

Clinical usefulness of concentrated ascites reinfusion therapy (CART) for gynecological cancer patients with refractory massive ascites due to cancerous peritonitis

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Summary

Purpose: Cell-free and concentrated ascites reinfusion therapy (CART) is intended to treat patients by ultrafiltration and reinfusion of their refractory ascites. In the CART system, bacteria and cancer cells in removed massive ascites are filtrated. Then, water is removed in the condenser, resulting in a higher protein concentration. The purpose of this study was to assess the clinical usefulness of CART in the treatment of refractory massive ascites in patients with cancerous peritonitis. **Materials and Methods:** CART was performed 13 times in four patients with ovarian and endometrial cancer. **Results:** Autologous protein with a higher concentration was intravenously administered. The amount of aspirated and condensed ascites was $3,190 \pm 1,086$ ml (975–4,500 ml) and 538 ± 249 ml (100–860 ml), respectively. Condensed albumin, albumin concentration, and concentration time were 43.2 ± 25.8 g, 8.2 ± 3.3 g/dl, and 73.3 ± 24.8 min (28–122 min), respectively. CART was effective in maintaining serum albumin concentrations, and it is possible to repeat infusion. During CART, patients performance status was 1–2 and vital signs were stable except for mild elevations in body temperature. Daily life was maintained without serious side-effects. **Conclusions:** The use of CART for gynecological cancer patients with refractory massive ascites due to cancerous peritonitis contributes to improvements in quality of life and relief of symptoms. With autologous infusion of condensed ascites, patients can avoid infection, allergic reactions, and administration of expensive blood products.

Key words: Cell-free and concentrated ascites reinfusion therapy; Gynecological cancer; Refractory massive ascites.

Introduction

Refractory ascites associated with cirrhosis and cancerous peritonitis causes a strong sense of fullness in the abdomen, respiratory discomfort, and significant decreases in quality of life (QOL). Abdominal drainage is valid, but its effect is transient and may also worsen nutritional status and immune status due to the loss of albumin and globulin, making it easier for patient to be readmitted due to the reaccumulation of ascites.

Cell-free and concentrated ascites reinfusion therapy (CART) is a technique which recovers protein components (albumin and globulin) from ascites after removal of cancer cells and bacteria using a filter. Recovered protein components can be reused in the blood vessels of the patient. CART has a long history in Japan. In 1977, Inoue *et al.* [1] reported a filtration concentration method with two kinds of hollow fibers for cancerous ascites. However, this system required complicated circuit and membrane clogging tending to occur in cancerous ascites. In 2011, a simpler and higher safety procedure was improved by Matsushita *et al.* [2] Their system includes a membrane cleaning function and enabled the processing of more ascites in a shorter period.

Advanced ovarian cancer is often accompanied by refractory ascites, which is closely associated with delays in commencing chemotherapy and the loss of QOL. In the

present study, the authors investigated the clinical usefulness of CART for gynecological cancer patients with refractory massive ascites due to cancerous peritonitis.

Materials and Methods

Four patients with refractory ascites (two with ovarian cancer and two with endometrial cancer) were enrolled in this study. All subjects underwent 12 CART at the Department of Obstetrics and Gynecology, Kagoshima University Hospital between December 2011 and April 2012.

Before abdominal paracentesis, a safe and effective puncture site was determined by abdominal ultrasound tomography, and paracentesis was then performed with a 16-G needle.

As much ascitic fluid as possible was collected in a collection bag by gravity flow. For ascites filtration and concentration, AHF-MOW and AHF-UP were used. CART in the present hospital was connected to the coupler in the membrane of the AHC-UP. This system has a concentrated 4,000 ml/hour water removal speed set to sink the dialysate. The concentrated fluid was intravenously administered with drip infusion at a speed of 100–150 ml/h. Patients with large amounts of endotoxin in their ascites were excluded from this study.

Results were expressed as the mean \pm standard deviation. The significance of changes due to the treatment was evaluated by the t-test. A $p < 0.05$ was considered significant.

Results

In this study, four patients with refractory ascites underwent 12 treatments of CART. Patient characteristics

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Table 1. — Outcome of CART in four cases of cancerous ascites

| Patient (age) (diagnosis) | Ascites (ml) | Ascites concentration (ml) | Albumin concentration (g/dl) | Processing time (min) | Serum albumin (g/dl) (pre-reinfusion/after reinfusion) |
|------------------------------------|-------------------|-------------------------------|---------------------------------|--------------------------|---|
| Case 1 (52) - Ovarian cancer | 3,475 | 390 | 6.1 | 78 | 1.8 / 2.1 |
| Case 2 (63) - Endometrial cancer | 975 | 110 | 3.0 | 30 | 2.0 / 2.4 |
| #2 | 1,265 | 100 | 6.9 | 28 | 2.0 / 2.1 |
| Case 3 (60) - Endometrial cancer | 3,375 | 545 | 9.3 | 80 | 3.6 / 3.6 |
| #2 | 2,275 | 370 | 12.6 | 60 | 3.3 / 3.3 |
| Case 4 (63) - Ovarian cancer | 3,400 | 550 | - | 65 | 2.3 / 2.6 |
| #2 | 4,500 | 860 | - | 75 | 2.6 / 3.2 |
| #3 | 4,400 | 860 | 2.5 | 97 | 3.2 / 3.5 |
| #4 | 3,700 | 755 | 9.3 | 122 | 3.5 / 3.5 |
| #5 | 3,875 | 780 | 9.9 | 85 | 3.4 / 3.4 |
| #6 | 3,075 | 520 | 9.6 | 80 | 3.2 / 3.2 |
| #7 | 3,870 | 620 | 12.6 | 80 | 3.2 / 3.2 |
| Mean \pm SD (standard deviation) | 3,190 \pm 1,086 | 538 \pm 249 | 8.18 \pm 3.3 | 73 \pm 25 | 2.8 \pm 0.6 / 3.0 \pm 0.5* |

* significance of the t-test: $p = 0.02$

are summarized in Table 1. A total of 3,190 ml (range 975 - 4,500) of ascites was filtrated and concentrated to 538 ml (range 100 - 860). The concentration of albumin in the concentrated fluid was 8.2 g/dl (range 2.5 - 12.6) and the average time to process the fluid collection was 73.3 min (range 28 - 122). Significant increases in plasma albumin concentrations were evident after CART ($p = 0.02$).

All patients complained of strong abdominal distension due to massive ascites. After CART, they could undergo anti-cancer chemotherapy without any abdominal distension and QOL was improved.

Discussion

Progression and recurrent gynecological cancer is accompanied by abdominal distention due to a large amount of ascites. Patients with massive ascites often face problems such as reduced QOL and treatment discontinuation in clinical practice. Abdominal paracentesis is chosen for the treatment of refractory ascites, but the effect has been transient. Therefore, nutritional status and immune status due to the loss of albumin are worsened. Alternatively, a peritoneo-venous shunt was reported for the treatment of refractory ascites [3, 4]. However, this treatment may bring about many serious complications including coagulation abnormalities, sepsis, and volume overload [5, 6].

Using cell free and concentrated ascites reinfusion therapy as key words, the authors conducted a Medline search of articles on CART in the English literature and found only eight reports. Reinfusion of ascites has been studied primarily as a therapeutic method for refractory ascites in liver cirrhosis [7]. CART can be performed safely in patients with ascites due to malignant tumors. After cell components such as bacteria, blood cells, and

cancer cells are removed, concentrated ascites can be re-infused. The current CART system became available from 1997, and its application was permitted by the Japanese National Insurance Scheme in 1981.

In the present study, the authors found that plasma albumin concentrations after CART therapy were significantly higher than pre-treatment concentrations ($p = 0.02$). CART was effective in maintaining serum albumin concentrations, and it is possible to repeat infusion. Autologous protein with a higher concentration was intravenously administered. All patients were relieved of strong abdominal distension and could undergo chemotherapy without discomfort. CART has the advantage of saving blood products through the use of a patient's own plasma protein, such that there is no risk of infection from an unknown pathogen.

In the current CART for refractory ascites associated with cancerous peritonitis, there were no serious side effects, with only one case of a slight fever. Some reports have shown the mechanism of the febrile reaction on reinfusion of ascites and its possible prevention. Katoh *et al.* [8] reported that in order to prevent fever occurring on reinfusion of ascites, a screen filter and depth filter were used in combination. Bernardi *et al.* [9] reported filters with a molecular weight cut-off of 300,000 decreased the incidence and grade of fever. Recently, it has been demonstrated that IL-6 exists in ascites [10], which may be considered as a cause of fever. The CART system used in this study is characterized to connect the coupler to the membrane of AHF-UP and flow the dialysate, and make the concentration such that the water removal rate of a 4,000 ml/h, monitoring dialysis pressure to a range that does not exceed 200 ml/h.

In conclusion, the authors performed CART for massive ascites in cancerous peritonitis with gynecologic cancer. They found that CART is safe and is expected to improve the symptoms, nutritional status, and QOL of

patients. They recommend that CART be more actively used as a supplementary treatment for cancerous peritonitis and palliation.

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