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【 CASE REPORT 】

Successful Introduction of Peritoneal Dialysis in an End-stage Renal Failure Patient with Idiopathic Aplastic Anemia

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Abstract:
A 45-year-old man with idiopathic aplastic anemia required renal replacement therapy (RRT) due to end-stage renal disease (ESRD). We succeeded in inserting the peritoneal dialysis (PD) catheter under cover of frequent red blood cell and platelet infusions because of severe pancytopenia. During the one-year period after starting PD using an ultraviolet-ray sterilization device, he developed severe leukopenia but no PD-related peritonitis or exit site/tunnel infection until he died of pneumonia. This case suggests that PD might be a suitable choice as RRT in ESRD patients with aplastic anemia, even in those with severe pancytopenia.

Key words: peritoneal dialysis, aplastic anemia, end stage renal disease, renal replacement therapy

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Introduction

Since aplastic anemia (AA) is often accompanied by pancytopenia, infection, and bleeding as life-threatening complications. Furthermore, hemosiderosis, immunosuppressive therapy, and chronic hypoxia due to severe anemia can lead to the development of severe renal injury in patients with AA, as with other hematologic diseases (1, 2). Therefore, end-stage renal disease (ESRD) is a lethal complication in patients with end-stage AA (3). Severe pancytopenia can also make the selection of renal replacement therapy (RRT) difficult.

Thus far, there have been only a few case reports of maintenance hemodialysis (HD) in patients with AA (4-6). The prognoses of these cases were poor because of the potential for the development of uncontrolled bleeding, manifesting as cerebral hemorrhaging and gastrointestinal bleeding, and/or sepsis, including pneumonia and infection related to the arteriovenous fistula (AVF) used as the vascular access site. Likewise, including the present case, there are only a few case reports of the peritoneal dialysis (PD) as RRT in patients with ESRD secondary to or accompanied by AA (7).

We herein report a case in which PD therapy was safely introduced in a patient with ESRD due to severe AA and successfully continued for approximately one year without any lethal infectious complications or bleeding related to the performance of PD therapy.

Case Report

A 45-year-old man with ESRD as a complication of idiopathic AA was admitted for commencement of RRT. He had been diagnosed with AA 24 years earlier (at 21 years old) based on pancytopenia and hypocellular bone marrow

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and started on methylprednisolone (mPSL) and antithymocyte globulin (ATG) as immunosuppressive therapies. The following year, anabolic steroid, granulocyte colony-stimulating factor (G-CSF), erythropoietin stimulating agent (ESA) and cyclosporine A (CyA) 200 mg/day had been added to improve his AA. Three years later, danazol was also added. However, his AA slowly worsened, and antilymphocyte globulin (ALG) was introduced when he was 39 years old. Since he developed leukocytopenia and thrombocytopenic purpura soon after starting ALG treatment, ALG was discontinued.

From 2008 to 2012, he required occasional blood transfusions of both red blood cells (RBCs) and/or platelets to control gingival and/or nasal bleeding and maintain his hemoglobin level above 5 g/dL and platelet count above 1-2×10^4/mm^3, respectively. In early 2010, deferasirox was added to prevent hemosiderosis, as his serum ferritin levels had markedly increased to approximately 2,000 ng/dL (8). However, because his serum creatinine level reached 2.94 mg/dL, the administration of deferasirox and CyA was stopped at the end of 2012. In August 2012, he developed left chronic subdural hematoma and right occipital lobe cerebral hemorrhaging. Due to progressive anemia, leukocytopenia and thrombocytopenia, the frequency of both RBC transfusions and platelet infusions was increased to weekly administration to keep his hemoglobin level around 5 g/dL and platelet count at 1×10^4, according to the guidelines for the diagnosis and management of adult AA (3), for the prevention of lethal bleeding, improvement of anemia-related symptoms and prevention of the deterioration of his quality of life.

However, purpura and recurrent gingival and nasal bleeding continued. Thereafter, his renal function gradually decreased, progressing to chronic kidney disease (CKD) stage 5. At this point, he was referred by the hematology unit at our hospital to the Department of Nephrology. A renal biopsy was not performed because of the risk of bleeding and his CKD stage at that time. The cause of CKD was suspected of being drug-induced renal injury, due to the use of CyA, drug-induced allergic purpura, renal ischemia due to severe anemia and hemosiderosis because of frequent blood transfusions. Until he developed ESRD, he had been followed up with supportive therapy for CKD. Once he developed ESRD, mild hepatic injury was also observed, possibly due to hemosiderosis. However, because his blood urea nitrogen (BUN) was over 100 mg/dL, his serum creatinine level was over 8 mg/dL, and his estimated glomerular filtration rate (eGFR) as a measurement of the residual renal function was less than 6.5 mL/min/1.73 m^2, he was given the options of PD or hemodialysis as RRT.

On admission, he complained of generalized fatigue and pruritus. Physical examination indicated that he was 174.4 cm tall, weighed 58.6 kg, and his body temperature was 37.2℃, blood pressure was 142/80 mmHg and heart rate was 98 beats/min in sinus rhythm. He did not have splenomegaly, and his conjunctiva was pale. Under regular usage of G-CSF and ESA and regular transfusion of platelets and RBCs, his clinical laboratory data were as follows: peripheral white blood cell (WBC) count, 1,200/mm^3 (polymorphoneutrophils, 57.7%; lymphocytes, 35.0%); RBC count, 187×10^4/mm^3; blood hemoglobin level, 5.7 g/dL; blood hematocrit level, 15.9%; reticulocytes 0.2×10^4/mm^3; blood platelet count, 1.1×10^4/mm^3 and C-reactive protein level, 0.11 mg/dL. His blood biochemistry data were as follows: urea nitrogen (BUN) 128 mg/dL, creatinine (Cre) 8.15 mg/dL, uric acid 7.0 mg/dL, sodium 141 mEq/L, potassium 4.9 mEq/L, Cl 109 mEq/L, calcium 8.6 mg/dL, phosphate 6.0 mg/dL, total protein 6.7 g/dL, albumin 3.5 g/dL, total bilirubin 0.3 mg/dL, aspartate aminotransferase (AST) 35 IU/L, alanine aminotransferase (ALT) 47 IU/L, IgG 902 mg/dL, IgA 79 mg/dL, IgM 22 mg/dL, Fe 300 μg/dL, TIBC 258 μg/dL, ferritin 6,584 ng/mL, beta-2 microglobulin 14.1 mg/dL and intact parathyroid hormone 491 pg/mL. His urinalysis results were as follows: protein +, occult blood 3, urinary RBC 40-50/high-power field (HPF), urinary WBC 1-2/HPF and urinary protein 0.29 g/day. A blood gas analysis (while breathing room air) showed a pH 7.272, HCO_3 15.7 mmol/L and actual base excess -9.8 mmol/L.

His clinical and laboratory data indicated the need for induction of RRT. Given the possibility of him developing ESRD requiring RRT, we had been carefully discussing the risks and benefits of HD and PD therapy with this patient over the past year (Table). Finally, based on the patient's desire and due to certain technically difficulties, PD was collectively chosen by the patient, his family, and us. To decrease the risks of perioperative bleeding and infection, we tried to keep his platelet count above 50,000/mm^3 and used cefazolin for perioperative antibiotic cover (Figure). To stop bleeding at the exit site of the PD catheter, pressure hemostasis was applied for over half a day when the catheter was inserted, and 20 units of platelet infusion was rapidly administered, which resulted in his platelet count being maintained at around 3×10^4/mm^3. During PD fluid bag change, we introduced a new ultraviolet-ray sterilization device (UVD), "TSUNAGU" (Baxter, Tokyo, Japan), to reduce the risk of peritonitis. Although PD fluid dwell was safely started after 18 days of PD catheter insertion, omental wrapping, which resulted in obstruction of the PD catheter, occurred as a rare PD-related complication three days after PD induction. To restore patency of the PD catheter, catheter repair by a forefinger along with the peritoneal wall anchor technique was performed while keeping the blood platelet counts at more than 5×10^4/mm^3 via prophylactic platelet infusion (green arrow in Figure) (9-11).

Once maintenance PD therapy was started, prophylactic platelet infusions were performed approximately twice a week to keep the blood platelet counts at approximately 2×10^4/mm^3, prevent PD catheter injury-related lethal bleeding in the peritoneal cavity and prevent exit-site bleeding. To preserve the patient's quality of life, RBC infusions were also performed once a week to keep hemoglobin levels at approximately 5 g/dL. With these precautions, maintenance PD therapy was able to be performed and continued for ap-

Table. Comparison of the Expected Advantages and Disadvantages of Hemodialysis and Peritoneal Dialysis.

	Peritoneal dialysis (PD)	Hemodialysis (HD)
Advantages	•Creation of a vascular access site, such as insertion of a double-lumen catheter into a central vein or an AV fistula, not required •Repeated puncture of the AV fistula and control of bleeding with every HD treatment not required •No risk of infection associated with AV fistula, especially during usage of artificial blood vessel	•AV fistula creation is easier than PD-catheter insertion when dealing with perioperative events such as bleeding. •No risk of PD-related peritonitis since PD bag changes are not required •No risk of PD catheter-related exit-site infection •No risk of PD catheter-related intraabdominal bleeding •Easy to perform frequent transfusion of RBCs and platelets through the AV fistula
Risks	•Infection and bleeding during the perioperative period of PD-catheter insertion •Risk of PD-related peritonitis •Risk of intraabdominal bleeding	•Infection and bleeding during the perioperative period of creating the vascular access for HD •Infection and bleeding during maintenance HD therapy

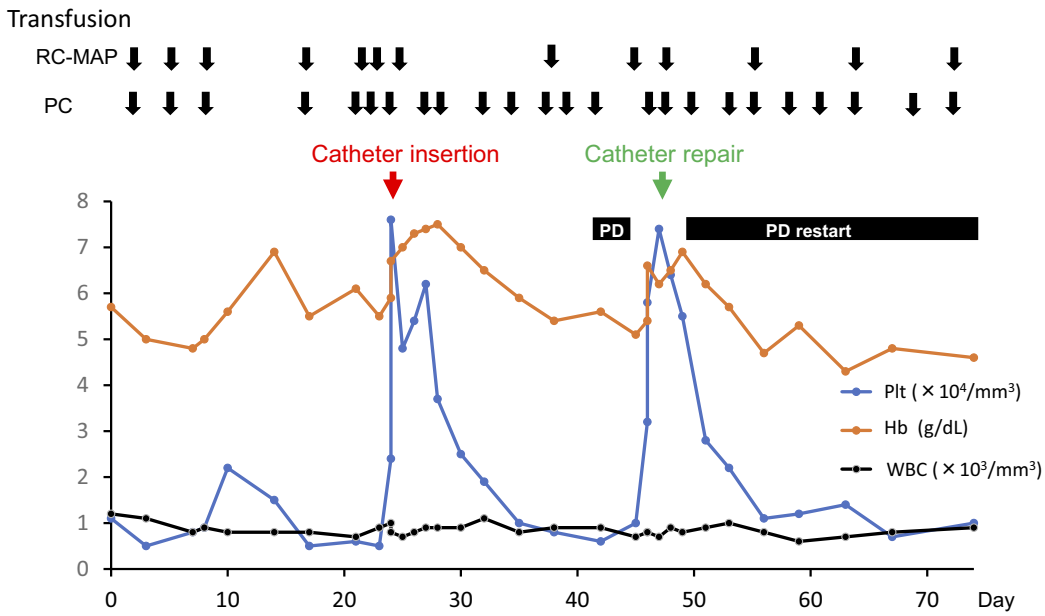

Figure. Clinical course of the patient at and around the period of peritoneal dialysis (PD) -catheter insertion, induction and catheter repair after omental wrapping. During his clinical course, the patient underwent two surgeries: PD-catheter insertion (red arrow) and catheter repair for omental wrapping (green arrow). Red blood cell-mannitol adenine phosphate (MAP): 2 units/time of red cell transfusion (black arrow), Platelet concentrate (PC): 10 units/time of platelet transfusion (black arrow). Plt: platelet count (blue line), WBC: white blood cell count (black line), and Hb: hemoglobin level (orange line)

proximately one year without intraabdominal bleeding, PD-related peritonitis or other potential complications related to PD therapy. However, the patient occasionally developed pneumonia due to leukopenia.

Of note, during our observation of his clinical course until the incidence of pneumonia, we did not use any prophylactic antibiotics regularly. One year after the induction of PD, he died of suspected fungal pneumonia with sepsis caused by *Enterococcus faecium* after an episode of culture-negative pneumonia.

Discussion

We encountered a case of AA with ESRD in which PD was safely started and maintained for approximately one year without any episodes of PD-related infection. In determining the most appropriate RRT in the present AA case, we compared the risks and benefits of PD and HD. As the

patient had severe pancytopenia, he and his family ultimately decided on PD. We realized that the main issues with PD in this case were the prevention of bleeding and infection during PD catheter insertion and abdominal bleeding during PD maintenance. Therefore, our patient regularly received platelet transfusions to prevent bleeding, and we used a UVD to decrease the risk of contamination by microorganisms during PDF bag changes.

Infections and bleeding are potentially lethal complications in patients with AA. In addition, these patients sometimes develop hemosiderosis due to frequent blood transfusions, leading to potentially lethal organ failure, such as hepatic insufficiency and heart failure (12, 13). In our patient, hemosiderosis due to frequent blood transfusions and adverse drug effects was expected (1). To date, there have been only a few reports of AA patients, including those with secondary AA, who developed ESRD that was managed by maintenance HD (4, 5, 14). Their prognoses were reportedly poor, with most patients dying within approximately half a year due to infection and/or bleeding. It is also possible that a significant number of primary AA patients die before consideration of RRT because of fatal infection and bleeding.

In the present case, the patient developed ESRD before the other complications. As such, PD therapy was recommended. Despite the use of G-CSF, ESA and/or blood transfusion for severe neutropenia and anemia, his neutrophil count was often in the 200-600/mm^3 range, his platelet count was less than 20,000/mm^3, and his reticulocyte count was often less than 1.0%. Therefore, he was categorized into the very severe AA class (15) when he was referred to our unit for ESRD. He decided to start PD therapy as RRT. In choosing PD as RRT for our patient, we had to consider the following four points: 1) control of bleeding associated with insertion of the PD catheter, 2) prevention of abdominal bleeding secondary to PD catheter-related peritoneal injuries, 3) prevention of exit-site bleeding and 4) prevention of PD-related peritonitis. To address these problems, we maintained the platelet count at $5\times10^4/mm^3$ to prevent surgical intervention-related bleeding and $3\times10^4/mm^3$ to prevent exit-site bleeding and unexpected intraabdominal bleeding related to the PD catheter, according to the guidelines for platelet infusions in patients with thrombocytopenia and other reports (9-11). Since PD-related peritonitis mainly occurs due to touch-contamination during the bag-change process at our hospital, as has also been previously reported (16-20), we introduced a new UV-sterilization device system, called "TSUNAGU" (Baxter Co.), which does not require the removal of the protective cover when connecting a new PDF bag. This system might be better able to maintain a sterile environment during most bag change procedures than the conventional "Clean Flash" UV-device system (Baxter Co.), which requires the protective cap be removed from the connecting tube by hand when changing PDF bags. The incidence of PD-related peritonitis might decrease with the use of this new system. The patient was also repeatedly trained by the attending physicians and nurses regarding the PD bag handling procedure in order to reduce opportunities for touch-contamination during PD bag changes. With these precautions, his PD therapy was able to be continued without severe bleeding or episodes of peritonitis.

This is the first report of the commencement and maintenance of PD in an ESRD patient with end-stage aplastic anemia. Our experience suggests that PD therapy might be a suitable choice for RRT in ESRD patients with severe AA with thrombocytopenia and leucopenia.

The authors state that they have no Conflict of Interest (COI).

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