

# Therapeutic Challenges to End-Stage Kidney Disease in a Patient with Tetralogy of Fallot



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**ABSTRACT:** In this report, we describe the case of an end-stage kidney disease patient with tetralogy of Fallot (TOF). A 33-year-old female with TOF was admitted to our hospital with complaints of general fatigue and appetite loss probably due to uremic milieu. She was ultimately treated with peritoneal dialysis (PD) with a favorable clinical course. TOF patients with chronic kidney disease are not exceptional, although the currently available information regarding the association between TOF and renal failure severe enough to require dialysis treatment is limited. We also discuss the complex processes of how and why PD was selected as a mode of chronic renal replacement therapy in this case.

**KEYWORDS:** end-stage kidney disease, peritoneal dialysis, tetralogy of Fallot, cyanotic nephropathy

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## Introduction

Tetralogy of Fallot (TOF) is a cyanotic congenital cardiac defect characterized by pulmonary outflow tract stenosis or obstruction, ventricular septal defect (VSD), overriding aortic root, and right ventricular hypertrophy.<sup>1</sup> Left without surgical correction, the overall survival was poor and over 90% of the patients die by 40 years of age.<sup>2,3</sup> There are some subsets of TOF patients with advanced chronic kidney disease (CKD); however, the association between TOF and renal failure severe enough to require dialysis treatment has been rarely reported in the literature.<sup>4,5</sup> In this report, we describe the case of an end-stage kidney disease patient with TOF. We also discuss the complex processes of how and why peritoneal dialysis (PD) was selected as a mode of chronic renal replacement therapy in this case. The patient has given her written consent for publication of this report.

## Case Report

A 33-year-old female with TOF managed by palliative surgery was admitted to our hospital with complaints of general fatigue and appetite loss at the end of December 2013. She was noted to be cyanosed at birth and had undergone Blalock–Taussig shunt at 2 years of age and palliative right ventricular outflow tract reconstruction, which is a procedure used to enlarge the ventricular outflow tract and main pulmonary artery, without inducing the closure of the concurrent VSD,<sup>6</sup> at 4 years of age. There was no known family history of congenital cardiac disease.

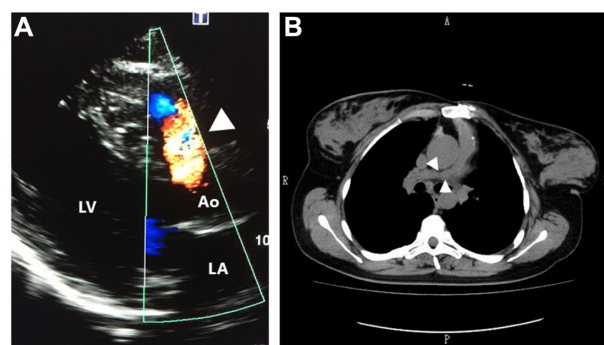
At 24 years of age, the patient's serum creatinine (sCr) levels were increased at approximately 1.3 mg/dL, and her sCr levels thereafter continued to increase gradually, but slowly. In 2012, at 32 years of age, she became hypertensive, and her sCr levels were approximately 3.1 to 3.4 mg/dL with 3+ for urine protein when the additional surgical correction for closure of the VSD was planned. She was then referred to our hospital. According to the clinical pictures and renal sonographic findings, which showed decreases in the renal long axis dimensions (right: 80 mm, left: 85 mm) with grade II renal cortex echogenicity, the patient was diagnosed with CKD<sup>7</sup> and subjected to contemporary and comprehensive renal care. Despite the successful control of her blood pressure to the ranges of 130–140/70–80 mmHg with losartan potassium and azelnidipine, her renal function steadily worsened during the last year, and she finally became aware of the symptoms at the end of December 2013 when her sCr and blood urea nitrogen (BUN) levels elevated up to 8.25 and 99 mg/dL, respectively. As a result, she was admitted for further workup.

A physical examination completed on this admission revealed the patient to be alert. The patient's blood pressure was 134/59 mmHg, her pulse was 78 beats/minute, and her temperature was 37.0 °C. Although the patient's oxygen saturation was 85% while she breathed ambient air, a chest X-ray film demonstrated neither an accumulation of fluid nor a sign of pulmonary infiltrates. There were no rashes or lymphadenopathy, and no petechiae were found. A laboratory evaluation revealed

the following results: white blood cell count, 9,000/ $\mu\text{L}$ ; red blood cell count,  $407 \times 10^4/\mu\text{L}$ ; hemoglobin (Hb), 12.1 g/dL; hematocrit, 36.4%; platelet count,  $19.5 \times 10^4/\mu\text{L}$ ; BUN, 111 mg/dL; sCr, 8.03 mg/dL; total protein, 7.7 g/dL; albumin, 4.7 g/dL; sodium, 139 mmol/L; potassium (K), 5.3 mmol/L; chloride, 108 mmol/L; calcium (Ca), 10.5 mg/dL; phosphorus (Pi), 7.2 mg/dL; aspartate aminotransferase, 13 U/L; alanine aminotransferase, 12 U/L; C-reactive protein, 0.02 mg/dL; and brain natriuretic peptide, 55.4 pg/mL. Her urine was 3+ for protein and + for occult blood and contained 1.3 g of protein in a 24-hour specimen, while the patient's creatinine clearance was 5.02 mL/minute. Transthoracic echocardiography disclosed a perimembranous VSD (maximum diameter of 21 mm), a bidirectional shunt with left-to-right shunting (2.55 m/second) predominance, and well contracting left ventricle (LV) with an LV ejection fraction of 63.8% (Fig. 1A), while chest computed tomography (CT) scans demonstrated right pulmonary artery stenosis (Fig. 1B). The patient was subjected to a transient session of hemodialysis (HD) treatment with repeated femoral vein puncture<sup>8</sup> between hospital days 2 and 14, during which time she began to feel well along with the decline in her sCr level. Finally, a Tenckhoff PD catheter was placed on hospital day 17 through a classic transverse surgical incision with a favorable postoperative course. PD using two daily exchanges (1.5 L of Midperiq<sup>®</sup>135  $\times$  2, Terumo Co.) with a total dwell of 12 hours was then initiated (Fig. 2). At the 1-year follow-up, the patient is still doing well with a daily urine output of approximately 1,100 to 1,300 mL. Considering the current therapeutic guidance for PD adequacy,<sup>9</sup> her solute clearance status expressed in terms of  $Kt/V_{\text{urea}}$ , where  $K$  is the clearance of urea,  $t$  is the treatment duration, and  $V$  is the urea distribution volume,<sup>10</sup> also appears to be favorable (a total  $Kt/V_{\text{urea}}$ : 1.9 [peritoneal  $Kt/V_{\text{urea}}$ : 0.8, residual renal  $Kt/V_{\text{urea}}$ : 1.1]).

## Discussion

Along with the decline in the mortality of patients with congenital heart diseases, it has become clear that various types of disturbed physiologies occur beyond the cardiovascular system.<sup>5,11</sup> Chronic renal insufficiency is one such late complication, and it may also be common even in adult subjects after obtaining the palliation of previous TOF.<sup>5,11</sup> Several morphological alterations, including glomerular enlargement, mesangial hypercellularity, glomerular capillary congestion, and segmental glomerular sclerosis, have been focused on as pathologic bases of the disease.<sup>5,12,13</sup> In the current patient, the absence of any pathological information precluded us from precisely evaluating the cause of end-stage kidney disease. However, we believe that numerous conditions, including previous surgical palliation and long-standing cyanotic conditions, could play a role in the establishment of her renal manifestations.<sup>5,11</sup> Alternatively, or in addition, the long-term use of various analgesics for relieving menstrual pain and a tension headache, which was revealed by our thorough clinical interview, might have played a role in our patient through

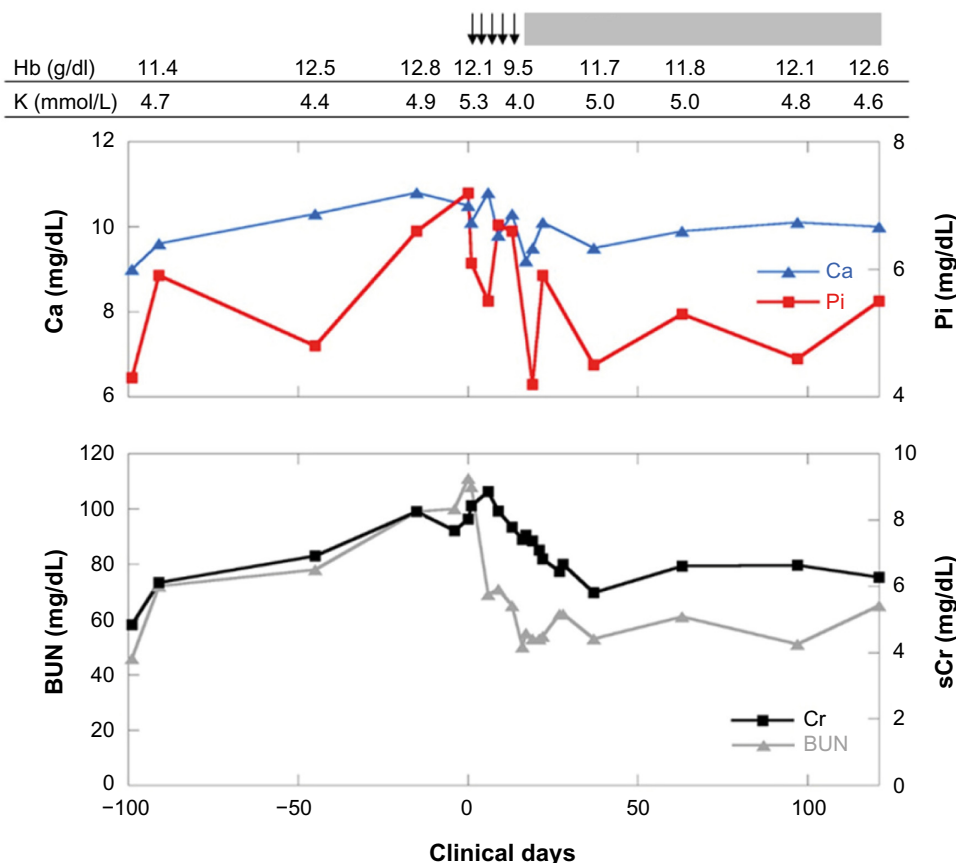


**Figure 1.** Cardiothoracic manifestations. The parasternal long-axis view of the echocardiogram with Doppler color flow mapping (A) demonstrated the bidirectional shunt with predominant left-to-right shunting (arrow heads) through the VSD, while the axial view of the chest CT (B) scan revealed right pulmonary artery origin stenosis (arrow heads).

their nephrotoxic nature.<sup>14</sup> Thus, the combination of TOF and CKD may not be surprising; however, the clinical significance of the current patient should be evaluated carefully in terms of the impact of the circulation disturbance due to cardiac anomaly on the therapeutic managements for end-stage kidney disease, including the choice of dialysis modality.

For many patients with end-stage kidney disease, a renal transplant is the treatment of choice as it replicates the standard renal physiology much more closely than dialysis treatments and offers an improved quality of life as well as survival benefits.<sup>15,16</sup> Despite the high risk of cardiac death before and after renal transplantation,<sup>17</sup> patients with cardiac disease or who are at high risk for cardiac disorders are still eligible for this procedure.<sup>18</sup> Moreover, it has been stated that patients with severe irreversible heart dysfunction should not be listed for kidney transplantation alone, while there may be select patients who are candidates for combined heart–kidney transplants.<sup>18</sup> The scarce information regarding renal transplantation among patients with unrepaired congenital heart disease precludes us from precisely evaluating the validity of such a strategy in the current case; however, the lack of readily available cadaveric or living renal transplantation in a timely manner, which leaves many subjects requiring dialysis,<sup>15,16</sup> obliged us to start dialysis treatment.

Considering the pathophysiologic characteristics of TOF,<sup>1,19,20</sup> we felt that avoiding the use of dialysis catheters as a means of either temporary or permanent vascular access for HD and the execution of periodic HD with peripheral vascular access should be mandatory in the current patient. Indeed, these devices may predispose patients with TOF to the detrimental pathologies such as pulmonary embolism, septicemia, infectious endocarditis, and paradoxical embolism,<sup>21–27</sup> although the available literature has seldom discussed pulmonary embolism in patients with TOF.<sup>28</sup> We must also recognize that in patients with an intrinsic cardiac anomaly, the creation of peripheral vascular access may result in severe



**Figure 2.** The changes in the BUN, sCr, Ca, Pi, K, and Hb values during the observation period. After five sessions of HD (arrows), PD was initiated. The number “0” is designated as the point of admission. Note that the patient’s sCr and BUN levels finally settled around 6 and 60 mg/dL, respectively.

cardiac failure.<sup>29</sup> Otherwise, it should be noted that bacteremia is less frequent in PD patients than in chronic HD patients with endovascular catheter, and no reports on infectious endocarditis in PD patients were available, despite the fact that septicemia is not exceptional in PD subjects<sup>30,31</sup>; therefore, PD does not appear to be an additional risk of infectious endocarditis among patients with end-stage kidney disease.<sup>31</sup> Alternatively, or in addition, the therapeutic nature of PD, including minimal variation in the intravascular volume status, reduction in cardiovascular stress, avoidance of peaks and troughs in uremic toxins, arrhythmia prevention, and the better preservation of residual renal function,<sup>10,32,33</sup> also encouraged us to promote the procedure as a good modality of renal replacement therapy for the current patient. One may argue against our concerns about the potential risks associated with a dialysis catheter and HD. Moreover, no one knows the impact of starting HD with repeated femoral vein puncturing for a transient vascular access on the risks of the concurrent development of thromboembolic and/or infectious events.<sup>8</sup> Nevertheless, it is necessary to take a proactive approach and not let lethal events become apparent. We believe that our policy regarding the application of tailored renal replacement therapy should be an appropriate therapeutic choice for the current patient. Apparently, we are always facing, as do most physicians at various times, different types of clinical challenges, as described herein.

There may be substantial variation in the type and intensity of managements provided to end-stage kidney disease patients with congenital heart disease, stemming from the uncertainty of the advantages and disadvantages of renal care in this population. A lack of prospective data suggests that numerous therapeutic decisions among such subjects are potentially empirical. Indeed, only a few anecdotal reports describing patients with TOF who began dialysis treatments during the observation periods for the disease are available.<sup>4,34,35</sup> PD with reduced dialysate exchanges may be less advantageous than full-dose PD in terms of ultrafiltration and dialytic clearance, while such a PD protocol may permit early incremental dialysis and provide favorable clinical significance.<sup>33,36,37</sup> At present, our patient appears to tolerate the PD program well with two daily dialysate exchanges; however, the validity of our strategy should be determined only when more experience with additional cases similar to ours has been accumulated. Thus, the establishment of an optimal management program for end-stage kidney disease patients with congenital heart disease should be a matter requiring continuous and careful attention.

#### Author Contributions

Drafted the manuscript: KO, TA. Contributed to the acquisition of the clinical data: TMiki, NO, TS, TMasuda, TMurakami, TI, ST. Provided a detailed review of the



contents and structure of the manuscript, resulting in significant changes to the original document: YA, SM, DN. All the authors have read and approved the final manuscript.

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