

Case series of heart transplantations in patients with transthyretin amyloidosis – University Hospital Centre Zagreb experience

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Introduction: Transthyretin amyloid cardiomyopathy (ATTR-CM) is characterized by deposition of amyloid fibrils in the myocardium which can lead to advanced heart failure (HF). Heart transplantation (HTx) is curative treatment option in patients who reach advanced HF stage, and it is recommended to combine HTx and liver transplantation (LTx) in cases of hereditary ATTR-CM to prevent further progression of the disease¹. We retrospectively analysed data of 6 ATTR-CM patients who received HTx or HTx and LTx in UHC Zagreb.

Case Series: Historically, the first patient was a female, aged 53 at the time of HTx. She had HF symptoms for 2 years prior HTx, and even though ATTR suspicion was made after first echocardiography, multiple tissue biopsies were negative for amyloid deposits. In 2011 she underwent HTx and histopathological analysis of explanted heart diagnosed ATTR-CM. One year following HTx there were signs of progression of the disease, predominantly polyneuropathy (PNP) but also signs of ATTR-CM of cardiac graft. She died 6 years after HTx due to infective complications.

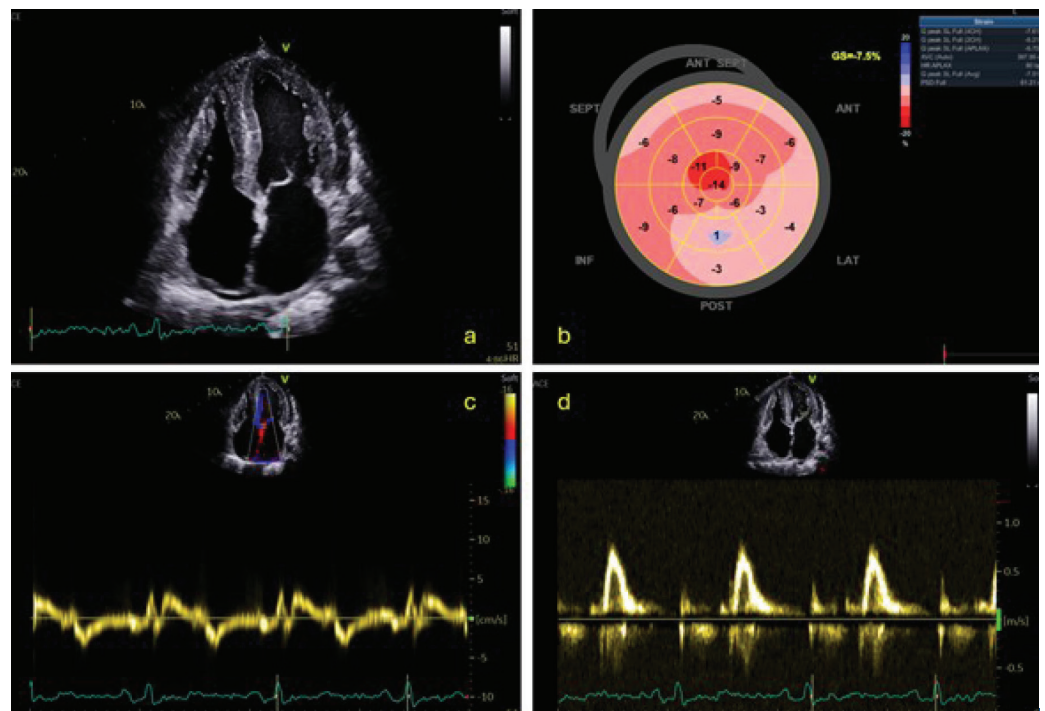


FIGURE 1. Echocardiography of patient 6. a) Apical 4 chamber view showing thickened left ventricular walls, b) Global longitudinal strain with typical apical sparing, c) Lateral annulus tissue doppler showing low velocities, d) Transmitral inflow doppler showing diastolic dysfunction

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The second patient was a female, aged 58 at the time of HTx. Five years following the first HF symptoms, the tissue biopsy was positive for amyloid deposits, and genetic testing proved Asp18Glu mutation. She underwent HTx in 2016, and from 2018 to 2019 was treated with tafamidis. LTx was never performed due to progression of PNP with infective complications, of which she died 4 years following HTx.

The third patient was male, aged 53 at time of HTx. He received HTx in 2019, a few months after positive genetic testing (Asp18Glu) and 4 years after the first HF symptoms. He received LTx in 2022 and died in 2024 due to infective complications.

The fourth patient, male, aged 64 at the time of HTx was the only patient transplanted in our centre with the wild type of ATTR-CM, also proven by tissue biopsy. He underwent HTx in 2019 and is still in regular follow-up.

The fifth and the sixth patient were both males, aged 47 and 52 at the time of HTx respectively. They both had positive family history and proven Asp18Glu mutation. They were both on tafamidis for more than 2 years before HTx. The first of the two received combined HTx and LTx in January 2023 and had one episode of early acute liver rejection that resolved completely. The second underwent combined HTx and LTx in August 2024, so far without complications. Complete patients' data are shown in **Table 1**, and typical echocardiogram before Htx is shown in **Figure 1**.

Conclusion: In patients with advanced heart failure due to hereditary ATTR-CM combined HTx and LTx is preferred therapy while outcomes following isolated HTx are hindered by continuous progression of the disease.

TABLE 1. Patient characteristics.

| | 1 | 2 | 3 | 4 | 5 | 6 |
|-----------------------------------|----------------------------|-------------------------------------|-------------------------------------|-----------------------------|----------------------|-------------------------------------|
| Gender | Female | Female | Male | Male | Male | Male |
| Age at HTx | 53 | 58 | 53 | 64 | 47 | 52 |
| Comorbidities | HA, Afib | Afib, Emphysema | CKD | HA, CKD, DM | Gastritis | Afib |
| HF symptom onset | 2009 | 2011 | 2015 | 2018 | 2019 | 2021 |
| ECHO signs of ATTR-CM | 2010 | 2012 | 2017 | 2014 | 2009 | 2021 |
| Polyneuropathy | Sensorimotor and autonomic | Sensorimotor and autonomic | Sensory, autonomic (CASS 2) | Autonomic (CASS 2) | Mild sensory | Sensorimotor and autonomic (CASS 3) |
| Genetics | / | Asp18Glu | Asp18Glu | negative | Asp18Glu | Asp18Glu |
| Tissue biopsy | negative | Fat pad + | Fat pad + | Fat pad + | Fat pad + | / |
| ECHO | | | | | | |
| - EF (%) | 25 | 25 | 30 | 45 | 45 | 45 |
| - GLS (%) | / | / | / | -5.1 | -8 | -9 |
| - IVSd (mm) | 20 | 15 | 28 | 25 | 18 | 22 |
| HTx | 18.04.2011 | 27.04.2016 | 30.05.2019 | 5.10.2019 | 04.01.2023 | 24.08.2024 |
| LTx | / | / | 03.06.2022 | / | 04.01.2023 | 24.08.2024 |
| Histopathology of explanted heart | amyloidosis | amyloidosis | amyloidosis | amyloidosis | amyloidosis | amyloidosis |
| Specific therapy | / | 2018-2019 | / | / | Feb. 2021- Jan. 2023 | Dec. 2022- Aug. 2024 |
| Complications | Infections, vision loss | Infections, vision and hearing loss | Infections, vision and hearing loss | CMV infection, osteoporosis | Liver rejection | / |
| Outcome | Died in Jul. 2017 | Died in Nov. 2020 | Died in Aug. 2024 | Follow-up | Follow-up | Follow-up |

Afib = atrial fibrillation; ATTR-CM = transthyretin amyloid cardiomyopathy; CASS = Composite Autonomic Severity Score; CI = cardiac index; CKD = chronic kidney disease; DM = diabetes mellitus; ECHO = echocardiography; EF = ejection fraction; GLS = global longitudinal strain; HA = arterial hypertension; HF = heart failure; HTx = heart transplantation; IVSd = interventricular septum diameter; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance.

LITERATURE

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