

Adenocarcinoma of the Stomach Associated with Pregnancy

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INTRODUCTION

Cancer associated with pregnancy is a rare condition. Some few reports¹⁾ on cancer of the breast with pregnancy were found in the English literature, however, cancer of the stomach with pregnancy is extremely rare, because the marked reduction in the incidence of cancer of the stomach has been found in the United States during the past forty years. The age adjusted deaths rate from cancer of the stomach per 100,000 population 1965 to 1967, were less than 10, both for males and females, as compared to those in Japan of about 70 during the same period²⁾.

In Japan gastric cancer comprises about half of the cases of cancer. In 1978, we collected and reported 44 cases of cancer of the stomach with pregnancy reported in Japanese literature from 1916 to 1974³⁾.

According to the reports of the results of the resected stomach carcinoma (1969 to 1973), cancer of the stomach in less than 40 years old females was 253 cases (12.5% in females patients) and 4.3% in all with stomach carcinoma⁴⁾.

The five-year survival rate for 250 cases who underwent operations was 65%. If they had any gastrointestinal symptoms in this condition, such symptoms as epigastric pain, nausea and vomiting were considered as those in pregnancy, because low incidence of cancer of the stomach in less than 30 years old females was extremely low in 1.9%. Most of them developed advanced carcinoma when diagnosis was given correctly.

We came across only five cases with gastric cancer with pregnancy mostly present

ing epigastric pain with nausea who were treated during the past 28 years as of 1984 at the First Department of Surgery of Nagasaki University.

We wish to present two patients who underwent emergent operations due to hematoemesis and colonic obstruction, respectively, and one case exploratory laparotomy with an anticancer drug, and emphasize that these should be kept in mind, especially when vomiting is persistent and extends over a prolonged period.

CASE REPORT

Case I. A 25-year-old woman gravida 3, para 1, abortuses 2 was admitted on July 18, 1970 with complaints of nausea and epigastric and lumbal pain. Her first infant delivered in July 1969 and the last menstrual period occurred on December 10, 1969. No past or family history of cancer was present. Since the end of May 1970, she had a history of continuous lumbar pain, but had no treatment.

In the middle of June, she began to complain epigastric pain with loss of appetite and followed by several episodes of vomiting. It was felt that her gastrointestinal symptoms were due to pregnancy by her private physician. In July she had complained of severe lumbar pain and noticed weight loss. She consulted an orthopedist, but nothing abnormal was found orthopedically.

On July 16, a routine upper GI series was performed. At this time, the patient was diagnosed as having cancer of the stomach and was transferred to our Department of Surgery.

At physical examination the patient was emaciated and showed an undernourished appearance, but she had no jaundice, edema, but a few small finger tip-sized lymphnodes were noticed in the left cervical region.

The heart sounds were clear to auscultation. The lung was normal. The abdomen was enlarged to a size compatible with a eight months' gestation. The uterine fundus was 5cm above the umbilicus. The fetus was in a cephalic presentation and the heart sounds were normal. There were tenderness and tumor-like resistance was palpable in the epigastrium.

Roentgenograph revealed irregularity and rigidity of both curvatures from the subcardial to antral portion forming a leather bottle appearance. Radiograph of the vertebral column noted the fetus were seen in the right lower abdominal region (Fig. 1).

With gastroendoscopy, irregular mucosal giant folds on the greater curvature of the

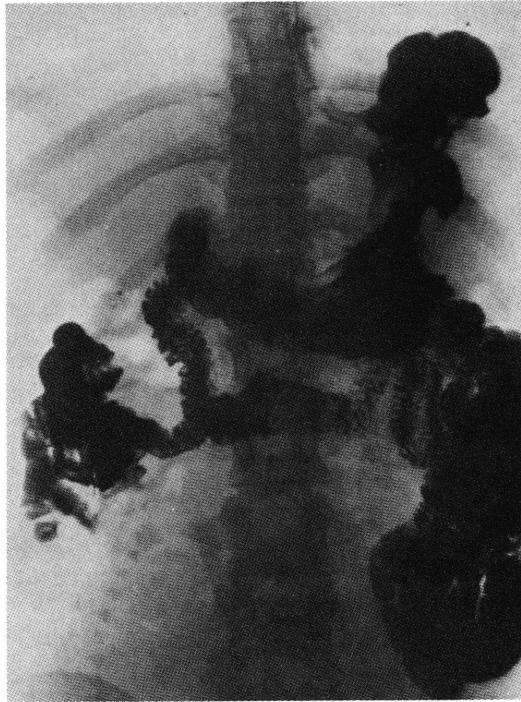


Fig. 1. Upper GI series shows irregularity and rigidity of gastric wall, forming leather bottle appearance. Vertebral column of the fetus is seen in the right lower quadrant.

body and a few irregular erosion with bleeding on the lesser curvature were found. The wall of the stomach showed marked decrease in distensibility. Preoperative diagnosis was linitis plastica, Borrmann's type 4 of carcinoma of the stomach.

Significant blood studies were hemoglobin 7.2g/dl, hematocrit 23%, red blood cell count $261 \times 10,000/\text{mm}^3$, white blood cell count $10,200/\text{mm}^3$, serum total protein level 5.9g/dl. Urinalysis was unremarkable except for positive protein.

Discussion between the obstetrician and the family was made as to which procedures were preferred in this patient, and a conclusion was reached that it was improper for her health to continue her pregnancy, and it was decided that abortion should be selected to relieve her complaints, though the possibility of curative resection of the stomach could not be expected. Abortion was induced using laminaria on July 23. She delivered a dead female infant unfortunately. On July 30, under general anesthesia, an upper midline incision was performed on her. A large amount of ascites was found. The stomach formed a leather bottle shape, and was invaded by carcinomatous infiltration with peritoneal implant and positive regional lymph nodes involved. The liver was clear of

metastasis. It was impossible to resect the stomach. Anticancer drugs of Mitomycin C 10mg and 5-FU 1000mg were remained in the abdominal cavity.

The pathological diagnosis of the resected lymph node of the lesser curvature was poorly differentiated adenocarcinoma. Her postoperative course was uneventful, but she died in of cachexia two months following laparotomy.

Case II. A 29-year-old woman gravida 2, parity 2 was admitted on July 8, 1983 to the First Department of Surgery, Nagasaki University Hospital because of massive bleeding due to early gastric coneer. Her second infant was delivered on May 24, 1983 and her post-pregnant course was uneventful. On the afternoon on July 6, she complained of dull abdominal pain in the epigastrium and noticed sudden dizziness and bowel sounds after dinner. One hour later she developed nausea and some bloody vomiting of bright red blood followed. The stools became tarry in the evening. She was admitted to the Nagasaki Municipal Adult Disease Hospital under a suspicion of peptic ulcer disease. After a day, emergent endoscopy of the upper digestive tract disclosed an unusual picture, but the esophagus appeared normal. On the lesser curvature of the cardiac portion of the stomach, a widely spreading irregular-shaped and depressed area with the nodular bottom and bleeding was observed. Hemostasis was achieved by laser irradiation. The endoscopic picture suggested early gastric cancer of IIc type.

Immediately she was transferred to our hospital for the purpose of operation. The patient appeared moderately pale. Pulse 102/min and blood pressure 80mmHg. The hemoglobin 8.8g/dl, red blood cell count $313 \times 10,000$. The hematocrit 27.3%. The heart and lung were normal. The abdomen was flat and soft without tenderness. Remarkable anemia was recognized. Blood transfusion and parental nutrition were begun. After the patient's general condition was improved, total gastrectomy was scheduled to perform. On July 11, she again began hematoemesis, and emergency laparotomy was performed. An upper midline incision was made. There was no ascites in the abdominal cavity. The stomach and duodenum were normal to inspection and palpation. There were neither regional lymphnodes involved nor peritoneal implants. The liver was clear of metastasis. Total gastrectomy with Roux-en-Y anastomosis was performed.

On the resected stomach, IIc type early gastric cancer of 7.5×5.4 cm was found located on the lesser curvature and posterior wall of the cardia.

Histological study revealed an extensive proliferation of signet ring cell carcinoma mostly limited to the mucosa with focal invasion into submucosal layer. There was no evidence of metastasis of lymphnodes.

No anticancer drug was administered after operation. Her postoperative course

was uncomplicated. Three years later the patient remained well and clinically free from recurrence.

Case III. A 35-year-old woman gravida 3, parity 3 was admitted on March 7, 1984 to the First Department of Surgery of Nagasaki University Hospital with complaints of abdominal colicky pain and vomiting. She delivered a third infant on December 15, 1983. During pregnancy she noticed hypertension, urinary protein and pretibial edema, but no gastrointestinal symptoms. After delivery she noted constipation with small-caliber "pencil" stools. She did not notice bloody stools and significant loss of weight.

On the evening of March 6, 1984, she began to complain of sudden colicky pain in the epigastrium and left hypochondrium. Barium enema revealed stenosis of the large bowel at the level of splenic flexure, and she was transferred under a suspicion of colon obstruction.

She was febrile at 38.4°C due to acute stagnation mastitis with breast pain for a few days. On admission, her general condition was ill. She had no jaundice and edema. Pulse 100/min, and blood pressure 112/64mmHg. The heart and lung were normal to auscultation. The hemoglobin 11.0g/dl. Hematocrit 35.1%, red blood cell count $434 \times 10,000/\text{mm}^3$, white blood cell count $9400/\text{mm}^3$, serum total protein level 6.4g/dl. On liver function tests, nothing abnormal was found. CEA was less than 1 (normal less than 4ng/ml).

The abdomen was slightly distended. There was slightly rigidity and resistance with tenderness in the left upper quadrant. A plain abdominal roentgenogram showed several small air-fluid levels in the right abdominal region, but no free gas. Only a small amount of gastric contents through a nasogastric tube passing into the stomach was aspirated.

Sedativa also did not fail to relieve her complaints. Emergency laparotomy was carried out. The midline incision was made from 5cm above the umbilicus to just above pubic symphysis. About 300ml of slightly bloody ascites were found in the abdominal cavity. Several peritoneal dissemination was seen on the mesenterium and mesocolon. Adults fist's-sized tumor was palpated at the splenic flexure of the colon, which was invaded from scirrhous carcinoma of the stomach directly. An enlargement of the incision upwards was made. Curative operation was impossible, but proximal gastrectomy combined with resection of spleen, tail of the pancreas and left hemicolectomy were carried out.

In the resected stomach linitis plastica and obstruction of the colon resulting from direct invasion of the tumor were observed.

Histologic finding showed an invasive proliferation of poorly differentiated

adenocarcinoma involving the whole layer of the stomach and pancreas. The primary site of carcinoma seemed to be in the body of the stomach. Ileus was thought to have been caused by peritonitis cancerosa. Her postoperative course was uneventful. She was discharged on April 10, but was readmitted complaining of abdominal fullness ten days later.

In the beginning of May, she developed jaundice and remarkable anemia. Four months after operation, she died of carcinomatous peritonitis.

REVIEW OF FIVE CASES

The 5 patients with cancer of the stomach treated surgically during the past 28 years at the First Department of Nagasaki University are listed in Table 1. The average age was 29.2 years, the extremes being 25 and 35 years. The average gravidity was 2.6 and the average parity was 1.2 pregnancies. Two patients delivered vaginally, three were aborted artificially, at 4, 4 and 8 months' gestation respectively. Family history of cancer of the stomach was present in one patient. Vomiting and nausea was encountered in 4 of them, and epigastric pain, in 4, abdominal mass, in 2, and hematoemesis, in 1.

The time from symptoms to diagnosis ranged from 2 days to twelve months with the average of 3.4 months. Two of them had sudden onset of abdominal pain caused by obstruction of the colon, and hematoemesis, respectively.

The diagnosis was made in 3 cases using upper GI series, 2 cases by endoscopy with biopsies, one, operatively.

The tumors of the stomach were located in one antrum and cardia respectively, the remaining being all the parts of the stomach. Glossy, Borrmann's type 3 and 4 were 2 cases respectively, one of them was the superficial spreading type (IIc).

Histologically, 4 of them were poorly differentiated adenocarcinoma, one, signet ring cell carcinoma. Treatment was primary surgical intervention, and two of them underwent total gastrectomy, one proximal resection of the stomach in early gastric cancer. Exploratory laparotomy and gastrojejunostomy were performed respectively in the remaining patients.

One of them was alive and well three years after operation. Four patients died in 38 days, 4 months and 7 months after operation from carcinomatous peritonitis.

Table 1. Cases of Cancer of the Stomach with Pregnancy

No.	1	2	3	4	5
Age	29	28	25	29	35
Family history	no	stomach ca.	no	no	no
Gravity	3	1	4	2	3
Parity	0	0	1	2	3
Abortion	3	1	3	0	0
Presenting symptoms	nausea abdom. mass	nausea vomiting abdom. pain	nausea epigastralgia	hematoemesis epigastral.	vomiting abdom. pain
Duration of complaints	3 mon.	12 mon.	2 mon.	2 days	1 day
Time of diagnosis	during preg.	post par.	during preg.	post par.	post par.
Diagnostic methods	X-P	X-P	X-P	endoscopy	operation
Obstetrial treatment	abortion (4mon.)	abortion (4mon.)	endoscopy abortion (8mon.)	—	—
Location of stomach cancer	corpus antrum	corpus antrum	all	cardia	all
Macroscopic finding	Borr. 3	Borr. 3	Borr. 4	IIC	Borr. 4
TNM classification	T ₄ N ₂ M ₁	T ₄ N ₂ M ₀	T ₄ N ₃ M ₁	T ₁ N ₀ M ₀	T ₄ N ₃ M ₁
Histologic finding	por. diff. ad-ca	∕	∕	signet cell	por. diff. ad-ca
Acidity of gastric juice	—	10mEq/L	—	—	—
Surgical procedure	gastro- jejunost.	total gastr.	expl. lapa.	total gastr.	proximal gaatrectomy
Survival from diagnosis	38 days	7 mon.	68 days	39 mon well alive	4 mon.

Table 2. Laboratory data and Presenting symptoms

	1	2	3	4	5
RBC	156×10 ⁴	320×10 ⁴	261×10 ⁴	418×10 ⁴	434×10 ⁴
Hb	30%	60%	7.2g/dl	8.1g/dl	11.0g/dl
Serum protein	5.5g/dl	7.2g/dl	5.9g/dl	5.5g/dl	6.4g/dl
Occult blood(stool)	(+)	(+)	(+)	(##)	—
Pretibial edema	(+)	(-)	(+)	(-)	(-)
Weight loss	(##)	(+)	(+)	(-)	(-)
Palpable mass	childhead	fist	resistense	no	no

DISCUSSION

Gastric carcinoma occurring in a young woman is very unusual. In 1961, BESTON and GOLDEN,¹⁾ reported 85 cases of cancer associated with pregnancy. The most frequent carcinoma is 20 cases each of carcinoma of the cervix and the breast, followed by 7 cases of thyroid cancer, 5 cases of colorectal cancer 5, but no gastric cancer.

YAMAGATA and UZUKA⁵⁾ observed that 15,486 women after delivery were associated with gastric cancer in 0.026%. In their studies, five of 469 female patients underwent surgical treatment for stomach cancer associated with pregnancy, while in 99 patients aged younger than 44 years, the incidence showed slightly high in 3.03%.

Owing to the sporadic occurrence of malignant disease and pregnancy, it is difficult for one to have clear concept of how to treat this condition.

Forty-four cases of cancer of the stomach with pregnancy from the 1916 to 1974 in Japan are found in literature.

In this report, a total of 44 cases of this disease have been reviewed and we wish to discuss the surgical treatment of malignancies.

The age was mentioned in 43 cases excluding one patient, and it ranged from 19 to 43 years, with the average age of 29.8 years. At the greatest fraction of 24 patients or 55.8% stood at the range of 25 to 29 years in the cases reviewed here.

In 1923, GOLOB⁹⁾ reported a 1-2% incidence of gastric carcinoma in patients under 30 years. In 1963, STOCK¹⁰⁾ summarized nine cases of gastric carcinoma occurring in patients aged 26-31, and all were initially diagnosed as peptic ulcer disease and a delay in correct diagnosis led to a poor prognosis in most of the cases. A majority of these cases have occurred in females, which is in agreement with the authors in that the incidence of gastric carcinoma in young people is at least equal to, or even more frequent, in women than in men.¹⁰⁾

The symptoms of gastric cancer were epigastric pain, anorexia, vomiting and weight loss. Particularly, abdominal pain has been reported as a first common symptom and observed in as many as 85% of patients by the time when the diagnosis of carcinoma of the stomach was made. In pregnancy, nausea and vomiting is encountered in 25% to 80% of pregnant woman. It may occur at different times throughout the day, but more commonly in the morning, and rarely the ability to eat is disturbed and weight loss is rare.¹³⁾ It usually begins at six weeks' gestation and may last up to 16 to 20 weeks' gestation.

Hyperemesis gravidarum is uncommon during the third trimester of pregnancy.

Peptic ulcer disease is also uncommon during pregnancy¹⁴⁾, probably owing to a placental histaminase known to peak at 24th to 29th week of gestation¹⁵⁾. In these collected series, the most common symptom was nausea and vomiting which occurred in 68.2%, followed by abdominal pain by 45.5%, palpable mass of abdomen, by 18.2%, weight loss and anorexia by 11.4%, respectively, and hematoemesis or melena by 11.3%.

Nausea with vomiting developed in the highest incidence of 83.3% in the first half of pregnancy, 60% in the latter half, but none did not complain in post partum. Abdominal pain in the first half of pregnancy and post partum, and weight loss with abdominal pain in post partum, are common symptoms. Therefore there is a high association of gastric cancer with pregnancy with these symptoms. The time from the appearance of symptoms to diagnosis ranged from four days to eleven months with the average of 3.5 months in the collected series which was just the same with our series of 3.4 months. The diagnosis can usually be made using barium contrast studies. With the combined use of gastroduodenoscopy, early small gastric cancers still confined to the gastric mucosa are detected as described in case 2, but 43.2% of them were diagnosed during pregnancy and post partum, respectively and 13.6% was found at autopsies. The diagnosis of cancer in these patients was initially delayed for the reason that the symptoms such as vomiting and abdominal pain were felt to be pregnancy related. In our series, the grossly type of cancer of the stomach using Borrmann's classification was type 3 and 4 in two cases respectively and early gastric cancer (superficial spreading) in one.

Tumors in 2 cases of Borrmann type 4 involved all parts of the stomach, and those of type 3 located from the body to the antrum, and in the rest one a depressed lesion was found on the lesser curvature in the cardiac area in one patient.

Preoperative acid study was performed in only one case. The value of free acid after stimulation using histamine showed hypoacidity of 10mEq/L. It has not been definitely established that pregnancy allows malignant conditions to spread more easily, but depressed maternal cell mediated immunity, especially in the last half of pregnancy, could be responsible for the increased mortality reported in pregnant women.⁶⁾

Clinically, PETERS⁷⁾ reported an 11% of five-year survival in women with breast carcinoma occurring in the last half of pregnancy, compared with 48% survival in women with breast carcinoma occurring in the first half of pregnancy, puerperium, or in non pregnant women. PURTILO⁸⁾ also showed that there was significant reduction in the maternal lymphocyte response to phytohaemagglutinin in most pregnant women, and that pregnancy was responsible for the growth of cancer of the stomach.

If the diagnosis is made, the treatment is generally directed to the removal of tumor, however, treatment varies slightly with the location of the lesion and trimester of pregnancy concerned.

McLEAN *et al.*¹¹⁾ expressed that before the 20th week of the pregnancy the treatment of the choice was immediate gastric resection without regard to pregnancy, and abortion should be performed first, followed by extensive operation. If pregnancy was advanced to 27 weeks, treatment would depend upon the stage of the disease, i. e., whether it was resectable (curable) or inoperable (advanced). When the cancer of the stomach is evidently advanced, it has been the policy to delay treatment until the 30th week of pregnancy and at that time a caesarean section and total abdominal hysterectomy should be followed with the appropriate palliative therapy. During the third trimester at or near term, medical induction of vaginal delivery is followed by the gastrectomy with regional lymphadenectomy within approximate time by 2 weeks. Vaginal delivery is to be preferred unless there is an obstetrical contraindication.

SIMS *et al.*¹⁶⁾ reported that a paraplegic young pregnant woman (30 weeks in gestation) presenting with gastric outlet obstruction following gastric bleeding, successfully underwent caesarean section and gastrectomy at the same time. After administration with two additional weeks of intensive intravenous hyperalimentation probably greatly reduced the operation risk for both the mother and the baby without significantly worsening of the long-term prognosis of the patients. They stressed that though the use of TPN in the obstetrical service is still rare, the need might arise in such pregnant patients with the problem of cancer.

There is general agreement that such complications as obstruction, perforation, severe hemorrhage are indications for immediate surgical intervention.¹¹⁾¹²⁾

In our collected series, though 34% delivered vaginally, on obstetrical treatment rather than surgical treatment for stomach cancer, artificial abortion was performed in 45.5% and caesarean section in 6.8%. As to surgical procedures for cancer, gastrectomy with adjunctive chemotherapy was primarily preferred. In our five cases, curative operation was performed on only one patient who had sudden onset of hemorrhage. In the remaining four cases, exploratory laparotomy with biopsy, gastrojejunostomy, proximal gastrectomy and total gastrectomy were palliatively done on each case. There was no operative death in these series. Histological findings showed poorly differentiated adenocarcinoma in 4 cases and signet ring cell carcinoma in one. None of the patients treated with noncurative operation remained alive more than 7 months, but all of four cases died of cancer, especially of cancerous peritonitis, with a median survival of 110 days from

diagnosis, which seems to be slightly lower than those without pregnancy, while the remaining one patient with early gastric cancer has been alive and well up to the present.

We conclude that pregnancy bears little relationship to survival except for the delay in diagnosis of cancer.

SUMMARY

Five patients in whom adenocarcinoma of the stomach associated with pregnancy has been evaluated. The age ranged from 25 to 35 years with a mean age of 29.5 years. In four patients the carcinoma was diagnosed during pregnancy, and one was diagnosed after delivery. Symptoms reported in the four patients included abdominal pain in 4, nausea and vomiting in 4, abdominal mass in 2, and hematoemesis in 2. The time from symptom to diagnosis was from 2 days to twelve months with the average of 3.4 months. Two of them had sudden onset of abdominal pain caused by obstruction of the colon at the splenic flexure, and hematemesis respectively. Two patients delivered vaginally, two were aborted artificially. Treatment was surgical intervention, and two of them underwent total gastrectomy, one proximal resection of the stomach in early gastric cancer. Exploratory laparotomy and gastrojejunostomy were performed respectively in the remaining patients. All except one patient whose carcinoma was limited in the submucosa, presented with more advanced disease being perigastric node involved. Macroscopically, there were two Borrmann's type 3, two type 4, and one early gastric cancer type IIc. Histologically, 4 of them were poorly differentiated adenocarcinoma, one signet ring cell carcinoma. Though four patients died from carcinoma within seven months after operation, one patient was alive and well with no evidence of recurrence 36 months after operation.

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