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Case Report

A case report validating the usefulness of cell-free and concentrated ascites reinfusion therapy for the treatment of exacerbation of chronic renal failure caused by lymphorrhea after surgery for bile duct cancer

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This is a case study on a 72-year-old man receiving continuous outpatient treatment since 2008 after a diagnosis of chronic renal failure due to diabetic nephropathy. In August 2010, he underwent pylorus-preserving pancreaticoduodenectomy for a middle bile duct carcinoma. He was transferred to our department at 39 days after surgery because of exacerbation of renal function, as well as prolonged ascites and anorexia after the surgery. The tests for malignant tumor, bacterial infection, tuberculosis, and ascitic fluid due to cirrhosis, done after his transfer, all showed negative results. Postoperative lymphorrhea was diagnosed on the basis of his clinical course and the feature of the ascites being similar to serum. Because the exacerbation of renal function was thought to be caused by a reduction of renal blood flow due to lymphorrhea, cell-free and concentrated ascites reinfusion therapy (CART) was performed for a total of two times. Consequently, the patient showed an increase in urine volume and improvement of renal function: creatinine was decreased to 1.99 mg/dL from 3.86 mg/dL. His course of ascites was observed conservatively with CART treatment, and the ascites gradually decreased and disappeared. We report a case that validates the usefulness of CART for treating exacerbation of chronic renal failure caused by lymphorrhea after surgery.

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Introduction

Lymphorrhea caused by lymphatic injury during abdominal surgery usually resolves spontaneously[1)]. This is helped by patient fasting in the postoperative period, as well as early formation of lymphatic collaterals, growth of lymphaticovenous connections, and regeneration of lymphatics[1)]. In rare cases, however, massive amount of ascites is produced in the early postoperative period, leading to the development of intractable ascites that is resistant to conservative therapy. When a copious lymphatic discharge occurs, it is often difficult to improve the patient's general condition, serum protein and electrolyte stores[2)].

The cell-free and concentrated ascites reinfusion therapy (CART) is a useful palliative maneuver in a patient with refactory ascites of various causes[3)]. CART is a treatment that could maintain serum albumin and globulin through filtration, concentration, and reinfusion of drained ascites[4)]. To date, there are no reports stating that CART is effective against exacerbation of impaired renal function caused by

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postoperative lymphorrhea.

We report a case that validates the usefulness of CART for treating exacerbation of chronic renal failure caused by lymphorrhea that occurred after an operation for cholangiocarcinoma.

Case Report

This is a case study on a 72-year-old man who has been receiving continuous outpatient treatment since 2008 after a diagnosis of chronic renal failure due to diabetic nephropathy. His creatinine levels reached 2.8 mg/dL during outpatient treatment. In August 2010, he underwent pylorus-preserving pancreaticoduodenectomy for a middle bile duct carcinoma. Although his postoperative course was favorable, rapid reduction of blood pressure, ascites, and decreased urine volume occurred on day 13 after surgery. The ascites were intractable and led to abdominal distension and appetite loss. The creatinine level increased to 5.49 mg/dL, and exacerbation of renal dysfunction was observed. Although administration of albumin and diuretics increased the urine volume and improved renal function slightly, his creatinine did not decrease from around 4.0 mg/dL. Therefore, he was transferred to our department on day 39 after surgery for intensive examination, as well as for treatment of ascites and renal dysfunction exacerbation. According to his medical history, he had a diagnosis of chronic myelogenous leukemia in 1999 and has been receiving medical treatment with imatinib.

On admission, his blood pressure was 107/74 mm Hg, pulse rate was 81 beats/min, and body temperature was 36.8℃. There were no abnormal cardiac, respiratory, or gastrointestinal sounds. Shifting dullness was observed. His clinical laboratory test findings are shown in Table 1. His blood test showed anemia (hemoglobin level, 8.1 g/dL), and biochemistry showed impaired renal function (blood urea nitrogen, 33 mg/dL; creatinine, 3.86 mg/dL) and hypoproteinemia (total protein, 5.3 g/dL; albumin, 2.8 g/dL). His blood gas analysis showed remarkable metabolic alkalosis. Abdominal paracentesis was performed after 4 days of admission of our department. The fluid was transparent and pale yellow. Ascitic fluid analysis showed white blood cell count of 200/mL, 61% of which were macrophages and 39% of which were lymphocytes. The fluid indicated that neutrophils were not increased ; however, the ascites were exudative. Cultures were negative for *Mycobacterium tuberculosis* and other bacteria, and the PCR results were also negative for *M. tuberculosis*. The cytodiagnosis was class I. Although a large quantity of ascitic fluid was detected on abdominal magnetic resonance imaging, there was no abnormality in the liver or portal veins (Figure 1). Lymphatic scintigraphy was performed because of the suspicion of postoperative lymphorrhea. However, no apparent efflux of radioisotope (RI) into the peritoneal cavity was observed.

On the basis of the above examinations, we excluded the possibilities of ascites due to malignant tumor, bacterial infection, tuberculosis, and cirrhosis. Although lymphatic scintigraphy showed no efflux of RI into the peritoneal cavity, postoperative lymphorrhea was diagnosed on the basis

Table1. Laboratory findings

<Peripheral blood>		<Blood chemistry>		<Urinalysis>	
WBC	4400 /μl	T-bil	0.5 mg/dl	Protein	1+
Seg	70 %	AST	22 IU/l	Occult blood	−
Lymph	14 %	ALT	7 IU/l		
Mono	9 %	LDH	208 IU/l	<Sediments>	
Eosino	6 %	BUN	33 mg/dl	RBC	1-2 /HPF
Baso	1 %	Cr	3.86 mg/dl	WBC	>100 /HPF
RBC	266×10^4 /μl	Na	135 mEq/l		
Hb	8.1 g/dl	K	2.9 mEq/l	< Fractional excresion(FE)>	
PLT	19.2×10^4/μl	Cl	91 mEq/l	FENa	2.2 %
		TP	5.3 g/dl	FEUrea	33.9 %
<Coagulation>		Alb	2.8 g/dl		
PT	80 %	Ca	8.3 mg/dl		
APTT	33.9 sec	P	3.5 mg/dl		
Fib	150 mg/dl	CRP	0.95 mg/dl		

of the patient's clinical progression and the feature of the ascites being approximately similar to serum (Table 2). In addition, the fractional excretion of urea (FEUrea) was 33.9%, which indicates prerenal failure. The fractional excretion of urea (FENa) might be affected by diuretics. Thus, the exacerbation of renal function was thought to be caused by a reduction in renal blood flow due to the decrease in the circulating fluid volume that occurred because of lymphorrhea. After CART was performed on the 19th and 26th day after hospitalization, an increase of urine volume and improvement of renal function (creatinine, 1.99 mg/dL) were noted. Although clinical progress was observed conservatively during CART treatment, the ascites gradually decreased and disappeared (Figure1). The patient's nutritional status and anorexia were improved, and he was discharged on the 49th day.

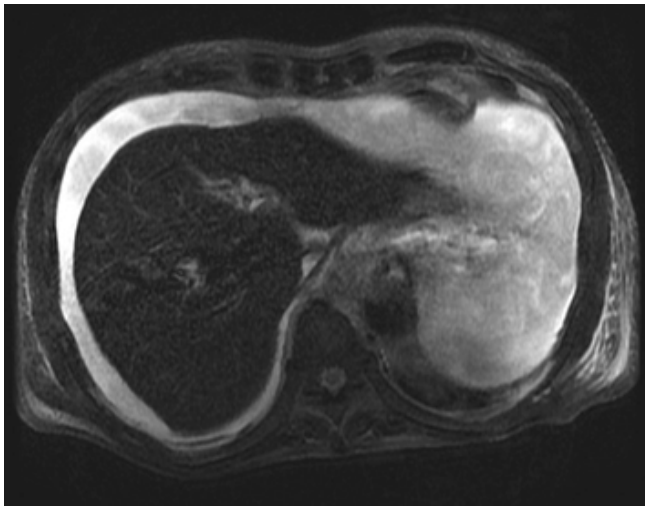

Figure1.T2-weighted magnetic resonance images showed a large amount of ascites.

Table2. Comparative evaluation of blood chemistry and ascites fluid

	Ascites fluid	Blood chemistry
BUN (mg/dl)	35	35
Cr (mg/dl)	3.8	3.88
TP (g/dl)	4.0	5.1
Alb (g/dl)	2.2	2.7
T-bil (mg/dl)	0.4	0.4
AST (IU/l)	12	22
ALT (IU/l)	5	7
LDH (IU/l)	148	150
γGTP (IU/l)	13	21
Glu (mg/dl)	169	226

Discussion

CART is performed according to the following procedures: ascitic fluid is drained from the patient's abdominal cavity; bacteria and cancer cells are removed from the ascitic fluid by filter; albumin and globulin, which are concentrated by dewatering the ascitic fluid, are returned to the patient's body[4]. CART is a useful palliative maneuver in a patient with ascites regardless of its cause. Here, we report the first case study that validates the usefulness of CART for the treatment of chronic renal failure exacerbation caused by postoperative lymphorrhea.

Lymphorrhea after intraabdominal surgery is thought to be caused by leakage of lymph fluid into the abdominal cavity due to transection of a lymphatic vessel and lymphatic damage. It is classified roughly into chylous ascites and hepatic lymphorrhea, according to the source of efflux. Chylous ascites is leaked from the intestinal lymph system and are chyliform due to chylomicrons. Hepatic lymphorrhea is leakage from the hepatic lymph system that has no lipid content, and therefore is a clear fluid. In addition, it has been reported that hepatic lymphorrhea is characterized as containing highly concentrated protein (as high as 50–80% of serum protein concentration)[5]. The lymphorrhea of the present patient is thought to be hepatic lymphorrhea because the fluid is clear and pale yellow and contains highly concentrated protein. In most instances, postoperative lymphatic leakage generally subsides spontaneously without special treatment. However, it becomes intractable in cases of substantial injury to major lymphatic vessels around the cisterna chylia and thoracic duct[2]. Notably, it was reported that compared to chylous ascites, hepatic lymphorrhea is prone to intractable form of postoperative lymphorrhea because it usually occurs by abdominal surgery with extensive lymph node dissection[6].

The complications of postoperative lymphorrhea are dehydration, circulatory failure, and renal failure due to the elimination of water and electrolytes caused by the leakage of lymph fluid into the abdominal cavity[2]. The FEUrea is a useful indicator to suggest the cause of renal failure, and FEUrea <35% indicates prerenal causes. Unlike when measuring the fractional excretion of sodium, FEUrea can be used even when patients are taking diuretics. As the FEUrea in our patient was 33.9%, prerenal factors might deteriorate his renal function. Thus, we consider that our patient showed exacerbation of chronic renal failure because of intravascular dehydration due to hypoalbuminemia and the leakage of lymph fluid into the abdominal cavity. In addition, undernutrition occurs from the elimination of protein and a reduction

in oral intake associated with the displacement of the gastrointestinal tract by the ascitic fluid, which leads to the deterioration of the patient's condition[7]. Drainage of the ascitic fluid was effective to restore appetite by the improvement of the gastrointestinal motility. However, drainage only was expected to cause significant protein loss because lymphorrhea is a protein-rich form of ascitic fluid. Therefore, we selected CART as the treatment method. As a result, it was suggested that the reinfusion of ascitic fluid after being drained and concentrated contributed to conservation of body protein and improvement of renal function by maintaining intravascular volume due to supplementing intravascular protein.

The treatment of postoperative lymphorrhea includes fasting, total parenteral nutrition, and CART as a conservative treatment, in addition to adhesion therapy, ligation of the damaged lymphatic vessel, peritoneovenous (PV) shunt, and transjugular intrahepatic portosystemic shunt[2]. According to the report by Aalami et al., two-thirds of patients with lymphorrhea may improve with conservative treatment alone, and one-third of patients require surgical treatment. It has been reported that remission of ascites due to postoperative lymphorrhea takes an average of 36 days during conservative treatment[8]. When no improvement was observed with conservative treatment, PV shunt or CART should be considered to improve the renal function and albumin levels. The PV shunt is an invasive treatment, whereas CART is an example of a conservative treatment that can supplement protein levels and remedy intravascular dehydration. Therefore, we selected CART as an effective supportive treatment to improve dehydration, renal failure, and elimination of protein. Table 3 shows a case study showing that postoperative lymphorrhea required PV shunt after CART[5,9-11]. Our literature search yielded reports of four cases. All of the patients underwent surgery for stomach cancer and had liver disease. They were treated with CART 3–12 times. They received a PV shunt approximately 1 to 5 months after surgery. Patients with liver disease may show a tendency to be intractable. Our patient developed no liver disease, which might be the reason why he could be treated successfully with CART alone, a conservative therapy. Moreover, there are several reports in which surgical treatment was performed in patients who did not respond to CART. In any case, it is important to improve refractory lymphorrhea at an early stage under a treatment including CART because refractory lymphorrhea causes a undernutrition.

CART is generally applicable in all patients who exhibit intractable ascites. Ascitic fluid can be concentrated and administered, thus supplementing albumin. Although albumin preparations derived from donated blood carry the risk of infection from unknown pathogens, CART involves no such risk because it is concentrated from the patient's own ascitic fluid. As an adverse effect of CART, fever caused by endotoxins in the concentrated ascitic fluid has been noted. Thus, it cannot be performed in cases involving the possibility of a high level of endotoxins in the ascitic fluid[11]. In addition, hemorrhaging is a possible complication of paracentesis. Although there was no serious complication for this case, CART should be performed paying attention to side effects.

Table3. Reports of postoperative refractory ascites treated with peritoneovenous shunt surgery after CART

No.	Age	Sex	Disease	Liver	CART before PV shunt	Timing of PV shunt	Author/year
1	58	F	Gastric cancer	HCV-Ab(+), Chronic hepatitis	3 times	55 POD	Kawahira/1994 [5]
2	44	F	Gastric cancer	Acute HB hepatitis	12 times	30 POD	Matsumoto/1995 [9]
3	62	F	Gastric cancer	HCV-Ab(+), LC	4 times	5 months	Yunoki/1998 [10]
4	56	M	Gastric cancer	HCV-Ab(+)	12 times	88 POD	Hosoki/2010 [11]

CART: concentration ascites reinfusion therapy, PV: peritoneovenous, F: female, M: male,
LC: liver chirrhosis, POD: postoperative day

Conclusion

We report a case of exacerbation of chronic renal failure associated with postoperative lymphorrhea, which was successfully treated by CART. CART is a useful supportive treatment for exacerbation of chronic renal failure due to postoperative lymphorrhea.

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