**CASE REPORT**

**Slowly Progressive Distal Muscular Atrophy of the Bilateral upper Limbs (O’Sullivan-McLeod Syndrome) Partially Alleviated by Intravenous Immunoglobulin Therapy**

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**Abstract**

We report a case of O’Sullivan-McLeod syndrome in a 59-year-old man, who had experienced slowly progressive weakening of both hands since he was 20 years of age. Mild hyperIgEemia and eosinophilia were present. Nerve conduction studies revealed reduced F wave-evoked frequencies for the median and ulnar nerves. Intravenous immunoglobulin (IVIG) at a dose of 400 mg/kg/day was given for 5 days. After IVIG, the muscle weakness of the distal upper extremities improved together with increased F wave-evoked frequencies. These effects lasted for a few months. These observations suggest that immune-mediated neural damage partially contributes to O’Sullivan-McLeod syndrome.

**Key words:** allergy, atopy, IgE, O’Sullivan-McLeod syndrome, motor neuron disease

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**Introduction**

O’Sullivan-McLeod syndrome is a rare disease involving slowly progressive weakening and atrophy of the hands with onset in the second to third decades of life (1). Although the disease is considered to be a variant type of spinal progressive muscular atrophy, its progression is extremely slow, extending for more than 20 years with muscle atrophy usually confined to the distal upper limbs (1). Although there are some similarities in its clinical manifestations to those of Hirayama disease (juvenile muscular atrophy of the distal upper extremities) (2), the latter usually stabilizes a few years after onset while the former shows a steady progression over decades. In general, both diseases have been assumed to be due to cord compression.

Here, we report a case of O’Sullivan-McLeod syndrome. In this case, distal weakness and atrophy in the hand muscles was progressive even after decompressive cervical laminectomy, suggesting that a non-compressive mechanism caused the lower motor neuron damage. Therefore, we examined the effectiveness of intravenous immunoglobulin (IVIG) therapy in this patient. Here, we describe the case and the response to IVIG immunotherapy.

**Case Report**

A 59-year-old right-handed Japanese man, with no relevant family history, had experienced slow progression of asymmetrical weakening of both hands since the age of 20 years. The initial sign was a slight discomfort swinging a bat when playing baseball. Before noticing the discomfort, his grasping power had been around 40 kg. He noted no sensory disturbance at that time. The rate of progress was relatively rapid during the first several years, and then became slower. The right/left hand grip powers at the ages of 26 and 33 years were 15 kg/10 kg and 10 kg/5 kg, respectively. When he was 44 years of age, he noted a sudden onset of numbness and pain that radiated from the neck to both hands. Therefore, he underwent a C4 through C7 laminectomy under suspicion of cervical spondylotic radiculopathy. Although the surgical treatment ameliorated the numbness and pain, the wasting of both hands continued to progress. Thereafter, he noted cold paresis in both hands. His grip power continued to decline and was around 1 kg when he was 59 years of age. In addition, he had suffered...
from a year-round nasal allergy for 20 years and had a contact allergy to copper. He had no history of poliomyelitis.

On physical examination, skin flares on both palms due to the copper contact allergy were observed. Cranial nerves were normal. Severe weakness and wasting of the intrinsic muscles of both hands, ulnar forearm flexors and radial extensor muscles were observed. Bilateral brachioradialis muscles and biceps brachii muscles were spared. The right/left hand grip powers were 2 kg/1 kg, with lateral pinch strengths of 1.5 kg/1 kg. The fingers showed irregular and fine tremulous movements (contraction fasciculation) upon extension. No abnormalities were observed in the lower extremities. Deep tendon reflexes were normal, and plantar responses were flexor. There were no sensory or autonomic abnormalities.

Cervical MRI revealed atrophy of the lower cervical spinal cord (Fig. 1A). No high-signal intensity lesion in the spinal cord on T2-weighted images or forward displacement of the dural sac was observed in a flexed position (Fig. 1B). Peripheral blood counts revealed mild eosinophilia (10%). Routine serum chemistries were normal. Serum IgE level was 249 IU/ml (normal, <240 IU/ml), but the relevant allergens were not specified in our hospital. Antinuclear antibodies, anti-SS-A antibody, anti-SS-B antibody, ScI-70, Jo-1, anti-RNP antibodies, anti-Sm antibody, MPO-ANCA, and PR3-ANCA were all negative. Serum complement levels were within normal levels. Cerebrospinal fluid examination was normal except for an elevated protein concentration (60 mg/dl; normal, <40 mg/dl), probably due to the post-laminectomy state. Nerve conduction studies revealed that the conduction velocities in the right median, right ulnar and right tibial nerves were all within their normal limits and there was no evidence of conduction blocks. F wave-evoked frequencies in the right median and right ulnar nerves were 25% and 31%, respectively, while the frequency in the right tibial nerve was 87%. Sensory nerve action potential amplitudes and conduction velocities in the right median, right ulnar and right sural nerves were normal. Needle electromyography of the right and left first dorsal interossei muscles showed fibrillation potentials and positive sharp waves at rest and polyphasic motor unit action potentials with reduced recruitment during voluntary contraction.

**Methods**

Prior to IVIG therapy, written informed consent was obtained from the patient. Intravenous infusion of immunoglobulins (Kaketsu Glovenin-I-Nichiyaku, Takeda Chemical Industries, Osaka) was administered at a dose of 400 mg/kg/day for 5 consecutive days. Motor and sensory conduction studies were performed according to standard techniques before and after the IVIG therapy. Compound muscle and sensory nerve action potential amplitudes, conduction velocities, F-wave response latencies and F-wave/M-response ratios were determined. We examined the ulnar, median, tibial and sural nerves. To evaluate the muscle power quantitatively, we measured hand grip strength as well as lateral pinch strength between the thumb and index finger.

**Results**

After the IVIG therapy, the patient was able to open his hands more than before (Fig. 1C and D). However, the tremulous movement of the fingers and muscle atrophy remained unchanged. The right/left hand grip powers rose from 2 kg/1 kg to 3.5 kg/1.5 kg. The lateral pinch power of the right hand also rose slightly from 1.5 kg to 2.5 kg, but the power of the left hand was unchanged. At 3 days after completing the therapy, the F wave-evoked frequencies increased from 25% to 50% in the right median nerve and from 31% to 37% in the right ulnar nerve. At 1 month after the therapy, the frequencies rose to 81% in the right median nerve and 56% in the right ulnar nerve. The mild eosinophilia and mild hyperIgEemia remained unchanged. The therapeutic effects lasted for a few months.

**Discussion**

In this report, we describe a patient with O’Sullivan-McLeod syndrome who had a partial response to IVIG therapy. The patient had the typical clinical features of O’Sullivan-McLeod syndrome; the intrinsic hand muscles and forearm were affected, the clinical course was slowly progressive without a stationary phase, and neither long tract sign nor sensory involvement was observed. Although a cervical laminectomy ameliorated the numbness and pain in both upper limbs, the muscle weakness was still progressive. Electrophysiologic findings were also compatible with lower motor neuron damage in the lower cervical spinal cord. In addition, a cervical MRI of our patient revealed lower cervical cord atrophy, which has previously been reported in O’Sullivan-McLeod syndrome (3). These findings suggest that our patient suffered from anterior horn cell impairment in the lower cervical cord manifesting as O’Sullivan-McLeod syndrome.

Although O’Sullivan-McLeod syndrome is considered to be a variant of spinal muscular atrophy (1), which involves the hands, its etiology remains uncertain. Petiot et al (4) reported localized T2-weighted high-signal intensity lesions in the anterior horns at the C6 to C7 spine levels. Such localized high-signal intensity lesions appear rather unusual for neurodegenerative disorders. Similar MRI findings have also been reported for Hirayama disease (5), which has similar clinical manifestations such as bilateral intrinsic hand muscle involvement and occasionally shows progression long after the stabilization phase (6). These common features suggest both diseases are possibly a continuum and have some common mechanism.

In Hirayama disease, flexion myelopathy-based circulatory insufficiency has been put forward as the main etiology (7, 8), and the lower cervical cord is considered to be most vulnerable because the dural sac is most tight around the
lower cervical cord on flexion. However, some patients present no evidence of flexion myelopathy (9). In the present patient, flexion myelopathy might have been present during the initial rapidly progressive phase and such flexion myelopathy might have caused motor neuron damage at the lower cervical cord. However, flexion MRI could not detect any compression after laminectomy in our patient, suggesting that flexion myelopathy does not sufficiently explain the late progression after the operation. A higher frequency of airway allergy and allergen-specific IgE together with a Th2 shift in peripheral blood CD4+ T cells has been identified in Hirayama disease (10, 11), while hyperIgEemia was reported to facilitate its progression (12). Moreover, Ochi et al (13) reported two Hirayama disease patients with airway allergies that partially responded to plasma exchange. The present patient also had an allergic tendency and IVIG immunotherapy was partially effective, even though the clinical course had been almost 40 years. These observations therefore suggest that an immunological mechanism may partly contribute to O’Sullivan-McLeod syndrome, similar to Hirayama disease.

References


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