

Reminder of important clinical lesson

Malignant gastric lymphoma with spontaneous perforation

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Correspondence to Dr Satoko Shimada, stomiya@juntendo.ac.jp**Summary**

Malignant gastric lymphoma, accounting only for 1% of primary gastric carcinoma, is usually a diffuse large B-cell lymphoma. Toyota *et al* reported that 37% of gastric perforations involved malignancy, generally gastric carcinoma. Fukuda *et al* found that less than 5% of malignant gastric lymphomas perforate. While it is relatively well known that perforations often take place during chemotherapy, they are rare in patients not receiving chemotherapy. To our knowledge, spontaneous perforation is rare in gastric malignant lymphoma, having been reported in the Japanese literature only 26 times, including this case, in the last 25 years.

BACKGROUND

Today, the standard treatment for aggressive gastric lymphoma has shifted from surgery to chemotherapy combined with rituximab; that is, CHOP-R.¹ There is as yet no established treatment strategy for gastric malignant lymphoma.² Its merits emphasise that outcomes of malignant gastric lymphoma with spontaneous perforation was poor (less than 2 years) compared to those without perforation.³ There were two reports in 1983 and 1993 mentioning the frequency of occurrence of spontaneous perforation having been 4.0% and 4.2%, respectively.^{4 5} However, Law *et al*⁶ did not find any spontaneous perforations in their 61 cases of patients with malignant gastric lymphoma. Patients in the Western country reached their peak of vulnerability to spontaneous perforation in their 60s; however, the incidence seen at younger ages, mean 56 years old in Japan. It was worldwide that men were more vulnerable to it than that of women. It was only our case that patient was ready for her scheduled operation which was 2 days prior, when the perforation occurred. Therefore, the choice of treatment including surgery should be carefully deliberated.

CASE PRESENTATION

An 85-year-old woman, whose medical, social and family histories were unremarkable, presented with anorexia and weight loss (a 6 kg decrease in the preceding 6 months). The patient also began to suffer from a lower back pain around on 25 March 2008. She consulted a neighbourhood doctor on 27 March.

INVESTIGATIONS

A subsequent endoscopic investigation identified a small number of ulcerations at the pyloric antrum of the stomach and pyloric stenosis. She was thus hospitalised, fasted and treated with fluids and proton pump inhibitors. Although her condition improved, endoscopic biopsy revealed that she had diffuse large B-cell lymphoma (DLBCL). She was discharged from the hospital in preparation of her treatment.

Status on admission in our hospital (3 June 2008): height 147 cm, weight 37 kg, temperature 36.6°C, blood

pressure 124/68 mm Hg. She was able to eat a small amount of food. There was a firm, immobile, clearly bounded and egg-sized lump at the left lower abdomen.

Lab data below showed that she had anaemia, increased lactate dehydrogenase (LDH) and interleukin (IL)-2 receptor; leucocytes 3990/ μ l, haemoglobin (Hb) 7.5 g/dl, platelets 44.1 \times 10/ μ l, C reactive protein 0.37 mg/dl, LDH 511 IU/l, IL-2 receptor 965 U/ml.

DIFFERENTIAL DIAGNOSIS

Gastric mucosa-associated lymphoid tissue lymphoma, Burkitt lymphoma, Hodgkin's lymphoma, peptic ulcer, gastric carcinoma, small lymphocytic lymphoma, mantle cell lymphoma, follicular lymphoma, GIST and melanoma.

TREATMENT

She was informed of her treatment choices, namely, chemotherapy plus radiotherapy, chemotherapy plus rituximab or surgery alone. She visited the gastroenterological outpatient department of our hospital for a second opinion on 22 April. Chemotherapy plus rituximab was recommended. However, she returned to our clinic on 20 May for yet another opinion. She was subsequently admitted to our ward on 3 June, scheduled to undergo surgery on 9 June. A central venous line was placed on 5 June. She was anaemic (Hb 7.5 g/dl), so she received 2 units of concentrated red blood cells over the next 2 days.

OUTCOME AND FOLLOW-UP

On 7 June, she complained of abdominal pain and was awake until 5:00 at the nurse station owing to anxiety and sleeplessness. Her temperature rose to 38.6°C. Emergency CT showed intraperitoneal free air under the diaphragm bilaterally, under the parietal peritoneum and within the portal hepatis, and a large amount of ascites. Malignant gastric lymphoma with spontaneous perforation and pancreatitis was diagnosed. The following emergency operations were performed: total gastrectomy, cholecystectomy and intraperitoneal drainage (figure 1). Upon incision of the abdomen, purulent ascites was observed. The entire stomach was sclerotic, with a 30 mm perforation on the

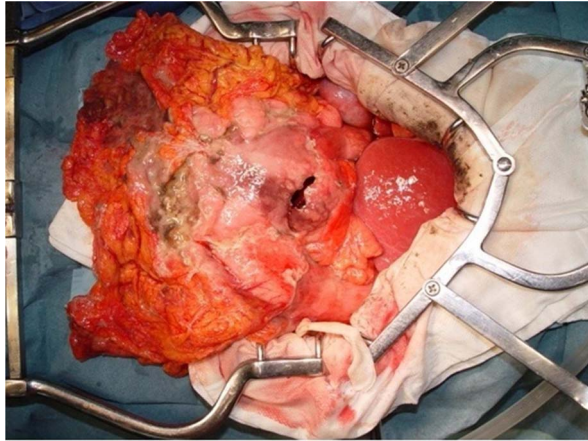


Figure 1 The entire stomach, with a 30 mm perforation on the large ulcerated tumour of the anterior pyloric antrum, is shown.

large ulcerated tumour of the anterior pyloric antrum. The ulcerated tumours measuring 65×60 mm and 90×85 mm were located at the anterior and posterior pyloric antrum, respectively (figure 2). Lymph nodes around the stomach were elastic and enlarged.

Pathological results reported ulcerative type with focal perforations, infiltrating the serosa. H&E staining showed diffuse, B-cell type and large-cell lymphoma. Immunohistochemical staining showed the tumour to be CD20 and CD79a positive, but CD3 and cyclin D1 negative (figure 3). The number of metastatic lymph nodes was 31/54. Dissemination to the major omentum was confirmed. The Lugano classification was considered to be Stage II1.

She recovered from the operation uneventfully and was discharged from the hospital 25 days postoperatively. She refused to undergo adjuvant chemotherapy and ascites recurred 4.5 months after surgery. She again refused any treatment then. She only began to take an opioid as a palliative care 6 months after surgery. The patient died 6.5 months after surgery.

DISCUSSION

Tanaka *et al* reported on 24 cases of malignant lymphoma with spontaneous perforation. Their 24 cases plus our

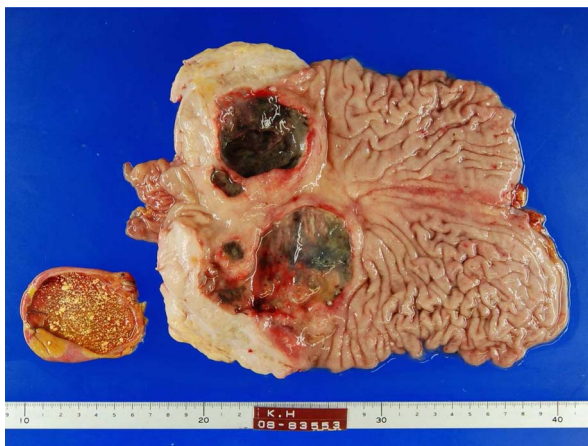


Figure 2 The gallbladder, ulcerated tumours measuring 65×60 mm and 90×85 mm located at the anterior and posterior of pyloric antrum, respectively, are shown.

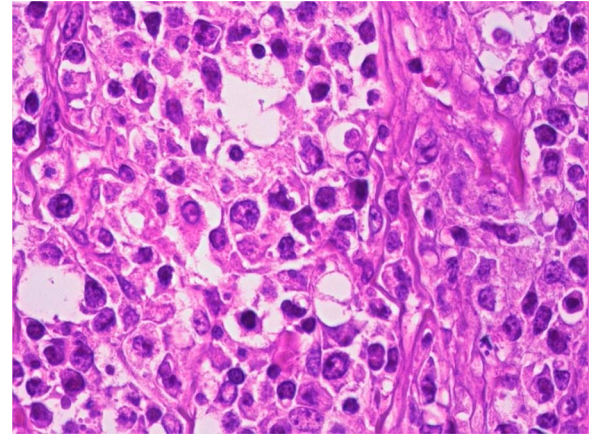


Figure 3 Pathological investigation: H&E staining showed diffuse, B-cell type, large-cell lymphoma. Magnification: ×40.

present case and an additional case reported in the meantime are presented in table 1. Perforation occurred in the body of the stomach in 15 cases and in the pylorus in 13 cases. Tumour sizes ranged from 15 to 250 mm, mean 67.6 mm. There were eight cases of excavated type and six of ulcerative type according to Sano's classification,⁷ suggesting tumours with ulceration to be common in perforation cases. Pathologically, diffuse large cell lymphoma was seen in 12 cases. According to Mitsunaga, pathology of malignant lymphoma often exists in conjunction with other tumour types. Large, ulcerative-type tumours are reportedly more likely to perforate.⁸

Tanaka *et al* also noted that pretreatment diagnosis is rare, occurring in only 6 of 24 cases. In the usual course of events, as soon as the diagnosis is made, treatment starts. It is widely known that perforation occasionally occurs in patients receiving chemotherapy. In contrast, spontaneous perforation of malignant gastric lymphoma is rare. The present patient was 85 years old and refused chemotherapy. However, the main tumour was 90 mm in size, raising the possibility of perforation regardless of whether chemotherapy was being administered.

Today, the standard treatment for aggressive gastric lymphoma has shifted from surgery to chemotherapy combined with rituximab; that is, CHOP-R. Aviles *et al* reported the 10-year survival rate of 589 patients with early stage primary gastric DLBCL, according to choice of treatment. The patients were divided into four treatment groups: surgery, surgery plus radiation, surgery plus chemotherapy and CHOP. The 10-year survival rates were 28%, 23%, 82% and 92%, respectively.⁹ It is somewhat surprising that patients who chose chemotherapy alone achieved the best result. Nevertheless, a simple comparison of results between Japan and Western nations is problematic. This is partly due to differences in the standard of management of gastric carcinoma. Gastric carcinoma is common in Japan, where the surgical death rate is less than 2%, whereas in Western nations, the rate is substantially higher partly because of D2 gastrectomy not having become standard yet. Nakamura *et al* compared the survival rate of patients choosing surgery to those selecting chemotherapy or radiotherapy, and found differences did not reach statistical significance. There is as

Table 1 Twenty-six reported cases of malignant gastric lymphoma with spontaneous perforation^{11–28}

	Age	Tumour size	Size of perforation	Outcome	Sex	Location	Sano's class	LSG class	Operation	Adjuvant chemotherapy
1985 Kanzaki	42	3.2×3.2 cm	0.5 cm	>18	M	M		Burkitt		VEMP
1987 Oda	43		6 mm	> 2	M	L		Non-Hodgkin's	Subtotal	
1989 Takeda	85							DLBC		
1990 Yamaguchi	57								Subtotal	Chemotherapy
1992 Ando	22	1.5×1.4 cm		>30	M	M		DMBC	Subtotal	CHO(P)
1992 Yanagi	65	18.5×10 cm	2×2.5 cm, 4.5×2.5 cm	>10	M	L		DLBC		CHOP
1994 Shinjyo	14		9×4 mm		F	L			Subtotal	Chemotherapy
1996 Uni	45		5 mm		F	M		DMBC	Subtotal	VEPA
1996 Mori	87				F	L		DMBC	Subtotal	
1997 Ono	43	25 cm	2 cm	>3	F	L		DLBC	Closure	CHOP
1997 Shiomi	71	15×13 cm	2 cm	7	M	M	Excavated	DLBC	Total	THP-COP
1997 Banyu	43	25 cm	2 cm		M	L		DLBC	Closure	CHOP
1997 Fukuda	45	8×9 cm	7 mm	>25	M	M		DMBC	Subtotal	VEPA
1998 Yanagisawa	72	7.5×6.0 cm		>15	M	M		DLBC	Subtotal	CHOP
1998 Yanagisawa	26	6.5×4.5		>14	M	M		DLBC	Subtotal	CHOP
1998 Housui	58		8 mm		F			DLBC	Total	Chemotherapy
1999 Miyamoto	46	3.0×2.8 cm	6 mm	>62	M	L		MALT		
2000 Yabuki	53	8×6 cm	1.0×0.5 cm	>28	M	M		DMBC	Subtotal	CHOP
2001 Hoshino	59	Nk	3 mm		F	M~L		DMBC	Total	Chemotherapy
2002 Yokoyama	64		10 mm		M	M		DLBC	Subtotal	CHOP
2005 Mori	65	3×3 cm	5 mm	2	F	M		DMBC	Total	CHOP
2006 Tanaka	65	10 cm							Total	
2007 Tanaka	84	9×8 cm	1 cm	>13	F	M	Excavated	DLBC	Subtotal	Chemotherapy
2007 Hirai	70			>3		L~M		DLBC	Total	Chemotherapy
2008 Matsunaga	73	4.5×2.0 cm	3 cm	>3	M	M		DLBC	Total	R-CHOP
2008 Our case	85	6.5×6 cm, 9×8.5 cm	30 mm	6	F	L	Excavated	DLBC	Total	

CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; DLBC, diffuse large B-cell; DMBC, diffuse medium B-cell; LSG, lymphoma study group classification; MALT, mucosa associated lymphoid tissue; THP-COP, pirarubicin, cyclophosphamide, vincristine, prednisone; VEMP, etoposide, cyclophosphamide, mitoxantrone, prednisone; VEPA, vincristine, cyclophosphamide, prednisolone, adriamycin.

yet no established treatment strategy for gastric malignant lymphoma. Its merits emphasize that outcomes of malignant gastric lymphoma with spontaneous perforation was poor (less than 2 years) compared to those without perforation.³ It seems that number of metastases to lymph nodes at the emergency surgery may predict the outcomes.^{2, 3, 10} The patient had spontaneous perforation 2 days prior to her scheduled operation in our case; the choice of treatment including surgery should be carefully deliberated.

Learning points

- ▶ Tumours with ulceration to be common in perforation cases.
- ▶ Large, ulcerative-type tumours are reportedly more likely to perforate.
- ▶ Outcomes of malignant gastric lymphoma with spontaneous perforation were poor (less than 2 years) compared to those without perforation.
- ▶ The choice of treatment including surgery should be carefully deliberated.

Competing interests None.

Patient consent Obtained.

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