Clinics in Surgery

Case Report
Published: 19 Sep, 2016

Treatment Strategy of Metastatic Gastrointestinal Stromal Tumor in Pregnancy

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Abstract

Treatment for metastatic gastrointestinal stromal tumor (GIST) is a challenge, particularly in pregnant female because of the absence of safety data concerning imatinib use during pregnancy. We report a case of metastatic GIST surgically resected during pregnancy with a favorable outcome. A treatment strategy for GIST in pregnant patients should be carefully discussed by a multidisciplinary team, based on the phase of pregnancy, tumor resectability, and patient's opinion in abortion. Patient counseling and education regarding the paucity of safety data cannot be overemphasized.

Keywords: Gastrointestinal stromal tumor; Pregnancy; Metastasis

Introduction

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract. The diagnostic criteria for GIST were first defined in 1983 with the discovery of tyrosine kinase receptor (CD117) mutations. Since then, the number of reported cases has been increasing [1,2]. GIST treatment was revolutionized by the development of molecular-targeted therapy using tyrosine kinase inhibitors, such as imatinib, which significantly improved the 5-year survival rate [3]. Although the incidence of GIST is increasing, it remains rare in women of child-bearing age. There are very few cases of GIST diagnosed or managed during pregnancy; a review of the literature yielded only five such case reports [3-7]. The optimal treatment strategy for metastatic GIST diagnosed during pregnancy is unknown and the absence of safety data concerning imatinib use during pregnancy further confounds the treatment decision [8]. Here, we report a case of metastatic GIST surgically resected during pregnancy with a favorable outcome.

Case Presentation

A healthy 20-year-old primigravid at 16 weeks presented to the hospital with severe abdominal pain. Ultrasonography revealed a 15.8 cm mass in the mid-epigastric area. Laboratory data were unremarkable with normal amylase and lipase levels. An MRI was not performed because the patient suffered from claustrophobia. Anon-contrast computed tomography (CT) scan revealed a 15 × 13 × 11cm complex heterogeneous mass which appeared to originate from the body of the pancreas and to protrude into the gastric wall (Figure 1). CT also revealed a 3 cm hypodense lesion on the left side of the liver concerning for metastasis, a moderate volume of ascites, and splenomegaly. Further evaluation with endoscopic retrograde cholangiopancreatography and endoscopic ultrasonography revealed the following: extrinsic compression of the gastric wall from the tumor; a large solid and cystic lesion with septations and well-defined margins; and no clear involvement of the gastric wall. Fine needle aspiration (FNA) was performed on the solid component of the tumor. Seven-hundred cc of thin, reddish-brown, fluid was aspirated from the cystic component. Cytological analyses of the aspirate showed no tumor cells or mucinous material. The tumor markers carcino-embryonic antigen and CA19-9 was not elevated. Pathology indicated a spindle cell tumor consistent with GIST.

Treatment and Follow-up

The following treatment options and risks were discussed with the patient: neoadjuvant imatinib therapy followed by resection in the late third trimester or immediate resection with adjuvant imatinib following delivery. The patient opted for surgery. She underwent surgical resection at 18 weeks gestation for a large tumor firmly adherent to both the distal portion of the pancreas and

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Received Date: *10 Aug 2016*
Accepted Date: *02 Sep 2016*
Published Date: *19 Sep 2016*

Citation:
Ikoma N, Harvin JA, Buryanek J, Lesslie DP. Treatment Strategy of Metastatic Gastrointestinal Stromal Tumor in Pregnancy. Clin Surg. 2016; 1: 1125.

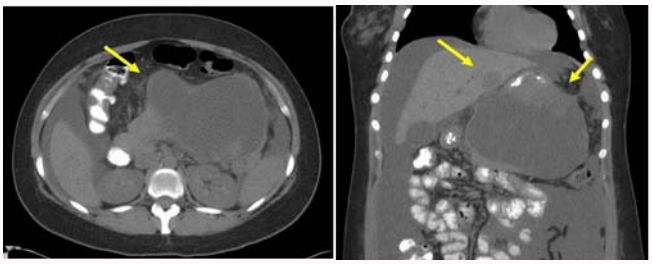

Figure 1: CT scan showed a 15 × 13 × 11 cm complex heterogeneous mass, apparently originating from the body of the pancreas and protruding into the gastric wall, and metastatic lesion in the liver.

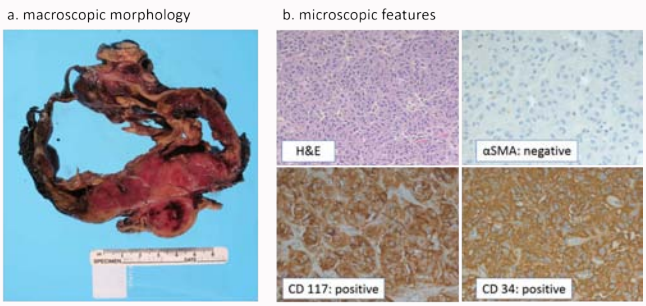

Figure 2: a. The gross morphology of the resection of the main tumor showed a mass involving primarily the distal portion of the stomach. The mass had been previously cystic, but had been previously ruptured. b. The H&E section showed the features of the epithelioid variant of GIST. Immunostains showed dual positivity for CD117 and CD34. Alpha SMA was negative in the tumor cells. Mitotic figures were counted as less than 5 per 50 high power fields. However, due to its large size (16.0 cm), it was placed in the high-risk category.

the posterior portion of the stomach. Upon inspection, the tumor appeared to originate from the stomach near the esophagogastric junction. She underwent en-bloc resection of the tumor by total gastrectomy, distal pancreatectomy, splenectomy, and a Roux-en-Y esophagojejunostomy. Intraoperative FNA of the liver lesion confirmed metastatic GIST; therefore, a lateral segment partial hepatectomy was performed leaving a clear margin. Histological analyses revealed: a 16 cm, low-grade GIST with a mitotic count < 5/50 high-power field (HPF); mixed spindle and epithelioid cell types; lymphovascular invasion was detected with 5 out of 9 lymph nodes being positive for metastasis. Immunohistochemistry revealed positivity for CD34 and CD117, but no alpha smooth muscle act in (SMA) (Figure 2). Mitotic figures were counted as less than 5 per 50 high power fields. She was diagnosed with pT4N1M1 stage IV GIST, and due to its large size (16.0 cm), it was placed in the high-risk category. Her postoperative course was favorable except for peri-pancreatic fluid collection that required percutaneous drain placement. The course of the pregnancy was favorable, and she delivered a healthy infant at 37 weeks gestation. Follow-up CT scans were negative for disease recurrence, and she was started on imatinib 400 mg/day for6 weeks after the delivery. At three years after the surgery she is doing well with no sign of recurrence.

Discussion

Since randomized trials are difficult to perform in pregnant women because of ethical considerations, consolidation of isolated case reports of rarely occurring diseases are important. A literature reviews uncovered 5 previous case reports of GIST in pregnancy (Table 1). Three patients underwent a simple resection without adjuvant therapy. One patient waited until 36 weeks and then underwent simultaneous resection of the tumor and a cesarean section. One patient was found to be pregnant during treatment with imatinib for metastatic GIST, which was continued throughout the pregnancy. None of these case reports indicated a complication of the pregnancy.

Current consensus recommends adjuvant imatinib use for high-risk tumors after complete resection of tumors, which has been shown to improve disease-free and overall survival [9,10]. However, the safety information concerning imatinib therapy in pregnancy is limited [4,11] and most of the data are derived from patients with chronic myeloid leukemia. Pye et al. [5] performed an analysis of 125 pregnancies with imatinib exposure, 50% resulted in a healthy live infant, 28% in elective termination, and 9.6% of fetuses were born with malformations. Although most deliveries followed by imatinib exposure had a successful outcome, there was an increased risk of fetus malformations; therefore, the current recommendation is that patients taking imatinib should use effective contraception or should discontinue the treatment if they conceive inadvertently.

On the basis of a literature review, a reasonable treatment strategy for GIST in pregnant patients should include the following: (1) Resection of the primary tumor and metastatic lesions, if feasible, especially if the tumor was diagnosed in the first or second trimester; (2) If the tumor is found in the later phase of pregnancy, one should consider waiting until 36 weeks gestation and then resect the tumor after or simultaneously with delivery; (3) Adjuvant imatinib administration should be considered for high-risk tumors, and should be started after child-birth; (4) For non-resectable metastatic GIST, continuation of the pregnancy and/or imatinib treatment should

Table 1: Reported cases of GIST diagnosed in pregnancy.

Year/author	Age	Pregwk at Dx	Size of tumor	Location of tumor	Surgery	TKI	Outcome
2012 Goel	25	16	NA	Chest and liver mets	None	Through- outpreg	Conceive during imatinib, and continued for metastatic disease. Normal birth at 36 weeks per C/S.
2012 Gozukara	21	15	17 cm	Omentum	During preg	None	N/A
2011 Stubbs	31	16	12 cm	Transverse mesocolon	Simultaneous with C/S at 36 wk	After delivery	Elective C/S and tumor resection at 36 weeks. Tumor grew 12cm to 17cm.
2009 Scherjon	25	10	17 cm	Jejunum	During pregnancy	After recurrence	Normal delivery at 41 wk. Recur 6 years later, treated with surgery and TKI.
2005 Lanzafame	29	22	4 cm	Stomach	During pregnancy	None	N/A
Presented case	20	16	16 cm	Stomach and liver mets	During pregnancy	After delivery	As described

Dx: Diagnosis; preg: Pregnancy; wk: Week; mets: Metastasis; TKI: Tyrosine Kinase Inhibitor; C/S: Caesarian Section; N/A: Information is not provided

be cautiously discussed with patients with collaboration from the multidisciplinary team. Patient counseling and education regarding the paucity of safety data cannot be overemphasized.

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