Unravelling complexity: A case of progressive cardiac involvement in hereditary amyloidosis after liver transplant

Edwin Lu, Akash Goyal, Katarzyna E Gil, Anna Hay, Mason Mocarski, Karolina M Zareba

Division of Cardiovascular Medicine, The Ohio State University, Columbus, United States

Correspondence to:
Karolina M Zareba, MD, FSCMR,
Associate Professor,
Division of Cardiovascular Medicine,
The Ohio State University,
473 W. 12th Ave, Suite 200
Columbus, OH USA 43210
phone: 1-614-293-8963
e-mail:
karolina.zareba@osumc.edu

DOI: 10.33963/v.phj.100188

Received:
March 8, 2024

Accepted:
April 9, 2024

Early publication date:
April 22, 2024

A 73-year-old Caucasian male with a past medical history of hypertension, hyperlipidemia, right bundle branch block, hereditary transthyretin amyloidosis (Leu78His variant, 3 affected first-degree relatives) status post orthotopic liver transplant (OLT) in 2006, presented to the emergency department with exertional dyspnea and presyncope. Initial evaluation was notable for bradycardia with high-grade atrioventricular block (AVB). Electrocardiography one year prior to the presentation demonstrated sinus rhythm with first-degree AVB and right bundle branch block. An echocardiogram performed at the same time revealed a mild increase in left ventricular (LV) wall thickness (1.3 cm) and normal LV ejection fraction (EF) of 57%. Cardiovascular magnetic resonance (CMR) or scintigraphy imaging was not performed before OLT in 2006. Given the AVB and history of amyloidosis, CMR was ordered.

CMR was performed at 1.5T (Magnetom Avanto, Siemens Healthineers, Germany) using standardized protocols with cine imaging, T1 mapping (Modified Look-Locker Inversion Recovery sequence), T2 mapping (T2-prepared balanced steady-state free precession), and late gadolinium enhancement imaging (phase-sensitive inversion recovery). The LV was top-normal in size (LV end-diastolic volume index 103 ml/m^2) and exhibited increased LV wall thickness (1.5 cm), with normal LV (57%) and right ventricular (RV) EF (58%). T2 signal was diffusely elevated (up to 57 ms; Figure 1). Pre-contrast native T1 was elevated in the septum (1142 ms) with extracellular volume fraction of 45% (Figure 1). CMR reference values for the myocardium were based on institutionally established normative control data and were as follows: native T1 1002 ± 41 ms, extracellular volume fraction 25 ± 3%, T2 47 ± 3 ms. There was evidence of altered gadolinium kinetics with prominent and diffuse late gadolinium enhancement in the basal LV segments, dense foci in the septal and lateral walls (Figure 1) with biatrial and partial RV enhancement. 99m-technetium pyrophosphate (Tc-99m PYP) imaging demonstrated a 3-hour heart/contralateral lung ratio of 1.99 and grade 3 myocardial uptake, which confirmed the CMR-based initial diagnosis of cardiac amyloidosis (Figure 1). Laboratory testing was negative for light-chain amyloidosis.

OLT is regarded as a definitive therapy for transthyretin amyloidosis due to halting production of the amyloidogenic transthyretin (TTR) protein. Despite improvement in patient mortality after OLT, progressive cardiomyopathy can still occur [1]. This is hypothesized to be due to continued deposition of wild-type TTR onto an amyloidogenic scaffold from pre-existing mutant TTR [2]. Progressive cardiac disease is not seen in patients undergoing both heart and liver transplant [3].

This case highlights the importance of CMR in cardiac monitoring in patients with amyloidosis, regardless of the type of treatment implemented [4]. The patient exhibited conduction disease for years prior to his index presentation. After CMR and Tc-PYP imaging, the patient underwent pacemaker implantation and was placed on tafamidis therapy. He remains on angiotensin receptor blocker and beta blocker (introduced due to frequent episodes of nonsustained ventricular tachycardia) with good tolerance. Given advancements in medical therapy for cardiac amyloidosis, early detection *via* CMR can alter management and should be considered in patients with amyloidosis even after OLT.

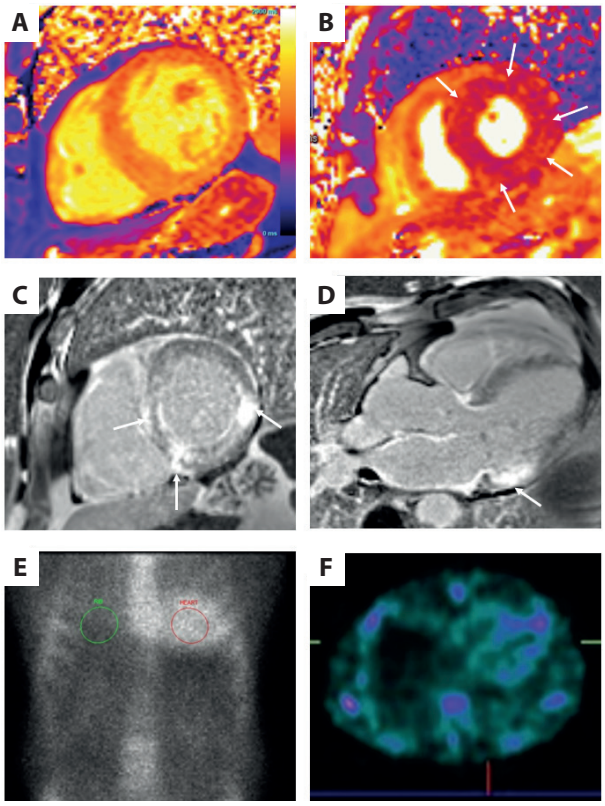

Figure 1. Native T1 color map with elevation of the septal T1 values on the mid-short-axis view (**A**); T2 systolic color map with diffuse T2 elevation on the mid-short-axis view (**B**; arrows); Late gadolinium enhancement imaging demonstrating extensive enhancement in the basal inferoseptal, inferior and inferolateral walls on the basal short-axis (**C**) and 3-chamber views (**D**); 3-hour technetium-99m pyrophosphate scintigraphy with the heart/contralateral lung ratio of 1.99 (**E**) and grade 3 myocardial uptake on technetium-99m pyrophosphate single-photon emission computed tomography (**F**)

Article information

Conflict of interest: None declared.

Funding: None.

REFERENCES

1. Dubrey S, Davidoff R, Skinner M, et al. Progression of ventricular wall thickening after liver transplantation for familial amyloidosis1. Transplantation. 1997; 64(1): 74–80, doi: 10.1097/00007890-199707150-00014.
2. Benson MD. Liver transplantation and transthyretin amyloidosis. Muscle Nerve. 2013; 47(2): 157–162, doi: 10.1002/mus.23521, indexed in Pubmed: 23169427.
3. Liepnieks JJ, Zhang LQ, Benson MD. Progression of transthyretin amyloid neuropathy after liver transplantation. Neurology. 2010; 75(4): 324–327, doi: 10.1212/WNL.0b013e3181ea15d4, indexed in Pubmed: 20660862.
4. Grzybowski J, Podolec P, Holcman K, et al. Diagnosis and treatment of transthyretin amyloidosis cardiomyopathy: A position statement of the Polish Cardiac Society. Kardiol Pol. 2023; 81(11): 1167–1185, doi: 10.33963/v.kp.97648, indexed in Pubmed: 37768101.