

Gastric Cancer in Pregnancy in China: Case Reports and a Mini-Review

Huanhong Zeng^{1*}, Xin Zhou¹, Haiting Xie¹, Yangyu Zhao² and Wei Fu¹

¹Department of General Surgery, Peking University Third Hospital, Beijing, China

²Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing, China

Abstract

Gastric cancer associated with pregnancy is quite rare, and it is often diagnosed late due to misinterpretation of clinic presentations as pregnancy-related digestive symptoms. Most pregnancy-associated gastric cancer is often at its advanced stage at the time of diagnosis. The difficulties in the early diagnosis of gastric cancer in pregnant women deter timely surgical treatment for the disease. We reviewed the existing literature using the key words “pregnancy” and “gastric cancer”. 65 cases, including 62 cases reported previously in China and 3 cases that we report here, were accumulated. The analysis of these and other 29 cases from Japan revealed that the pathology of such kind of tumor mostly were poorly differentiated diffuse carcinomas. Some further examinations should be conducted timely on the pregnant patients with persistent gastrointestinal symptoms for the differential diagnosis of hyperemesis gravidarum. As soon as gastric cancer was diagnosed, a therapeutic plan should be promptly made by obstetric and gastric cancer specialists.

Keywords: Gastric cancer; Pregnancy; Diagnosis

Introduction

Cancer associated with pregnancy is rare. The incidence of cancer during pregnancy accounts for approximately 0.1% [1]. As women defer childbearing to the third or fourth decade of life, this rare coexistence is likely to become more common. The common malignancies associated with pregnancy include malignant melanoma, breast cancer, cervical cancer, lymphoma, ovarian cancer, gastrointestinal cancer and genitourinary cancer [2]. Gastric cancer in pregnancy is often diagnosed late due to misinterpretation of clinic presentations as pregnancy-related digestive symptoms. The difficulties in the early diagnosis of gastric cancer in pregnant women deter timely surgical treatment of the disease.

In an analysis by Sakamoto et al. that includes 137 cases of pregnancy-associated gastric cancer from Japan, most cancer were at advanced or late stages at the time of diagnosis, which to a large extent would cause dilemma for surgeons [3]. Here we reported our cases and reviewed literatures from China in order to analyze the clinicopathological characters of pregnancy-associated gastric cancer and shed light on the early diagnostic strategies.

Materials and Methods

1. The database of Peking University Third Hospital was searched for the cases of pregnancy-associated gastric cancer that were treated at the Department of General Surgery from 2001 to 2014.

2. A literature search was conducted on China National Knowledge Infrastructure (CNKI), VIP database, WANFANG DATA, and the China Biology Medicine Disc by using “gastric cancer” and “pregnancy” as key words. Inclusion criteria were as follows: (1) literatures were published in the last two decades, (2) original documents and detailed clinic and pathological data were preserved, (3) not less than 3 cases of gastric cancer during pregnancy or within 1 year after delivery were reported in the article.

Results

Case report

Among 863 gastric cancer patients, 3 were associated with pregnancy. The clinicopathological data of these cases were illustrated in Table I. These 3 patients all experienced nausea and vomiting

during the second or third trimester, while they were diagnosed with hyperemesis gravidarum or pregnancy-associated manifestation and with no further investigation or treatment. When admitted to our hospital, their symptoms failed to improve and laboratory tests showed anemia and hypoalbuminemia. Through gastrointestinal endoscopy, they were all diagnosed as gastric cancer. Two pregnant women chose induced labor to terminate their pregnancy. Due to advanced tumor stage and multiple metastases, one of the patients lost the chance of tumor resection. Other two accepted the surgical treatment. Despite all this, three patients all died of the progression of cancer from one to six months after the diagnosis.

Literature research

There are a total of 65 cases included in our study, three of which are from our department and 62 from 9 literatures [4-11]. In order to help clinicians formulate the best treatment plan, we present a comparison of the data collected from China and Japan.

Two tables (Table II and III) show the clinicopathological features of the 65 patients from China and 29 patients from Japan. Most of the patients (76.9%) were diagnosed by gastroscopy. With respect to the stage of gastric cancer, all patients were found to have advanced gastric cancer. The most common macroscopic feature was the infiltrative type (Borrmann III and IV) (76.5%). Regarding the pathological features, the diffuse type (poorly differentiated adenocarcinoma, mucinous adenocarcinoma, signet ring cell cancer) was most common (92.3%). In regard to the obstetric management of pregnant women with gastric cancer, no detailed record was reported in Chinese patients.

***Corresponding author:** Huanhong Zeng, Department of General Surgery, Peking University Third Hospital, No. 49 North Huayuan Road, Haidian District, Beijing 100191, China, Tel: 86-10-82267312; E-mail: zeng_bjmu@163.com

Received August 05, 2014; **Accepted** November 18, 2015; **Published** November 25, 2015

Citation: Zeng H, Zhou X, Xie H, Zhao Y, Fu W. Gastric Cancer in Pregnancy in China: Case Reports and a Mini-Review. Journal of Surgery [Jurnalul de chirurgie]. 2015; 11(4): 165-168 DOI:[10.7438/1584-9341-11-4-9](https://doi.org/10.7438/1584-9341-11-4-9)

Copyright: © 2015 Zeng H, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Table I: Clinicopathological data of 3 cases treated in Peking University Third Hospital.

Patient age(years)	Weeks of gestation	Symptoms					Pathology		Treatment
		Abdominal pain	Abdominal distension	Nausea and vomiting	Melena	Weight loss	Macroscopic type	Histological type	
29	26	-	-	+	+	+	Borrmann III	Moderately differentiated adenocarcinoma	Pancreaticoduodenectomy
31	24	-	+	+	-	-	Borrmann IV	Poorly differentiated adenocarcinoma	No surgery
36	post-partum	+	-	+	-	+	Borrmann III	Poorly differentiated adenocarcinoma	Palliative subtotal gastrectomy

Table II: Clinical features of Chinese and Japanese patients diagnosed with pregnancy-associated gastric cancer.

	China (1993-2014)	Japan (1988-2007)
No. of patients [No. (%)]	65	29
Patient age (years)		
20-29	26(40.0)	9(31.0)
30-39	8(12.3)	13(44.8)
>40	1(1.5)	7(24.1)
Unknown	30(46.2)	0
Weeks of gestation [No. (%)]		
<24	11(16.9)	9(31.0)
24-27	6(9.2)	2(6.8)
≥28	13(20.0)	13(44.8)
post-partum	35(35.8)	5(17.2)
Diagnostic method [No. (%)]		
Endoscopy	50(76.9)	22(75.8)
Ultrasound	1(1.5)	0
Upper GI series	9(13.8)	0
Palpable tumor or lymph nodes	0	1(3.4)
Laparotomy	2(3.1)	3(10.3)
Unknown	3(4.6)	3(10.3)
Disease status [No. (%)]		
Early	0	2(7.0)
Advanced	65(100.0)	26(89.7)
Unknown	0	1(3.4)

According to the record of Japanese cases in the last two decades, a majority of patients (7/9) prior to week 24 of gestation selected surgical intervention after termination of pregnancy. All the patients (13/13) at week 28 of gestation and beyond implemented cesarean section or vaginal delivery, as well as two patients at week 24 to 27 of gestation carried out cesarean section. The survival rate of gastric cancer for the patients with pregnancy is far lower than those without pregnancy at the corresponding time period (Table III).

Discussion

As far is known, there is no clear definition of gastric cancer associated with pregnancy. In current literature, patients who are diagnosed with gastric cancer during pregnancy or within one year of childbirth are included [1,3,12,13]. Although the incidence of gastric cancer is in the second place among all malignancies around the world, the rate of gastric cancer during pregnancy is reported to be only 0.016% in Japan, a gastric cancer prevailing area [14]. In South Korea, among 14,563 patients with primary gastric cancer admitted at Seoul National University Hospital, only 15 patients (0.103%) were identified as pregnancy-associated [1]. There were only 3 patients (0.36%) with gastric cancer associated with pregnancy admitted at Department of General Surgery in the Third Hospital of Peking University, among 838 patients with primary gastric cancer during the period of 2001 to 2014.

Many factors may lead to the delayed diagnosis of gastric cancer associated with pregnancy. First of all, the incidence of gastric cancer

associated with pregnancy is uncommon. For this reason, gastric cancer might not be the first differential diagnosis for pregnant women with digestive symptoms in most of the cases. Secondly, gastric cancer symptoms can easily be concealed by pregnancy-related digestive symptoms. Pregnancy can decrease the secretion of acid in the stomach and increase mucus production at the same time. On the other hand, histaminase produced by the placenta deactivates histamine function. These factors will decrease the body sensitivity to cancerous ulcer injury. Jaspers et al. pointed out that the incidence of gastric cancer was not obviously different between pregnant women and other young people, but there was often a delay in diagnosis in pregnant women due to the lack of attention to upper abdominal discomfort during pregnancy [13]. Finally, the diagnostic measures are especially restricted for pregnant women. For instance, radiological examinations are not suitable for pregnant women and the safety of endoscopy is also questioned. All our 3 cases were delayed in diagnosis. One was considered to be hyperemesis gravidarum, and the other two were mistaken for digestive symptoms associated with pregnancy.

In our opinion, the causes of the poor prognosis of gastric cancer in pregnancy could be coming from many aspects. Firstly, most patients were found to have advanced cancer on diagnosis. Our data revealed that in all reported cases the tumors were diagnosed at an advanced stage. 83.6% of patients underwent surgery but only 14.3% of them had curative resection. In the Japanese data, 26 out of 29 patients had advanced gastric cancer at diagnosis. Secondly, a majority of patients had highly malignant tumor. In China, the percentage of infiltrative type (Borrmann III and IV) is 76.9%, and the percentage of diffuse type (poorly differentiated adenocarcinoma, mucus adenocarcinoma, signet ring cell cancer) is 92.3%, of which signet ring cell cancer accounts for 30.8%. Sakamoto et al. analyzed the pathology of the tumors in the 61 patients whose data were available [3]. The results showed that the percentage of infiltrative type and diffuse type were 83.6% and 86.9% respectively in gastric cancer associated with pregnancy.; Thirdly, the change of local biology in the stomach promotes the development of neoplasms during pregnancy. According to a report by Lanciers et al, *H. pylori* infection rate is significantly higher for pregnant women than non-pregnant women [15]. Given that circulatory blood flow increases and immunity attenuates during pregnancy, pregnant women are particularly susceptible to the rapid growth and spread of cancer [14]; besides, treatment is comparably restricted due to pregnancy. Ueo et al. have recommended that surgical treatment for gastric cancer should be immediately performed without regard for the pregnancy when gastric cancer is diagnosed prior to week 24 of gestation; At weeks 25 to 29 of gestation, the decision should depend on the stage of the gastric cancer as well as the resectability of the tumor; For week 30 of gestation and beyond, obstetric treatment followed by surgical intervention is recommended to guarantee the infant to be viable by cesarean section or vaginal delivery [12]. As the definition of abortion in Japan was revised in 1993, the above three categories correspond to prior to 22 weeks, 22 to 27 weeks as well as 28 weeks and beyond, respectively [3]. In our cases, two patients at week 23 to 27 underwent pregnancy termination because of their late tumor stage or poor nutritional condition, and then were delayed for the time of surgery or adjuvant therapy.

Table III: Pathology of tumors, surgical treatment, prognosis and obstetric management in Chinese and Japanese patient diagnosed with pregnancy-associated gastric cancer.

	China	Japan
Macroscopic type		
Localized type	1(1.5)	4(13.8)
Infiltrative type	50(76.9)	20(67.0)
Unknown	14(21.5)	5(17.2)
Histological type		
Intestinal type	5(7.7)	4(13.8)
Diffuse type	60(92.3)	19(65.5)
Signet ring cell type	20(30.8)	9(31.0)
Unknown	0	6(20.7)
Resectability		
No surgery	8(12.3)	7(24.1)
Surgery	57(87.7)	21(72.4)
Exploration or bypass	23(35.4)	4(13.8)
Gastrectomy	34(52.3)	17(58.6)
Unknown	0	1(3.4)
Management of obstetrics		
Abortion or induction of labor	11(16.9)	9(31.0)
Cesarean section or vaginal delivery	10(15.4)	15(51.7)
Diagnosed after delivery	37(56.9)	5(17.2)
Unknown	7(10.8)	0
Prognosis		
Patient alive at 12 months	8(12.3) ^b	10(37.0) ^a
Patient alive at 24 months	3(4.6) ^b	6(22.2) ^a
Patient alive at 36 months	2(3.1) ^b	

^aThe prognosis of 27 Japanese patients was recorded.

^bThe prognosis of 62 Chinese patients was recorded.

The impact of gastric cancer associated with pregnancy on fetus should be taken into account when deciding treatment. The perinatal mortality of the fetus is greatly influenced by the treatment methods. According to the statistical data from Jaspers's data, the prognosis for the fetus is favorable with 72% surviving. For pregnancies ≥ 30 weeks, only two babies died out of 29 cases [13]. With the development of perinatal medicine, fetal survival rate has gradually increased. The other factor impacting fetal survival is the potential occurrence of fetal tumor metastasis. Neonates delivered with concomitant placental or villous cancer involvement should be considered a high-risk population. Alexander et al. found that fetal risk of melanoma metastasis is approximately 22% with placental involvement [16]. There were less than 10 case reports of gastric carcinoma metastatic to the placenta, none of which found villous invasion or fetal metastasis.

On the basis of the clinical and pathological features of gastric cancer associated with pregnancy, early diagnosis is the only possibility for the better outcome. Eliakim et al. indicated that digestive symptoms would gradually remit after 16 weeks of gestation in 90% of patients with hyperemesis gravidarum and completely remit by 20 weeks in 99% of patients [17]. Most researchers emphasized that active examinations should be taken into account for pregnant women with persisting digestive symptoms. At present, the ultrasonography and gastroscopy are the main methods for gastric cancer patients in pregnancy.

Compared with endoscopy, ultrasonography could display both the intragastric and perigastric lesions and also the depth of invasion, with the advantage of noninvasion, economy and repeatability. Seevaratnam et al. made a meta-analysis about preoperative imaging for TNM staging of gastric cancer. The results showed the primary tumor detection rates ranged from 90.7 to 100 and the overall accuracy was $67.8\% \pm 10.8\%$ for ultrasonography [18]. Ultrasonography has guiding significance for further investigation. One of our cases showed a lesion of gastric wall by ultrasound, and then underwent endoscopy. But it is

debatable to diagnose the lesion of gastric fundus, tiny gastric cancer and small gastric cancer by ultrasonography.

Magnetic resonance imaging may be used to diagnose pregnancy-related gastric cancer. M. Anzidei et al. found that MRI and 64-MDCT accuracy levels did not differ in advanced stages of disease, whereas MRI was superior in identifying early gastric cancer [19]. K. M. Jang et al. analyzed a series of data of the patients who underwent gadoteric acid-enhanced MRI with diffusion-weighted imaging and multidetector contrast-enhanced abdominal computed tomography imaging [20]. They pointed out that the diagnostic accuracy and sensitivity of combined conventional and DW MRI set for detection of gastric cancer was significantly higher than that of the CT imaging set or the conventional MRI set. But it is still not clear whether MRI or gadoteric acid is safe for pregnant women or fetuses. MRI might be a valid alternative in clinical practice after finding a safer contrast agent instead of gadoteric acid.

Endoscopy can diagnose gastric cancer definitively and provide pathological biopsy. The safety of gastroscopy in pregnancy might hesitate pregnant patients. The potential risks of endoscopy include arrhythmia, hypertension, hypotension, hypoxemia, malformation, premature and so on. The research by Cappell et al. including 83 patients showed that gastroscopy didn't induce labor or result in congenital malformation [21]. No significant endoscopic complications occurred and none of the infants had a congenital malformation in the neonatal nursery. And compared with normal control group, neonatal Apgar scores were no significantly different. Another retrospective evaluation of 60 pregnant women also showed that endoscopy could be safely performed in pregnancy with no maternal and fetal complications [22]. American Society for Gastrointestinal Endoscopy outlined the main indications for endoscopy in pregnancy and general principles that apply to endoscopy in the Guidelines for Endoscopy in Pregnant and lactating Women. The safety of endoscopy could be greatly improved by following these indications and general principles [23].

Conclusion

In conclusion, the features of gastric cancer associated with pregnancy are the delayed diagnosis, high degree of malignancy and poor prognosis. Further examinations should be conducted timely in pregnant patients with persistent gastrointestinal symptoms for the differential diagnosis of hyperemesis gravidarum. When gastric cancer was diagnosed, a therapeutic plan should be promptly made by obstetrics and gastric cancer specialists.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Reference

1. Lee HJ, Lee IK, Kim JW, Lee KU, Choe KJ et al. (2009) Clinical characteristics of gastric cancer associated with pregnancy. *Dig Surg* 26: 31-36.
2. Pentheroudakis G, Pavlidis N (2006) Cancer and pregnancy: poena magna, not anymore. *Eur J Cancer* 42: 126-140.
3. Sakamoto K, Kanda T, Ohashi M, Kurabayashi T, Serikawa T, et al. (2009) Management of patients with pregnancy-associated gastric cancer in Japan: a mini-review. *Int J Clin Oncol* 14: 392-396.
4. Chen ZK (2000) An analysis of misdiagnosis of four cases of gastric cancer associated with pregnancy. *Chin J Dig Endosc* 17: 59.
5. Wei JW (2007) An analysis of four cases of gastric cancer associated with pregnancy. *Chin J Perinat Med* 10: 191-193.
6. Zheng ZQ, Xu JR, Chen GG (2000) A clinical analysis of 10 cases of gastric cancer associated with pregnancy. *Zhejiang Medicine* 22: 348-349.
7. Chen GG, Tang WH (2007) A clinical analysis of four cases of gastric cancer associated with pregnancy. *Zhejiang Clinical Medicine* 9: 26-28.

8. Dai D, Chen J, Wang S (1995) [Stomach cancer in pregnancy and breast feeding: report of 17 cases]. *Zhonghua Wai Ke Za Zhi* 33: 768-769.
9. Lu SY, Hao JM, Xing Y, Wang ZH (2005) A clinical analysis of 3 misdiagnosed cases with pregnancy-related gastric cancer. *Chinese Journal of Family Planning* 1: 48-49.
10. Guo QY (1999) Three cases of primary gastric cancer associated with pregnancy. *Central China Medical Journal* 23: 164.
11. Sun H (1994) Four cases of gastric cancer associated with pregnancy in the youth. *Journal of Ningxia Medical College* 16: 69-70.
12. Ueo H, Matsuoka H, Tamura S, Sato K, Tsunematsu Y, et al. (1991) Prognosis in gastric cancer associated with pregnancy. *World J Surg* 15: 293-297, discussion 298.
13. Jaspers VK, Gillessen A, Quakernack K (1999) Gastric cancer in pregnancy: do pregnancy, age or female sex alter the prognosis? Case reports and review. *Eur J Obstet Gynecol Reprod Biol* 87: 13-22.
14. Yoshida M, Matsuda H, Furuya K (2009) Successful treatment of gastric cancer in pregnancy. *Taiwan J Obstet Gynecol* 48: 282-285.
15. Lanciers S, Despinasse B, Mehta DI, Blecker U (1999) Increased susceptibility to *Helicobacter pylori* infection in pregnancy. *Infect Dis Obstet Gynecol* 7: 195-198.
16. Alexander A, Samlowski WE, Grossman D, Bruggers CS, Harris RM, et al. (2003) Metastatic melanoma in pregnancy: risk of transplacental metastases in the infant. *J Clin Oncol* 21: 2179-2186.
17. Eliakim R, Abulafia O, Sherer DM (2000) Hyperemesis gravidarum: a current review. *Am J Perinatol* 17: 207-218.
18. Seevaratnam R, Cardoso R, McGregor C, Lourenco L, Mahar A, et al. (2012) How useful is preoperative imaging for tumor, node, metastasis (TNM) staging of gastric cancer? A meta-analysis. *Gastric Cancer* 15 Suppl 1: S3-18.
19. Anzidei M, Napoli A, Zaccagna F, Di Paolo P, Zini C, et al. (2009) Diagnostic performance of 64-MDCT and 1.5-T MRI with high-resolution sequences in the T staging of gastric cancer: a comparative analysis with histopathology. *Radiol Med* 114: 1065-1079.
20. Jang KM, Kim SH2, Lee SJ1, Lee MW1, Choi D1, et al. (2014) Upper abdominal gadoxetic acid-enhanced and diffusion-weighted MRI for the detection of gastric cancer: Comparison with two-dimensional multidetector row CT. *Clin Radiol* 69: 827-835.
21. Cappell MS, Colon VJ, Sidhom OA (1996) A study of eight medical centers of the safety and clinical efficacy of esophagogastroduodenoscopy in 83 pregnant females with follow-up of fetal outcome with comparison control groups. *Am J Gastroenterol* 91: 348-354.
22. Debby A, Golan A, Sadan O, Glezerman M, Shirin H (2008) Clinical utility of esophagogastroduodenoscopy in the management of recurrent and intractable vomiting in pregnancy. *J Reprod Med* 53: 347-351.
23. ASGE Standard of Practice Committee, Shergill AK, Ben-Menachem T, Chandrasekhara V, Chathadi K, et al. (2012) Guidelines for endoscopy in pregnant and lactating women. *Gastrointest Endosc* 76: 18-24.