Abstract

We present a case of neurosarcoidosis showing bilateral carpal tunnel syndrome which disappeared without any medication. This patient was also suffering from motor and sensory disturbance caused by peripheral neuropathy of the four extremities. Magnetic resonance image showed transient swelling of the median nerve, and subperineurial edema was unexpectedly observed in some fascicles in sural nerve biopsy. We hypothesize that the carpal tunnel syndrome in this case was induced by the intercanal high pressure due to edema inside the tunnel, which might be related to the high level of serum IL-2.

Key words: sarcoidosis, peripheral neuropathy, swelling, carpal tunnel syndrome, interleukin-2, MRI

Introduction

Sarcoidosis is an idiopathic multi-system disease and neurological disorders are recognized in only about 5% of all cases. Only about half of all patients with neurosarcoidosis present with clinical neurological symptoms (1, 2). The most frequent manifestation is multiple fluctuating and remitting cranial nerve palsies. Non-cranial neuropathy also occurs in 15 to 40% of patients with neurosarcoidosis. Electrophysiological test usually suggests distal symmetric or multifocal axonal neuropathy (3, 4). In a large series of patients with neurosarcoidosis, peripheral neuropathy evidently occurred in 6 to 18% (1). However, an abnormal neuroimage of swelling peripheral nerves has not been reported. We present a case of neurosarcoidosis showing transient swelling of a median nerve on magnetic resonance image (MRI). We hypothesize that this swelling was induced by the intercanal high pressure due to edema inside the carpal tunnel, which might be related to the high level of serum IL-2.

Case Report

A 70-year-old woman noticed increasing difficulty with needlework in autumn of 1999. In February 2000, she felt severe general fatigue and muscle pain of both the upper extremities. Two days later, she noticed mild dysesthesia of the distal fingers. All her fingers became weak and insensitive in the following week. She also felt dysesthesia and sensory loss in both feet, and she easily fell on gentle slopes or stairs. At the beginning of March, she could not move her feet anymore. In the middle of March, she became able to move her fingers a little, and dysesthesia of the fingers was also slightly reduced, but the symptoms of the lower extremities were unchanged. She was admitted to our hospital on March 21.

The results of the general physical examination were normal. Mental state was normal. There was no clinical evidence of cranial nerve disturbance. Moderate distal dominant weakness with patchy distribution of dysesthesia and sensory loss in both the extremities existed, but autonomic dysfunction was not found. Vibration sense was completely absent, but position sense was preserved in all four extremities. Deep tendon reflex of the limbs was completely absent. She could not stand by herself mainly because of the lack of deep sensation. Both median nerves and the left tibial nerve were palpable. The median nerves were bulging and rough at the wrist. Bilateral Tinel’s sign and Phalen’s sign were positive. She could not bend her wrists due to pain, and dysesthesia of the thumb and forefinger was stronger than the other three fingers. She was diagnosed as having bilateral carpal tunnel syndrome.
Transient Swelling of Peripheral Nerves in a Case of Neurosarcoidosis

Blood cell count, other blood serum and chemical studies including thyroid function tests, antinuclear antibodies were all normal. The levels of angiotensin-converting enzyme and lysozyme were not elevated. Erythrocyte sedimentation rate was 9 mm per hour, and C-reactive protein was normal. However, the level of interleukin-2 (IL-2) was 2.7 U/ml (normal range, 0 to 0.8) and corresponding IL-2 receptors (IL-2R) numbered 719 (normal range, 220 to 530), which were clearly elevated. Cerebrospinal fluid was clear and colorless and contained 1 monocyte per cubic millimeter, 55 mg/dl of glucose and 63mg/dl of protein. The Mantoux tuberculin test was negative. A computed tomographic examination of the chest showed right-sided paratracheal and subcarinal lymphadenopathy with multiple small nodules scattered in both upper lobes. Gallium scanning test showed abnormal uptake of the bilateral hilar lymph nodes. Bronchoalveolar lavage fluid had a total cell count of 26×10⁶/ml, and 62% of the cells were lymphocytes. T lymphocytes (T-cells) accounted for 95% of the lymphocytes, and the CD4/CD8 ratio was 4.92, which were all evidently elevated and seemed characteristic of sarcoidosis. Scalene node biopsy showed a gathering of epithelioid cells. From all these results, the patient was diagnosed with sarcoidosis. One month after admission, serum level of IL-2 was re-examined and showed 1.4 U/ml, which was a reduction of 48%.

Motor conduction velocity (MCV) was markedly slow, and the amplitude of motor action potentials was low in median, ulnar, peroneal and posterior tibial nerves. Distal motor latency of the median nerves recorded from abductor pollicis brevis was 20.2 ms on the right side and 11.4 ms on the left side. Right-handed amplitude evoked by supramaximal stimulation was 3.25 mV at the distal site of the carpal tunnel and 0.91 mv at the proximal site, which indicated evident temporal dispersion. MCV of the median nerve ranged from 11.5 to 38.9 m/s, which was especially delayed through the carpal tunnel. Sensory nerve action potentials were undetectable in median, ulnar and sural nerves. Amplitude obtained by the stimulation of the left facial nerve was reduced, and the blink reflex was also abnormal even though she had no evidence of facial palsy.

The median nerve at the right wrist was evaluated by MRI. The nerve was thick, and its signal showed diffuse high intensity on the T₂-weighted image without enhancement (Fig. 1A). After 10 days, MRI showed a thinner nerve than before, and the high intensity lesion had disappeared without any treatment (Fig. 1B). At the same time, she could bend her fingers more easily than before. Dysesthesia of the thumb and index fingers was milder, and the swelling of the median nerve at the wrist was decreased. Distal latency of the motor nerve conduction of the median nerve became clearly shortened, and the amplitude became larger.

A fragment of the right sural nerve was obtained on March 23, the third day after her admission. No granuloma or infiltration of the inflammatory cells was observed in any section. The subperineurial space of the nerve fascicle was edematous. The density of myelinated fibers was 7,247 per square millimeter with many cluster formations and thinly myelinated fibers, which indicated the alteration in size distribution. Onion bulb formations were not observed (Fig. 1C and D).

Oral corticosteroid treatment of 45 mg daily was started, resulting in improvement of superficial and vibration sense of the four extremities. One month later, she was able to easily use a spoon and walk without a cane for a short distance.

Discussion

The present patient showed subacute progression of mononeuropathy multiplex with bilateral carpal tunnel syndrome, which was consistent with the electrophysiological studies. The median nerve showed swelling and high intensity at the site of the carpal tunnel on T₂-weighted MRI. The swelling of the nerve decreased within ten days without any treatment. MRI demonstrated a thinner nerve, motor conduction study revealed shortened distal latency and larger amplitude of the median nerve in parallel with the clinical improvement. Although there was a thick edematous space under the perineurium with many cluster formations and thinly myelinated fibers, granuloma and infiltration of the inflammatory cells were not observed in a biopsy specimen of the sural nerve.

In previous neurosarcoidosis, granulomas in the endoneurium or epineurium and loss of axons and myelin have been observed. The mechanism of nerve damage is still controversial. Nemni et al considered demyelination to be the primary disorder rather than axonal injury (2). Vital et al emphasized the role of ischemia due to vascular disease (5), and Oh argued that the main reason for involvement was panangitis and periangitis as well as compression by sarcoid tissue (6). However, as observed in the present case, thick edema under the perineurium without evidence of infiltration of the inflammatory cells or vasculitis is not common. Niemer et al (7) investigated the relationship between sarcoidosis and carpal tunnel syndrome. In this study, 44% of patients reported symptoms and/or signs of carpal tunnel syndrome, which was higher than the 14.4% found in the general population. They proposed several mechanisms for carpal tunnel syndrome in sarcoidosis such as synovitis of the wrist and direct deposition of granulomas in the transverse carpal ligament. But they did not prove the cause of carpal tunnel syndrome in sarcoidosis (7). There was some possibility that granulomas and inflammation existed in another part of the nerves which was not investigated, however, interestingly in our case, IL-2, which is known to cause carpal tunnel syndrome, was elevated.

The side effect of IL-2 infusion is believed to be due to widespread exaggeration of the physiologic action of IL-2 as a cytokine: capillary leak syndrome causes transfer of fluid from vascular compartments to the extravascular spaces (8). This phenomenon may lead to subperineurial space edema of the median nerve in the anatomically narrow carpal tunnel,
which could cause intercanal high pressure, resulting in carpal tunnel syndrome. Subperineurial space edema has some relevance to the permeability changes associated with the breakdown of the blood-nerve barrier. In the present case, subperineurial space edema was not observed in every fascicle and nerve swelling was improved within 10 days, which indicated the possibility of mild dysfunction and easy restoration of the barrier.

Current concepts of the pathogenesis of sarcoidosis suggest that the T-cells play an important part in modulating the formation of granulomas. It is known that under the active condition, activated helper T-cells in the lung release IL-2 spontaneously (9). The inflammatory macrophages express IL-2R with a high concentration in the blood, and this expression may be involved in the pathogenesis of pulmonary sarcoidosis (10). In the present case, the serum levels of IL-2 and IL-2R were high, and this might have played an important role in the activation of the neurosarcoidosis.

The prognosis of neurosarcoidosis of the peripheral nerve is not uniform and is unpredictable. Steroid therapy is sufficient treatment, and some patients improve before steroids are given (11), as in the present case. The reason for the spontaneous improvement is unknown. However, if the subperineurial space edema was a cause of the neurosarcoiudosis, it is comprehensible that the intercanal high pressure of the carpal tunnel progresses or improves in parallel with the level of edema.

In conclusion, we hypothesize that the carpal tunnel syndrome in the present case was induced by the intercanal high pressure caused by edema inside the narrow tunnel, which was related to the high level of serum IL-2. Neural edema at compression sites is one of the causes of neuropathy in sarcoidosis.

References


