



## Case report

# Successful treatment of refractory hepatic lymphorrhea after gastrectomy for early gastric cancer, using surgical ligation and subsequent OK-432 (Picibanil) sclerotherapy

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### Abstract

**Postoperative hepatic lymphorrhea is a very rare complication after abdominal surgery. Hepatic lymphorrhea, not containing chyle, involves an internal lymph fistula between the lymphatic channels toward the cisterna chyli and the peritoneal cavity. Over the past 20 years, 17 cases have been reported in Japan. Here, we report a further case, of a patient with successfully treated intractable hepatic lymphorrhea following gastrectomy for early gastric cancer. We review 18 cases, including the present case, with respect to the management of postoperative lymphorrhea refractory to conventional medical treatment.**

**Key words** Hepatic lymphorrhea · Gastrectomy · Surgical ligation · OK-432 (Picibanil) sclerotherapy

### Introduction

Chylous ascites following abdominal surgery is a rare complication [1], but it has been reported after various surgical procedures, including abdominal aortic surgery [2], retroperitoneal lymph node dissection [3], esophagectomy [4,5], pancreaticoduodenectomy [6], and gastrectomy [7]. Although there are many reports in the English-language literature describing the diagnosis, causes, and treatment of chylous ascites [8,9], little is known about hepatic lymphorrhea, not containing chyle, following abdominal surgery. To our knowledge, there has not been any report of hepatic lymphorrhea following abdominal surgery in the English-language literature. However, over the past 20 years, 17 cases have been reported in Japan [10–22].

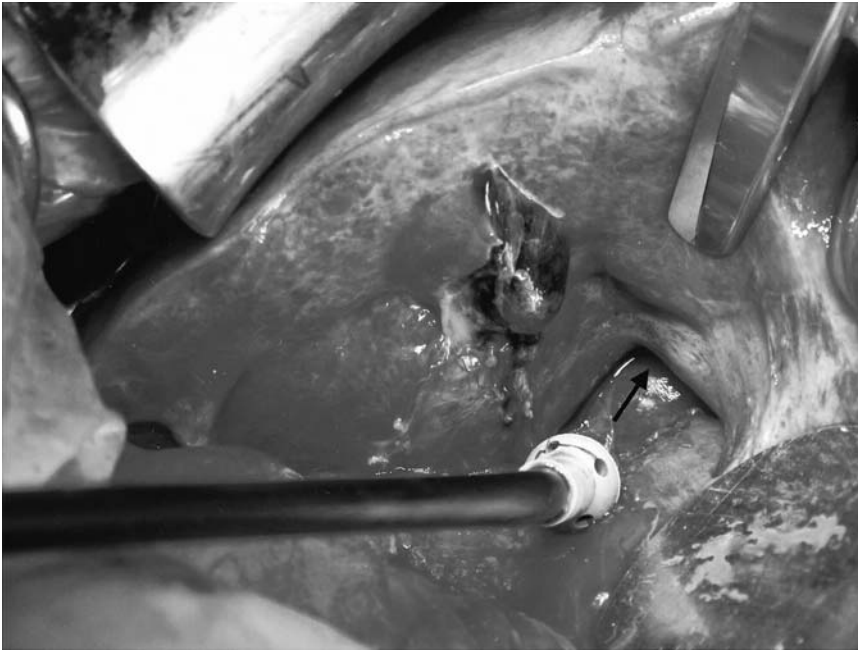
Hepatic lymphorrhea, not containing chyle, involves an internal lymph fistula between the lymphatic channels toward the cisterna chyli and the peritoneal cavity,

resulting from probable lymphatic duct injuries during lymph node dissection for a gastric malignancy. Gastrectomy with lymph node dissection is performed acceptably in most Japanese institutions; however, lymphorrhea is frequently encountered after gastric surgery, although the postoperative lymphatic leakage generally stops spontaneously without treatment. There is, though, little information about a standard treatment for postoperative lymphorrhea, which is highly refractory to any conventional medical treatments such as cessation of oral intake, total parenteral nutrition (TPN) management, diuretic therapy, intravenous reinfusion of ascites, or therapeutic paracentesis.

Here, we present a case of intractable lymphorrhea in a patient who was successfully treated with surgical lymph vessel ligation, and subsequent OK-432 (Picibanil; Chugai Pharmaceutical, Tokyo, Japan) sclerotherapy. Additionally, we review the present case and the 17 previous reports noted above, and discuss management options.

### Case report

A 66-year-old man was referred to our department for medical treatment for refractory ascites. One year before admission, he had undergone, in our department, a total gastrectomy with lymphadenectomy for early gastric cancer. Because preoperative study showed that the tumor had probably invaded to the submucosal layer, we performed extended lymph node dissection, including the regional lymph nodes and additional lymph nodes, along the common hepatic artery. His postoperative course was uneventful. The final, pathological staging was T1 (SM), N0, H0, P0, M0, stage IA according to the *Japanese classification of gastric carcinoma*, second edition [23]. He had chronic B-type viral hepatitis, and was non-cirrhotic, but with normal liver function tests. There was no evidence of recurrence on the basis of



**Fig. 1.** A few minutes after the injection of patent blue violet solution into the liver bed, a dye-stained lymphatic duct (*arrow*) was easily identified

clinical observations, biological tests, and imaging studies done on an outpatient basis.

About 4 months after the curative surgery for gastric cancer, abdominal distension gradually developed. He was admitted to the Internal Medicine Department at our hospital for the assessment of abdominal distension and liver function. Bilateral pitting edema of the legs and massive ascites was noted. Laboratory tests and imaging studies indicated that the massive ascites may be responsible for postoperative lymphorrhea not associated with liver dysfunction due to the chronic B-type viral hepatitis. Finally, fluid analysis obtained from diagnostic paracentesis demonstrated that the ascitic fluid was clear-colored, and he was diagnosed with non-chylous lymphorrhea by biochemical tests of the fluid. Cytological examination of the fluid revealed no evidence of peritoneal cancer recurrence. Total parenteral nutrition (TPN), diuretic therapy, and therapeutic paracentesis were begun. Neither symptomatic relief nor a decrease in abdominal size was achieved despite these therapies being carried out over a 6-month period. Although lymphoscintigraphy did not show an obvious lymphatic leakage point, we decided to perform surgical intervention because the ascites was non-responsive to all the conservative therapies used.

Exploratory laparotomy was performed after medical treatment had been given for over 120 days. There was a large amount of clear ascitic fluid but no evidence of peritoneal recurrence of gastric cancer. To detect the lymphatic channels causing lymphorrhea, we used 2% patent blue violet dye (Wako Pure Chemical Industries, Osaka, Japan), a dye used for lymphatic mapping. Because the lymphorrhea would probably have been

caused by an injury to the lymphatic ducts during lymph node dissection, we injected this solution into the liver bed. The dye-stained lymphatic ducts were easily identified (Fig. 1) and successfully ligated. However, we could not achieve complete resolution of the lymph leak because other lymphatic leaks emerged posterior to the hepatoduodenal ligament. Therefore, fibrin glue was applied to treat minor lymphatic leakages.

The small amount of lymphatic outflow from the drain tube was postoperatively treated with an injection of OK-432 (Picibanil). Repeated sclerotherapeutic sessions (six times in total), using a total dose of 45 KE, led to the complete disappearance of the ascites within 67 days. No adverse effects were observed, except for a temporary mild fever and some slight abdominal pain. The patient has continued to do well, without hepatic lymphorrhea or cancer recurrence, 6 months after being discharged.

## Discussion

Intraabdominal lymphorrhea, without chylous ascites, occurring after abdominal surgery is a rare complication, resulting from an internal lymph fistula between the lymphatic channels toward the cisterna chyli and the peritoneal cavity. Although small lymph leaks are commonly seen during lymphadenectomy, they rarely cause lymphorrhea because of the abundance of collateral lymphatic channels in the abdominal cavity. In most cases, they remain clinically asymptomatic or unrecognized. Despite the large number of abdominal surgeries that have been performed, little is known about post-

**Table 1.** Characteristics of 18 patients with hepatic lymphorrhea after gastric surgery

Case no.	Author	Age/Sex (years)	Liver disease (medical history)	Diagnosis	Operation	Onset of lymphorrhea (postoperative days)
1	Miyagawa, 1983 <sup>a</sup>	65/M	HBsAg (+)	GC (advanced stage)	TG	1
2	Nakashima, 1985 [10]	58/M	None	GC (advanced stage)	DG	6
3	Nakano, 1987 <sup>a</sup>	49/M	None	GC (advanced stage)	TG	1
4	Kawata, 1989 [11]	52/M	Liver cirrhosis	GC (early stage)	DG	7
5	Umehara, 1989 [12]	59/M	None	GC (advanced stage)	TG	8
6	Kaneko, 1991 [13]	44/M	None	GC (early stage)	DG	35
7	Imai, 1992 [14]	34/M	Liver dysfunction	Gastric leiomyosarcoma	TG	6
8	Shimizu, 1992 [15]	62/M	Liver cirrhosis	GC (early stage)	DG	1
9	Ota, 1993 [16]	70/M	CH	GC (early stage)	DG	63
10	Mitsuno, 1993	42/M	CH	GC (early stage)	DG	5
11	Sasaki, 1994 [17]	54/M	Liver cirrhosis	GC (early stage)	DG	7
12	Kawahira, 1994 [18]	58/M	CH	GC (advanced stage)	DG	32
13	Matsumoto, 1995 [19]	44/M	CH	GC (advanced stage)	DG	3
14	Tada, 1996 [20]	79/M	CH	GC (early stage)	DG	1
15	Tada, 1996 [20]	57/M	CH	GC (early stage)	DG	1
16	Takahata, 1998 [21]	49/M	CH	GC (advanced stage)	DG	1
17	Yoshida, 2000 [22]	55/M	Liver cirrhosis	GC (advanced stage)	DG	60
18	Present report, 2002	66/M	CH	GC (early stage)	TG	120

None, no hepatic disease; CH, chronic hepatitis; GC, gastric cancer; TG, total gastrectomy; DG, distal gastrectomy

<sup>a</sup>Cited in reference 14

**Table 2.** Therapies for and clinical outcome of hepatic lymphorrhea

Case no.	Prior treatment (duration; days)	Treatment	Time to complete resolution (days) <sup>a</sup>
1	Medical treatment (183)	Surgical ligation	13
2	Medical treatment (30)	Surgical ligation + antibiotics + sclerotherapy	30
3	Medical treatment (47)	Surgical ligation	14
4	Medical treatment (101)	Surgical ligation + fibrin glue + sclerotherapy	37
5	Medical treatment (97)	Surgical ligation	28
6	Medical treatment (63)	Surgical ligation + PV shunt	30
7	Medical treatment, sclerotherapy, PV shunt (111)	Reoperation + antibiotics + sclerotherapy	7
8	Medical treatment, sclerotherapy, PV shunt (630)	Surgical ligation	30
9	Medical treatment (60)	Surgical ligation + fibrin glue	50
10	Medical treatment (105)	PV shunt	?
11	Medical treatment (60)	OK-432 sclerotherapy (50 KE, 4 times)	150
12	Medical treatment, PV shunt (238)	Surgical ligation + fibrin glue + OK-432 sclerotherapy	10
13	Medical treatment, surgical ligation, PV shunt (288)	Re-re-surgical ligation + fibrin glue	14
14	Medical treatment (34)	OK-432 sclerotherapy (75 KE, 6 times)	54
15	Medical treatment (25)	OK-432 sclerotherapy (25 KE, 3 times)	47
16	Medical treatment (44)	Surgical ligation + fibrin glue + OK-432 sclerotherapy	12
17	Medical treatment (120)	OK-432 sclerotherapy (20 KE, 2 times)	43
18	Medical treatment (180)	Surgical ligation + fibrin glue + OK-432 sclerotherapy	67

Medical treatment: total parenteral nutrition (TPN), diuretics, paracentesis, and/or reinfusion

PV, peritoneo-venous

<sup>a</sup>Duration from the beginning of treatment to complete disappearance of lymphorrhea

operative hepatic lymphorrhea. To our knowledge, there has not been any report of hepatic lymphorrhea following abdominal surgery in the English-language medical literature, although there are many reports

about chylous ascites after various abdominal surgeries [1–7]. To clarify the clinical features, we reviewed the 17 cases reported in the Japanese medical literature plus the present case (Tables 1 and 2).

**Table 3.** Comparison between treatments and variables, including clinical outcome

Variable	A. Surgical treatment ( <i>n</i> = 14)	B. Sclerotherapy alone ( <i>n</i> = 4)	<i>P</i> value <sup>a</sup>
1. Medical history			
Liver cirrhosis	2	2	
Chronic hepatitis	7	2	0.53
2. Gastric cancer			
Advanced stage	7	1	
Early stage	6	3	0.58
3. Operation			
Total gastrectomy	5	0	
Distal gastrectomy	9	4	0.28
4. Onset of postoperative lymphorrhea (postoperative days)	21 ± 34	18 ± 28	0.88
5. Duration of prior treatment (days)	156 ± 157	60 ± 43	0.25
6. Time to complete resolution (days)	23 ± 13	74 ± 51	<0.01

A, Direct surgical ligation was performed; if required, fibrin glue sprinkle, supportive sclerotherapy, and PV shunting were added

B, Paracenteses, followed by intraperitoneal OK-432 injection without any surgical treatment

Data values are given as means ± SD, or as numbers

<sup>a</sup>Fisher's exact test or Mann-Whitney U-test

The patients were 13 men and 5 women, ranging in age from 34 to 79 years (mean, 55 years). All patients were diagnosed as having a gastric malignancy, including gastric cancer (advanced stage, 8; early stage, 9) and gastric leiomyosarcoma (1), and they underwent either distal gastrectomy (13) or total gastrectomy (5). Thirteen (72%) had a medical history of liver disease: laboratory liver dysfunction (1), chronic hepatitis (8), and liver cirrhosis (4). The mean time from gastric surgery to the onset of lymphorrhea was 20 days (range, 1 to 120 days). After the diagnosis of postoperative lymphorrhea was established, all patients were treated conventionally by diet, TPN, diuretics, therapeutic paracentesis, and/or intravenous reinfusion of ascites. However, none of the patients responded to any of these conservative therapies after durations of treatments ranging from 25 to 630 days (mean, 134 days).

Although there was no significant association between the duration of medical treatment and the presence (or degree) of liver disease, these observations suggest that such intractable lymphorrhea may be caused not only by injury to the lymphatic ducts during lymph node dissection but also by increased lymph flow and lymph production secondary to chronic liver disease.

Table 2 shows that various types of therapies for refractory lymphorrhea have been used, and that the therapeutic strategies pursued have not been uniform. Kaas et al. [1] indicated that no relaparotomies for ligation of lymph fistula were necessary because complete resolution was achieved by conservative management or peritonea-venous (PV) shunt insertion. In contrast, Haukaas et al. [3] have reported that direct surgical closure is a valid treatment option in patients with persistent chylous fistula after retroperitoneal lymph node dissection.

After conventional medical treatment, various regimens were used to treat the intractable hepatic lymph-

orrhea (Table 2). These regimens were divided into two groups. In group A (surgical treatment), direct surgical ligation was performed, if required, and fibrin glue sprinkle, supportive sclerotherapy, and PV shunting were added. In group B (sclerotherapy alone), paracentesis was followed by an intraperitoneal OK-432 injection without any surgical treatment.

Most importantly, as shown in Table 3, the time to complete resolution in group A was significantly shorter than that in group B ( $P < 0.01$ ). The most effective therapy for intractable lymphorrhea appears to have been surgical ligation of lymph fistula with supportive sclerotherapy and/or fibrin glue sprinkle. Even if the preoperative imaging study does not show an obvious leakage point, surgical ligation should be performed, together with intraoperative injection of dye such as patent blue violet [24].

Peritoneo-venous shunting has become a less common technique recently, because of the high associated morbidity, such obstruction, vascular thrombosis, infections, sepsis, and disseminated intravascular coagulopathy (DIC) [8,9]. Table 2 also shows that almost all patients with a PV shunt insertion underwent additional surgery to treat subsequent complications. Although the insertion of a PV shunt is recommended as one of the management techniques for refractory chylous ascites [1,25], the results indicate that PV shunt insertion should be avoided if possible, because of the resulting longer duration of treatment.

In conclusion, hepatic lymphorrhea after gastrectomy with lymph node dissection was generally refractory to conventional medical treatment, and often occurred in patients with liver disease. The analysis of data reported in 18 cases suggests that early surgical exploration with direct ligation of leaking lymphatics may be the first choice of treatment in the management of intractable lymphorrhea and that the timing of surgical intervention may also be important. In the face of failing con-

ventional medical treatments for refractory lymphorrhea, a surgeon should try to perform direct ligation of any lymph leaks as soon as possible, before the patient's general condition deteriorates further.

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