CASE REPORT

Pregnancy and gastric cancer: diagnostic and treatment dilemma

Nawar Hussain,¹ Navaneethakrishnan Selvakumari,¹ Frances Afadapa,² Olubusola Amu²

¹Obstetrics and Gynaecology, Royal Oldham Hospital, Greater Manchester, UK

²Women & Children's Division, Royal Oldham Hospital, Greater Manchester, UK

Correspondence to

Dr Nawar Hussain,
nawar2001@hotmail.com

Accepted 28 March 2018

SUMMARY

Gastric cancer in pregnancy is an extremely rare entity. The incidence of gastric cancer is more in elderly patients and higher in the male population. Gastric cancer symptoms can be nausea, vomiting and epigastric discomfort which is similar to early pregnancy symptoms. This leads to a misinterpretation and delay in the diagnosis during pregnancy. Gastric cancer in pregnancy is associated with poor prognosis because of its delayed diagnosis at an advance stage. We present our patient here, with this rare clinical diagnosis and with no suspicion in a young healthy woman.

BACKGROUND

A healthy 27-year-old woman had multiple admissions to the hospital with a history of vomiting and epigastric pain while she was pregnant. At one occasion, she had perforation of gastric ulcer, which required laparotomy, and repairing of the perforation.

An endoscopy was arranged for her, after she had normal vaginal delivery at 37 weeks, and a biopsy was taken which revealed a poorly differentiated adenocarcinoma, while the CT and MRI revealed an sT2/T3 N1 gastric cancer. The patient died a few months later.

CASE PRESENTATION

A healthy 27-year-old, primip, 18-week pregnant, non-smoker woman with no history of alcohol abuse nor any medical history was presented with a dull achy generalised abdominal pain for 3 days. On examination, observations were normal: general abdominal tenderness and fundal height was normal. There were 3+ketones in the urinalysis; her haemoglobin was 11 g/dL with a platelet count of $321 \times 10^9/L$. Her white cell count was $9.9 \times 10^9/L$, she had a C reactive protein of 16.2 mg/L and her amylase was 70 U/L. The liver and renal function tests were both normal. An assessment of hyperemesis gravidarum was made with the possibility of a viral infection.

Antiemetics and analgesia were given. The patient was later sent home as her symptoms improved.

At 24-week gestation, the patient was readmitted with a history of coffee ground vomiting and upper abdominal pain. Examination revealed stable observations, with mild tenderness over the epigastric area. As the patient's condition deteriorated rapidly within the next 48 hours, she had a laparotomy,

which revealed a large amount of dark-coloured fluid, clots and gastric contents in the abdomen, and a perforation of 1 cm diameter on the upper portion of the lesser curvature of the stomach, which had been repaired.

The patient was then admitted to the high dependency unit with a nasogastric tube, intra-abdominal drain in situ. She was put on intravenous meropenem, clindamycin and gentamicin.

On day 7, postoperative day, while she still had a spiking temperature, her blood culture grew methicillin-resistant *Staphylococcus aureus*; therefore, vancomycin had been added to the antibiotic regimen, and gentamicin was stopped.

Her clinical condition improved over the next 10 days and she was sent home 18 days post operation with a plan to have a regular antenatal review and gastroscopy after delivery. Two weeks later, the patient was readmitted to the hospital with epigastric pain and nausea. The gastroscopy showed a 1 cm acute duodenal ulcer with no active bleeding. She had a course of 72 hours intravenous omeprazole. She made a good recovery and went home a few days later.

At 30-week pregnancy, she developed diarrhoea and vomiting. Her stool culture grew a *Clostridium difficile*, for which vancomycin was started. Then, 2 days later, her urine culture grew *Escherichia coli*, and meropenem was added. A full 7-day course of meropenem and a 10-day course of vancomycin were given before she was discharged home. The patient had serial growth scans throughout the pregnancy which reflected a normally growing fetus with an expected weight of over the 10th centile.

At 37 weeks, the patient had a spontaneous rupture of the membrane followed by normal labour progress and the delivery of a healthy male baby of 2450 g. Apgar Scores were 9 and 10 at 1 and 5 min, retrospectively.

Then, 4 weeks later, the patient had another admission as she was presented with vomiting, haematemesis and melaena.

INVESTIGATIONS

An endoscopy performed on this occasion showed a poorly differentiated adenocarcinoma (figure 1), and *Helicobacter pylori* was negative.

CT scan revealed a circumferential mural thickening of the antral part of the stomach and bulky head of the pancreas but no focal abnormality nor peripancreatic inflammatory changes. Normal liver,

To cite: Hussain N, Selvakumari N, Afadapa F, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222963

Figure 1 Pictures from second endoscopy showing gastric cancer.

spleen, adrenals and kidney with neither ascites nor abnormal pelvic mass seen. These findings had been confirmed by the MRI which showed a gastric body bulk tumour.

Further endoscopy was performed after chemotherapy, which revealed further growth beyond the stent that was inserted.

DIFFERENTIAL DIAGNOSIS

Hyperemesis gravidarum

Severe protracted nausea and vomiting occurred during early stage of the pregnancy associated with dehydration, electrolyte disturbances and more than 5% weight loss of prepregnancy weight. Diagnosis is usually made by history, examination and investigation. Symptoms usually settle with antiemetics.¹

Peptic ulcer

It could be a duodenal or gastric ulcer, caused by mucosal damage by pepsin and gastric acid secretion. The most common cause is *H. pylori* and non-steroidal anti-inflammatory drugs. It is associated with epigastric pain, which usually improves by eating or with an antacid.²

Zollinger-Ellison syndrome

It is a clinical syndrome, which is caused by extra secretion of gastrin by a neuroendocrine tumour—gastrinoma, which in most of the cases present in the duodenum (60%) or in the pancreas (40%). This causes a refractory peptic ulcer. It is diagnosed by the presence of fasting hypergastrinaemia (high gastrin).³

Gastric cancer

Its symptoms can be similar to peptic ulcer and may also be associated with dysphagia, weight loss, pain, feeling full after eating a small amount of food, vomiting and bleeding.⁴

TREATMENT

The patient had one course of radiotherapy and three courses of chemotherapy. During this course of treatment, she had a stent insertion to improve gastric outlet obstruction. This was followed by further endoscopy, which confirmed the extension of the tumour beyond the stent.

OUTCOME AND FOLLOW-UP

A CT scan was performed post chemotherapy, showing a good response. The plan was to have a laparoscopy to assess her suitability for operation. But her condition deteriorated later and she developed a swelling of her legs and arms due to multiple thrombosis associated with metastasis.

DISCUSSION

It is evident that the delayed diagnosis occurred due to a cross over between the similarity of pregnancy-related symptoms and gastrointestinal upset, although the differentials, for example, Zollinger-Ellison syndrome and gastric cancer always need to be considered carefully. Moreover, gastric cancer in itself is a rare condition in this cohort and would therefore not be likely as a differential until more serious symptoms appear when diagnosed in the later stages. Gastric cancer is usually incurable as it is unresectable with disease progression.

This case highlights the need for further investigations at an earlier stage if symptoms are not resolving by simple measures, and this will include biopsy of gastric ulcers during laparotomy, as it may have diagnosed the cancer at an early stage. It is possible that an earlier diagnosis may considerably improve patient outcomes.

The importance of gastric cancer associated with pregnancy is derived from its rarity and its difficulty in diagnosis especially with gastric cancer symptoms mimicking pregnancy-related symptoms, which lead to a delay in diagnosis. Most cases diagnosed at later stages are incurable and unresectable. In addition, offering surgery can also be challenging with fetal prematurity.

In the UK, age-specific incidence rates rise sharply from around age 60–64. With a male:female ratio of around 18:10 (1 in 67 men and 1 in 135 women will be diagnosed with stomach cancer during their lifetime)⁴ The risks of developing gastric cancer include age, genetics and exposure to risk factors: while *H. pylori* infection is the main potentially avoidable risk factor for stomach cancer, linked to an estimated 32% of stomach cancer.

Consuming too much salt (24%), and smoking (22%), ionising radiation and certain occupational exposures, low fruit and vegetable diet are considered as contributing factors. Alcohol and obesity might increase the risk but there is no clear evidence.⁴ The diagnosis of gastric cancer during pregnancy is usually delayed as its symptoms are masked by pregnancy-related symptoms, which can explain poor survival rate.^{5,6} Ninety-three per cent are diagnosed in advanced stage, and 60% of cases are unresectable.⁷ The yearly survival rate is 46.7%.⁷

Endoscopic examination is recommended for severe abdominal pain and vomiting which may not be improved by the usual management.^{5,8} The poor prognosis of the gastric cancer during the pregnancy is due to delayed diagnosis, restricted therapeutic approach in pregnancy, hormonal and biological changes in the pregnancy as well as the immunosuppression effect of the pregnancy.⁸ The management of the gastric cancer includes surgery, chemotherapy and radiotherapy. Management will depend on the stage of the disease and the gestational age. Termination of pregnancy should be offered to those who are less than 24 weeks of gestation followed by surgery. While those who are 24–32 weeks' pregnant can offer a course of dexamethasone followed by caesarean section and gastrectomy at the same setting.⁹ Those who are 32-week pregnant or more, vaginal delivery should be offered as soon as possible to facilitate the surgical management.⁹

We did a Medline and Embase search using the following keywords: gastric cancer, pregnancy, cancer in pregnancy, adenocarcinoma in pregnancy, perforation between 2000 and 2014. We collected 23 cases but only managed to review 22 (table 1). Most common presenting complaint was abdominal pain and vomiting. While in most cases, the histology revealed a poorly differentiated adenocarcinoma; all cases were presented in an advanced stage.

Table 1 Gastric cancer case reports between 2000 and 2014

Case no	Country	Age at the time of diagnosis	Gestational age at the time of diagnosis	Main complaint	Unusual presentation	Management	Survived
1	Belgrade	38	24	Abdominal pain and vomiting	Krukenberg tumour	Palliative	No ⁶
2	USA	22	28	Rapidly increasing abdominal girth		Surgical	No ¹⁰
3	North Ireland	35	22	Vomiting, upper abdominal pain and melaena		Palliative	No ¹¹
4	USA	32	28	Tachycardia and dyspnoea	Pericardial tamponade	Palliative	No ¹²
5	Italy	30	37	Backache	Bilateral erythematous breast hypertrophy	Palliative	No ¹³
6	Singapore	24	35	Obstructive jaundice	No abdominal pain	Palliative	No ¹⁴
7	Ireland	33	17	Vomiting, pain and weight loss		Palliative	No ¹⁵
8	Israel	26	26	Abdominal pain	Placenta and amniotic fluid metastasis	Palliative	No ¹⁶
9	Japan	37	23	Vomiting and abdominal pain		Surgery	No ¹⁷
10	Turkey	29	31	Abdominal pain, backache and vomiting		Surgery and chemotherapy	No ¹⁸
11	Japan	36	26	Backache	Idiopathic thrombocytopenia	Chemotherapy	Unknown ¹⁹
12	Japan	31	41		DIC and low platelets	Palliative	No ²⁰
13	Germany	37	36		Sister Mary Joseph's nodule	Surgery and chemotherapy	Unknown ²¹
14	Turkey	27	16	Abdominal pain and vomiting		Survived ²²	
15	Spain	39	18		Sever anaemia	Surgery	No ²³
16	Greece	27	22		Virilising ovarian Krukenberg tumour	Surgery, chemotherapy and radiotherapy	Loss follow-up ²⁴
17	Malaysia	27	16	Severe epigastric pain		Palliative	No ²⁵
18	Belgrade	31	27	Abdominal pain and swelling		Surgery and chemotherapy	No ²⁶
19	Turkey	30	26	Abdominal pain, nausea and vomiting		Surgery and chemotherapy	Unknown ²⁷
20	Belgrade	18	23	Hyperemesis		Surgery	Unknown ²⁸
21	Switzerland	34	35	Epigastric pain	Bilateral Krukenberg tumours	Surgery and chemotherapy	No ²⁹
22	Turkey	22	2 weeks after premature labour at 24 weeks gestation	Nausea, vomiting and abdominal pain		Palliative	No ³⁰

DIC, Disseminated intravascular coagulation.

CONCLUSION

Gastric cancer during pregnancy is very rare and is usually presented in an advanced stage. Further investigation, including biopsy of gastric lesion, for cases, which do not respond to simple management, is crucial for early diagnosis of the disease. While many had unusual presentation, 16 out of 22 cases in the report died shortly after diagnosis.

Learning points

- Gastric cancer is very rare in pregnancy.
- Symptoms of gastric cancer may be masked by pregnancy symptoms.
- Delayed diagnosis and treatment contribute to the bad outcome.
- One of the deferential diagnoses should be if vomiting in pregnancy is not responding to usual treatment.

Acknowledgements I would like to acknowledge Mr Najib Khan for helping them with publication of this case report.

Contributors NH: wrote the case report and the discussion. NS: discussed planning and helped with discussion. FA: helped with discussion and reviewed the whole case report. OA: helped with planning and reviewing the whole case report.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Royal College of obstetricians and Gynaecologists. The management of nausea and vomiting of pregnancy and hyperemesis gravidarum (Green-top Guideline No. 69). 2016.
- 2 Ramakrishnan K, Salinas RC. Peptic ulcer disease. *Am Fam Physician* 2007;76:1005–12.
- 3 Ito T, Cadiot G, Jensen RT. Diagnosis of Zollinger-Ellison syndrome: increasingly difficult. *World J Gastroenterol* 2012;18:5495–503.
- 4 Cancer research UK. <https://www.cancerresearchuk.org/>
- 5 Al-Ibrahim A, Parrish J, Dunn E, et al. Pregnancy and maternal outcomes in women with prior or current gastrointestinal malignancies. *J Obstet Gynaecol Can* 2014;36:34–41.
- 6 Glisic A, Atanackovic J. Krukenberg tumor in pregnancy. The lethal outcome. *Pathol Oncol Res* 2006;12:108–10.
- 7 Lee HJ, Lee IK, Kim JW, et al. Clinical characteristics of gastric cancer associated with pregnancy. *Dig Surg* 2009;26:31–6.

- 8 Ueo H, Matsuoka H, Tamura S, *et al.* Prognosis in gastric cancer associated with pregnancy. *World J Surg* 1991;15:293–7.
- 9 Chan YM, Ngai SW, Lao TT. Gastric adenocarcinoma presenting with persistent, mild gastrointestinal symptoms in pregnancy. A case report. *J Reprod Med* 1999;44:986–8.
- 10 Baker AM, Haeri S, Shafer A, *et al.* Maternal gastric carcinoma metastatic to the placenta. *Eur J Obstet Gynecol Reprod Biol* 2010;153:225–6.
- 11 Miller K, Zawislak A, Gannon C, *et al.* Maternal gastric adenocarcinoma with placental metastases: what is the fetal risk? *Pediatr Dev Pathol* 2012;15:237–9.
- 12 Bacic B, Mistic Z, Kovacic V, *et al.* Gastric carcinoma presenting as pericardial tamponade during pregnancy. *Turk J Gastroenterol* 2009;20:276–8.
- 13 Mandato VD, Pirillo D, Gelli MC, *et al.* Gastric cancer in a pregnant woman presenting with low back pain and bilateral erythematous breast hypertrophy mimicking primary inflammatory breast carcinoma. *Anticancer Res* 2011;31:681–5.
- 14 Chong VH, Lim CC. Advanced disseminated gastric carcinoma in pregnancy. *Singapore Med J* 2003;44:471–2.
- 15 Kamal Y, Sheehan S, Geary M. Gastric carcinoma: an unusual cause of vomiting in pregnancy. *J Obstet Gynaecol* 2004;24:820–9.
- 16 Khatib F, Shaya M, Samueloff A. Gastric carcinoma with metastasis to the placenta and amniotic fluid: case report and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 2003;107:208–9.
- 17 Sakamoto K, Kanda T, Ohashi M, *et al.* Management of patients with pregnancy-associated gastric cancer in Japan: a mini-review. *Int J Clin Oncol* 2009;14:392–6.
- 18 Yücesoy G, Büyükgöbüz O, Yıldız K, *et al.* Gastric carcinoma diagnosed at the third trimester: a case report. *Arch Gynecol Obstet* 2006;274:47–9.
- 19 Takai H, Kondoh E, Sato Y, *et al.* Disseminated intravascular coagulation as the presenting sign of gastric cancer during pregnancy. *J Obstet Gynaecol Res* 2011;37:1717–9.
- 20 Kurabayashi T, Isii K, Suzuki M, *et al.* Advanced gastric cancer and a concomitant pregnancy associated with disseminated intravascular coagulation. *Am J Perinatol* 2004;21:295–8.
- 21 Fill S, Taran A, Schulz HU, *et al.* Sister Mary Joseph's nodule as the first sign of pregnancy-associated gastric cancer: a case report. *World J Gastroenterol* 2008;14:951–3.
- 22 Özdemir I, Pehlivan M, Demirci F. Gastric cancer in pregnancy. *Int J Gynaecol Obstet* 2003;82:207–8.
- 23 Ayestaran C, Matorras R, Ramon O, *et al.* Fulminating gastric cancer in a pregnant woman, after 18 weeks of gestation, recipient of oocytes. *Acta Obstet Gynecol Scand* 2000;79:86–7.
- 24 Papakonstantinou E, Liapis A, Kairi-Vassilatou E, *et al.* Virilizing ovarian Krukenberg tumor in a 27-year-old pregnant woman. A case report and literature review. *Eur J Gynaecol Oncol* 2011;32:331–3.
- 25 Jasmi AY, Normala B, al-Amin MD. Perforated malignant gastric ulcer in a pregnant young adult: a case report. *Med J Malaysia* 2000;55:135–7.
- 26 Stojnic J, Stefanovic A, Jeremic K, *et al.* Krukenberg tumor of gastric origin in pregnancy with dismal outcome. *Eur J Gynaecol Oncol* 2011;32:356–8.
- 27 Çalışkan E, Sener M, Nursal TZ, *et al.* Thoracic epidural anesthesia and analgesia for gastric resection at 26 week pregnant woman. *Agri* 2006;18:20–3.
- 28 Gojnic M, Dugalic V, Vidaković S, *et al.* Hyperemesis or stomach carcinoma in pregnancy--a true diagnosis with two lives saved: a case report. *Clin Exp Obstet Gynecol* 2005;32:201–2.
- 29 Sandmeier D, Lobrinus JA, Vial Y, *et al.* Bilateral Krukenberg tumor of the ovary during pregnancy. *Eur J Gynaecol Oncol* 2000;21:58–60.
- 30 Kurt M, Aksoy S, Cizginer S, *et al.* Gastric cancer and the coincidental finding of herpetic esophagitis immediately after pregnancy: a case report. *J Reprod Med* 2007;52:425–7.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow