of the findings, and an esophagogastroduodenoscopy was performed. The examination revealed a 5x4 cm raised mass near the greater curvature of the lower gastric body, adjacent to the gastro-pyloric junction, with two ulcers in the center, surrounded by irregular, nodular mucosa (Fig. 2C). Biopsy samples were taken from the ulcer edges for pathological examination, with gastric cancer highly suspected. Biopsy and ascitic fluid samples were fixed in 10% neutral-buffered formalin at room temperature for 12-24 h. Paraffin-embedded sections were cut at 4 μ m. Routine H&E staining was performed at RT (hematoxylin 5 min, eosin 2 min). Cytospin smears of ascitic fluid were prepared by centrifugation at 1,500 x g for 10 min at room temperature, then fixed in 95% ethanol for 10 min and stained with H&E under the same as aforementioned. All slides were examined with an Olympus BX43 light microscope.

Pathological results from the gastroscopic biopsy indicated poorly differentiated gastric carcinoma, partially composed of signet ring cell carcinoma, classified as Lauren's mixed type. Concurrently, ascitic fluid cytology revealed proliferated mesothelial cells, small lymphocytes, macrophages and scattered atypical cells with irregular nuclei and mitotic figures, suggesting a possible tumor origin (Fig. 2D-F).

Given the confirmed diagnosis of gastric cancer, the patient and family were fully informed of the condition. Termination of pregnancy and specialized treatment were recommended; however, after discussion, the family of the patient opted for discharge and palliative care at a local hospital. The patient passed away 3 days after discharge as confirmed by telephone follow-up with the family. Fig. 3 presents a timeline of the medical journey of the patient.

Discussion

The incidence of gastric cancer during pregnancy is low (0.026-0.100% of all pregnancies); however, the maternal prognosis is poor, with reported 1- and 2-year survival rates of 18.3 and 15.1%, respectively (3). Due to the non-specificity of symptoms and the limitations of diagnostic methods during pregnancy, most patients are diagnosed at an advanced stage. However, early detection is crucial for prognosis, as poor outcomes are common when diagnosis is delayed. Therefore, prompt attention to maternal symptoms and targeted examinations are crucial for early diagnosis (7).

The symptoms of gastric cancer during pregnancy are atypical, which markedly interferes with clinical diagnosis and treatment. Symptoms such as nausea, vomiting, anorexia and weight loss in early pregnancy are often attributed to pregnancy itself and treated symptomatically. However, nausea and vomiting occurring after 9 weeks of gestation warrant exclusion of other causes, such as common hepatitis, pancreatitis or acute abdominal conditions. Most of these can be diagnosed through routine laboratory tests and ultrasonography (8). As early diagnosis is beneficial for improving the prognosis of the

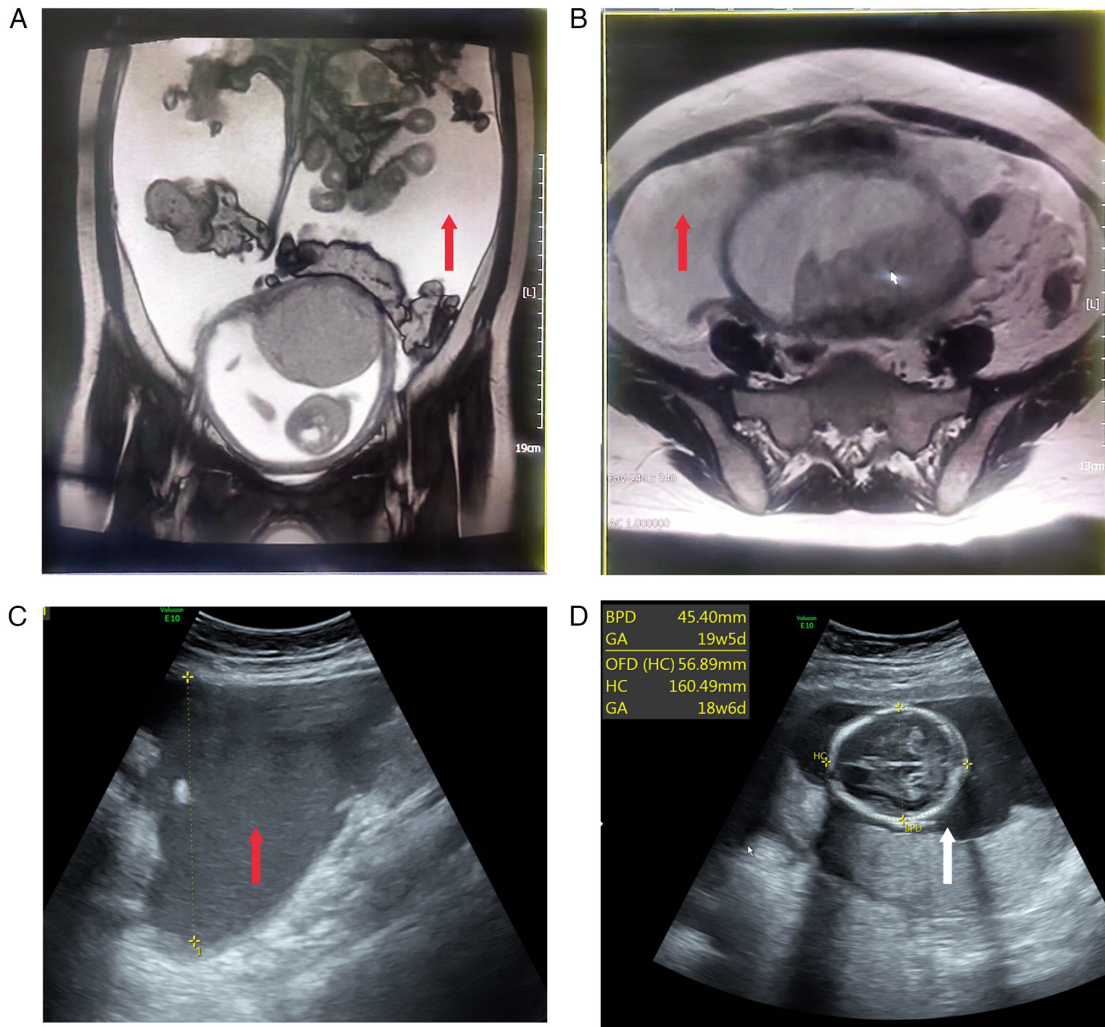


Figure 1. Pelvic magnetic resonance imaging and ultrasonography showing maternal ascites and the intrauterine fetus. (A) Coronal view and (B) transverse section of pelvic MRI, with ascites indicated by the red arrow. (C) Abdominal ultrasound, with ascites indicated by the red arrow. (D) Obstetric ultrasound, with the fetus indicated by the white arrow.

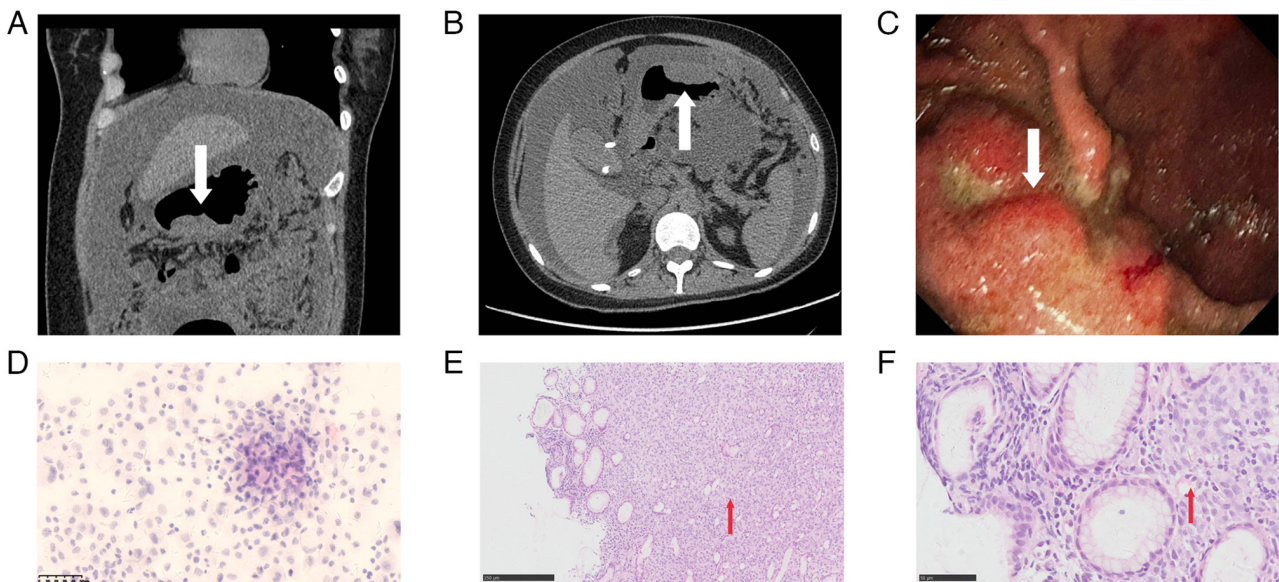


Figure 2. Abdominal computed tomography, endoscopy, cytology and histology of gastric signet-ring cell carcinoma. (A) Coronal view and (B) transverse section of abdominal CT, with the tumor indicated by the white arrow. (C) Endoscopic view of the gastric lesion, with the tumor indicated by the white arrow. (D) Cytological smear of ascitic fluid (magnification, x400). (E) Microscopic examination of the biopsy (magnification, x100). (F) Microscopic examination of the biopsy, revealing gastric primary malignant cells with the signet ring cell indicated by the red arrow (magnification, x400).

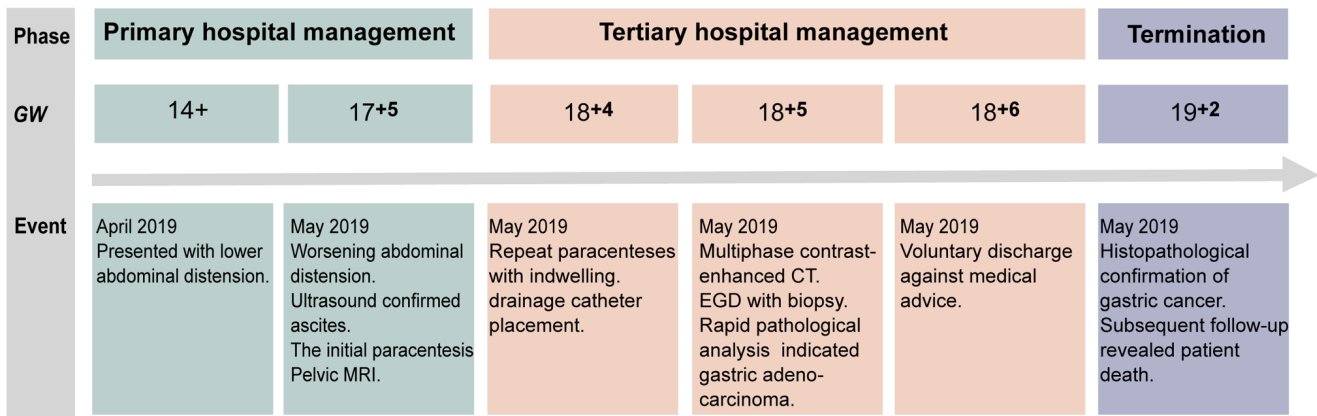


Figure 3. Timeline of the medical journey of the patient. GW, gestation week; EGD, esophagogastroduodenoscopy.

patient, attention should be paid to the onset and duration of gastrointestinal symptoms (7). Typically, pregnancy-related nausea and vomiting markedly improve after 20 weeks of gestation (9,10). Therefore, women with persistent gastrointestinal symptoms should undergo active examination to rule out gastrointestinal diseases. Ultimately, nausea and vomiting during pregnancy are diagnoses of exclusion.

Imaging for malignant tumors in the digestive system primarily relies on gastroscopy and CT (1); however, due to safety considerations during pregnancy and the extremely low incidence of malignant tumors in the digestive system, these two methods are rarely employed, often leading to delays in diagnosis and treatment and missed opportunities for optimal therapy (11). Currently, gastric window ultrasonography and gastroscopy are the primary diagnostic methods available for pregnant women. Compared with gastroscopy, ultrasonography offers advantages such as being non-invasive, cost-effective, highly repeatable and capable of clearly displaying intra-gastric cavities, gastric walls and perigastric lesions with the aid of gastrointestinal contrast agents. It can also observe the depth of gastric cancer infiltration, making it more acceptable to patients (12). Nevertheless, its diagnostic significance for lesions at the gastric fundus, micro-gastric cancers and small gastric cancers warrants further investigation (13).

Concerns about the safety of gastroscopy, including the risks of hypoxemia or hypotension during the procedure that may lead to fetal death, miscarriage or preterm birth, as well as the potential impact of medications on the fetus, contribute to the low utilization rate of gastroscopy in pregnant women. Nevertheless, gastroscopy holds unique significance in the diagnosis of gastric cancer (12). A Swedish nationwide cohort study reported that women undergoing any form of endoscopy during pregnancy faced an increased risk of preterm birth and delivery of small for gestational age infants (14). However, when focusing on women without inflammatory bowel disease, celiac disease or liver disease, this association disappeared, indicating that under certain conditions, endoscopy may be safe and feasible during pregnancy (14). In 2012, the American Society for Gastrointestinal Endoscopy released guidelines for the use of gastrointestinal endoscopy in pregnant and lactating women, providing guidance for the safe use of gastrointestinal endoscopy in pregnant women. Strict adherence to endoscopy

indications during pregnancy includes: Obvious or persistent gastrointestinal bleeding; severe or refractory nausea, vomiting or abdominal pain; dysphagia or odynophagia; strong suspicion of colonic masses; severe diarrhea with negative test results; gallstone pancreatitis, gallstone cholangiopathy or cholangitis; and bile duct or pancreatic duct injury. General principles include: Strictly adhering to indications; scheduling endoscopy during the second trimester if not an emergency; using the lowest dose of sedative drugs; preferring Class A or B drugs; minimizing procedure duration; lying on the left side to avoid supine hypotensive syndrome; obstetric consultation for fetal heart rate monitoring before and after anesthesia; and avoiding use in certain obstetric complications such as placental abruption, rapid labor, rupture of membranes or eclampsia (12). CT scans are not absolutely contraindicated during pregnancy. According to the Diagnostic Imaging Guidelines in Pregnancy and Lactation (no. 723) issued by the American College of Obstetricians and Gynecologists (15), the radiation dose for pelvic CT is 50 mGy; however, with the help of low-exposure techniques, the dose can be reduced to 2.5 mGy to achieve diagnostic efficacy, which is far below the threshold for teratogenic radiation dose before 25 weeks of gestation.

The large-scale case series reviews on gastric cancer during pregnancy include a study of 137 cases of pregnancy-associated gastric cancer in Japan published in 2009 (16) and a study involving 65 Chinese patients published in 2015 (17). These studies reported that approximately one-third of the cases were detected postnatally, and >90% of the cases were advanced stage gastric cancer. The 1- and 2-year survival rates for the tumors were both <20%. Moreover, after adjusting for age, sex and cancer stage, a retrospective study in Korea reported that the median survival time during pregnancy was ~7 months, which was lower than the 15-month median survival time observed in non-pregnant women; however, this difference was not statistically significant. The study also reported that the time to diagnosis during pregnancy was markedly longer than that in non-pregnant individuals (18). Therefore, persistent gastrointestinal symptoms in pregnant women require thorough evaluation to facilitate early diagnosis.

Pregnancy-associated gastric cancer presents two conflicting issues: On the one hand, it is ideal to initiate surgical intervention as early as possible to increase the

chances of maternal recovery from gastric cancer; but on the other hand, there is a viewpoint that the pregnancy should be continued as long as safely possible to ensure fetal safety. Treatment plans depend on the cancer stage and fetal development at diagnosis. In line with current practices in China, it is generally agreed that for pregnancies at ≥ 28 weeks, surgical intervention should follow cesarean or vaginal delivery (16). For pregnancies at < 28 weeks, decisions regarding whether to continue the pregnancy and proceed with surgery should be made after considering the cancer stage, specialized principles for managing gastrointestinal tumors and thorough communication with the patient (16).

The most common metastatic sites for gastric carcinoma include peritoneal surfaces, the liver, spleen, ovaries, lung and brain. Gastric cancer infrequently metastasizes to the bone (1). A literature search of English publications over the past 5 years identified the metastatic sites of gastric cancer during pregnancy as the placenta (19-21), ovaries (22-25), lungs (26), bones (27,28) and breasts (29). Moreover, a notable clinical concern associated with placental metastasis is fetal metastasis (20), which is not always obvious at birth; however, to date, no case reports of fetal metastasis have been documented, to the best of our knowledge. A total of one case of uterine metastasis during pregnancy has been reported (30).

The present case has certain limitations that require acknowledgment. Specifically, *H. pylori* status remained undetermined due to the discharge of the patient before diagnostic confirmation, precluding timely microbial evaluation. This gap is clinically significant given the well-documented role of *H. pylori* in gastric carcinogenesis. The World Health Organization International Agency for Research on Cancer classifies *H. pylori* as a Group I carcinogen, with cohort studies demonstrating its association with $\sim 89\%$ of non-cardia gastric carcinomas (31). Whilst pregnancy necessitates careful diagnostic modality selection, with ^{13}C -urea breath tests and serological assays as preferred safety considerations, the inability to ascertain infection status in the present case limits etiological interpretation. This underscores the need for protocols ensuring pre-discharge microbial testing in similar cases. Furthermore, the association between gestational gastric cancer and *H. pylori* infection remains poorly characterized, highlighting a critical research gap.

In the present case, ascitic cytology slides were prepared at an outside institution and could not be retrieved for in-house review. As a result, representative images of ascitic cytology and the corresponding ultrasound were unavailable, which may limit the completeness of our imaging and cytological documentation.

In conclusion, the present case report highlights the rarity and notable maternal mortality rate associated with gastric cancer diagnosed during pregnancy. The presented case exemplifies the difficulties in early detection due to non-specific symptoms and diagnostic constraints during pregnancy. Despite an extensive diagnostic workup, the condition of the patient deteriorated swiftly, underscoring the necessity for prompt assessment of maternal symptoms and focused diagnostic procedures. The present paper delineates the poor prognosis associated with pregnancy-associated gastric cancer, with most cases identified at an advanced stage. Additionally, the report emphasizes the critical importance of

addressing the unique challenges presented by the coexistence of cancer and pregnancy when strategizing treatment plans. The metastatic capacity of gastric cancer during pregnancy complicates clinical management further. Collectively, the present case underscores the imperative for increased awareness, timely diagnosis and personalized treatment approaches to enhance outcomes for both the mother and fetus in instances of pregnancy-associated gastric cancer.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JN and HY designed the study and analyzed patient data. YS and YG advised on patient treatment. JN, YG, YS and HY confirm the authenticity of all the raw data. All authors agree to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Peking University First Hospital Medical Science Research Ethics Committee (approval no. 164-002) and performed according to the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Patient consent for publication

Written informed consent was obtained from the family of the patient for publication of the present case report.

Competing interests

The authors declare that they have no competing interests.

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