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A rare maternal gastrointestinal stromal tumor found in the second trimester of pregnancy: A case report

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ABSTRACT

Gastrointestinal stromal tumors are rare, and in pregnancy they are extremely rare. We present a case of a maternal gastrointestinal stromal tumor found in the second trimester of pregnancy. A 29-year-old woman, gravida 1 para 0, complained of bloody vomiting at 14 weeks of gestation. She had no significant medical history. We performed plain computed tomography and upper gastrointestinal endoscopy. Precise examination revealed a large mass in the stomach and an exposed blood vessel on the surface. An exposed blood vessel can be harmful for mother and fetus as it might rupture during the pregnancy. We performed a distal gastrectomy at 16 weeks of gestation. Histology confirmed a localized gastrointestinal stromal tumor with a high risk of recurrence, and adjuvant imatinib was recommended. The patient elected to delay adjuvant imatinib until after delivery. The postoperative and antenatal course was favorable, and the patient was followed up by ultrasound every 2 months after the operation. After she gave birth at 40 weeks of gestation, she started adjuvant imatinib 400 mg/day. There was no evidence of recurrence 1 year after surgery. There are no guidelines for the management of gastrointestinal stromal tumors in pregnancy. Given the treatment challenges, we believe that pregnant patients should be managed by a multidisciplinary team with expertise in gastrointestinal tumors and fetal-maternal medicine.

1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract, with an estimated annual incidence of only 10 to 20 cases per million [1]. They present very rarely in pregnancy, and there are few reported cases in the literature. The management of pregnant patients presenting with GISTs poses a challenge to both general surgeons and obstetricians. We present a rare case of maternal GIST found in the second trimester of pregnancy.

2. Case Report

A 29-year-old woman, gravida 1 para 0, visited an internal medicine clinic complaining of bloody vomiting at 14 weeks of gestation. She had no significant medical history. Upper gastrointestinal endoscopy demonstrated a large irregular mass in the stomach, following which she was referred to hospital. Her hemoglobin level was 11.6 g/dL. Plain computed tomography of the chest and upper abdomen showed an irregular 6-cm mass restricted to the stomach (Fig. 1). There was no evidence of metastasis. Upper gastrointestinal endoscopy revealed that the detected stomach mass was on the greater curvature of the pyloric zone. A 1-cm ulcer was found at the top of the mass with exposed blood vessels at risk of rupture. An exposed blood vessel can be very harmful to the mother and fetus if it ruptures during the pregnancy.

After consultation with surgeons, gastroenterologists, and neonatologists, we performed an open distal gastrectomy under general anesthesia at 16 weeks of gestation. The pathological diagnosis was GIST. The resected stomach tumor was 60 mm, with mitosis noted in 15/50 high-power fields (HPF). There was no tumor rupture or vascular invasion. All resection margins were clear. The pathological findings of the tumor were consistent with typical pathological characteristics of GIST: CD34(+) and c-KIT(+). Some histological findings (size >5 cm, mitosis >5/50 HPF) indicated a high risk of recurrence. Adjuvant imatinib (a small-molecule tyrosine kinase inhibitor) is recommended for localized GISTs with a high risk of recurrence [1]. The patient opted to delay the initiation of adjuvant imatinib therapy until after delivery.

The postoperative and antenatal course was favorable, and the patient was followed up by ultrasound every two months after the operation. She gave birth by vaginal delivery at 40 weeks of gestation. The baby weighed 3446 g, which was appropriate for gestational age. Adjuvant imatinib 400 mg/day was started 7.5 months after the operation. Two weeks after she started taking imatinib, the patient experienced eyelid edema as an adverse reaction, but it troubled her little. There was no evidence of recurrence 1 year following the operation. The

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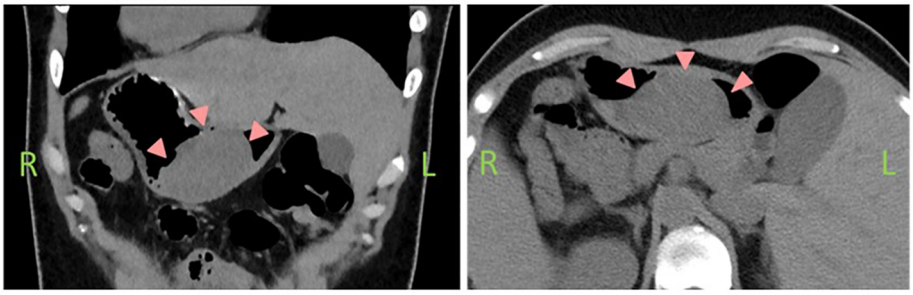

Fig. 1. Plain computed tomography scan of the chest and upper abdomen. An irregular 6-cm mass is seen in the stomach (arrows). There is no evidence of metastasis.

intention was for the patient to continue therapy for 3 years and to maintain long-term follow-up.

3. Discussion

In this case, GIST was diagnosed after the patient presented with bloody vomiting at 14 weeks of gestation. The tumor was resected successfully, and the patient delivered a healthy, full-term infant. There was no sign of recurrence one year after the resection, and the patient was under continuous follow-up while on imatinib therapy.

GIST is the most common mesenchymal tumor of the gastrointestinal (GI) tract, originating from interstitial cells of Cajal [2]. Most GISTs have active mutations in c-KIT (75–80%) or CD34 (80–85%) [1]. These tumors most commonly occur in patients over the age of 50 years, primarily in the stomach (60%) and jejunum and ileum (30%), and to a lesser degree in the duodenum (4–5%), rectum (4%), colon and appendix (1–2%), esophagus (<1%), and omentum/peritoneum (extra GI-GIST). Some patients present with abdominal pain, vomiting, GI bleeding, anemia, or fatigue. The tumors very rarely present during pregnancy.

We found ten reported cases of GIST in pregnancy (Table 1) [3–12]. Their average time at diagnosis was 18 weeks of gestation (13–28 weeks). The primary treatment for localized or resectable GIST was surgery, and the best chance for cure was complete surgical excision of the tumor with clear margins [1]. Tumor resection was performed in 3 out of the 10 cases. However, there is no guideline on the appropriate timing of the surgery in pregnant women with GISTs. A multidisciplinary approach is needed for improved maternal and fetal prognosis. In our case, the risk of tumor vessel rupture outweighed the risks to the fetus due to anesthesia and surgical invasion, and therefore we performed the surgery in the second trimester of pregnancy. For pregnant women with cancer, the optimal time for delivery is usually between 35 and 37 weeks of gestation [2]. Among the studies that we reviewed, there were reports of three patients who had received postpartum resection after scheduled cesarean sections performed at 35–36 weeks of gestation.

Prognosis is based on molecular biomarkers, tumor size, mitotic rate, location, rupture, resectability, and the presence of metastasis [3]. The Miettinen classification and modified Fletcher classification are generally used to evaluate the risk of GIST recurrence (Table 2) [1]. According to these classifications, our patient had a high risk of recurrence: a 50–60% chance of recurrence up to 10 years after the operation [1]. Kanda et al. reported that for high-risk GIST patients with macroscopically complete resections in Japan, the recurrence-free and overall survival rates were 94.7% and 96.8% at one year and 57.3% and 87.1% at three years, respectively [13]. Adjuvant imatinib therapy is generally recommended for patients with a high risk of recurrence [1,14]. In one randomized trial of patients who had complete resection of a primary GIST, the estimated 1-year recurrence-free survival after surgery was 98% in the imatinib group versus 83% in the placebo group (hazard

Table 1
Summary of reported cases of GIST during pregnancy.

Case	References	Maternal age	Gestational week at diagnosis	Tumor size	Tumor site	Metastatic disease	Treatment	Gestational week at delivery	Birth weight	Fetal outcome	Maternal outcome
1	Igras 2012[3]	42	20th	10 cm	Retro peritoneum	None	Surgery (pp)	36th e-CS	–	Healthy	NED
2	Gouzukara 2012[4]	21	15th	17 cm	Pelvis	None	Surgery (ip)	–	–	Unknown	Unknown
3	Stubbs 2011[5]	31	16th	12 cm	Lower abdomen	None	Surgery (pp) Imatinib (pp)	36th s-CS	2150 g	Healthy	Unknown
4	Scherjon 2009[6]	25	10th	10 cm	Uterus	Spleen	Surgery (ip) Imatinib (pp)	41st NVD	3990 g	Healthy	SD
5	Lanfazame 2006[7]	29	22nd	4 cm	Stomach	None	Surgery	–	–	Unknown	Unknown
6	Valente 1996[8]	32	28th	13 cm	Stomach	Peritoneum	Surgery (ip)	28th e-CS (fetal distress)	1100 g	Healthy	NED for 9 M
7	Goel 2013[9]	25	13th	16 cm	Abdomen	Liver Lung	Imatinib (Ip)	36th e-CS (fetal distress)	2000 g	Healthy	NED for 12 M
8	Charif 2014[10]	42	20th	23 cm	Epigastric	None	Surgery (pp) Imatinib (pp)	35th s-CS	–	Healthy	PR
9	Coveney 2011[11]	42	23rd	11 cm	Left adnexsa	None	Surgery (pp)	37th e-CS (preeclampsia)	–	Healthy	NED
10	Haloob 2013[12]	31	18th	10 cm	Epigastric	None	Surgery (pp) Imatinib (pp)	36th s-CS	2150 g	Healthy	Unknown
11	This case	29	14th	6 cm	Stomach	None	Surgery (ip) Imatinib (pp)	39th NVD	3446 g	Healthy	NED for 8 M

ip: in pregnancy, pp.: postpartum, NED: no evidence of disease, PR: partial response, SD: stable disease, e-CS: emergency cesarean section, s-CS: selective cesarean section, NVD: normal vaginal delivery.

Table 2
Miettinen classification to evaluate the risk of recurrence.
Adapted from Miettinen and Lasota, Seminars in Diagnostic Pathology 2006: 23(2) 70–83.

Mitotic rate (50HPF)	Tumor size (cm)	Stomach	Duodenum	Jejunum or ileum	Rectum
≦5	≦2	None 0%	None 0%	None 0%	None 0%
	> 2 ≦5	Very low 1.9%	Low 4.3%	Low 8.3%	Low 8.5%
	> 5 ≦10	Low 3.6%	Moderate 24%	Insufficient data	Insufficient data
	> 10	Moderate 10%	High 52%	High 34%	High 57%
> 5	≦2	None 0%	High	None	High 54%
	> 2 ≦5	Moderate 16%	High 73%	High 50%	High 52%
	> 5 ≦10	High 56%	High 85%	Insufficient data	Insufficient data
	> 10	High 86%	High 90%	High 86%	High 71%

HPF: high-power fields.

ratio 0.35, 95% CI 0.22–0.53; $p < 0.0001$) [14]. Another trial reported that the most frequent imatinib-related adverse reaction of any grade was eyelid edema (48.4%), followed by neutropenia (40.6%), leukopenia (39.1%), nausea (39.1%), rash (37.5%), and peripheral edema (37.5%), most of which were mild and manageable [13].

The safety of imatinib administration during pregnancy is yet to be established because of limited data. The report by Pye et al. concerning imatinib administration during the gestational period in 180 pregnant women revealed that 50% delivered normal infants, whereas the rest of the pregnancies ended either in elective termination or in spontaneous abortion. Some fetal abnormalities were also documented [15]. The data for imatinib administration during breastfeeding are equally limited. Although a few breastfed infants experienced no adverse effects during maternal use of imatinib, no long-term follow-up data are available. Some authors recommend that breastfeeding be discontinued during imatinib therapy. We think that it is an important piece of information and should be offered to patients to help them make better individualized informed decisions.

GIST in pregnancy is extremely rare. Further studies are needed to develop guidelines for the management of GISTs during pregnancy. Given the treatment challenges, pregnant patients should be managed by a multidisciplinary team with expertise in GI tumors and fetal-maternal medicine.

Contributors

Naoko Tanaka contributed to conception and design and drafting of the manuscript.

Shoko Tamada contributed to critical revision of the manuscript for important intellectual content.

Naoko Ueno contributed to critical revision of the manuscript for important intellectual content.

Makoto Ishida contributed to critical revision of the manuscript for important intellectual content.

Junichi Kodama contributed to critical revision of the manuscript for important intellectual content and supervision.

Tetsushi Kubota contributed to critical revision of the manuscript for important intellectual content.

All authors approved the final article.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

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