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CASE REPORT
Heart failure

Wild-type transthyretin amyloid cardiomyopathy complicated by spinal canal stenosis, carpal tunnel syndrome, and rotator cuff tears: a case report

Seiji Takashio *, Masato Nishi, Yuichiro Tsuruta , and Kenichi Tsujita

Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, chuo-ku, Kumamoto, Kumamoto 860-8556, Japan

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Background Wild-type transthyretin amyloid cardiomyopathy (ATTRwt-CM) is receiving increasing attention due to the availability of novel treatment options. Carpal tunnel syndrome (CTS) and lumbar spinal canal stenosis are known early symptoms of transthyretin (TTR) amyloidosis preceding the cardiac involvement and are considered as 'Red Flags' for transthyretin amyloid cardiomyopathy (ATTR-CM).

Case summary A 67-year-old man with a history of lumbar spinal canal stenosis for the last 10 years, right rotator cuff tears for the last 4 years, and bilateral CTS for the last 1 year was scheduled for orthopaedic surgery for lumbar spinal canal stenosis. Investigations revealed severe left ventricular hypertrophy and hypertroponinaemia, which were suggestive of cardiac amyloidosis. Cardiac magnetic resonance imaging and ^{99m}Tc-labelled pyrophosphate scintigraphy demonstrated positive findings for ATTR-CM. Transthyretin deposition was found in both the myocardium and the yellow ligamentum excised during surgery. There was no transthyretin mutation on genetic testing. The final diagnosis was ATTRwt-CM.

Discussion Transthyretin deposition in the ligaments or tendons has been observed in a number of patients with CTS, spinal canal stenosis, and rotator cuff tears. These orthopaedic diseases are predictive for the future occurrence of ATTR-CM. In addition, the coexistence of these multiple diseases might strongly predict ATTR-CM. This knowledge needs to be shared with orthopaedicians and cardiologists for the early diagnosis of ATTR-CM.

Keywords Case report • Transthyretin amyloid cardiomyopathy • Lumbar spinal canal stenosis • Carpal tunnel syndrome • Rotator cuff tears

Learning points

- Carpal tunnel syndrome (CTS) and lumbar spinal canal stenosis are known early symptoms of transthyretin amyloidosis preceding the cardiac involvement.
- Coexistence of CTS, lumbar spinal canal stenosis, and rotator cuff tears might be predictive of the future occurrence of transthyretin amyloid cardiomyopathy (ATTR-CM).
- This knowledge needs to be shared with orthopaedicians and cardiologists for the early diagnosis of ATTR-CM.

* Corresponding author. Tel: +81 96 373 5175, Fax: +81 96 362 3256, Email: s-takash@kumamoto-u.ac.jp
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Introduction

Wild-type transthyretin amyloid cardiomyopathy (ATTRwt-CM) is a progressive and infiltrative cardiomyopathy leading to increased ventricular wall thickness, diastolic dysfunction, and cardiac conduction system diseases.[1] ATTRwt-CM is potentially present in elderly patients with heart failure and is receiving increasing attention due to the availability of novel treatment options.[2,3] It has been reported that several orthopaedic conditions such as bilateral carpal tunnel syndrome (CTS), lumbar spinal canal stenosis, and tendon rupture are known to precede the diagnosis of ATTRwt-CM.[4–8] Therefore, patients with these orthopaedic conditions are considered to be at high risk for ATTRwt-CM.

We present here, the case of a patient with ATTRwt-CM, diagnosed during preoperative evaluation for lumbar spinal canal stenosis and confirmed transthyretin (TTR) deposition in the myocardium and surgically excised yellow ligament.

Timeline

50 years	Diagnosed with hypertension and dyslipidaemia
57 years	He had lumbago and was diagnosed with lumbar spinal canal stenosis
63 years	He had right rotator cuff tears and underwent surgery
65 years	He was diagnosed with diabetes mellitus
66 years	He developed bilateral carpal tunnel syndrome and underwent surgery
67 years	His lumbago aggravated and made it difficult for him to walk. The orthopaedician decided to perform surgery. The preoperative evaluation revealed left ventricular hypertrophy on echocardiography with hypertroponinaemia

Case presentation

A 67-year-old man visited the orthopaedic unit of our institution for worsening lumbago due to lumbar spinal canal stenosis, which was diagnosed 10 years ago. He could not walk well without support. Magnetic resonance imaging (MRI) revealed stenosis of the lumbar spinal canal and compression of the spinal cord (*Figure 1*). Surgical intervention was decided for his treatment.

He was diagnosed with hypertension and dyslipidaemia at the age of 50 years, and diabetes mellitus at the age of 65 years; these conditions were controlled with medications (candesartan 8 mg and teneligliptin 20 mg). He experienced right rotator cuff tears at the age of 63 years and bilateral CTS at the age of 66 years and underwent surgery for both conditions. Electrocardiography showed sinus rhythm, biatrial load, prolonged PQ interval (211 ms), and ST-segment depression in leads II, III, aVF, and V5–6 (*Figure 2*). X-ray showed enlargement of the cardiac silhouette; therefore, he was referred to the cardiologist.

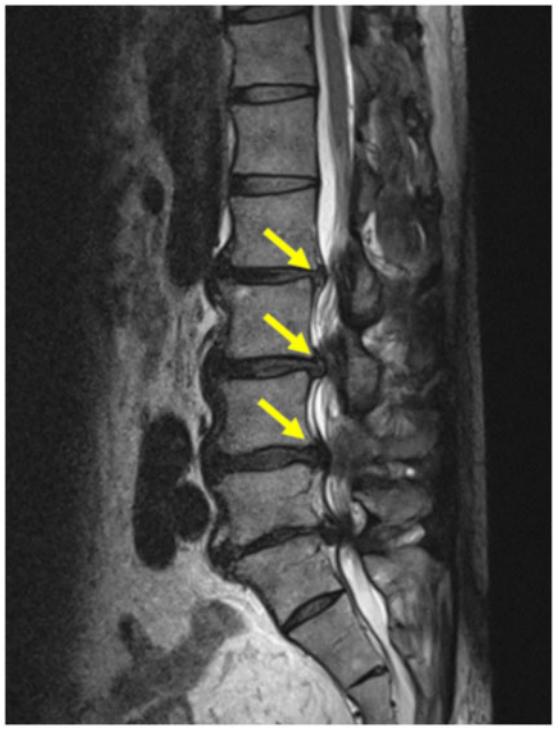


Figure 1 Lumbar spine magnetic resonance imaging showed stenosis of the lumbar spinal canal due to thickening of the ligaments and compression of the spinal cord (yellow arrow).

His heart rate was 80 b.p.m., and blood pressure was 114/75 mmHg. Auscultation detected no cardiac murmur and there was no oedema of the lower legs. He had no family history of amyloidosis and reported no exertional dyspnoea in daily life, but his activity was limited due to severe lumbago. There was a high concentration of B-type natriuretic peptide [358.5 pg/mL (normal range: <18.4 pg/mL)] and high-sensitivity cardiac troponin T level [0.0890 ng/mL (normal range: <0.014 ng/mL)]. Transthoracic echocardiogram examination revealed left ventricular hypertrophy (interventricular septum: 13.7 mm) and reduced left ventricular ejection fraction (38%) (*Figure 3A–D* and *Videos 1-2*). Apical sparing of left ventricular longitudinal strain was observed on speckle-tracking analysis (*Figure 3E*), and the global longitudinal strain was reduced (-6.8%). From the above medical history, echocardiographic findings, and hypertroponinaemia, we suspected cardiac amyloidosis. Contrast-enhanced cardiac MRI revealed diffuse transmural late gadolinium enhancement and a dark blood pool with marked increased in native T1 value (1440 ms, reference value in our institute is 1225 ± 35 ms), extracellular volume (63%) and mild increase of native T2 value (47 ms, reference value in our institute is 40–43 ms) (*Figure 4A–C*). ^{99m}Tc-labelled pyrophosphate scintigraphy demonstrated higher uptake of the tracer compared to that in the bone (Perugini grade 3) and increased heart to contralateral ratio (2.98) (*Figure 4D*). There was no evidence of the presence of monoclonal protein evaluated by free light chain and urine immunofixation assays. Coronary angiography revealed no significant stenosis. Endomyocardial biopsy revealed amyloid deposition

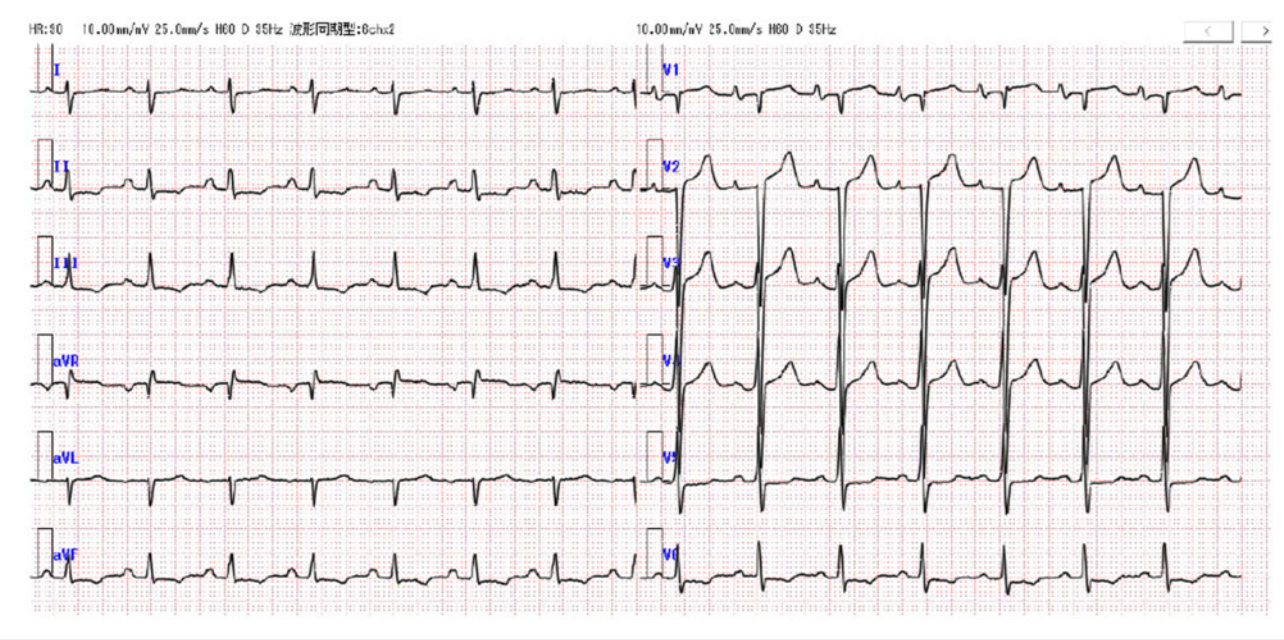


Figure 2 Twelve-lead electrocardiogram showed sinus rhythm, biatrial load, and ST-segment depression in leads II, III, aVF, and V5–6.

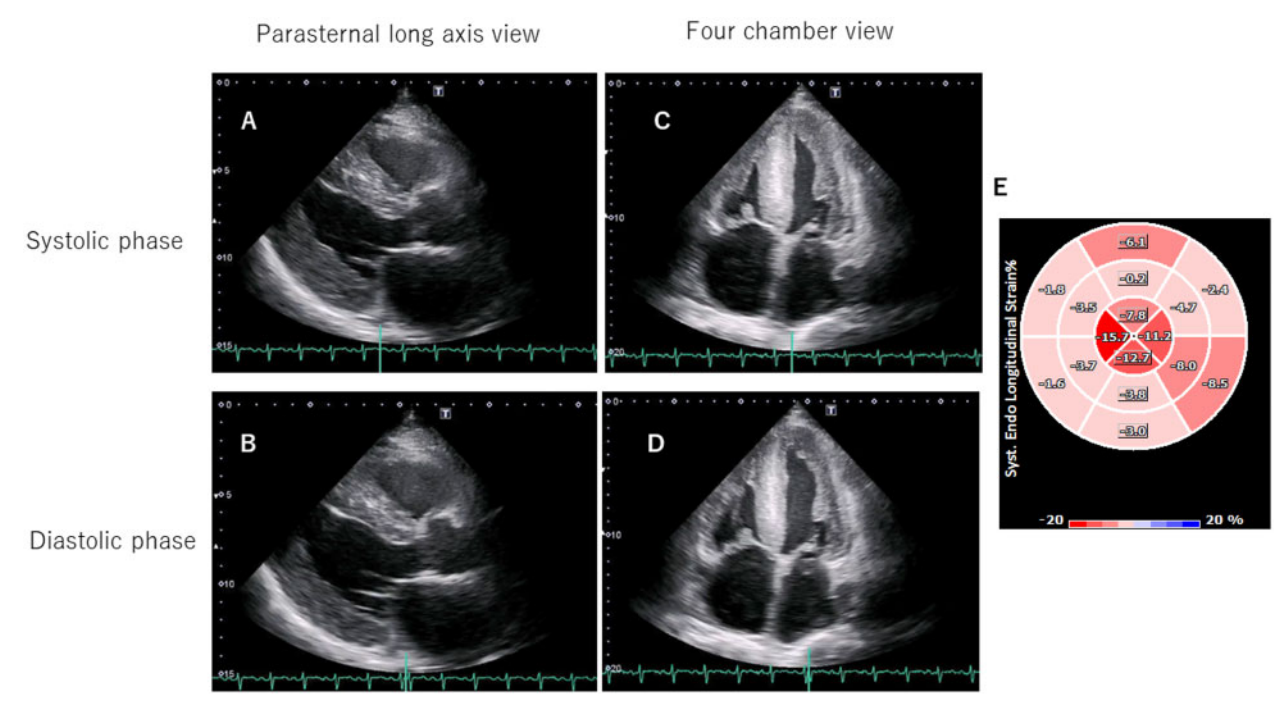
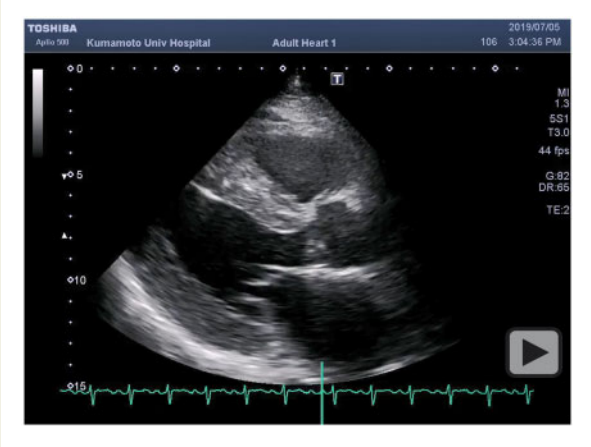
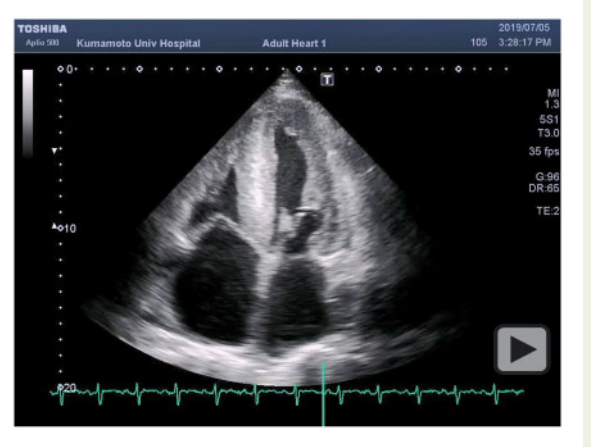


Figure 3 Echocardiography showed left ventricular hypertrophy and reduced left ventricular systolic function (see *Video 1*). Parasternal long-axis view in systolic (*A*) and diastolic phase (*B*). Four-chamber view in systolic (*C*) and diastolic phase (*D*). Apical sparing is noted on the bull's-eye map of left ventricular longitudinal strain (*E*).

in the myocardium (*Figure 5A and B*). Immunohistochemical staining revealed the amyloid precursor protein was TTR and no *TTR* mutation was found on genetic testing. The patient was eventually diagnosed as ATTRwt-CM complicated with lumbar spinal canal stenosis. Furosemide 20 mg and tafamidis 80 mg were added to treat his heart failure and ATTRwt-CM, respectively.



Video 1 Parasternal long axis view.



Video 2 Four chamber view.

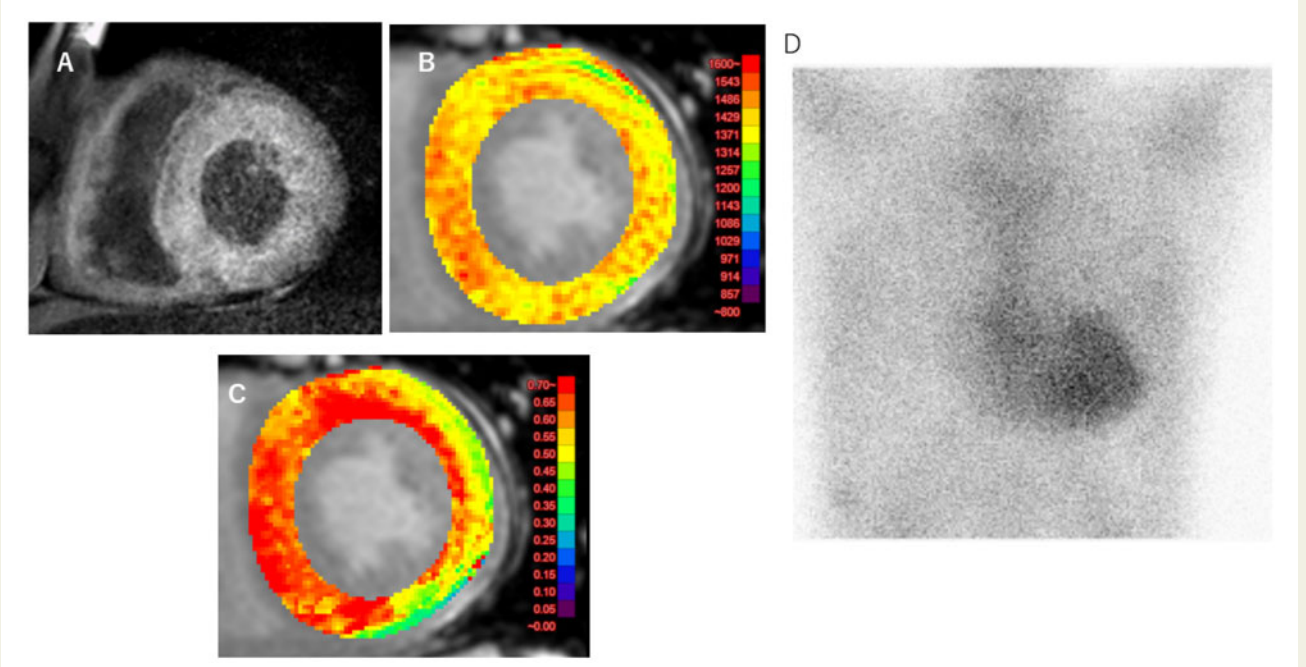


Figure 4 Contrast-enhanced cardiac magnetic resonance imaging showed transmural late gadolinium enhancement and a dark blood pool (*A*) with marked increased native T1 value (*B*) and extracellular volume (*C*). ^{99m}Tc-labelled pyrophosphate scintigraphy demonstrated positive uptake of tracer in the heart (Perugini grade 3) (*D*).

Since he had compensated heart failure, orthopaedic surgery for lumbar spinal canal stenosis was performed without any complications. The yellow ligamentum excised during surgery was sent for pathological evaluation. TTR amyloid deposition was found in the resected specimens (*Figure 5C–E*).

Six months after the diagnosis of ATTRwt-CM, he underwent catheter ablation for atrial tachycardia. Currently, 1 year has passed since the diagnosis of ATTRwt-CM. His heart failure symptoms were well controlled and unrestricted in daily life. In echocardiography, left ventricular hypertrophy was slightly advanced (interventricular septum: 15.8 mm); however, left ventricular ejection fraction (38%) and cardiac biomarkers did not change (B-type natriuretic peptide: 246.4 pg/mL, high-sensitivity cardiac troponin T: 0.0759 ng/mL).

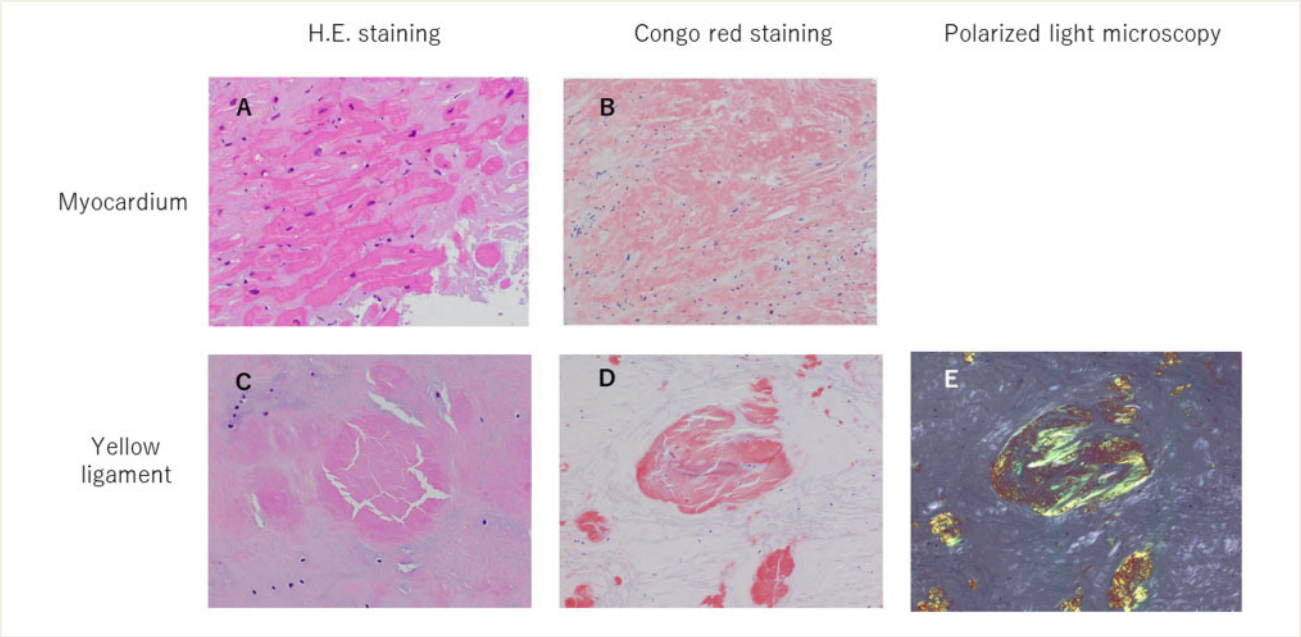


Figure 5 Amyloid deposition was observed in the myocardium (*A* and *B*) and yellow ligament (*C* and *D*) on H.E and Congo red staining and polarized light microscopy (*E*).

Discussion

In recent times, ATTRwt-CM has received increased attention because (i) it is a hidden cause of heart failure in the elderly, (ii) establishment of a diagnostic algorithm by bone scintigraphy, and (iii) potential benefit from emerging therapies. Early detection and accurate diagnosis are important for the improvement in clinical outcomes in patients with ATTRwt-CM.

Bilateral CTS is the most common early non-cardiac antecedent and is present in ~50% of the patients with ATTRwt-CM, 5–7 years before the diagnosis.[4–8] It has been reported that patients who underwent surgical treatment for CTS were associated with a higher risk of amyloidosis and heart failure in the future, compared to matched controls.[9] ATTRwt leads to complications related to lumbar spinal canal stenosis (14–22% of patients) and tendon rupture.[7,8,10] Carpal tunnel syndrome and spinal stenosis results in compression of the median nerve and spinal cord due to thickening of the ligamentum and tendons. It has been reported that TTR amyloid deposition is frequently observed in the tendons and ligaments. Sueyoshi *et al.*[11] evaluated the occurrence of TTR amyloid deposition in surgically excised specimens in three orthopaedic diseases. They revealed that there were TTR amyloid depositions in 18/54 (33%) cases of CTS (flexor tenosynovium specimens), 5/21 (24%) cases of rotator cuff tears (rotator cuff tendon specimens), and 16/36 (44%) cases of lumbar canal stenosis (yellow ligament specimens). These results suggested that TTR deposition is seen in a significant number of patients with these orthopaedic conditions.

In our case, this patient had history of lumbar canal stenosis for the last 10 years, right rotator cuff tears since 4 years, and CTS since 1 year. There was no confirmation of TTR deposition in the previously excised surgical specimens; however, it is possible that he already had progressive TTR deposition for more than 10 years and accumulation of TTR amyloid deposition in the myocardium. His activity was limited due to lumbago; therefore, symptoms of heart failure were not manifested. However, transmural late gadolinium enhancement pattern and increased extracellular volume were observed in cardiac MRI. These results suggested that ATTR-CM had already reached an advanced stage.[12] Transthyretin deposition was observed both in the myocardium and in the yellow ligament. This result suggested that TTR deposition was the common cause of his cardiomyopathy and lumbar spinal canal stenosis.

Carpal tunnel syndrome, spinal canal stenosis, and rotator cuff tears have TTR deposition on the ligaments or tendons as a common condition and are predictive for the future occurrence of ATTR-CM. In addition, the coexistence of these diseases might strongly predict a future occurrence of ATTR-CM. This knowledge needs to be shared with orthopaedicians and cardiologists for the early diagnosis of ATTR-CM.

Lead author biography

Seiji Takashio is a 40-year-old doctor working in Kumamoto University, Kumamoto, Japan. He performed a fellowship in National Cerebral and Cardiovascular Center, Osaka, Japan. His areas of interest include heart failure and cardiomyopathy, especially cardiac amyloidosis.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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