IMAGES IN NUCLEAR CARDIOLOGY

ATTR Amyloidosis Concomitant with Parkinsonism and Cardiac Sympathetic Neuropathy

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Wild-type transthyretin amyloidosis (ATTRwt) is an infiltrative disease in which amyloid fibrils derived from transthyretin are deposited in various tissues without mutations in *TTR* gene. Symptoms mainly manifest in joints, ligaments, and the heart, leading to carpal tunnel syndrome, spinal canal stenosis, cardiac hypertrophy, arrhythmia, and heart failure (1). ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy is widely used to evaluate cardiac sympathetic innervation in patients with chronic heart failure. In addition, it is applied to the differential diagnosis of Parkinson's disease from other neurodegenerative parkinsonism, characterized by reduced accumulation of ^{123}I-MIBG in the heart (2). Here we report the case of ATTRwt presenting parkinsonism concomitant with reduced accumulation of ^{123}I-MIBG scintigraphy in the heart.

Case report

A 76-year-old man was referred to our hospital due to worsening leg edema and shortness of breath. He had a three-year history of dyskinesia and gait disturbance. He presented parkinsonism, including muscle rigidity, slouching gait, and bradykinesia at the time of admission. A 12-lead electrocardiogram showed atrial fibrillation. Chest X-ray showed cardiac enlargement, pulmonary congestion, and pleural effusion. Blood tests showed renal dysfunction (estimated glomerular filtration rate 48 ml/min/1.73 m^2) and elevated B-type natriuretic peptide levels (303 pg/ml). Echocardiography revealed diffuse left ventricular hypertrophy with severe hypokinesis, and the left ventricular ejection fraction was 24%. ^{123}I-MIBG scintigraphy showed early heart-to-mediastinum (H/M) ratio was 1.83 and late H/M ratio was 1.35 (the normal range in our hospital is ≥2.2), wash-out rate was 69.7% (the normal range in our hospital is ≤30%) (Figure 1). Oral medications for Parkinson's disease were started, but he presented the progression of movement disorder, suggesting that his parkinsonism was caused other than Parkinson's disease. Coronary angiography revealed no significant coronary artery stenosis. Cardiovascular magnetic resonance imaging showed gadolinium delayed contrast enhancement in the base of the left ventricle and in diffuse right ventricle. We performed ^{99m}Tc-pyrophosphate scintigraphy (PYP), obtaining planar images 3 hours after injection of ^{99m}Tc-PYP. The heart to contralateral (H/CL) ratio was 1.59 (the normal ratio is <1.3), and visual scoring showed grade 3 accumulation throughout the left ventricle (Figure 2). Right ventricular endomyocardial biopsy revealed positive for both Congo Red staining and transthyretin immunostaining (Figure 3). No genetic mutation was detected in the *TTR* gene analysis. Serum immunoglobulin light chain κ / λ ratio was within normal range, and urinary Bence-Johns protein was negative. Based on these results, he was diagnosed with ATTRwt. Medications for heart failure including angiotensin-converting enzyme inhibitor, β-blocker, and a loop diuretic improved shortness of breath and leg edema. The left ventricular ejection fraction was recovered to 57%. Tafamidis treatment was introduced, and he continued to receive the medications.

Discussion

ATTRwt affects not only solid organ tissues but also autonomic nervous system including cardiac sympathetic nerves (3). ^{123}I-MIBG scintigraphy is useful in the evaluation

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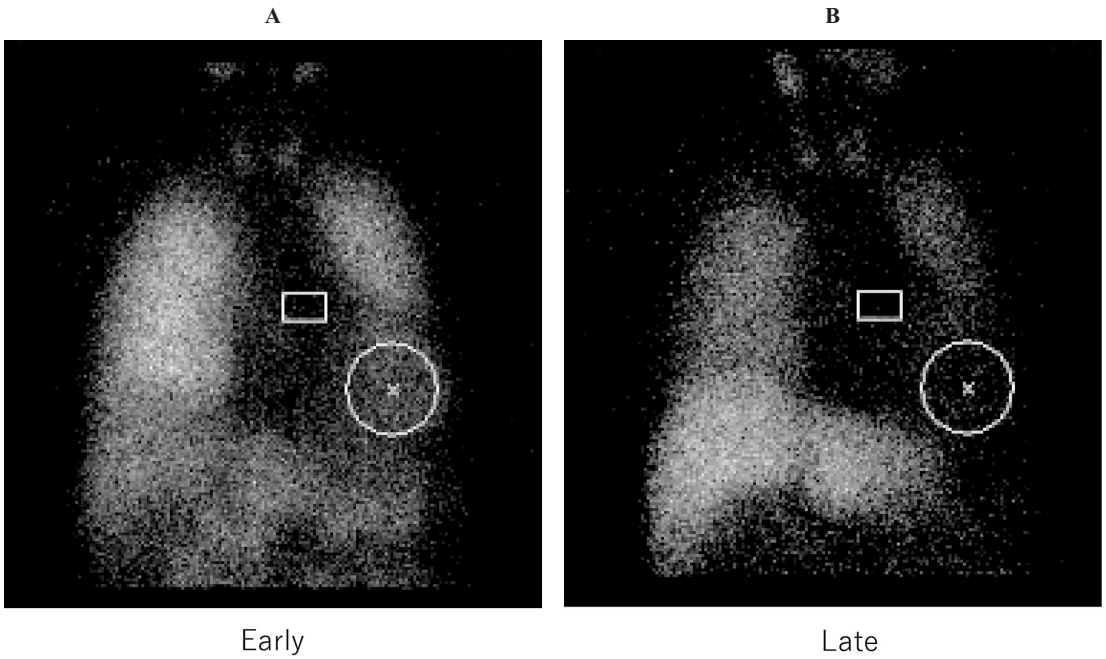

Figure 1 ^{123}I-MIBG scintigraphy showed a decreased H/M ratio (early 1.83, late 1.35, the normal range is ≥2.2 in our hospital) and increased wash-out rate (69.7%, the normal range in our hospital is ≤30%). Early phase (**A**) and Late phase (**B**).

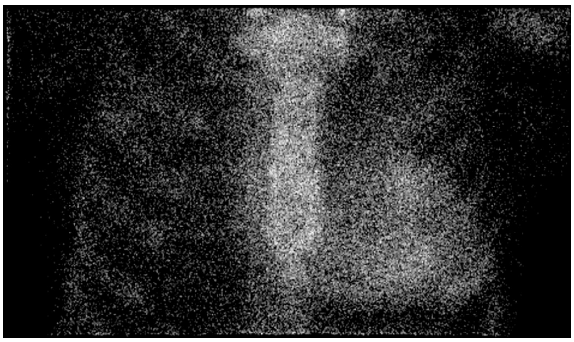

Figure 2 ^{99m}Tc-Pyrophosphate scintigraphy showed increased H/CL ratio (1. 59, the normal ratio is <1. 3) and grade 3 accumulation throughout the left ventricle.

of abnormal myocardial sympathetic nervous function, and a H/M ratio <1. 6 in late-stage image is considered a poor prognostic factor in hereditary ATTR (4). In this case, the finding of decreased H/M ratio was initially attributed to both Parkinson's disease and ATTRwt affecting cardiac autonomic nervous dysfunction. However, because the medication against Parkinson's disease did not work well, the pathophysiological condition of parkinsonism might be caused by other than Parkinson's disease, and modified by ATTRwt. Although the precise mechanisms by which TTR amyloid affects the nervous system are currently unclear, the neuropathy caused by ATTRwt may involve both of the central nervous system and cardiac sympathetic nerves, leading to exacerbation of parkinsonism and heart failure. Maetzler et al. reported that TTR levels in cerebrospinal fluid correlated negatively with amyloid β1–42, total tau, and phospho-tau levels, suggesting neuroprotective role of TTR (5). Although ^{123}I-MIBG scintigraphy has not yet been performed after the heart failure therapy, it would be interesting to confirm the recovery of H/M ratio and wash-out rate to assess the treatment effect of heart failure therapy and tafamidis in this case. It can provide additional data of the severity of heart failure and involvement of ATTR on sympathetic nerve function. The relationship between ATTRwt and parkinsonism is not fully understood, but this case suggests the diverse pathophysiology of ATTRwt.

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Conflicts of interest

The authors declare no conflict of interest.

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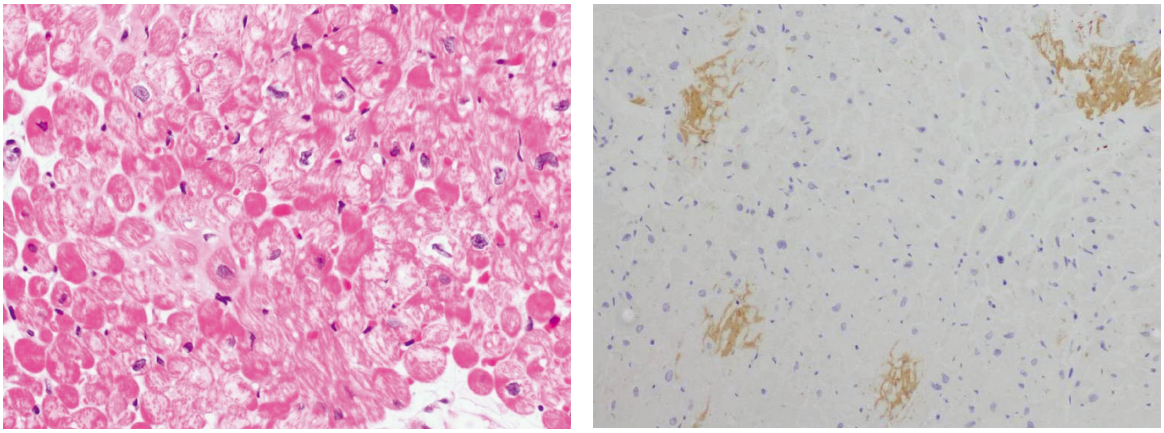

A B

Figure 3 Right ventricular myocardial biopsy showed positive for Congo Red staining (**A**) and immunostaining for transthyretin (**B**).

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