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Carpal Tunnel Syndrome in AL Amyloidosis

Takashi Isobe, Nobuhiko Mizuno, Shinzo Kubota, Tadanobu Chinzei, Munetada Oimomi and Shigeaki Baba

Having an initial sign and symptom of carpal tunnel syndrome, a 67 year-old Japanese female was hospitalized. She was found to have AL amyloidosis, associated with carpal tunnel syndrome, edema, pleural effusion, serum IgG (λ) -monoclonal protein, urinary Bence Jones protein of lambda type, plasma cell proliferations of 22.6% out of nucleated cell count of 11.1 x 10^9/μl in aspirated bone marrow specimen, no evidence of osteolytic shadow on bone x-ray survey, slight enlargement of liver, and electrocardiographic abnormality of low voltage in limb leads. She died of cardio-pulmonary insufficiency. At autopsy, the pathological diagnosis was plasma cell dyscrasia and primary amyloidosis involving heart, lung, tongue, carpal joints, and transverse colon, with perivascular amyloid deposits in various organs.

Key Words
Carpal tunnel syndrome, Monoclonal immunoglobulin, Primary amyloidosis, Myeloma-associated amyloidosis, Prognosis of AL amyloidosis.

INTRODUCTION

Varieties of clinical features are a hallmark of systemic amyloidosis (1 ~ 4). Patients with AL amyloidosis show a different combination of syndromes occurred and directly related to the amyloid deposits in various organs in AL amyloidosis. Such syndromes related to AL amyloid include carpal tunnel syndrome, nephrotic syndrome, congestive heart failure, peripheral neuropathy and orthostatic hypotension. In the present study, the initial sign and symptom of carpal tunnel syndrome was clearly noted. The significance, survival and prognosis of AL amyloidosis is discussed.

CASE PERSSENTATION

F. Fuj., 67 year-old Japanese female, visited the hospital with a chief complaint of dysesthesia of hands at her age of 66. Her family history showed uterine carcinoma with her sister. Past history was non contributory. History of the present illness started in 1970 at the age of 61 with bilateral carpal tunnel syndrome which included dysesthesia of both carpal joint and peripheral area particularly 2nd, 3rd and 4th fingers, bilaterally, followed by noted muscle atrophy of thenar eminence of the palmar surface. Symptoms of carpal tunnel syndrome increased its intensity for the following years in an association of pain and moderate moter disturbance, i.e. difficulty of flexion of both fingers. An electromyogram showed no abnormality at rest and
voluntary waves of muscles including m. biceps brachii, m. extensor digitorum, m. opponens pollicis and m. flexor carpi ulnaris. A x-ray survey of bones showed generalized osteoporosis of mild form. Cervical spines on x-ray showed no abnormality. At the age of 64, she visited a hospital with a high-grade (> 39°C) fever, persistent cough and pitting edema in the legs. She was found to have pleural effusion followed by administration of intramuscular injections of streptomycin with oral medication of PAS and INAH for 6 months, showing a minor improvement. Around this time, an erythrocyte sedimentation rate was 140 mm per hour, an abnormality of serum protein with proteinuria, and febrile state prompted her hospitalization to the Second Department of Medicine, Kobe University Hospital. On admission, she was anemic, with a hemoglobin 9.2 g/dl. Other data included a white blood cell of 6,500/μl a platelet count of 20.0 x 10^4/μl, an ESR 157 mm/hr, CRP 3+, a serum total protein 5.0 g/dl including albumin 2.0 g/dl and abnormal monoclonal peak in gamma mobility which was immunologically identified as IgG (λ) - M-protein, urinary protein of daily excretion of approximate 8 gm/day without obvious Bence Jones protein at this time, plasma cells 22.6% out of 11.1 x 10^4/μl nucleated cells in a bone marrow aspirate, a serum cholesterol 253 mg/dl and a blood urea nitrogen 20 mg/dl. On X-ray survey, there was no evidence of osteolytic lesions. A clinical diagnosis was thus plasma cell dyscrasia. High-dose intermittent melphalan and prednisolone administration were instituted, with a subjective and objective improvement. She was discharged from the hospital with a continuous low dose of prednisolone, 5.0 – 7.5 mg per day at the out-patient clinic. Eight months later at her age of 65, she had an episode of fever with cough and sputum, which was improved by intake of antibiotics of penicillin. At the age of 66, one year and 8 months after the first hospitalization, she was readmitted because of relapsed carpal tunnel syndrome, general fatigue, exertional dyspnea and generalized edema. On admission, there was no fever, no oliguria or no chest pain at this time. She was well-nourished with moderate stature, regular pulse 90/min., a body temperature 36.3°C, a blood pressure 90/54 mmHg and a respiration rate 22/min. Physical examination revealed pale skin, generalized edema, telangiectasis on bilateral check, obvious macroglossia, slight enlargement of the heart to the left, slight enlargement of the liver below the right costal margin, with smooth surface and slight tenderness. There was no splenomegaly or no ascites. Moderate edema on bilateral extremities was present. Neurological examinations were nothing particular, except an obvious muscle atrophy of thenar eminence of the palmar surface and bilateral carpal tunnel syndrome.

Laboratory examination revealed proteinuria ranging 8 to 10 gm of daily excretion, negative glucosuria, urobilinogen normal, negative occult blood, a red blood cell 264 x 10^4/μl, a hemoglobin 9.1 g/dl, a hematocrit 26.9%, a white blood cell 4,400 including neutrophil 51%, eosinophil 6%, monocyte 12% and lymphocyte 31%, a platelet count 17.3 x 10^4/μl, an ESR 156 mm/hr, CRP (−), RA
Figure 1. Serum and urinary protein electrophoresis at the age of 67. Monoclonal spike in gamma mobility is noted in the serum (upper) and monoclonal spike in slow-gamma mobility is noted in the urine (lower). An immunologic analysis identified as IgG(λ)MP in the serum and BJP lambda in the urine, respectively.

(−), STS (−), ANF (−), bleeding time 4'30", fibrinogen 504 mg/dl, fasting blood sugar 96 mg/dl, GOT 27 IU/l, GPT 15 IU/l, CPK 131 mU/l, Ca 7.7 mg/dl, P 3.5 mg/dl, Fe 92 μg/dl, BUN 24 mg/dl, serum Cr 1.8 mg/dl, uric acid 5.1 mg/dl, PSP excretion test 6.4% (15 minutes) and 29.8% (120 minutes), β-lipoprotein 1,400 mg/dl, triglyceride 243 mg/dl,
17 ORCS 2.4 mg/day, serum total protein 5.5 g/dl with albumin 1.9 g/dl and monoclonal gamma-globulin 1.8 g/dl identified as IgG (A)-M-protein, IgG 2.813 mg/dl, IgA 38 mg/dl, IgM 80 mg/dl, and positive urinary Bence Jones protein of lambda type (Figure 1). A bone marrow aspirate showed 12.2% of plasma cells out of 18.2 x 10^4 nucleated cells. Repeated check up of ECG demonstrated noted differences of findings of the two tracings between the 1st admission at the age of 65 and 2nd admission at age 67, demonstrating lowering voltage of limb leads and inverted T in V6 lead in an ECG at age 67. A chest X-ray showed a cardio-thoracic ratio of 57.3%, with reticulo-nodular pattern in the peripheral lung field. On X-ray survey of the bone, there was no evidence of osteolytic lesion. After admission to the hospital, she was given digitoxin 0.04 mg a day plus Lasix 40 mg a day, with a mild improvement on exertional dyspnea, only for a short period of time. She had a downhill course, suffering from dyspnea, fever, leucocytosis, moist rales of bilateral lung fields, and oliguria. Without any marked effects of a combination of antibiotics, intravenous immunoglobulin, cyclophosphamide and prednisolone, she developed nausea, vomiting, and massive bleeding from gastro-intestinal tracts. She died of ventricular fibrillation during blood transfusion on March 30, 1976. At autopsy, pathological findings demonstrated plasma cell dyscrasia (diffuse, without tumor formation of plasma cells) and primary amyloidosis. Amyloid deposits were shown mainly, in the heart, lung, tongue, carpal joints, and transverse colon, along with perivascular amyloid deposits in various organs.

DISCUSSION

Carpal tunnel syndrome was noted in the present case, as the major sign and symptom at the onset in the present case, which was definitely proved to be due to amyloid deposit at autopsy. Kyle and his associates (3) described the analysis of amyloidosis patients by reviewing 236 cases on clinical features and laboratory findings. As to AL amyloidosis, they examined 132 cases of primary amyloidosis and 61 cases of myeloma-associated amyloidosis. Incidence of carpal tunnel syndrome was 16% (21 of 132) in primary type and 33% (20 of 61) in myeloma-associated type. Among various syndromes related to AL amyloidosis, carpal tunnel syndrome, nephrotic syndrome, congestive heart failure, sprue, peripheral neuropathy, and obvious orthostatic hypotension have been known. As to the incidence, besides carpal tunnel syndrome, the nephrotic (32% in primary type and 11% in myeloma-associated), congestive heart failure (26% and 30%), sprue (5% and 5%), peripheral neuropathy (17% and 5%) and orthostatic hypotension (16% and 8%). Regarding the presence of these syndrome before clinico-pathological diagnosis, time duration of the existence of syndrome prior to diagnosis is clinically important in relation to providing a significant clue to the possible diagnosis. Referring to Kyle's data, the time duration was as follows: carpal-tunnel syndrome (34 months in primary type AL amy-
Figure 2. Electrocardiograms of January 28, 1974, December 16, 1975 and March 25, 1976. Serial tracings demonstrate cardiac abnormalities in the present case of AL amyloidosis.
loidosis vs. 18 months in myeloma-associated AL amyloidosis), nephrotic syndrome (10 mo. vs. 4 mo.), congestive heart failure (11 mo. vs. 9 mo.), sprue (29 months vs. 17 mo.), peripheral neuropathy (20 mo. vs. 4 mo.), and orthostatic hypotension (17 mo. vs. 5 mo.). Therefore, the appearance of carpal-tunnel syndrome in clinical medicine has to be considered the possible presence of systemic amyloidosis. Clinically, carpal tunnel syndrome is seen in 2 different types of amyloidosis; the one in AL and the other in Aβ2M among patients with long-term hemodialysis. Other than amyloidosis, carpal tunnel syndrome virtually occurs among patients with rheumatoid arthritis, acromegaly, Sheie's syndrome of mucopolysaccharide deposition seen in children and vitamin B₆ deficiency. Physicians have to keep in mind of clinical significance of carpal tunnel syndrome.

Considering the prognosis of patients with AL amyloidosis, Kyle and his associates (4) analyzed 168 cases with these syndromes with an interesting observation. Median survival after the diagnosis of AL amyloidosis was 12 months. There were different ranges of median survival; carpal tunnel syndrome (23 months with 28 cases) nephrotic syndrome (16 mo. with 37 cases), congestive heart failure (4 mo. with 38 cases), peripheral neuropathy (50 mo. with 11 cases), and orthostatic hypotension (12 mo. with 17 cases). Therefore, it is conceivable that carpal tunnel syndrome gives a clue to diagnosis, with rather long-term survival, only in case carpal tunnel syndrome alone would be present. However, combinations of heart failure and carpal tunnel syndrome could will be found in AL amyloidosis, as seen in the present case. It is worthy of having these informations of AL amyloidosis, when physicians observe clinical features of patients in clinical medicine.

REFERENCES