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Cardiac amyloidosis in a kidney transplant recipient

Bahareh Marghoob[1*], Mohammad Hassan Fallahkohan[2]

[1]Iran University of Medical Sciences, Hasheminejad Kidney Center, School of Medicine, Nephrology Department, Tehran, Iran
[2]Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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ABSTRACT

Systemic amyloidosis is a collection of diseases caused by the deposition of protein fibrils in organ tissues, leading to significant morbidity. Cardiac amyloidosis, a rare and debilitating condition, can affect any organ in the body. The two primary types of cardiac amyloidosis are systemic light chain (AL) amyloidosis, which is more common and related to light chain overproduction in the bone marrow, and wild-type transthyretin cardiac amyloidosis (ATTRwt). This case report describes a unique and uncommon case of cardiac amyloidosis observed in a patient following kidney transplant, which was effectively managed using a novel therapeutic regimen.

Case Report

Implication for health policy/practice/research/medical education:
This case report describes a cardiac AL amyloidosis observed in a kidney transplant patient, which was diagnosed and effectively managed with a daratumumab-based chemotherapy regimen (Dara-CyBorD), supporting the current literature.

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Introduction

Amyloidosis is characterized by the extracellular deposition of fibrils composed of low molecular weight subunits derived from various serum proteins (1). Over 38 distinct types of amyloid diseases have been identified, with the kidneys, heart, autonomic nervous system, and liver being the most commonly involved organs. Cardiac amyloidosis can lead to hypertrophy of the cardiac walls, resulting in impaired cardiac function, arrhythmias, heart block, restrictive cardiomyopathy, or heart failure with preserved ejection fraction.

The two major forms of cardiac amyloidosis are AL amyloidosis, caused by the deposition of immunoglobulin light chains, and ATTR (transthyretin amyloidosis) amyloidosis, which can be hereditary (familial) or age-related (wild-type). In ATTR amyloidosis, the transthyretin protein misfolds and deposits in the myocardium with similar symptoms to AL amyloidosis but with different pathophysiology. Certain genetic variants, such as Ile68Leu and Leu111Met, are linked to the cardiac phenotype of ATTR amyloidosis (2,3).

Clinically, amyloidosis should be suspected in patients presenting with unexplained left ventricular hypertrophy, heart failure accompanied by bilateral carpal tunnel syndrome, peripheral neuropathy, renal failure, or aortic stenosis. Echocardiographic findings, such as myocardial granular sparkling, low-flow, low-gradient aortic stenosis, and abnormal left ventricular global longitudinal strain, further support the diagnosis (4,5).

The diagnosis of cardiac amyloidosis, as well as AL amyloidosis, relies on the detection of monoclonal light chains. A disproportion in the usual 2:1 ratio of kappa to lambda light chains and the presence of clonal free lambda light chains in serum or urine are key diagnostic markers. The use of immunofixation electrophoresis of serum and urine, combined with a serum free light chain assay, has a

*Corresponding author: Bahareh Marghoob,
Email: baharehmarghoob@yahoo.com

sensitivity of over 95% for detecting AL amyloidosis (6).

This case report describes a rare instance of cardiac amyloidosis in a patient following kidney transplantation, illustrating the diagnostic and therapeutic challenges associated with this condition.

Case Presentation

A 53-year-old male presented to Hasheminejad kidney center with a chief complaint of breathlessness. He had undergone kidney transplantation from a living unrelated donor two years prior, following hemodialysis for one year. His medical history included diabetic kidney disease and hypertension for over a decade. Post-transplantation, the patient became hypotensive, and all antihypertensive medications were gradually discontinued. He reported chest discomfort and palpitations on exertion but had no other comorbidities.

Physical examination revealed no significant abnormalities. Jugular venous pressure was normal, and there was no evidence of regional lymphadenopathy or lower extremity edema. Laboratory investigations showed normal serum creatinine, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), electrolytes, and troponin levels. However, the brain natriuretic peptide (NT-proBNP) level was elevated at 1441 pg/mL. Serum and urine protein electrophoresis were unremarkable, but the free kappa to lambda light chain ratio was elevated at 2.8, and beta2 microglobulin was 2.8 µg/ml. No proteinuria or hematuria was detected.

Imaging studies, including ultrasonography of the transplanted kidney, revealed normal size, echogenicity of cortical parenchyma, and normal peak systolic arterial velocity and resistive index of Doppler parameters. Electrocardiography (ECG) was otherwise normal, normal sinus rhythm without ST-segment changes. Echocardiography demonstrated normal chamber sizes and function, with no signs of aortic stenosis, but biventricular wall thickening was observed. Left ventricular ejection fraction and pulmonary artery pressure were within normal limits.

Bone marrow aspiration and biopsy showed normal cellularity and composition, with no amyloid deposits and negative Congo red staining. Immunohistochemistry (IHC) and immune-phenotyping identified approximately 3% plasma cells (CD138-positive). Cardiac magnetic resonance imaging (MRI) findings were consistent with amyloidosis, and subsequent myocardial biopsy confirmed the presence of focal amyloid deposits with positive Congo red staining. Meanwhile, the IHC of the myocardial tissue demonstrated kappa and lambda light chain deposition, incongruent with AL amyloidosis (Figures 1 and 2). Neurological investigations via electromyography and nerve conduction velocity studies revealed polyneuropathy consistent with diabetic neuropathy.

Results

The patient was diagnosed with AL amyloidosis and initiated on a daratumumab-based chemotherapy regimen (Dara-CyBorD) aligned with the hematology-oncology consult. Following the initiation of chemotherapy, his symptoms improved. Mycophenolate mofetil (MMF) was discontinued to avoid over-immunosuppression. At the most recent follow-up, his serum creatinine level was 0.8 mg/dL, indicating stable renal function.

Discussion

Amyloid cardiomyopathy is an incrementing but often underdiagnosed cause of heart failure and arrhythmias, particularly in older adults (7). The global incidence of AL amyloidosis is estimated to range from 8 to 14 cases per million per year, with a higher incidence noted in individuals aged 18–64 years (8,9). In healthy individuals,

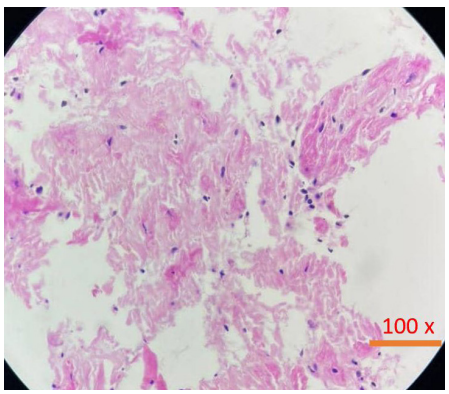

Figure 1. Eosinophilic amorphous aggregates on hematoxylin and eosin (H&E) staining of myocardial biopsy tissue.

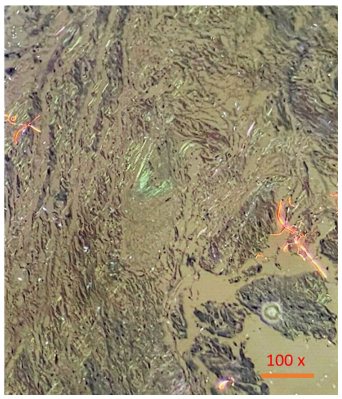

Figure 2. Apple-green birefringence on Congo red staining under polarized light microscopy, indicative of amyloid deposits.

approximately two-thirds of light chains are kappa and one-third are lambda; this ratio is reversed in AL amyloidosis.

Diagnostic delays are common, with 20%–30% of patients presenting with congestive heart failure at diagnosis, and 50%–70% with subsequent development of cardiac amyloid infiltration. Early recognition and treatment are paramount, with therapeutic strategies focusing on anti-plasma cell therapy to reduce free light chain levels and supportive care. Combination chemotherapy regimens, such as daratumumab (anti-CD38), cyclophosphamide, bortezomib (proteasome inhibitor), and high dose dexamethasone (Dara-CyBorD), are commonly utilized (10).

Conclusion

This case shows the diagnostic and therapeutic challenges of cardiac amyloidosis in a post-kidney transplant patient. The 53-year-old male was successfully treated with a Dara-CyBorD regimen following a definitive diagnosis of AL amyloidosis via cardiac biopsy. This emphasizes the importance of early diagnosis, multidisciplinary collaboration, and tailored therapeutic approaches to improve outcomes in patients with cardiac amyloidosis.

Authors' contribution

Conceptualization: Bahareh Marghoob.
Data curation: Bahareh Marghoob.
Formal analysis: Bahareh Marghoob.
Funding acquisition: Bahareh Marghoob.
Investigation: Bahareh Marghoob, Mohammad Hassan Fallahkohan.
Methodology: Bahareh Marghoob.
Project administration: Bahareh Marghoob.
Resources: Bahareh Marghoob.
Software: Mohammad Hassan Fallahkohan.
Supervision: Bahareh Marghoob.
Validation: Mohammad Hassan Fallahkohan.
Visualization: Bahareh Marghoob.
Writing–original draft: Bahareh Marghoob.
Writing–review & editing: Bahareh Marghoob.

Conflicts of interest

The authors declare that they have no conflicts of interests.

Ethical issues

This case report was conducted in accordance with the World Medical Association Declaration of Helsinki. The patient provided written informed consent. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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