TRANSPLANT QUIZ

# From combined heart–kidney to kidney transplantation program: what nephrologists should know about dilated cardiomyopathy

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## CASE

A 42-year-old hemodialysis (HD) patient was investigated in our department for symptomatic heart failure (HF) despite daily home dialysis. He had a history of living donor kidney transplantation at the age of 18 that lasted 7 years. Home dialysis was then started. At the age of 40, he developed acute heart failure symptoms.

Echocardiography revealed severe dilated cardiomyopathy (DCM). Coronarography and myocardial perfusion scintigraphy showed no abnormal findings. Betablockers were administrated, and RAAS inhibitor dosing was optimized. Dyspnea persisted, and patient was referred to our department.

At admission, blood pressure was 116/82 mmHg, and pulse 68 beats/min. No peripheral edema was observed. Dry weight was 62.5 kg. Patient was anuric. Hemoglobin level was 9.8 g/dl, highly sensitive troponin level was 62 ng/ml, and BNP level was 1527 ng/ml. The liver enzyme levels were normal. C-reactive protein was 4.2 mg/ml. Vitamin level, zinc levels, and thyroid function were normal.

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**Key words**
apheresis, cardiac failure, dialysis

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*Abbreviations used*

| | |
|---|---|
| SGLT2 | Sodium/glucose cotransporter 2 |
| RAAS | Renin-angiotensin-aldosterone system |
| CCP | Cyclic citrullinated peptid |
| Sm | Smith |
| SSA | Sjögren's syndrome-related antigen A |

## Quiz

1. Which treatment would have the best efficacy to rapidly improve symptoms of HF in this context?
   A. SGLT2 inhibitors
   B. Spironolactone
   C. **Daily ultrafiltration**
   D. Hydrochlorothiazide
   E. Dual RAAS blockade

Despite achieving a normal dry weight and decreasing the BNP level, the LVEF remained low (20%) and the cardiac index was 1.53 l/min/m². Medical treatment includes administration of Betablockers and RAAS inhibitor at optimum dose.

2. Which diagnosis do you suspect?
   A. Diabetic cardiomyopathy
   B. Ischemic cardiomyopathy
   C. thiamine deficiency
   D. **idiopathic DCM**
   E. auto-immune DCM
   F. Chagas disease


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3. A autoimmune dilated cardiomyopathy is suspected. Which antibodies are strongly associated with this condition?
   A. Anti-DNA antibodies
   B. Anti-Sm antibodies
   C. Anti-CCP antibodies
   D. **Anti-beta1adrenergic receptor antibodies**
   E. Anti-SSA antibodies
4. Laboratory tests confirmed the diagnosis of autoimmune dilated cardiomyopathy. Which specific treatment has shown the best level of evidence in this condition?
   A. **Immunoadsorption**
   B. Cyclophosphamide
   C. Mycophenolate mofetil
   D. Intravenous immunoglobulins
   E. Glucocorticoids
5. If symptoms of heart failure and LVEF do not improve after the above-mentioned treatment, which treatment would you consider based on current evidence?
   A. Plasma exchange
   B. Hemoperfusion
   C. **Dual heart-kidney transplantation**
   D. IdeS (Specific Immunoglobulin G (IgG)-Cleaving Enzyme from *Streptococcus pyogenes*)
   E. Azathioprine
   F. Rituximab

## Discussion

Dilated cardiomyopathy (DCM) is associated with multiple causes that include coronary artery disease, vitamin deficiencies, or abnormal thyroid function. In advanced stages, when the decreased left ventricular ejection fraction (LVEF) is irreversible, a heart transplantation is indicated.

In case of heart failure in hemodialysis patient, fluid overload (FO) is the first cause to exclude. FO may be related to inadequate dialysis dose, food intake, or decrease in urinary output. Despite achieving a normal dry weight and decreasing the BNP level, the LVEF remained low (20%) and the cardiac index was 1.53 l/min/$m^2$. Medical treatment includes administration of betablockers and RAAS inhibitor at optimum dose. Data on mineralocorticoid antagonist receptor (MRA) such as spironolactone in hemodialysis are promising but not currently recommended.

The patient was registered on a waiting list for combined heart–kidney transplantation.

In rare cases, DCM can be triggered by autoantibodies [1]. Etiologic investigations showed positivity for anti-M2 muscarinic receptor (anti-M2r) and anti-beta1 adrenergic receptor (anti-B1ar) antibodies (E.R.D.E, AAK Diagnostik, Berlin, Germany).

The patient started immunoadsorption (IA) twice weekly during 6 weeks combined with hemodialysis. The clinical status improved shorty after IA initiation and the LEVF rapidly improved up to 42% at M3 (Fig. 1). IA was maintained monthly, and the LEVF remained stable, allowing removal from the heart transplantation waiting list. Concomitantly, IA had a slight effect on anti-HLA immunization, as 5 out of 8 major Class I anti-HLA antibodies decreased below 2000 MFI after apherisis. Similarly, levels of anti-M2r and anti-B1ar antibody titers decreased slightly based on a semi-quantitative evaluation. Twenty months after IA initiation, the patient exhibits no signs of cardiac failure, undergoes daily home HD and monthly IA maintenance sessions, and is still waiting for a kidney transplant.

Dilated cardiomyopathy is a peculiar condition in which autoimmunity plays a major role and progressive cardiac chamber dilatation and remodeling finally leads to congestive HF. Autoantibodies against various myocyte structural and functional proteins have been identified in DCM. In particular, the pathogenetic role of autoantibodies against b1-adrenoreceptors has been extensively studied in experimental models and in humans [2,3]. IA is the main treatment for autoimmune DCM [4]. A recent report has shown efficacy of IA with a complete response in 48% of patients based on clinical and/or radiological signs [5].

The diagnosis of autoimmune DCM in a HD patient is challenging because of the multiple causes related to patient comorbidities and HD efficacy. The latter

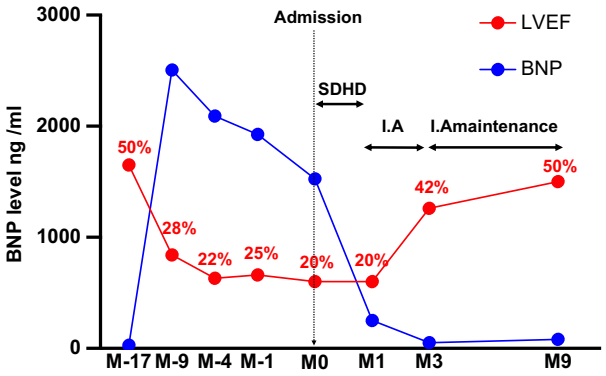


**Figure 1** Kinetic of BNP (Blue) and left ventricular ejection function, LVEJ (red) prior and after the treatment by immunoadsorption (IA) induction and maintenance. SDHD, intensive short daily hemodialysis.



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include fluid overload, myocardial infarctions, arrhythmia, and vitamin deficiency. Therefore, DCM may be underdiagnosed [1].

In conclusion, we advocated for the in-depth diagnosis of DCM in a hemodialysis patient before transplantation evaluation. Given the specificity of auto anti-M2r and/or anti-B1ar antibodies in DCM, clinicians should consider IA to improve LEVF.

## Conflict of interest

The authors declare no competing financial interest.

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