Successful Peritoneal Dialysis for the Treatment of Inotrope-Dependent End-Stage Heart Failure

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Summary

Extra- and/or intracorporeal renal replacement therapy can improve the cardiorenal hemodynamics in patients with advanced heart failure (HF) refractory to medical therapy and renal failure. Here, we report the case of a 51-year-old woman with inotrope-dependent end-stage HF and chronic renal failure due to anthracycline-induced cardiomyopathy, in whom the induction of hemodiafiltration and subsequent chronic peritoneal dialysis (PD) provided a dramatic improvement of her cardiac hemodynamics from restrictive to almost normal physiology assessed by echocardiography and cardiac catheterization. The patient returned to office work with New York Heart Association functional class I-II symptoms for at least 3 years with continuous ambulatory PD after hospital discharge.

Key words: Renal failure, Cardiac hemodynamics

Heart failure (HF) is a progressive disorder whose treatment options are limited and typically ineffective once patients develop end-stage HF. Mortality is especially high when such patients have coexisting chronic renal failure. Under these conditions, extra- and/or intracorporeal renal replacement therapy can improve the cardiorenal hemodynamics. Previous studies and case reports have demonstrated that peritoneal dialysis (PD) improves HF symptoms and cardiac function and reduces readmission rates. However, no investigators have assessed the effects of PD on cardiac hemodynamics using cardiac catheterization. Here, we report the case of a 51-year-old woman with severe inotrope-dependent HF and chronic renal failure, in whom the induction of hemodiafiltration (HDF) and subsequent chronic PD provided a dramatic improvement of her cardiac hemodynamics from restrictive to almost normal physiology assessed by echocardiography and cardiac catheterization. She returned to office work with New York Heart Association (NYHA) functional class I-II symptoms for at least 3 years after hospital discharge.

Case Report

A 51-year-old woman was admitted to our hospital due to worsening of chronic HF. She had a past medical history of acute myeloid leukemia at the age of 29, at which time she had a normal electrocardiogram (Figure 1, top left), and was treated with anthracycline-based chemotherapy (a total dose of 1,005 mg/m²) and achieved complete remission. At the age of 38, chest X-ray pointed out cardiomegaly and poor R-wave progression in leads V1-V4, as well as left axis deviation and wide QRS complex on electrocardiogram (Figure 1, top right). Echocardiography revealed a decreased left ventricular ejection fraction (LVEF) of 30% (Teichholz’s method). When she was 45 years old, she developed congestive HF requiring hospitalization for the first time. The histological findings of the endocardial biopsy sample (Figure 2) showed atrophy and dropout of cardiomyocytes associated with interstitial fibrosis, especially in the endocardial area. No significant inflammatory infiltration, epithelioid cells, granuloma formation, or deposition of amyloid was observed. There was no late gadolinium enhancement lesion on cardiac magnetic resonance imaging. Invasive coronary angiography showed no coronary artery disease. Based on a careful clinical assessment including the above-mentioned imaging and histological assessments, she was diagnosed with anthracycline-induced cardiomyopathy, and beta-blocker treatment was started. Renal dysfunction with an estimated glomerular filtration rate (eGFR) of < 60 mL/minute/1.73 m² was first detected when she was 47 years old. There were no abnormal urinalysis findings, and ultrasound images showed no renal atrophy. When she was 50 years old, she was hospitalized for worsening of HF, and a cardiac resynchronization therapy defibrillator was implanted. However, she was rehospitalized soon thereafter and required pericardial drainage for exudative pericardial effusion, continuous inotropic infusion, and adaptive servo ventilation. Right and left heart catheterization revealed...
Figure 1. Normal electrocardiogram at the age of 29 (top left). There was poor R-wave progression in leads V1-V4, left axis deviation, and wide QRS complex at the age of 38 (top right). Electrocardiogram on hospital admission showed atrial sensed and ventricular paced rhythm and low QRS voltage (bottom left). The low QRS voltage slightly improved before the induction of HDF (bottom middle). At discharge, further increases in the QRS voltage were shown (bottom right).

Figure 2. Hematoxylin and eosin staining showing atrophy and dropout of cardiomyocytes in the endocardial region (left). Picro-Sirius Red staining showing the size variance of cardiomyocytes and apparent collagen accumulation around cardiomyocytes (right) (scale bar: 100μm).
restrictive cardiac physiology\textsuperscript{14} with left ventricular (LV) and right ventricular (RV) end-diastolic pressure of 23 and 20 mmHg, respectively, after the removal of the pericardial effusion (Figure 3). Pericardial effusion developed rapidly within 1 month after pericardial drainage.

Upon her final hospital admission at the age of 51, she complained of dyspnea on mild effort and significant peripheral edema. Her oral HF treatment was carvedilol 7.5 mg/day, candesartan 4 mg/day, azosemide 120 mg/day, spironolactone 12.5 mg/day, tolvaptan 15 mg/day, and pi-mobendan 2.5 mg/day. Her blood pressure was 80/45 mmHg and pulse rate was 60 bpm. Chest X-ray showed marked cardiomegaly with a cardiothoracic ratio of 85%, but there was no obvious pulmonary venous congestion or pleural effusion (Figure 4, left). Electrocardiogram showed atrial sensed and ventricular paced rhythm and low QRS voltage (Figure 1, bottom left). Laboratory tests revealed markedly elevated plasma B-type natriuretic peptide (BNP) level (1,119 pg/mL), mild anemia (hemoglobin: 11.4 g/dL), decreased renal function (creatinine [Cr] 2.71 mg/dL, creatinine clearance [CCr] 22.1 mL/minute), hyponatremia (135 mmol/L), and hyperkalemia (6.2 mmol/L) (Table I). Arterial blood gases indicated primary metabolic acidosis and compensated respiratory alkalosis (pH 7.335, PaCO\textsubscript{2} 27.3 mmHg, PaO\textsubscript{2} 98.4 mmHg, HCO\textsubscript{3}\textsuperscript{−} 14.3 mmol/L, and base excess −10.2 mmol/L on room air) (Ta-
Table I. Comparisons of Clinical and Laboratory Data

|                           | On hospital admission | Before HDF (on inotrope) | At hospital discharge | 1 year after discharge |
|---------------------------|-----------------------|---------------------------|-----------------------|------------------------|
| NYHA functional class     | IV                    | III                       | II                    | II                     |
| Body weight (kg)          | 53.5                  | 46.7                      | 50.3                  | 48.8                   |
| Pericardial effusion      | Present               | Present                   | Absent                | Absent                 |
| Plasma BNP (pg/mL)        | 1,119                 | 806                       | 243                   | 133                    |
| Hemoglobin (g/dL)         | 11.4                  | 10.7                      | 12.3                  | 11.9                   |
| Serum sodium (mmol/L)     | 135                   | 133                       | 129                   | 133                    |
| Serum potassium (mmol/L)  | 6.2                   | 5.8                       | 4.9                   | 4.5                    |
| Serum creatinine (mg/dL)  | 2.71                  | 1.82                      | 2.86                  | 2.37                   |
| HCO₃⁻ (mmol/L)            | 14.3                  | 20.7                      | 25.6                  | 27.1                   |

HDF indicates hemodiafiltration; and BNP, B-type natriuretic peptide.

Figure 5. Echocardiography on hospital admission (top), before the induction of HDF (second row), at discharge (third row), and one year after discharge (bottom).

The cytokines or uremic toxins were not measured. Ultrasound images showed no renal atrophy and no signs of renal artery stenosis, but the arterial renal resistance index was distinctly above 0.7, with intermittent renal venous waveform patterns in both kidneys, suggesting increased intrarenal pressure. Therefore, it was presumed that renal congestion plays an important role in the progression of renal dysfunction, although chemotherapy-induced nephrotoxicity has not been ruled out because renal biopsy was not performed. Echocardiography showed four-chamber dilatation, a reduced LVEF of 21% assessed by the modified Simpson method, a reduced cardiac index assessed by Doppler echocardiography, grade III diastolic dysfunction, severe tricuspid regurgitation, dilated inferior vena cava (IVC) with reduced respiratory change, and mild-to-moderate pericardial effusion (Figure 5, top; Table II). Right heart catheterization (RHC) revealed high mean pulmonary artery wedge pressure (PAWP) of 21 mmHg and right atrial pressure (RAP) of 19 mmHg with a reduced cardiac index of 2.11 L/minute/m² measured using Fick’s method (Figure 6, top; Table III). In addition, the RV developed pressure, obtained by subtracting the end-
diastolic pressure from the peak systolic pressure, was only 18 mmHg, which indicates combined left- and rightsided HF rather than isolated left-sided HF. The patient required continuous inotropic infusion (maximal dose of dobutamine: 5.0 μg/kg/minute, maximal dose of milrinone: 0.0625 μg/kg/minute) and intravenous furosemide administration (maximal daily dose of 60 mg) for 7 weeks, but this failed to improve her condition, including persistent metabolic acidosis and exudative pericardial effusion requiring pericardial drainage despite her decreased body weight (Figure 4, middle; Table I), even though the low QRS voltage slightly improved on electrocardiogram (Figure 1, bottom middle). Echocardiography after the pericardial drainage revealed worsening of the diastolic function with an increase in the peak flow velocity and shortening of mitral early diastolic filling (E-velocity), as well as persistent severe tricuspid regurgitation despite mild increases in LVEF assessed by the modified Simpson method (Figure 5, second row; Table II). RHC showed no obvious reduction of intracardiac pressure even after the removal of the pericardial effusion: mean PAWP (before/after drainage: 18/18 mmHg), mean pulmonary artery pressure (26/26 mmHg), RV end-diastolic pressure (15/15 mmHg), and mean RAP (14/16 mmHg) despite mild increases in the cardiac index assessed by the thermodilution method and Doppler echocardiography (Tables II, III). Therefore, HDF was initiated with the clinical assumption that chronic latent uremia was contributing to refractory decompensated HF. Although her body weight remained unchanged, her HF symptoms obviously improved and the dosage of dobutamine was successfully decreased from 5.0 to 1.5 μg/kg/minute after HDF. The BNP level was changed from 806 pg/mL just before the induction of HDF to 674 pg/mL 1 month after the initiation of HDF. Therefore, HDF was switched to PD 5 weeks after initiation. Her general condition gradually improved during a total of 5 months of PD using 1.0 L of 2.5% dextrose and icodextrin in a two-exchange-per-day regimen, and her BNP level decreased to 243 pg/mL and metabolic acidosis improved (Table I). Chest X-ray showed a remarkable decrease in the cardiothoracic ratio to 67% (Figure 4, right), and electrocardiogram showed further increases in the QRS voltage (Figure 1 bottom right). Echocardiography showed an increased cardiac index, mild prolongation of the deceleration time of E-velocity and increases in the peak flow velocity at atrial contraction (A-velocity), reduced tricuspid regurgitation, and decreased IVC diameter (Figure 5, third row; Table II). RHC showed markedly decreased mean PAWP, mean RAP (10 and 6 mmHg, respectively), and an increased cardiac index to 3.14 L/minute/m² when compared with the baseline value measured by Fick’s method (Figure 6, bottom; Table III). She left the hospital with NYHA class II symptoms. Surprisingly, she gained about 3.5 kg body weight during the 5-month PD. During hospitalization, her oral medications remained unchanged except for an increased pirombendan dose from 2.5 mg/day to 5 mg/day, replacement of candesartan 4 mg/day by perindopril (initial dose: 4 mg/day, final dose: 8 mg/day), and additional administration of trichlormethiazide 2 mg/day. Finally, her echocardiography revealed an increased LVEF to 33% assessed by the modified Simpson method, an increased cardiac index to 2.32 L/minute/m² assessed by Doppler echocardiography, improved diastolic function to grade I (18), decreased IVC diameter, and disappearance of pericardial effusion 1 year after hospital discharge (Figure 5, bottom; Table II). She returned to office work with NYHA class I-II symptoms for at least 3 years with continuous ambulatory PD thereafter (Table I).

### Discussion

Advanced HF, also defined as stage D HF, is refractory to medical treatment, especially when patients have
coexisting chronic renal failure. Under these conditions, extra- and/or intracorporeal renal replacement therapy can improve cardiorenal hemodynamics. It reduces the intravascular volume, corrects acid-base and electrolyte imbalances, and removes uremic toxins, including cytokines. HDF but not hemodialysis was adopted for initial renal replacement therapy for rapid reduction of intravascular volume and amelioration of uremic manifestations because HDF more effectively removes moderate-molecular-weight molecules and improves uremia-related complications compared to hemodialysis. After successful HDF, the patient received chronic PD but not HD. Long-term HD leads to an increase in preload due to arteriovenous fistula and can cause hemodynamic and electrolyte instability due to rapid fluid removal, which are associated with an increased risk of cardiovascular events in patients with HF. In addition, HD is known to be associated with poor recovery of renal function. In contrast, chronic PD provides a continuous and gentle correction of the above-described uremic milieu. PD promotes slow and effective peritoneal ultrafiltration that preserves better residual renal function, and it is less invasive and more tolerated by patients with HF than extracorporeal renal replacement therapy, offering an improvement of clinical symptoms and quality of life. In fact, previous studies and case reports have reported favorable results of PD in the setting of chronic refractory HF. Although PD is used primarily for the treatment of end-stage renal disease with an eGFR of <15 mL/minute/1.73 m², these clinical reports revealed that PD reduces hospitalization rates, improves the HF functional status, and increases the LVEF even if the individuals did not reach end-stage renal disease. Thus, PD may reasonably be expected to benefit patients with severe HF and chronic renal failure (particularly those with residual renal function). Interestingly, Sánchez, et al. demonstrated that the pulmonary artery systolic pressure estimated by echocardiography decreased from 44 ± 12 to 27 ± 9 mmHg after six-month PD in patients with refractory HF and chronic kidney disease (GFR: 35 ± 6 mL/minute). However, there have been no reports of studies evaluating the hemodynamic effects of PD using cardiac catheterization. Surprisingly, five-month PD normalized intracardiac pressure without affecting renal function in the present patient, in whom baseline car-

Figure 6. RHC on hospital admission (top) and at discharge (bottom). PAP indicates pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; RVP, right ventricular pressure; and RAP, right atrial pressure.
diac catheterization showed restrictive cardiac physiology despite receiving maximal medical therapy and cardiac re-synchronization therapy. Since her body weight increased during the five-month in-hospital PD, the improvement of her cardiac hemodynamics can be mainly explained by PD-induced nonhemodynamic mechanisms, including acid-base control, nutritional improvement, and removal of inflammation-inducing substances such as tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) and IL-6. The use of the peritoneal membrane in PD may remove inflammation-inducing substances much more effectively compared to the dialyzer membrane in hemodialysis.22) Indeed, Oncel, et al. demonstrated that the serum TNF-α and IL-6 levels of patients on continuous ambulatory PD were significantly lower than with hemodialysis.22) In addition, the use of an icodextrin-containing PD solution may have had favorable effects on the uremic milieu and metabolic control and thus, the cardiac hemodynamics in the present study.12) Meanwhile, it should be noted that patients with poor comprehensive understanding and management abilities for daily PD procedure are not suitable for home-based chronic PD. In addition, the amount of fluid removed depends on multiple factors, including the type and concentration of the osmotic agent, the temporal distribution of dialysis fluid exchanges, and the characteristics of the peritoneal membrane,22) and thus, the maintenance of an adequate fluid balance is difficult in certain patients with HF, particularly those with no residual renal function.

We concluded that, in the present case, the induction of HDF and subsequent long-term PD provided a dramatic improvement of cardiac hemodynamics, which led to the reversal of inotrope-dependent stage D to stage C HF with very mild symptoms.

Conclusion

PD can be a useful therapy for advanced HF refractory to medical therapy with renal failure.

Disclosures

Conflicts of interest: Masaaki Ito received departmental research grant support equal to or more than 500,000 yen per year from Daiichi Sankyo Company Limited and Bristol-Myers Squibb K.K. Kaoru Dohi received honoraria equal to or more than 500,000 yen per year from Otsuka Pharma Inc. Masaaki Ito received honoraria equal to or more than 500,000 yen per year from Daiichi Sankyo Company Limited, Takeda Pharmaceutical Company Limited, Bayer Holding Ltd., Mitsubishi Tanabe Pharma Corporation, and Mochida Pharmaceutical Co., Ltd. The other authors declared no conflicts of interest.

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Table III. Comparisons of Hemodynamic Parameters During Hospitalization

| Parameter                          | On hospital admission | Before HDF (on inotrope) | At discharge |
|-----------------------------------|-----------------------|--------------------------|-------------|
| Mean PAWP (mmHg)                  | 21                    | 18*                      | 10          |
| Mean PAP (mmHg)                   | 23                    | 26*                      | 17          |
| Mean RAP (mmHg)                   | 19                    | 16*                      | 6           |
| Cardiac index (L/minute/m²)       | 2.75                  | 3.10                     | 2.60        |
| Cardiac index (L/minute/m²) (Fick’s method) | 2.11                  | No data                  | 3.14        |
| Systolic blood pressure (mmHg)    | 86                    | 117*                     | 82          |
| Heart rate (bpm)                  | 61                    | 73*                      | 63          |

HDF indicates hemodiafiltration; PAWP, pulmonary artery wedge pressure; PAP, pulmonary artery pressure; and RAP, right atrial pressure. *Data obtained immediately after pericardial drainage.
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