Original Article

Management of high-output chylous ascites after D2-lymphadenectomy in patients with gastric cancer: a multi-center study

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Background: This study aimed to propose treatment strategies for high-output chylous ascites (CA) developed after gastric cancer surgery.

Methods: The data of patients with CA after gastric cancer surgery in three high volume Training and Research Hospitals between 2005 and 2015 were retrospectively evaluated.

Results: Nine patients out of 436 gastrectomies were detected with CA. The mean amount of daily fistula output was 939 mL. Treatment consisted of cessation of oral feeding, total parenteral nutrition (TPN), somatostatin analogs administration, clamping and/or removal of the drainage tube, diuretic administration and diet therapy with medium-chain triglycerides (MCTs) alone or in combination. The mean fistula closure time and length of hospital stay were 23 and 24 days respectively. Hemopneumothorax developed during right subclavian vein catheterisation for TPN implementation in one patient. There was no mortality.

Conclusions: Combined cessation of oral feeding and TPN are usually used for treatment of CA as first-line treatment. However, TPN is no harmless. Although our data are limited they do allow us to conclude that diet with MCT's may use for medical treatment of CA as first-line.

Keywords: Chylous ascites (CA); gastric cancer; lymphadenectomy (LA)

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Introduction

The lymphatic system was described by Asellius in 1627 and chylous ascites (CA) was first reported by Morton in 1691 (1,2). It is defined as the leakage of milk-like triglyceride-rich lymphatic fluid from lymphatic system to the peritoneal cavity (3). CA generally occurs as a result of disturbances of cisterna chyli, the thoracic duct, or their major tributaries (4-6). It may be seen after congenital defects of the lymphatic system, oncological abdominal surgery, abdominal aortic and vena cava surgery, nephrectomy, retroperitoneal lymphadenectomy (LA), blunt abdominal trauma, portacaval and mesocaval shunt procedures, bacterial peritonitis, pelvic irradiation, pelvic surgery, peritoneal dialysis, liver cirrhosis, abdominal tuberculosis, inflammatory disease, spinal surgery, or after a variety of other benign or malignant processes (1-3,7-11). In this study we aimed to put forward treatment strategies for high output CA with life threatening complications developed after D2-lymphadenectomy (D2-LA) performed for gastric cancer.

Methods

The data of patients with CA after gastric cancer surgery in three high-volume Training and Research Hospitals between 2005 and 2015were retrospectively evaluated. Gastric cancer surgery was performed by surgeons experienced in gastric cancer surgery and specifically trained in National Cancer Center (NCC) in Tokyo/Japan. Patients were analyzed for age, gender, tumor localization, surgery type, resected and metastatic lymph nodes number, day of lymphatic leakage (LL), daily fistula output, diagnosis of CA, tumor-node-metastasis (TNM) classification, choice of treatment, morbidity, mortality, day of fistula closure and hospital stay duration. Informed consent were provided in all patients.

Results

Nine out of 436 patients with gastrectomy were identified with CA (2.06%). Five of these were women and four were men. The mean age of patients was 59.5 (range, 31–73) years. Tumor localization was distal in four patients. Proximal and middle tumour locations were found in two patients and one patient had diffuse gastric cancer. Six and three patients underwent total gastrectomy (TG) and subtotal gastrectomy (STG) plus D2-LA respectively. One patient underwent additional patient mediastinal LA while another patient received additional splenectomy (SP) plus distal pancreas resection. Intraoperative lymphatic fluid leakage was seen in one patient and the lymphatic duct was sutured. The mean number of resected lymph node was 33.8 (range, 20–48) and the mean number of metastatic lymph nodes was 8.7 (range, 0–26). There was no lymph node metastasis in two patients. According to the TNM staging, five patients were Stage III (55.6%), two Stage II (22.2%) and two Stage I (22.2%). Only one patient (11.2%) had early gastric cancer. Interestingly this patient had attended the emergency department with only pyloric stenosis findings. Oral feeding was started postoperatively with the mean time of 3.9 (range, 2–5) days. The mean time of noticing postoperative LL was 5.9 days (range, 5–7). Suspicion of CA was based on the macroscopic appearance of the drainage fluid and was confirmed with biochemical tests. Mean daily fistula output was 939 (range, 600–1,500) cc. The treatment regimen either solely or combined included cessation of oral feeding and total parenteral nutrition (TPN), periferial parental nutrition (PPN), or Sandostatin analogs (Somatosan, CuraMED Pharma GmbH, Karlsruhe, Germany) administration, removal of the drainage tube, diuretic administration, clamping of drainage tube and diet treatment with medium-chain triglycerides (MCTs) including MCT oil (Ses Handels-Und Service GmbH, Köln, Germany), Basic-f (Numil, Istanbul, Turkey) and Fantomalt (Nutricia, the Netherlands). Meantime to fistula closure was 23 (range, 8–51) days. Mean length of hospital stay was 24 (range, 11–45) days. The detailed features of the patients are seen on *Table 1*. Hemopneumothorax occurred in one patient during right subclavian vein catheterization for TPN implementation and was treated with tube thoracostomy. In addition, grade I Clavien-Dindo surgical complication including wound infection was observed in patient who TPN administration. No mortality was occurred.

Statistical analysis

Only descriptive analysis was used because of limited of cases.

Discussion

CA is a rare condition and usually occurs as a complication of abdominal surgery. The incidence is stated as between 0.17–1.10% (12-14) while the level in our study was 2.06%. CA might cause permanent protein loss, nutrition impairment, metabolic complications, prolonged hospital stay, increased costs and life-threatening complications such as sepsis, severe dyspnea and death (6,15).

The lymphatic system is an important route through which protein and liquids pass from the intestinal lumen to vascular system. Another interesting point is, it also plays an important role in the absorption of fat and fat soluble vitamins (1,16). Under normal circumstances lymphatic fluid and interstitial fluid share the same concentration and osmotic pressure (16). Lymphatic fluid flows from the lymph nodes to prenodal collecting lymphatic vessels and then through postnodal lymphatic vessels respectively into lymphatic trunci, cisterna chyli and ends up in ductus thoracicus. This one way flow happens by means of smooth muscles and valves present in the collecting lymphatics (3).

CA might occur for a number of reasons. Crumley *et al*. (17) stated two criteria for postoperative CA in their study; one of them is the impairment of lymphatic circulation and resection during operation. The second is the increased pressure in lymphatics compared to the abdominal cavity and tissue pressure. Malignant invasion

Table 1 Patient and treatment characteristics

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Mean values
Age	72	73	48	73	62	73	49	31	55	59.5 (31.0–73.0)
Gender	E	K	K	E	K	K	K	E	E	E/K: 4/5
BMI	24	16	18	23	27	24	26	23	25	22.6 (16.0–27.0)
Albumin	Normal	Low	Normal	Normal	Low	Normal	Normal	Normal	Normal	–
Hgb	Normal	Normal	Normal	Normal	Low	Normal	Normal	Low	Normal	–
CRP	Normal	Normal	Normal	Normal	High	Normal	Normal	Normal	Normal	–
Localization	1/3 upper	1/3 distal	1/3 distal	1/3 middle	1/3 upper	Linitis plastica	1/3 distal	1/3 distal	1/3 middle	–
Surgery type	TG + D2-LA + M-LA	STG + D2-LA	STG + D2-LA	TG + D2-LA + SP + DP	TG + D2-LA	TG + D2-LA	STG + D2-LA	TG + D2-LA	TG + D2-LA	–
Peroperatuar LL	No	No	Yes	No	No	No	No	No	No	–
Resected lymph node No.	40	24	30	31	42	27	20	42	48	33.8 (20.0–48.0)
Metastatic lymph node No.	2	0	0	9	2	9	9	21	26	8.7 (0–26.0)
Vascular invasion	No	No	No	Yes	No	Yes	No	Yes	Yes	–
Lymphatic invasion	No	No	No	Yes	No	Yes	No	Yes	Yes	–
Neural invasion	No	No	No	Yes	Yes	Yes	No	Yes	No	–
T stage	T3	T1b	T2	T4a	T3	T4b	T3	T4a	T4a	–
N stage	N1	N0	N0	N3	N1	N3	N3	N3	N3	–
TNM stage	IIB	IA	IB	IIIC	IIB	IIIC	IIIB	IIIC	IIIC	–
Start days of oral feeding	5	4	4	2	4	5	5	3	3	3.9 (2.0–5.0)
Start time of LL (day)	7	6	5	7	5	6	7	5	5	5.9 (5.0–7.0)
Flow of LL (cc/day)	600	1,000	1,500	1,000	900	800	700	750	1,200	939 [600–1,500]
Cessation time of oral feeding (day)	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	–
TPN	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	–
PPN	No	No	Yes	No	No	Yes	No	No	No	–
Sandostatin administration	No	No	Yes	No	Yes	No	No	No	Yes	–
Removal of drainage tube	Yes	Yes	Yes	No	No	No	No	No	No	–
Removal of drainage tube + diuretic administration	Yes	No	Yes	No	No	No	No	No	Yes	–
Clamping of drainage tube + diuretic administration	No	No	Yes	No	No	No	No	No	Yes	–
Diet with MCTs	No	No	Yes	No	Yes	No	No	No	Yes	–
Fistula closure duration (day)	15	9	51	20	22	22	15	8	45	23 [8–51]
Hospital stay duration (day)	15	11	40	20	22	30	20	11	45	24 [11–45]

BMI, body mass index; TG, total gastrectomy; LA, lymphadenectomy; D2-LA, D2-lymphadenectomy; M-LA, mediastinal lymphadenectomy; STG, subtotal gastrectomy; SP, splenectomy; DP, distaly pancreatectomy; LL, lymphatic leakage; TNM, tumor-node-metastasis; TPN, total parental nutrition; PPN, periferial parental nutrition; MCTs, medium-chain triglycerides.

can causes deterioration and fibrosis of lymphatic system and consequently due to the obstruction occurred in distal segments, lymphatic fluid may extravasate and CA may occur (12).

Clinical presentation of CA includes nonspecific findings such as abdominal distension, indigestion, nausea and vomiting (18,19). An important clinical observation is milk-like fluid in the drainage tube or paracentesis (20). In our series, perioperative high-volume LL was observed in one patient and although the lymphatic ducts were primarily ligated, CA still developed in the postoperative period. A diagnosis was made with the postoperative appearance of a milky appearance lymphatic fluid from the drainage tubes in all other patients.

Griniatsos *et al*. (16) suggested criteria for CA diagnosis which included aspiration and drainage tube fluids should not be hemorrhagic, should not contain high levels of amylase and bilirubin, but should contain high triglyceride and be milky or creamy in appearances. Our diagnosis was based on the suspicion of the presence of milky/creamy drainage fluid and this was confirmed with biochemical tests.

Kuboki *et al*. (21) reported in their study that dissection of para-aortic area, retroperitoneal invasion and early enteral feeding are independent risk factors for CA. In another study, the number of resected lymph nodes and concomitant vascular resection were presented as independent risk factors for postoperative pancreatic surgery (22). All patients in our series underwent D2-LA according to Japanese gastric cancer treatment guidelines (23). The average number of resected lymph nodes was 33.8. With regard to the extent of retroperitoneal dissection and the number of resected lymph nodes, the results correlate with the literature.

Many patients had high T, N and TNM stages in our series. Also 55.5% of the patients were over the age of 60. The presence and absence of lymphatic, vascular and neural invasion were histopathologically similar. There was no important difference in preoperative hemoglobin and albumin values. In terms of body mass index (BMI), two patients were thin. Most patients (6/9) underwent TG.

First-line treatment of CA usually includes cessation of oral feeding plus TPN (24-26). Diuretic administration, solely or combined with other treatments, is another treatment approach (27). Another treatment modality is the implementation of a diet solely with MCTs (with 6–12 carbon). MCTs might decrease lymphatic flow and provide regular nutrition because it is directly transported to intestinal cells (3). Cárdenas *et al*. recommended a diet with MCTs as the first-line medical care (1). Except for MCTs in one patient, all of the treatment modalities implemented in our study failed. Moreover during TPN implementation the patient encountered life threatening catheterisation complications and was subsequently treated with diet containing MCTs.

Some authors have presented somatostatin or octreotide administration as an effective treatment but the detailed mechanism of this treatment is not yet understood. Somatostatin might reduce LL within 24–72 hours (2,28-32).

In patients where the conservative treatment remains ineffective, surgical intervention is advised (16,25). Sixty seven percent of patients with CA were cured with conservative treatment, while 33% required surgical intervention in the study of Aalami *et al*. (25). Sometimes a major leakage area cannot be observed even during surgical exploration (27).

In our study, cessation of oral feeding, TPN, PPN, sandostatin analogs administration, removal of the drainage tube (drainage tube was removed while fistula flow between 500–1,000 cc per day), clamping the drainage tube (drainage tube was clamped while fistula flow between 1,000–1,500 cc per day), diuretic administration and diet treatment with MCTs were applied solely or in combination with other treatments as treatment. Removal of the drainage tube was successful in one patient. In this patient stopping of LL was attributed to the increased intra-abdominal pressure from accumulating lymphatic fluid due to the removal of drainage tube and subsequent peritoneal absorption. In another patient diuretic administration in addition to the removal of drainage tube was successful. Oral feeding was not stopped in both patients.

In another patient (case No. 3) clamping the drainage tube was applied. However this failed. TPN was planned for this patient but hemopneumothorax occurred during right subclavian vein catheterization. The treatment continued with cessation of oral feeding, PPN, sandostatin analogs and diuretic administration, clamping of the drainage tube followed by the removal of drainage tube. Although CA regressed, it resumed 2 days after oral feeding and the patient was finally successfully treated with a diet including protein, carbohydrate and MCTs.

Three other patients were treated by cessation of oral feeding and TPN, two patients were treated by cessation of oral feeding in addition to TPN and diet with MCTs and the last one patient was cured by cessation of oral feeding, TPN and sandostatin analogs administration. None of the patients required surgical exploration.

This study has some shortcomings. The most important is limited number of cases. However, the studies including high volume CA are limited in the literature. Another; satisfactory statistical analysis couldn't done accordingly limited number of cases.

Conclusions

All our results suggest that CA is an important complication after D2-LA although it is rarely seen. Surgeons should be aware of abnormalities in lymphatic system and operate carefully and meticulously in order to avoid these complications. Injured lymphatic ducts should be ligated. Usually, first-line treatment of CA usually includes cessation of oral feeding plus TPN. But TPN has own complications and it no harmless. We suggest, diet with MCTs and/or removal of drainage tube might be used as first-line medical treatment for reduce side effects and length of hospital stay because of they are noninvasive and more convenient treatment options for treatment of CA.

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Footnote

Conflicts of Interest: This article has been presented as "Oral Presentation" at "10th National Congresson Trauma and Emergency Surgery 28 October–1 November, 2015, Antalya, Turkey".

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