Senile Systemic Amyloidosis Starting as Bilateral Carpal and Left Ulnar Tunnel Syndrome

Key words: senile systemic amyloidosis, abdominal fat aspiration biopsy, transthyretin, carpal tunnel syndrome

This report concerns an elderly man whose disease started as bilateral carpal tunnel syndrome (CTS) followed by cardiomyopathy. He was diagnosed as having senile systemic amyloidosis (SSA) as evidenced by wild type transthyretin-derived amyloid deposition.

The patient developed numbness and dysesthesia of both hands at the age of 65. An electrocardiogram obtained the following year showed complete left bundle branch block. He had congestive heart failure when he was 74, for which diuretics were administered. He had a 15-year history of mild hypertension but had not taken any medication for this disorder. There was no family history of cardiac diseases or neuromuscular disorders. When he was examined at the age of 75, a grade 2 precordial systolic murmur was heard. Neurological examination indicated severe atrophy of the bilateral thenar muscles and left dorsal interossei of the hand muscles (Fig. 1A). Pinprick sensation was reduced in the first, second and third fingers of the right hand and in all fingers of the left hand. Tinel’s sign and Phalen’s maneuver were positive for both hands. Motor nerve conduction velocity (MCV) and sensory nerve conduction velocity (SCV) of the right median nerve were not evoked. Right ulnar MCV was delayed (44 m/s, normal >55 m/s). Left median MCV

Figure 1. A: Hands of the patient. Both thenar muscles are atrophied as are the left dorsal interossei of the hand muscles. Flexion contracture of all fingers and the clawhand phenomenon are seen in the left hand. B: \(^{99m}\)Tc-PYP scintigram. Myocardial scintigram using \(^{99m}\)Tc-PYP shows high uptake of radioactive tracer, indicating severe amyloid deposition on the myocardium. C: Congo red staining of the biopsied abdominal wall fat tissue. Amyloid deposition is visible around fat cells (Congo red staining, \(x23\)). D, E: Histopathological findings of the tenosynovial tissue in the left carpal tunnel. D: Congo red staining shows amyloid deposits in the connective tissues (Congo red staining, \(x54\)). E: Tissue amyloid was specifically immunolabeled only by the anti-TTR antibody (Immunostaining for anti-TTR antibody, \(x54\)). F: MALDI/TOF mass spectrometry of immunoprecipitate from the patient’s serum. The wild type of TTR with two major ion peaks was detected (Left: ion peak of normal monomer TTR; right: ion peak of normal TTR with cysteine covalently attached).
was delayed (37 m/s, normal >50 m/s) and SCV was not evoked. Left ulnar MCV was delayed (37 m/s). No abnormalities were found in laboratory examination results. Cardiomegaly (cardio-thoracic ratio: 56%) was seen on the chest X-ray, and the echocardiogram showed concentric hypertrophy of the left ventricular wall with a 22 mm interventricular septal thickness and LV dysfunction with a % fractional shortening of 19.5% (normal: 30–50%). A myocardial scintigram using technetium-99m pyrophosphate (1) showed a high uptake of radioactive tracer (Fig. 1B). Surgical release of both carpal tunnels and the left ulnar tunnel was carried out.

For immunohistochemical analysis of the amyloid protein, antibodies to five major amyloid fibril proteins were used (2): IgG light chain κ (Aκ), IgG light chain λ (Aλ), serum amyloid A protein (AA), transthyretin (ATTR), and β2-microglobulin (Aβ2M). The tissue amyloid in the left carpal tunnel was specifically immunolabeled only by the anti-TTR antibody (Fig. 1D, E). Abdominal fat aspiration biopsy was performed, and alkaline Congo red staining identified amyloid deposition in the tissue. To confirm this finding, an abdominal skin biopsy was performed and also showed amyloid deposition in the subcutaneous fatty tissue (Fig. 1C). A matrix-assisted laser desorption ionization/time-of-flight (MALDI/TOF) mass spectrometry system was used to detect variant forms of TTR in immunoprecipitated serum TTR molecules (3), but showed only the wild type of TTR in our patient (Fig. 1F). Direct DNA sequencing of all four exons of the TTR gene did not detect any mutation.

Histopathological and immunohistochemical examinations of amyloid and molecular analysis of TTR demonstrated that our patient was affected by SSA as seen in clinical pictures of CTS and cardiac amyloidosis. An autopsy study conducted outside Japan identified SSA in at least 25% of the population over the age of 80 (4), but among Japanese this disease is extremely rare.

It has been reported that abdominal fat aspiration biopsy is useful for screening for amyloid deposition in systemic amyloidosis including AL, AA, and FAP (5). However, few reports have indicated the value of this technique for the histopathological diagnosis of SSA. In our patient significant amounts of amyloid deposition were observed in the abdominal fat tissue, in addition to the amyloid deposition detected in gastric, duodenal and ileal mucosal biopsies. Abdominal fat aspiration biopsy, which is a simple procedure, may therefore be helpful for the histopathological diagnosis of SSA.

The patient we describe here is different from the patient reported in the following article: Takei Y et al. Senile systemic amyloidosis starting as bilateral carpal tunnel syndrome. Amyloid: The Journal of Protein Folding Disorders 9 (4): 252–255, 2002.

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References


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