A young woman with slender hands

A young woman developed slowly increasing atrophy and weakness of the small hand muscles, beginning in her late teens. All other musculature was unaffected. A thorough work-up and literature search eventually revealed a very rare diagnosis.

The relatively slow symptom progression meant that a neurodegenerative disease, such as spinal muscular atrophy, was an obvious possible diagnosis. However, it would be unusual for only the small hand muscles to be affected.

The number of needle pricks in the EMG test was limited, as the patient was afraid of needles, but electromyography from the right extremity revealed chronic peripheral neurogenic changes in the abductor digiti minimi muscles innervated by the ulnar and median nerves, especially the thenar, hypothenar, lumbricals and interossei (Fig. 1, Fig. 2). There was no definite atrophy or paresis of the forearm musculature. She had normal flexion and extension power in the wrist, such that more proximal ulnar- and median-innervated musculature, as well as radial-innervated musculature, was judged to be intact. There was no visible atrophy or paresis of the upper arm or shoulder girdle musculature, and there was normal muscle fullness with good symmetrical power in both lower extremities.

Fine finger movements were reduced in speed, reflecting the paresis, but otherwise normal. No fasciculations were observed and tests of coordination were unremarkable. The patient reported normal sensation for all types of sensory stimuli. Reflexes were of average liveliness and symmetry, and plantar reflexes were flexor. She had no neck pain, free movement of the cervical spine and was negative for Lhermitte’s sign. Cranial nerve examination and mental status were unremarkable.

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Other possible diagnoses we initially took into consideration were benign forms of motor neuron disease, structural lesions of the cervical spine, a form of motoric neuropathy and neurogenic thoracic outlet syndrome. The possibility of an atypical form of plexus neuritis was also considered, although we regarded this as less likely because there was no pain. The clinical picture was fairly unusual – with findings suggestive of an isolated lower motor neuron involvement delimited to medullary level C6 to Th1.

An extensive work-up was performed with blood tests, MRI of the head and medulla, and cerebrospinal fluid examination. A clinical neurophysiological examination with needle electromyography (EMG) from both upper extremities and the lower right extremity, as well as electro-myography (EMG) from both right extremities, was also carried out.

Blood tests, including creatine kinase (CK), which was checked several times, were completely normal. Ganglioside (GM1) antibodies were negative. Cerebrospinal fluid examination yielded normal results.

MRI of the spinal cord showed marked atrophy from C4 to Th2 and two longitudinal symmetrical T2-weighted hyperintense lesions from C2 to Th2 (Fig. 3, Fig. 4), confined to the anterior horn area of the medulla. The changes were not considered consistent with syringomyelia, demyelinating plaques, tumour or transverse myelitis. MRI of the head was normal.

In the upper extremities, sensory and motor nerve conduction velocities for the median and ulnar nerves were within normal ranges. Low motor response amplitudes were recorded for the left median and both ulnar nerves, in the order of 0.7–2.5 mV (normally > 4–5 mV, but atrophy will affect the amplitude). F-responses were delayed in both ulnar nerves, approximately 30–35 ms (normally < 28 ms), difficult to detect for the right median nerve and in the upper range of normal for the left median nerve. Neurographic examination, including F-responses in the lower extremities, was normal.

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minimi muscle and extensor group, while in the first dorsal interosseous, subacute peripheral neurogenic changes were seen with signs of mild denervation. There was no evidence of fasciculations in the muscles examined. EMG findings were normal in the proximal musculature of both the upper and lower extremity.

The patient had an unusual clinical condition and very unusual MRI findings in the spinal cord. After conferring with several neuroradiologists, we were no closer to an aetiological diagnosis. While we were still leaning towards a form of distal spinal muscular atrophy, neurophysiological examination did not reveal the classic changes expected in spinal muscular atrophies, wherein the proximal musculature and lower extremities are usually the most affected. In our patient, most changes were seen distally in the upper extremities. Delayed F-response with normal conduction velocities suggested a proximal abnormality near the nerve root.

There was no neurophysiological evidence for amyotrophic lateral sclerosis, nothing to suggest simultaneous denervation and reinnervation in most of the muscles examined, and no spontaneous activity. Non-reduced amplitudes proximally compared with distally, and negative GM1 antibody status, argued against multifocal motor neuropathy with conduction block. Normal ulnar and median distal latencies meant that there was also no evidence for pathology of Guyon’s canal or the carpal tunnel. Creatine kinase was normal and there were no EMG changes typical of myopathy.

Another possible cause of atrophy and paresis of the small hand muscles is neurogenic thoracic outlet syndrome. This condition results from compression of the brachial plexus, often by a cervical rib, and generally begins with pain or paresthesia in the ulnar region of the arm. In our patient, no anomalies were detected in the cervical spine. As she had never had pain or paresthesia either, this differential diagnosis was also regarded as unlikely.

Following an internet search we found an article from 1978 in which O’Sullivan & McLeod described six patients with chronic distal spinal muscular atrophy affecting the hands (1). These patients had a 10–30 year history of slowly progressive wasting and weakness of the small hand muscles, and in all six individuals, clinical abnormalities were limited to the hands.

According to the authors there was no clinical or radiological evidence for peripheral or proximal nerve root involvement or for a disorder of the central nervous system. Neurophysiological examinations confirmed that the muscle atrophy was the result of a chronic partial denervation. Motor and sensory nerve conduction velocities were normal, and cervical myelography revealed no pathology. Clinical, radiological and neurophysiological findings were interpreted as consistent with a chronic degeneration of motor anterior horn cells. The condition has subsequently been named O’Sullivan-McLeod syndrome.

In our patient, there has been no definite progression of the condition in ten years, based on clinical and MRI data.

Discussion

Spinal muscular atrophies (SMA) are a heterogeneous group of disorders that usually begin with weakness in proximal muscle groups as a result of slowly progressive lower motor neuron degeneration. Most spinal muscular atrophies are hereditary, but sporadic cases also occur. Rarer and localized variants with distal musculature involvement and relatively good prognosis have been described (2, 3).

In other forms of distal spinal muscular atrophy, such as SMA-V, both upper and lower extremities are affected. Charcot-Marie-Tooth type 2D (CMT) is an inherited polyneuropathy with a similar phenotype to SMA-V (4). The main difference between these two conditions is distal sensory loss in patients with Charcot-Marie-Tooth type 2D. Both conditions show autosomal dominant inheritance and are therefore unlikely in our patient, although the possibility of a de novo mutation remains. The anamnesis provided
The condition most often affects young men. 

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Amyotrophy. Forearm and upper arm. Hirayama disease is hand muscles, whereas Hirayama disease as van-McLeod syndrome, clinical findings are more prevalent in Asians than in Caucasians (5). Bilateral manifestations of the anterior horn cells extending from C6 to C7. The diameter of the cervical medulla was considered normal.

The aetiology of O'Sullivan-McLeod syndrome is unknown, although it is presumably a neurodegenerative disorder. There is no evidence that the condition is hereditary. A pathophysiological mechanism similar to that of Hirayama disease is conceivable, but has not been described in the literature. There has been discussion as to whether immunemediated neuronal damage may be a contributory factor in the pathogenesis, based on a case report in which transient improvement of muscle wastage was seen after treatment with intravenous immunoglobulin (13). Other than this single report, no specific treatment has been described. Because the condition is very rare, it will not be possible to conduct randomised controlled trials; however, the prognosis seems to be good.

**Conclusion**

O'Sullivan-McLeod syndrome is a rare form of distal spinal muscular atrophy with relatively good prognosis. The diagnosis is based upon clinical and neuropsychological examinations and characteristic MRI changes with segmental atrophy in the cervical medulla and hyperintense lesions in the anterior motor neuron area.

The patient has consented to publication of this article.

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