O'Sullivan–McLeod syndrome: clinical features, neuroradiology and nosology

Introduction

It is more than 35 years since O'Sullivan and McLeod (1978) described a series of patients with slowly progressive wasting of the hand and forearm musculature. These patients had investigation features suggestive of an anterior horn cell (motor neurone) disease which the authors characterized as a chronic distal spinal muscular atrophy. Few cases using the nomenclature of O'Sullivan–McLeod syndrome have subsequently been published (Serratrice, 1984; Gaio et al, 1989; Petiot et al, 2000; Kawano et al, 2007).

This article presents a further case of O'Sullivan–McLeod syndrome with neurophysiological and neuroradiological investigation, in order to raise awareness of this condition, which has been under-recognized in classifications of motor neurone diseases (Donaghy, 1999), and also to clarify its nosology.

Discussion

The initial publications on O'Sullivan-McLeod syndrome defined the condition as a chronic spinal muscular atrophy with onset in adolescence or young adulthood. The disease was characterized clinically by weakness and atrophy of the small hand muscles sometimes extending to the forearms, in the absence of sensory or pyramidal signs, and neurophysiologically by neurogenic electromyography recordings and normal nerve conduction studies. These publications (O'Sullivan and McLeod, 1978; Serratrice, 1984) predated the availability of magnetic resonance imaging studies. These have been reported to show focal cervical cord atrophy (Gaio et al, 1989; Kawano et al, 2007), and in one case symmetrical T2-weighted high signal in the region of the anterior horn cells was seen (Petiot et al, 2000), akin to the neuroimaging changes seen in this case.

Similarities between O'Sullivan–McLeod syndrome and Hirayama disease (Hirayama et al, 1959) have been noted (Kawano et al, 2007). The latter terminology has been used for a juvenile onset muscular atrophy of the distal upper extremity, usually unilateral and predominantly occurring in males, characterized by progressive arm wasting and weakness over a few years followed by spontaneous arrest such that wasting and weakness deteriorate no further. Owing to the favourable long-term prognosis pathological studies are rare but have suggested the presence of ischaemic change in the lower cervical anterior horns (Hirayama, 2000).

While neurogenic findings on electromyography are typical, abnormalities in nerve conduction studies, in particular reductions in compound muscle action potentials of affected muscles, may be seen (Hirayama, 2000). Neuroradiological investigations have suggested that Hirayama disease may be the result of dynamic compression of the spinal cord, secondary to forward displacement of the posterior cervical dural sac during neck flexion. This results in anterior-posterior flattening of the cord, atrophy, and occasionally T2-weighted hyperintensity in the grey matter of the anterior horns (e.g. Desai and Melanson, 2011; Huang and Chen, 2011). Diffusion tensor imaging and transcranial magnetic stimulation studies support the integrity of the supraspinal corticospinal tracts in Hirayama disease, suggesting that this is a pure spinal motor neurone disorder (Boelmans et al, 2013).

Based on the overlap in clinical, neurophysiology and neuroradiology findings, it would seem that O'Sullivan–McLeod syndrome and Hirayama disease are closely related if not identical conditions. This nosology may have distinct implications

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Case Report

A 29-year-old right-handed man reported 18 months of slowly progressive weakness and wasting in his left arm and hand, such that he had difficulty lifting the arm, flexing the elbow and abducting the fingers. More recently, he had begun to develop similar symptoms in the right arm. He reported some mild pain in the proximal upper limbs. There was no cranial nerve, lower limb, sphincter or sensory symptomatology. His past medical history was unremarkable and there was no family history of neuromuscular disease.

Salient findings on neurological examination were wasting of biceps, triceps, deltoids and intrinsic hand muscles, more evident on the left than right, with commensurate weakness, and bilateral scapular winging. Tendon reflexes were depressed in the upper limbs, with absence of the triceps jerk bilaterally. The rest of the neurological examination was normal.

Routine blood tests, including creatine kinase and genetic testing for facioscapulohumeral dystrophy, were negative or within normal limits. Nerve conduction studies were normal with no evidence of conduction block. Electromyography showed denervation changes, mostly chronic, associated with fasciculations in the left deltoid, biceps, spinati and extensor digitorum communis and right biceps, indicating that the wasting was neurogenic. Repeat electromyography 8 months later confirmed these findings: again active denervation changes were few. Analysis of CSF was entirely normal. Magnetic resonance imaging of the brain was normal, but magnetic resonance imaging of the cervical spine showed a long segment of high signal change and volume loss involving the anteromedial aspect of the cord from around C3 to C6, which on the axial views was confined to the anterior horns (*Figure 1*).

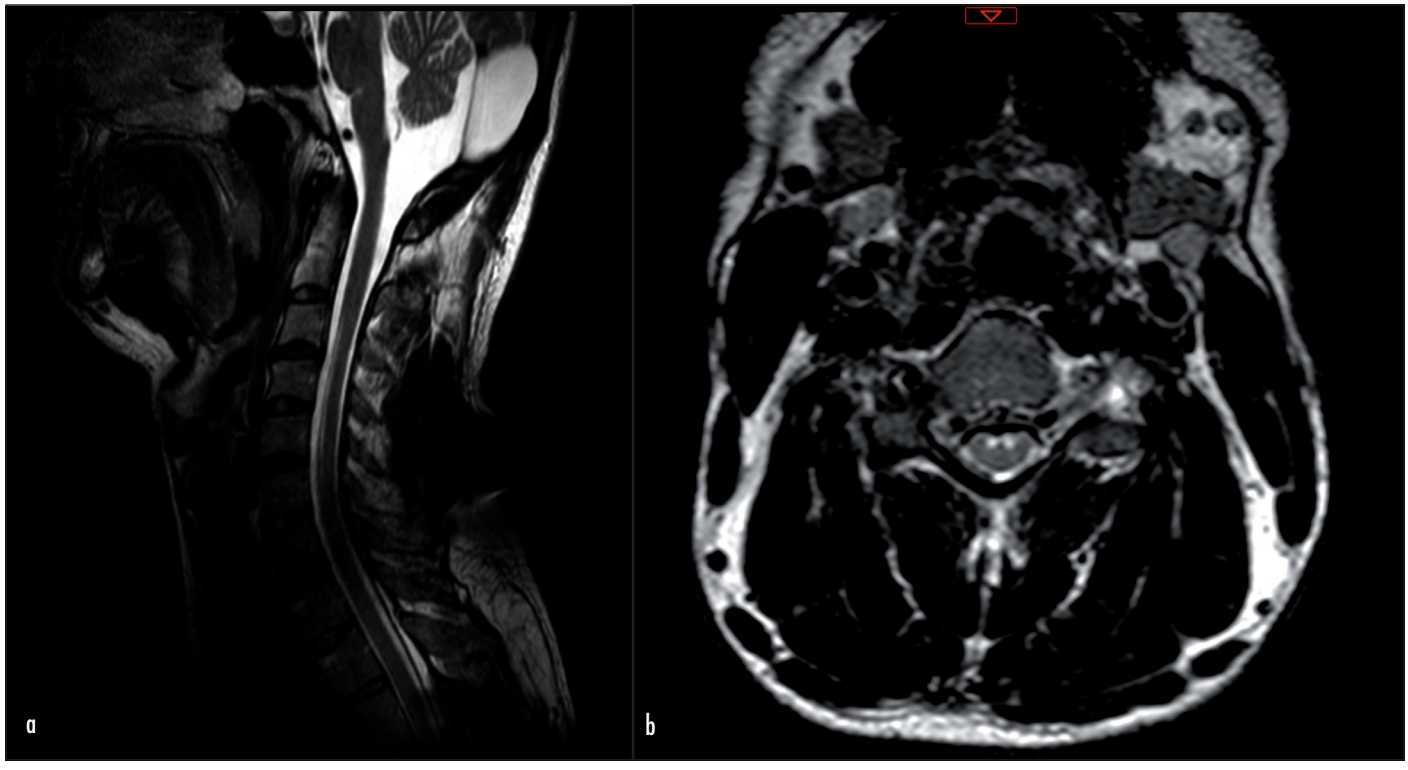

Figure 1. Magnetic resonance imaging of cervical spine, showing (a) increased signal intensity in the anterior spinal cord (sagittal image) (b) which is confined to the anterior horns (axial image), so-called 'snake eyes' appearance.

for treatment: no specific treatment for O'Sullivan–McLeod syndrome is known, although in one case transient improvement was noted following administration of intravenous immunoglobulin (Kawano et al, 2007). However, the presumed compressive aetiology of Hirayama disease has prompted the suggestion that application of a cervical collar to minimize neck flexion may prevent progressive muscular weakness if instituted early in the disease course (Hirayama, 2000).

Future investigations which might confirm or refute the proposed nosology include studies of hyperIgEaemia in both conditions (Ito et al, 2005), and pathological studies, for example using immunostaining for TDP-43 which might define whether or not these are primary anterior horn cell disorders (as for other focal anterior horn cell disorders, such as focal onset sensory and motor neuropathy, FOSMN: B Ziso et al, unpublished observations, 2014) or simply the consequence of focal ischaemia. **BJHM**

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LEARNING POINTS

- O'Sullivan–McLeod syndrome is a chronic distal spinal muscular atrophy.
- Although rare, awareness of O'Sullivan–McLeod syndrome is clinically relevant since this condition enters the differential diagnosis of motor neurone disease.
- The clinical, neurophysiological and neuroradiological features of O'Sullivan–McLeod syndrome overlap with those of Hirayama disease, another juvenile onset muscular atrophy.
- This clinical overlap may reflect clinical identity, which may have implications for understanding disease pathogenesis (compressive flexion myelopathy) and treatment (neck stabilization with a collar).