

Plasma filtration with dialysis for the treatment of capillary leak syndrome occurring secondary to surgery for colon cancer-related perforating peritonitis

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Abstract

The use of plasma filtration with dialysis (PDF) may be considered when treating the acute phase of capillary leak syndrome (CLS). To the best of our knowledge, this is the first report using PDF for CLS.

KEYWORDS

blood purification therapy, GEDI, IVIG, steroid pulse therapy, vascular permeability

1 | BACKGROUND

We present a case of capillary leak syndrome in a patient who underwent surgery for colon cancer-associated perforating peritonitis. We treated the patient with plasma filtration with dialysis (PDF). PDF ameliorated the capillary leak, and the patient's blood pressure gradually increased. Thus, PDF might be useful in such cases.

Capillary leak syndrome (CLS) is a very serious condition of unknown cause, first reported by Clarkson in 1960.¹ The characteristics of CLS are hypotension, hemoconcentration, and low plasma albumin levels; however, there are no clear diagnostic criteria.²⁻⁸ Certain autoimmune systems may be involved in the disease. Various treatments have been attempted, including fluid resuscitation, renal replacement therapy, corticosteroid administration, high-dose intravenous immunoglobulin (IVIG), and plasma exchange (PE).⁴⁻⁶ We present a case of CLS that developed after surgery for colon cancer perforating peritonitis wherein we treated the patient with plasma filtration with dialysis (PDF). Moreover, we obtained new information about this condition during the course of treatment.

2 | CASE PRESENTATION

An 84-year-old woman was admitted to the general ward of our hospital with the chief complaints of stomachache and diarrhea. She was a known case of myasthenia gravis; she had undergone thymoma extraction 6 years ago, after which she had started taking prednisolone 6mg/day and tacrolimus 3mg/day. On admission, computed tomography (CT) showed ascending colon cancer. Three days later, she underwent colon stenting with an endoscope. She complained of feverishness and a severe stomachache that night. The CT scan was re-examined, and free air was found in the abdominal cavity. She was immediately taken in for emergency surgery. She underwent a right hemicolectomy and ileostomy through open surgery.

After surgery, she was admitted to the intensive care unit (ICU), where she was orally intubated and ventilated. Extracellular fluid was administered at 200 mL/h, and noradrenaline was administered at 0.3 μ . Her vital signs were as follows: body temperature 35.8°C, blood pressure 108/65 mm Hg, pulse 122/min, respiratory rate 15/min under sedation. Meropenem 3g/day and daptomycin 350mg/

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TABLE 1 Blood test results on admission to the ICU

Peripheral blood			Biochemistry			Immunological test		
WBC	16.9	$\times 10^4/\mu\text{L}$	CRP	1.1	mg/dL	RF	<5	IU/mL
Basophil	0.6	%	Na	139	mEq/L	Antinuclear antibody	negative	
Eosinophil	0.1	%	K,	4.1	mEq/L	PR3-ANCA	<1.0	U/mL
Lymphocyte	6.3	%	Cl	105	mEq/L	MPO-ANCA	<1.0	U/mL
Monocyte	0.6	%	Alb	4.8	g/dL	IgG	454	mg/dL
Neutrophil	92.4	%	AST	30	U/L	IgM	57	mg/dL
Hb	16.9	g/dL	ALT	25	U/L	IgA	63	mg/dL
Ht	51.2	%	LDH,	271	U/L	Kappa chain	9.6	mg/dL
PLT	22.1	$\times 10^4/\mu\text{L}$	ALP	173	U/L	Lambda chain	1.7	mg/dL
			γ GTP	30	U/L	C3	42	mg/dL
			T-Bil	0.9	mg/dL	C4	12	mg/dL
			BUN	14	mg/dL	BJP	negative	
			Cr	0.85	mg/dL	C-1 esterase inhibitor	62	%
			Lactate	0.8	mmol/L	Estradiol	36	pg/mL

day were used as antibiotics. Table 1 shows the blood test parameters on admission to the ICU. The blood pressure started dropping 5 hours after the operation; the fluid volume was increased to 500 mL/h, but the blood pressure did not rise. Therefore, 7 hours after the operation, continuous administration of hydrocortisone (200 mg/day) and continuous hemodiafiltration (CHDF) were introduced. We were using the EV1000[®] (Edwards Life Science, Ltd) for hemodynamic monitoring. Based on the data provided by the EV1000[®], especially the global end-diastolic volume index (GEDI), up to 17 hours after the operation, we gradually reduced the infusion volume. The day after the operation, the infusion was 200 mL/h. By the 2nd postoperative day, the infusion could be reduced to 100 mL/h; however, after a while, the blood pressure began to decrease. The infusion volume was therefore again increased to 500 mL/h. On the 3rd postoperative day, it was not possible to reduce the amount of the fluid, and we had to increase the infusion to 1000 mL/h. Although her condition was initially attributed to uncontrolled sepsis, her C-reactive protein level, white blood cell count, and procalcitonin level had improved on the third postoperative day; moreover, no bacteria were detected in the postoperative culture specimens. In addition, the serum albumin level was extremely low (0.7 mg/dL), due to which we suspected CLS for the first time. We conducted blood tests, which revealed increased level of kappa light chain M protein (9.6 mg/dL). Urinary Bence Jones protein was negative and C-1 esterase inhibitor level was low (Table 1). Based on these results, we diagnosed CLS. At the time of diagnosis, her condition was quite critical, with the blood pressure dropping to 48/30 mm Hg despite an infusion speed of 1000 mL/h. Therefore, PDF was introduced in preparation for administration of a high dose of IVIG (0.4 g/

kg/day). An Evacuer[®] Plus (Kawasumi Chemical Industry, Ltd.) EC-2A filter was used as the membrane plasma separator. As previously described,^{9,10} the blood, dialysate, and filtrate flow rates were set to 100 mL/min, 400 mL/h, and 380 mL/h, respectively. A 25% albumin solution was infused at 20 mL/h as a supplemental liquid. We planned to transfuse fresh frozen plasma (FFP) when monitoring indicated coagulopathy progression, as appropriate; finally, 480 mL of FFP was administered. The filtration flow rate was set at 800 mL/h. Nafamostat mesylate was infused as an anticoagulant at 30 mg/h.

After PDF was started, her blood pressure gradually increased. About 2 hours later, her blood pressure was 132/70 mmHg. Soon after that, IVIG was started. The infusion speed was gradually decreased, and 9 hours after PDF started, the infusion speed was 60 mL/h. The pulmonary vascular permeability index (PVPI) provided by the EV1000[®] was decreased 2.2 to 1.5. The PDF was continued for 39 hours, and we continued CHDF. As the patient's condition was stable, CHDF was stopped for approximately 37 h after PDF. Subsequently, her blood pressure gradually decreased. We reintroduced PDF as soon as we expected the CLS to relapse. In addition, steroid pulse therapy (methylprednisolone 1 g/day) was also initiated, as PDF alone raised concerns about the patient relapsing. Her condition began to improve and stabilized again.

However, after the PDF was stopped, the patient reverted to her initial state in approximately 2 days. We therefore used PDF for the third time. PDF was effective, but the patient relapsed a few days later. Although PDF was effective and the GEDI increased with every introduction of PDF, the patient relapsed a few days later and died. The ICU course is shown in Figure 1.

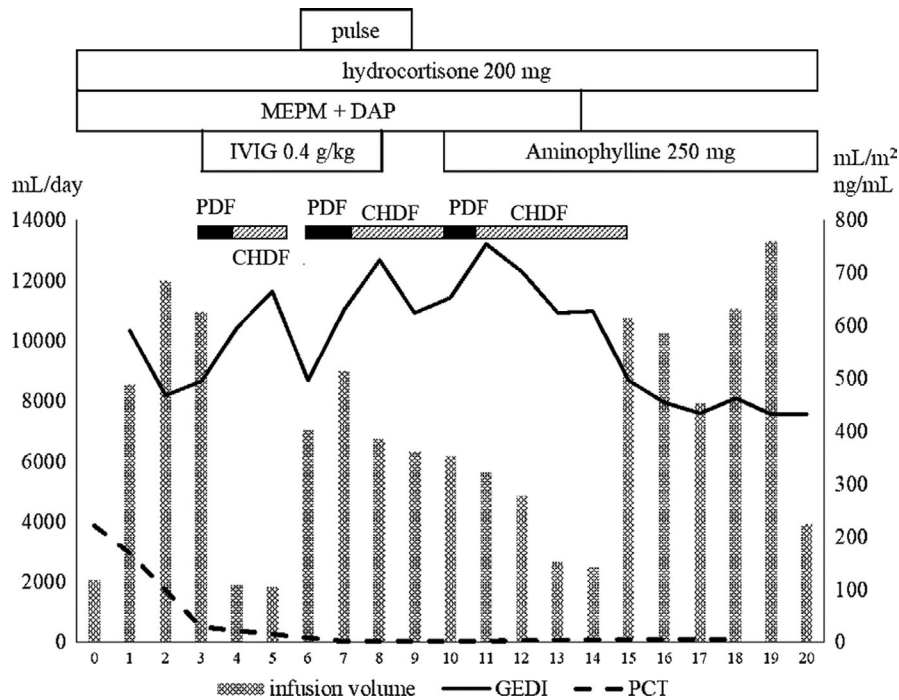


FIGURE 1 Clinical course in the ICU. Abbreviations; pulse: steroid pulse (methylprednisolone 1 g/day), MEPM: meropenem, DAP: daptomycin, IVIG: intravenous immunoglobulin, PDF: plasma filtration with dialysis

3 | DISCUSSION AND CONCLUSIONS

We obtained two new findings from this case. First, to the best of our knowledge, this is the first case to use PDF for CLS. Second, we speculated that the substances that are therapeutic targets for CLS are likely to be included in the medium molecule region.

We introduced PDF to treat CLS. PDF is a blood purification method in which a dialysate is recirculated to the outside of a hollow fiber while performing plasma exchange with FFP or an albumin solution using a membrane type plasma separator Evacuer[®] Plus (Kawasumi Chemical Industry, Ltd.) EC-2A filter. PDF is said to be able to remove small and medium-sized harmful substances while retaining useful substances in the large molecule region, such as immunoglobulin and coagulation factors. Therefore, the major advantage of PDF compared to PE is that it can reduce the use of FFP.¹¹ Reducing the use of FFP can lower the cost of treatment and reduce the risk of blood transfusion complications. In addition, previous reports have shown that PDF increases adiponectin levels in patients with liver failure; thus, it may be useful as a treatment for patients with liver failure.¹²

In this case, PDF showed a remarkable effect, due to which we can surmise that substances within the treatment target of PDF may be the cause of CLS. PDF may ameliorate capillary leaks. In Japan, PDF is treated as PE for insurance claims, so the use of PDFs is limited to those with PE insurance coverage. However, this patient also had myasthenia gravis and was covered by insurance for PE, due to which performing PDF was not a problem. In other circumstances,

the cost can be an issue with using PDF. Therefore, unless the physician is very confident about the diagnosis, PDF should be used with extreme caution.

The findings obtained in this case can be useful to plan treatment for CLS in future cases. If substances in the middle molecular area are responsible for increased vascular permeability, immunoglobulin and M protein will not be directly responsible. There are reports of vascular endothelial growth factor and angiopoietin 2 as substances in the middle molecular region and they reflected the clinical course.⁸ Together with the results of this study, it may be that such substances are the cause of CLS.

CLS is a rare syndrome, difficult to diagnose, and has an uncertain etiology. Although our patient did not show any hemoconcentration, she was diagnosed as having CLS due to prominent hypotension and decrease in GEDI and hypoalbuminemia. In this case, the recurrence of sepsis could not be ruled out, but there were no major problems during surgery, the appropriate antibiotics had been administered, and blood test results had showed improvement. Finally, while we diagnosed CLS based on the presence of monoclonal M protein, this diagnosis cannot be completely confirmed. Other differential diseases, such as ovarian hyper-stimulation syndrome and hereditary angioedema, were ruled out based on serum estradiol level and C1 esterase inhibitor level, respectively. Although there have been reports of CLS complicated with cancer,⁷ the relationship between cancer and CLS is unclear. In addition, CLS occurring with myasthenia gravis has not been reported in the past, and it is unclear whether the two diseases are related. In this case, it was not possible to completely improve the vascular permeability. The patient may not have been completely cured due to persisting malignancy

or metastasis. However, PDF may be useful in overcoming the acute phase of CLS.

In summary, an 84-year-old woman with a history of myasthenia gravis underwent surgery for colon cancer-related perforating peritonitis. After surgery, CLS developed and was treated using PDF. PDF was considered to be an effective treatment that covers the therapeutic target of CLS and may ameliorate capillary leak. The use of PDF may be considered when treating the acute phase of CLS. To the best of our knowledge, this is the first report using PDF for CLS.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

GS wrote and drafted the manuscript. GS, RI, SY, HS, YN, MW, and MH helped to draft the manuscript. All authors read and approved the final manuscript.

ETHICAL APPROVAL

We got the patient's family consent for this report.

DATA AVAILABILITY STATEMENT

All data described during this case report are included in this article.

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