Amyotrophic lateral sclerosis presenting as upper limb weakness in a 35 year old female: a case report

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Chiropractors regularly assess and provide treatment for a variety of neuromuscular complaints. Many of these respond well to conservative care however some represent conditions that must be referred for further evaluation. This article chronicles the management of a patient who presented with upper limb weakness and was subsequently diagnosed with amyotrophic lateral sclerosis (ALS). Chiropractors should be informed of the nature and presentation of this disease to facilitate early diagnosis and treatment. (JCCA 2011; 55(3):204–210)

KEY WORDS: amyotrophic lateral sclerosis, upper limb weakness, chiropractor

Introduction

ALS is characterized by relentless degeneration of both upper motor neurons (UMN) and lower motor neurons (LMN) leading to progressive muscular paralysis and death usually within five years.¹ Recent studies report yearly incidence rates ranging from 1.5 to 2.5 cases / 100,000 population.² The disease principally affects people aged 50–60 years with only 5% of patients having onset before the age of 30 years. It is usually not inherited with genetics involved in a minority of cases.³

A 2008 study published in Neurology showed that limb weakness is the most common symptom at disease onset followed by dysarthria, dysphagia, cramps, fasciculations and shortness of breath.⁴ These LMN signs are often accompanied with the clinical signs of UMN disease: overactive tendon reflexes, clonus and Babinski responses.⁵ After the disease begins, it follows a typical progressive Les chiropraticiens évaluent régulièrement et offrent des traitements pour diverses douleurs neuromusculaires. La plupart de ces douleurs réagissent bien au traitement conservateur, mais certaines constituent des états pathologiques nécessitant un examen plus approfondi. Cet article explique la gestion d'un patient qui présentait une faiblesse des membres supérieurs, et pour qui l'on a émis un diagnostic de sclérose latérale amyotrophique (SLA). Les chiropraticiens doivent être informés de la nature et de l'aspect de cette maladie afin de faciliter le diagnostic hâtif et le traitement de cette maladie. (JCCA 2011; 55(3):204–210)

MOTS CLÉS : sclérose latérale amyotrophique, faiblesse des membres supérieurs, chiropraticien

course and it eventually affects almost all voluntary muscles. The cause of death is usually respiratory compromise related to diaphragm and intercostal weakness.⁶

Chiropractors frequently assess and treat patients for limb complaints.⁷ While many of these complaints, for example carpal tunnel syndrome^{8,9} and spinal radiculop-athy^{10,11,12} often respond well to treatment some are more serious neuromuscular conditions that require appropriate referral. ALS is one such disease that can mimic some of the limb conditions which are seen in chiropractic practice and may need to be considered as a differential diagnosis.

The purpose of this case report is to describe the presentation of a patient with upper limb weakness that she believed was secondary to her occupational demands as administrative assistant. Her condition had been previously diagnosed by her medical doctor as carpal tunnel syndrome. She was diagnosed with ALS by a neurologist

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one month after her presentation to a chiropractic clinic and died 15 months later.

Case Presentation

A 35 year old, right-handed female presented to a chiropractic clinic with a complaint of progressive weakness in the right upper limb. She described the weakness as no hand strength and a loss of dexterity in the third, fourth and fifth digits. Upon further questioning it was revealed that she found handwriting difficult, was prone to dropping cups of coffee and that recently it had taken her 10 minutes to put on her pants. This condition began six weeks prior to her appointment at the clinic. She felt her symptoms were related to a time she was working 48 hours a week doing data entry.

She described associated pain and tingling in the right third, fourth and fifth digits, pain in multiple areas in the right upper limb and bilateral cervico-thoracic pain. She reported visible muscular twitching in both hands. These symptoms were aggravated when she worked and relieved when, for extended periods, she did not work. Heat and a hand therapy ball had not provided relief of symptoms. She denied past history of a similar complaint.

She had previously seen her medical doctor for this complaint. The doctor felt her symptoms were due to carpal tunnel syndrome and had scheduled an electromyogram in three months. No previous imaging had been completed. Past medical history revealed asthma for which she required previous hospitalization and ongoing medications. She reported a motor vehicle accident five months earlier but did not sustain injury. Maternal family history revealed stroke and arthritis while paternal history revealed type 1 diabetes and occupational claw-hand. The patient was a widow with no children of her own.

The patient appeared in discomfort and dysarthria was noted throughout the visit. Postural exam revealed an elevated right scapula and hypertrophy in the bilateral cervico-thoracic musculature. Spinal joint fixations were noted in the cervical and thoracic spine. Cervical spine range of motion was full and pain-free in all planes. Tender myofascial trigger points were noted in the right medial intermuscular septum, flexor carpi ulnaris and tunnel of Guyon. Generalized muscular tension was palpated in the right flexors and extensors of the forearm. Fasciculations were observed in the right triceps. A normal Babinski response was elicited. An upper limb motor strength exam revealed weakness in the flexors and extensors of the right wrist as well as in flexion and abduction of the right digits. Decreased sensation was documented in the palmar surfaces of digits four and five as well as the medial aspect of the hand, forearm and arm which corresponds to C6, C7 and C8 dermatomes. Severe hyper-reflexia was elicited bilaterally in the C5, C6, C7, L4 and S1 deep tendon reflexes. Elevated arm stress test revealed the patient was unable to flex her right fifth digit and after the test, fasciculations were noted in the thenar eminence bilaterally.

The patient was treated for her musculoskeletal findings. Treatment involved a prone adjustment of her midthoracic spine and Active Release Techniques® to the affected soft tissues. The patient's cervical spine was not treated with a high-velocity, low-amplitude manipulation. This decision was based on the presence of the neurological signs and symptoms in case of a possible cervical myelopathy, space occupying lesion affecting a nerve root or vertebrobasilar insufficiency.¹³ The case was discussed with a colleague at the clinic and it was agreed the patient was to be referred to her medical doctor for a neurological consult. This referral was discussed with the patient at her next chiropractic appointment and no treatment was done. She saw a neurologist one month later.

Management and Outcome

The neurologist noted in her report that the patient described progressive hand weakness, dysarthria, twitching in the extremities, dysphagia as well as new symptoms including cramping in the left forearm, intermittent blurred vision and difficulty walking. Examination revealed tongue weakness and mild spastic dysarthria. Bilateral atrophy of her hands and fasciculation in the right biceps and triceps were observed. Strength in the deltoids was 4/5 bilaterally and 3/5 in the hands bilaterally, graded on the Medical Research Council Muscle Strength Grading System,¹⁴ however the right arm was slightly weaker than the left throughout. Motor testing in the lower extremities was normal. Reflexes were graded as pathologically brisk in the arms and in the right leg. Three positive UMN signs were noted bilaterally: a Hoffman sign,¹⁵ a crossed knee adductor response¹⁶ and a spastic catch¹⁷ (Table 1). Sensory testing was normal. Gait was described as normal except difficulty with heel walking.

Right ulnar and median motor nerve conduction studies demonstrated moderately diminished amplitudes. Right

Table 1Description of the UMN signs15,16,17

Hoffman Sign – A sudden nipping of the nail of the index, middle or ring finger produces flexion of the terminal phalanx of the thumb and of the second or third phalanx of some other finger.

Crossed Knee Adductor Response – The patient is sitting or lying supine, the examiner taps the adductor tendons on the medial distal thigh with a reflex hammer. The crossed adductor response describes adduction of the contralateral leg when the adductor tendons are tapped. Under normal circumstances, only the leg which the hammer hits should adduct.

Spastic Catch – The limb is passively and quickly moved through its range of motion. As the limb moves, it seems to catch. This catch is followed by a slow relaxation through the remainder of the movement. No catch is demonstrated if the limb is moved slowly.

median mixed palmar, superficial radial and sural sensory studies were normal. Electromyography studies showed active denervation in all muscles studied including the right first dorsal interosseous muscle, pronator teres, deltoid and medial gastrocnemius as well as the tibialis anterior bilaterally.

It was noted that the patient demonstrated clinical and/ or electrophysiological evidence of LMN involvement at at least two spinal levels and UMN involvement at three spinal levels. It was further noted this meets the criteria for probable to definite ALS. Riluzole, the established disease modifying medication, which has been shown to modestly slow progression and lengthen survival in ALS^{18,19} was prescribed. Lithium was also prescribed. A 2008 paper revealed promising results for lithium slowing disease course in a pilot study and its neuroprotective effects in an animal model study;²⁰ however, subsequently the drug failed to show evidence of benefit in a larger, randomized, double-blind, placebo-controlled trial.²¹

The neurologist referred the patient for an MRI of her brain and cervical spine. The MRI study conducted two months later, showed hyperintense signal along the corticospinal tract in the brain bilaterally with a cervical spine examination within normal limits. This verified the diagnosis.

A progression of symptoms was reported when the patient was re-evaluated by the neurologist one month later. Examination showed moderate bifacial and tongue weakness as well as fasciculations in the tongue. Strength remained relatively preserved in the upper extremity bilaterally except marked weakness was noted in the intrinsic hand muscles graded at 0–1/5. It was noted that the patient's family physician had recently prescribed ativan, a medication with anxiolytic and sedative properties²² as well as citalopram, a selective serotonin reuptake inhibitor.²³ The patient also presented to an ALS clinic that day and was assessed by a multidisciplinary team composed of an occupational therapist, registered dietician, social worker, speech language pathologist and registered nurse.

Three months later the patient was re-assessed. The neurologist's notes from that visit reveal progression in her dysphagia and increased weakness in hands and legs. It was noted the patient's forced vital lung capacity was at 60% of predicted. Consequently she was referred to a gastroenterologist for feeding tube placement. The note of this referral is the last entry available. The patient died nine months later.

Discussion & Conclusion

ALS involves progressive muscular paralysis reflecting degeneration of the motor neurons in the primary motor cortex, brainstem and spinal cord. Male gender, aging, a positive family history and military service are established risk factors for the development of the disease while smoking, exposure to toxins (e.g. lead), repeated head injury, playing football professionally and a family history of non-ALS neurodegenerative diseases (e.g. Parkinson's disease) are proposed yet unconfirmed. The hypothesis most authors favor is a complex interaction of factors.^{24,25}

The precise molecular pathway causing degeneration is unknown. It is likely interplay between several pathogenic cellular mechanisms including cell injury through excitotoxicity of postsynaptic glutamate receptors, oxidative stress, mitochondrial dysfunction, impaired axonal transport, neurofilament and protein aggregation in neural tissues, immune deregulation based inflammatory dysfunction and deficits in neurotrophic factors signaling pathways.²⁵ The disease has pathological hallmarks. UMN disease is indicated by the loss of motor cortex cells with variable astrocytic gliosis affecting cortical grey and underlying white matter. Additional characteristics include axonal loss within the descending pyramidal tracts as well as myelin pallor and gliosis in the corticospinal tracts. LMN pathology affects the anterior horn motor cells of the spinal cord and brainstem. At autopsy loss of motor neurons can be as high as 50% and the remaining neurons are atrophied and contain characteristic intraneuronal inclusions.²⁵

Investigative medicine plays an important role in the confirmation of diagnosis and the exclusion of mimic disorders. Standard electrophysiological studies include nerve conduction studies and conventional electromyography (EMG). Typically, EMG reveals evidence of denervation and chronic neurogenic changes. In the absence of concomitant entrapment or other neuropathies, nerve conduction studies are normal or near normal.²⁶ MRI has a dual value. It aids in the exclusion of treatable structural lesions that mimic ALS and it often reveals abnormalities reflective of the disease's degeneration. The most common finding in ALS is hyperintensity of the corticospinal tract.^{27,28}

Diagnosis is based on the presence of characteristic clinical findings in conjunction with investigations to exclude "ALS-mimics" (Table $2^{25,29}$) which are distinct disorders with a similar presentation. Signs suggestive of a combined UMN and LMN disease that is progressive and cannot be explained by any other disease process is required for the diagnosis.³⁰ The World Federation of Neurology Research Group on Motor Neuron Diseases developed the 1994 El Escorial Diagnostic Criteria to aid in the classification of patients suspected of having ALS. In 2000 the Revised El Escorial Diagnostic Criteria was published (Table $3^{25,30}$).

There are two types of typical ALS, spinal onset and bulbar onset, named according to the type of symptoms that first manifest. Spinal onset is 1.5 to 4 times as common as bulbar onset depending on classification criteria and has a better prognosis than bulbar onset.^{29,31} ALS has variant syndromes involving motor neuron disease with distinctive clinical presentations and prognosis. These include primary lateral sclerosis (PLS) which is a UMN disease in which patients have no LMN signs.³² Progressive muscular atrophy (PMA), on the other hand, is a pure LMN disease.³³ Additional variants include flail leg and Table 2Conditions that may mimic ALS

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STRUCTURAL DISORDERS

- Syringomyelia or syringobulbia
- Cervical spondylotic myelopathy
- Central nervous system (CNS) tumors
- Arnold-Chiari malformations
- Cervical disc herniations
- Lumbo-sacral radiculopathy

IMMUNE AND INFLAMMATORY DISORDERS

- Multifocal motor neuropathy
- Multiple sclerosis
- Myasthenia gravis
- Inclusion body myositis

METABOLIC DISORDERS

- Hyperthyroidism
- Hyperparathyroidism

OTHER CNS DEGENERATIVE DISORDERS

- Parkinson disease

INFECTIOUS DISORDERS

- Creutzfeldt-Jakob disease
- Syphilis

HEREDITARY NEUROLOGICAL DISORDERS – Kennedy's disease

flail arm syndromes. Flail arm syndrome is a LMN disorder of the upper limbs while flail leg syndrome is a LMN disorder of lower limbs.³⁴ PLS and the flail syndromes have a more benign course than ALS however PMA has a prognosis almost as poor as ALS.^{32,33,34} These syndromes are considered variants because they share molecular findings and at autopsy both UMN and LMN involvement is visualized.⁵

ALS has a predictable progressive, rapid and widespread clinical course. A 28-year retrospective study pub-

Table 3Summary of Revised El Escorial Diagnostic
Criteria for diagnosing ALS25,30

The clinical diagnosis of ALS, without pathological confirmation, may be categorized into various levels of certainty by clinical assessment alone, depending on the presence of UMN and LMN signs together in the same topographical anatomical region in either the brainstem (bulbar cranial motor neurons) or the cervical, thoracic, or lumbosacral spinal cord (anterior horn motor neurons).

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| Diagnostic Category | Clinical Features |
|--|--|
| • Definite ALS | • UMN & LMN signs in the bulbar region and in at least 2 spinal regions or UMN & LMN in 3 spinal regions |
| • Probable ALS | • UMN & LMN signs in 2 regions with at least some UMN signs rostral to the LMN signs |
| • Probable ALS (laboratory supported) | • UMN & LMN signs in 1 region or UMN signs in 1 region and LMN dysfunction defined by EMG in at least 2 regions |
| • Possible ALS | UMN & LMN signs in 1 region (together) UMN signs in 2 or more regions LMN signs rostral to the UMN signs without evidence for Probable ALS(laboratory supported) |

lished in 2004 showed median survival from symptom onset ranges from 2.4 years for bulbar onset and 3.1 years in spinal onset with a long term survival observed in only 6% of patients.³¹ Riluzole, which has been hypothesized

to inhibit the release and effects of glutamate, has been shown to extend survival.³⁵ A 2007 study showed that riluzole therapy increased survival rates at 12 months by approximately 10% and prolonged life by 6 months independent of other interventions.³⁶ Additional prognostic factor include age of symptom onset, time from symptom onset to diagnosis, El Escorial diagnostic category at presentation and baseline respiratory function.²⁵

In the absence of a cure, the goal of ALS care is to enable the patient to achieve maximal functioning and maintain autonomy for as long as possible. Helping the patient overcome communication and ambulation difficulties as well as managing ventilation and nutrition are key independence issues. Furthermore all efforts should be made to improve quality of life through treatments for the associated physical symptoms including cramps, spasticity, pain, sialorrhea, fatigue and insomnia, constipation, aspiration and laryngospasm. The psychological symptoms that ALS patients face such as fear, hopelessness, depression and anxiety as well as cognitive impairment need to be attended to.⁶ A multidisciplinary approach is essential. It has been shown to improve quality of life³⁷ as well as improve prognosis and lengthen survival³⁸ in recent studies.

This case highlights important aspects of the disease. As is most common in ALS, the presenting symptom was limb weakness. The patient presented to our clinic with LMN signs in two regions evidenced by dysarthria and the weakness and fasciculation in the upper limb as well as UMN signs in two regions displayed by pathological reflexes in the upper and lower limb. This presentation is compatible with possible-probable ALS.^{25,30} This was unknown to the author at the time; however, there were sufficient signs and symptoms to warrant concern and recommend a neurological consult. Following the investigations by the neurologist, a diagnosis of ALS was established. In spite of the medication and multidisciplinary care, the patient's deterioration was progressive, rapid and relentless.

There were aspects of the case that initially confounded the diagnosis. The onset of symptoms appeared related to increased hours at work and they were relieved by rest. On examination, the patient did demonstrate sensory findings which would not be expected with ALS however it is likely there was a musculoskeletal condition such as a nerve entrapment. Additionally, a normal Babinski response was elicited which would suggest that there was not an UMN lesion.

A literature search for previously published studies on this topic was done. The PubMed and Index to Chiropractic Literature databases were searched with the terms ("Amyotrophic Lateral Sclerosis" [Mesh] or "Amyotrophic Lateral Sclerosis" or "Lou Gehrig's disease") and ("Manipulation, Chiropractic" [Mesh] or "Musculoskeletal Manipulations" [Mesh] or "chiropract*" or "manipulat*" or "spinal manipulation") revealed no results for articles detailing the involvement of chiropractors with ALS. It is possible that chiropractic is a safe and effective palliative option for the musculoskeletal effects of the disease similar to its benefits for tardive dyskinesia³⁹ and multiple sclerosis⁴⁰ outlined in previous studies; however, research specifically into its benefits for ALS patients is required before a more definitive statement can be made. The need for a controlled trial into the role chiropractic has in relieving the chronic pain of neuromuscular diseases was stated in a 2005 study published in Archive of Physical Medicine and Rehabilitation, after it was revealed chiropractic care was the most effective treatment option and the only one that continued to be used by most patients who tried it.⁴¹

Chiropractors can contribute to the early detection of ALS by being cognizant of its nature and presentation. Early ALS diagnosis has become increasingly important as this facilitates arrangement of the best care and enables early administration of disease modifying medication as a potential means to improve quality of life in patients with this devastating disease.^{26,42}

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