

Progression of myocardial sympathetic denervation assessed by ¹²³I-MIBG imaging in familial amyloid polyneuropathy and the effect of liver transplantation

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Abstract

Introduction

Familial amyloid polyneuropathy (FAP) is a rare disease caused by systemic deposition of amyloidogenic variants of the transthyretin (TTR) protein. The TTR-V30M mutation is caused by the substitution of valine by methionine at position 30 and mainly affects the peripheral and autonomic nervous systems. Cardiovascular manifestations are common and are due to autonomic denervation and to amyloid deposition in the heart. Cardiac sympathetic denervation detected by iodine-123 labeled metaiodobenzylguanidine (MIBG) is an important prognostic marker in TTR-V30M FAP. Liver transplantation, widely used to halt neurological involvement, appears to have a varying effect on the progression of amyloid cardiomyopathy. Its effect on the progression of cardiac denervation remains unknown.

Methods

In this observational study, patients with the TTR-V30M mutation underwent annual cardiac assessment and serial MIBG imaging with quantification of the late heart-to-mediastinum (H/M) ratio.

Results

We studied 232 patients (median age 40 years, 54.7% female, 37.9% asymptomatic at the time of inclusion) who were followed for a median of 4.5 years and underwent a total of 558 MIBG scans. During follow-up, 47 patients (20.3%) died. MIBG scintigraphy at inclusion was a strong predictor of prognosis, with the risk of death increasing by 27.8% for each one-tenth reduction in the late H/M ratio. The late H/M ratio decreased with age (0.082/year, $p < 0.001$), but progression of cardiac denervation was so slow that annual repetition of MIBG imaging did not increase its prognostic accuracy. During follow-up, 70 symptomatic patients underwent liver transplantation. The late H/M ratio decreased by 0.19/year until transplantation but no statistically significant differences were detected after the procedure.

Conclusions

Cardiac denervation is common during the progression of TTR-V30M FAP and quantification of the late H/M ratio on MIBG scintigraphy is valuable for prognostic stratification of these patients. Liver transplantation stabilizes cardiac denervation, without recovery or further deterioration in cardiac MIBG uptake after the procedure.

Keywords:

Amyloid; Scintigraphy; Liver transplantation