OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2025;10(3):239-246 *Online Türk Sağlık Bilimleri Dergisi 2025;10(3):239-246*

Evaluation of Cases Diagnosed with Cervical Myelopathy or Syringomyelia Referred with a Preliminary Diagnosis of Amyotrophic Lateral Sclerosis

Amiyotrofik Lateral Skleroz Ön Tanısıyla Sevk Edilen Servikal Miyelopati veya Siringomiyeli Tanısı Almış Olguların Değerlendirilmesi

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ABSTRACT

Objective: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease involving both upper and lower motor neurons. Upper motor neuron signs include spasticity and hyperreflexia, while lower motor neuron signs include weakness, muscle atrophy, and fasciculations. Because of these signs, ALS can be confused with cervical spondylotic myelopathy (CSM), syringomyelia, and similar diseases. This study aimed to evaluate the clinical and demographic characteristics of patients diagnosed with CSM or syringomyelia after initially being referred with suspected ALS.

Materials and Methods: Ten patients referred to our neurology clinic between January 2018 and June 2020, with a preliminary diagnosis of ALS, were evaluated. Those patients later diagnosed with CSM or syringomyelia after neurological examination, including electromyography (EMG) and magnetic resonance imaging (MRI), were included in the study.

Results: Ten patients (mean age 65.6 years) were analysed. Thenar and hypothenar atrophy was observed in 8 patients (80%). EMG revealed fasciculations and subacute denervation in cervical myotomes in all patients; 1patietnt had lumbar involvement. EMG of rectus abdominis and genioglossus muscles was normal. Thenar and hypothenar atrophy, fasciculation, and denervation in cervical and lumbar myotomes on EMG are similar to ALS signs. A normal rectus abdominis and genioglossus muscle EMG excludes the diagnosis of ALS.

Conclusions: CSM and syringomyelia should be considered in the differential diagnosis of ALS. A detailed history, neurological examination, EMG, and MRI are essential for diagnostic accuracy.

Keywords: Amyotrophic lateral sclerosis, cervical spondylotic myelopathy, syringomyelia

ÖZ

Amaç: Amiyotrofik lateral skleroz (ALS), hem üst hem de alt motor nöronların dejenerasyonu ile karakterize, ilerleyici bir nörodejeneratif hastalıktır. Üst motor nöron bulguları arasında spastisite ve hiperrefleksi; alt motor nöron bulguları arasında ise kas güçsüzlüğü, atrofi ve fasikülasyonlar yer alır. Bu bulgular nedeniyle ALS, servikal spondilotik miyelopati (SSM), siringomiyeli ve benzeri hastalıklarla karıştırılabilir Bu çalışmada, ALS şüphesiyle sevk edilen ve CSM veya siringomiyeli tanısı alan hastaların klinik ve demografik özelliklerinin değerlendirilmesi amaçlanmıştır.

Materyal ve Metot: Ocak 2018 – Haziran 2020 tarihleri arasında nöroloji kliniğimize ALS ön tanısıyla sevk edilen 10 hasta değerlendirildi. Nörolojik muayene, elektromiyografi (EMG) ve manyetik rezonans görüntüleme (MRG) sonrasında CSM veya siringomiyeli tanısı konulan hastalar çalışmaya alındı.

Bulgular: On hasta (ortalama yaş 65,6 yıl) analiz edildi. 8 hastada (%80) tenar ve hipotenar atrofi gözlendi. EMG'de tüm hastalarda servikal miyotomlarda fasikülasyonlar ve denervasyon görüldü; 1 hastada lomber bölgede tutulum vardı. Rektus abdominis ve genioglossus kaslarının EMG'si normaldi. Tenar ve hipotenar atrofi gözlenmesi, EMG'de servikal ve lomber miyotomlarda fasikülasyon ve denervasyon görülmesi ALS ile benzerlik göstermektedir. Rektus abdominis ve genioglossus kaslarının EMG'sinin normal olması ALS tanısından uzaklaştırmaktadır.

Sonuç: ALS ayırıcı tanısında CSM ve siringomiyeli düşünülmelidir. Ayrıntılı öykü, nörolojik muayene, EMG ve MRG tanı doğruluğu için gereklidir.

Anahtar Kelimeler: Amiyotrofik lateral skleroz, servikal spondilotik miyelopati, siringomiyeli

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Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 23/04/2025
Kabul Tarihi/ Accepted: 15/08/2025
Online Yayın Tarihi/ Published: 15/09/2025

Atıf / Cited: Uçaroğlu Can N. Evaluation of Cases Diagnosed with Cervical Myelopathy or Syringomyelia Referred with a Preliminary Diagnosis of Amyotrophic Lateral Sclerosis. *Online Türk Sağlık Bilimleri Dergisi* 2025;10(3):239-246. doi: 10.26453/otjhs.1682365

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a gradually worsening neurodegenerative disease involving the motor neurons situated in the spinal cord, cerebral cortex, and brainstem. Its incidence is reportedly 1.68 per 100,000, and recent data show a rising prevalence worldwide. Male sex is a known risk factor, and disease onset typically occurs between the ages of 51 and 66 years. An ALS diagnosis is based on clinical history, findings, neurophysiological testing, and exclusion of other diseases. It presents with simultaneous upper and lower motor neuron degeneration.[1] Upper motor neuron (UMN) signs are detected clinically, while lower motor neuron (LMN) signs are confirmed by diagnostic procedures such as nerve conduction analysis and needle electromyography (EMG).[2]

Cervical spondylotic myelopathy (CSM), the most severe outcome of cervical spondylosis, is the leading cause of acquired spinal cord dysfunction. Its incidence in North America is at least 4 per 100,000.[3] CSM usually develops between the ages of 50 and 60 years and presents with neck, shoulder, or arm pain as well as hand weakness, leg weakness, and gait disorder. Upon examination, findings include muscle atrophy, hyperreflexia, sensory loss, and spastic paresis of the lower limbs.[4] LMN signs appear at the lesion level, while UMN signs appear below. Upper limb signs may be unilateral; lower limb signs are always bilateral.[5] Diagnosis is supported by magnetic resonance imaging (MRI) showing spinal cord changes such as oedema, gliosis, or myelomalacia on T2 sequences.[6] Electromyography (EMG) helps in ruling out ALS.

Syringomyelia is a fluid-filled cavity (syrinx) in the spinal cord (typically in the mid-lower cervical region), which causes chronic sensory and motor loss.[7,8] Symptoms vary by syrinx location. Involvement of the anterior horns causes segmental atrophy and weakness. Damage to the central grey matter causes temperature sensation and loss of pain. Involvement of lateral columns leads to spasticity, paraparesis, and hyperreflexia. Syringomyelia can mimic ALS but progresses slowly and includes sensory symptoms. MRI confirms diagnosis.[9] CSM may also mimic ALS and cause diagnostic delays.

This study aimed to evaluate and compare the clinical, radiological and electrophysiological features of patients who were initially referred with a preliminary diagnosis of ALS. Still, it was later diagnosed with CSM or syringomyelia after detailed examinations.

MATERIALS AND METHODS

Ethics Committee Approval: Approval was granted by the Ethics Committee of Sakarya University Faculty of Medicine (Date: 10.07.2020, decision no: E.6172), and all procedures were performed in accordance with the Helsinki Declaration

Study: This study retrospectively reviewed the medical records of 10 patients who presented to our neurology clinic in Turkey with a preliminary diagnosis of ALS between 1 January 2018 and 1 June 2020. Based on medical history, detailed neurological examination, spinal MRI, sensory and motor nerve conduction studies and concentric needle electromyography (EMG), ALS was excluded in all patients. These patients were diagnosed with CSM or syringomyelia. The radiological findings were evaluated by MRI. We selected only patients for whom cervical cord MRI showed radiological signs of CSM and syringomyelia.

Analysis: All participants underwent sensory and motor nerve conduction studies and EMG of the thenar and hypothenar muscles as a conventional diagnosis method. During motor nerve examination, thenar and hypothenar compound muscle action potential (CMAP) values were recorded at the abductor pollicis brevis (APB) and abductor digiti minimi (ADM) in response to stimulation of the median and ulnar nerves, respectively. In sensory nerve examination, the median and ulnar nerves were stimulated at the wrist.

Deep tendon reflexes are an important part of the neurological examination used to assess the integrity of the peripheral and central nervous systems. Reflex responses are graded on a scale from 0 to 4+:

Grade 0: No response.

Grade 1+: Diminished or sluggish response.

Grade 2+: Average, normal response.

Grade 3+: Brisker than average (the reflex is more active than normal, but not necessarily abnormal).

Grade 4+: Very brisk, hyperactive with clonus (this is an exaggerated reflex response, often accompanied by clonus, which is typically abnormal and suggests an upper motor neurone lesion or central nervous system pathology).

Exclusion Criteria: 1) history of spinal cord tumor or abnormalities of the cervical vertebrae; 2) focal or multifocal neuropathy; 3) brachial plexus lesion; 4) muscular dystrophy; or 5) injury or infection at presentation.

Statistical Analyses: The statistical component of the study was handled via SPSS version 21.0, with numerical results presented as mean ± standard deviation, number, and percentage.

RESULTS

The mean age of the patients in this research was 64.90 ± 9.26 years, with an age range of 51 to 78 years. The 10 patients comparised 6 (60%) males and 4 (40%) females. Four patients (40%) took med-

ications for hypertension, and 2 (20%) for diabetes mellitus. One patient (10%) was diagnosed with chronic kidney disease (CKD). The mean time from onset to diagnosis was 3.25 ± 3.01 years. Table 1 shows a summary of the demographic characteristics of the study participants. These patients, along with their demographic characteristics, are detailed in Table 1.

Regarding the presenting symptoms, five patients exhibited isolated unilateral upper extremity weakness, two had bilateral upper extremity weakness, three demonstrated lower extremity weakness accompanied by gait disorder, and one patient displayed weakness in both the upper and lower extremities, coupled with gait disorder. In addition to these complaints, all patients had neck and back pain, and two patients had spasticity in the lower extremities.

Neurological examination findings included thenar and hypothenar muscle atrophy in eight patients, gait disorder and mild spasticity in the lower extremities in four patients, increased deep tendon reflexes in the lower extremities in eight patients, and cape-like sensory deficits in three patients. Seven patients had significant muscle atrophy. No patients were diagnosed with dysphagia or dyspnoea. In six patients, spinal MRI showed narrowing of the canal diameter, low signal intensity on the T1-weighted sequence, high signal intensity on the T2-weighted sequence, and atrophy of the medulla spinalis on cervical spinal MRI, so they were evaluated in favour of CSM. In four patients, cervical spinal MRI showed hypointensity on T1, hyperintensity on T2, and no contrast enhancement on contrast-enhanced examinations, which are findings compatible with syringomyelia. A 78-year-old male patient (Case 6) presented complaining of weakness in the left hand. During the general physical examination, muscle atrophy and contracture were observed in the left hand. Upon neurological examination, atrophy was observed in the left-hand intrinsic muscles and hypoesthesia in the left upper extremity. Cervical MRI showed a syrinx extending from C3 to C7. The dilated spinal canal appears as a centrally located intramedullary elongated/ tubular structure with high T2W and low T1W signal intensity. There is no evidence of contrast-enhancing intraspinal masses or abnormal enhancement. Figure 1 shows the cervical spinal MRI findings of Case 6: atrophy in the left-hand intrinsic muscles.

Table 1. Demographic characteristics of patients.

Demographic characteristics	Data
Age (years), Mean±SD	64.90 ± 9.26
Gender (male), n (%)	6 (60.0)
Hypertension, n (%)	4 (40.0)
Diabetes mellitus, n (%)	2 (20.0)
Chronic kidney disease, n (%)	1 (10.0)
Time to final diagnosis (years), Mean±SD	3.25 ± 3.01

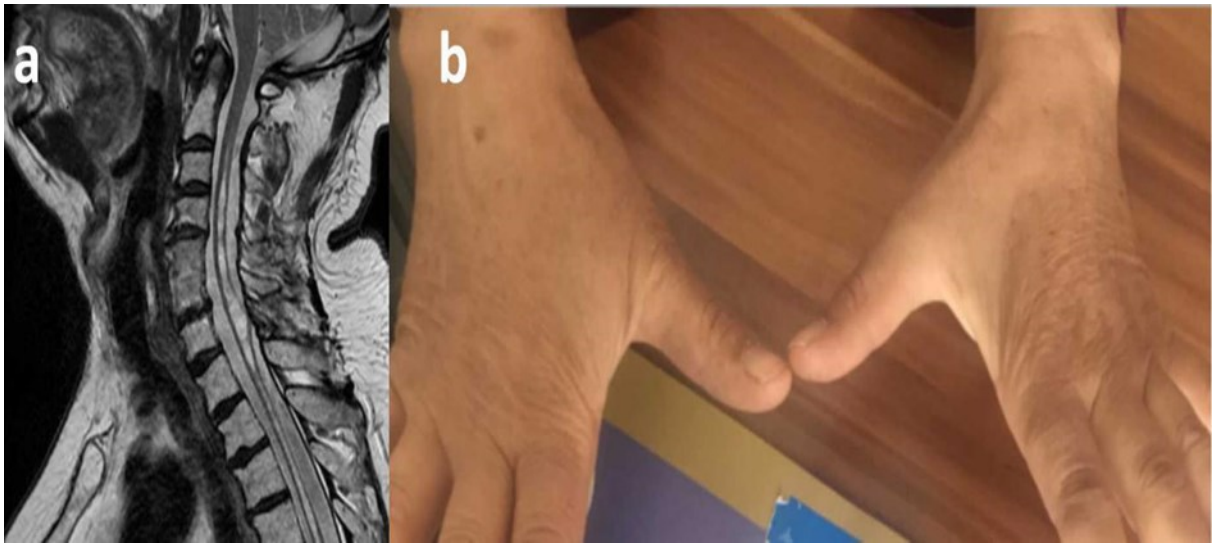

Figure 1. MRI of the cervical spine in a patient with cervical syringomyelia (case 6) (a) and atrophy of the intrinsic muscles of the left hand (b).

Another 78-year-old male patient (Case 7) presented complaining of weakness in the right-hand. This patient had no sensory complaints or pain. Upon examination, atrophy was observed in the right-hand intrinsic muscles. Cervical spondylotic myelopathy was detected on cervical spinal MRI. Cervical spinal MRI findings and atrophy in the hand muscles are shown in Figure 2.

Table 2 illustrates a summary of the clinical features of the study participants.

Sensory nerve action potentials and conduction velocities were normal, even in advanced atrophic extremities. The paraspinal muscle, rectus abdominis, and genioglossus concentric needle EMG examinations of the patients were normal. These findings were atypical for ALS, and the predominance of denervation in the upper extremities suggested an underlying spinal cord pathology. Based on spinal MRI results and concentric needle EMG findings, six patients were diagnosed with CSM, and four patients were diagnosed with syringomyelia. The patients were referred for neurosurgical consultation and evaluated for the need for surgery. Table 3 summarises the neurological symptoms/neurological examination findings, and laboratory findings. Performed as part of the general screening protocol, six patients were diagnosed with CSM and four patients with syringomyelia. All these individuals were directed towards the neurosurgery department.

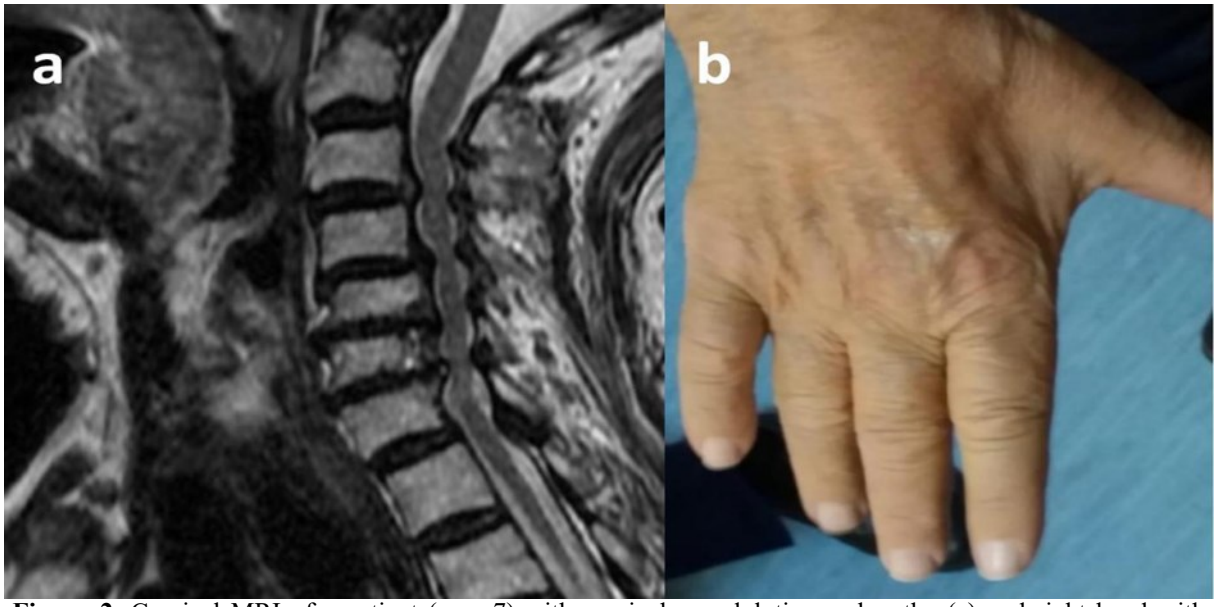

Figure 2. Cervical MRI of a patient (case 7) with cervical spondylotic myelopathy (a) and right hand with marked intrinsic muscle atrophy (b).

Table 2. Clinical features of the participants.

Clinical Features	n (%)
Unilateral upper extremity weakness	5 (50.0)
Bilateral upper extremity weakness	2 (20.0)
Lower extremity weakness and gait disorder	3 (30.0)
Weakness in both the upper and lower extremities, with a gait disorder	1 (10.0)
Unilateral thenar and hypothenar atrophy	5 (50.0)
Bilateral thenar and hypothenar atrophy	3 (30.0)
Gait disorders and spasticity in the lower extremities	4 (40.0)
Increased deep tendon reflexes in both lower extremities	8 (80.0)
Cape-like sensory deficits (pain and temperature sensation)	3 (30.0)
Cervical spinal MRI findings consistent with CSM	6 (60.0)
Cervical spinal MRI findings consistent with syringomyelia,	4 (40.0)

Table 3. Clinical characteristics, neurological symptoms/neurological examination findings, and laboratory findings of the patients (N=10).

	Gender	Age (years)	Comorbidities	Time from symptom onset to diagnosis (years)	Complaints	Neurological examination	MRI	EMG	Diagnosis
Patient 1	M	73	HT	0.5	Paraesthesia and loss of muscle strength in legs, gait disorder	Exaggerated DTR and spasticity in both lower extremities	C3-C4, C4-C5, C5-C6, C6-C7, C7-C8 disc protrusions and spinal cord compression C5-C7 myelomalacia	Chronic neurogenic MUPs and positive spikes and fibrillations in bilateral C5-C6-C7 roots innervated muscles	CSM
Patient 2	M	65	HT	10	Paraesthesia and loss of muscle strength in the left hand	Atrophy of the intrinsic muscles of the left hand, hypoesthesia in the left arm	C2-C3, C4-C5, C5-C6 disc protrusions and spinal cord compression, myelomalacia in the spinal cord at C5-C6 level	Chronic neurogenic MUPs and positive spikes and fibrillations in bilateral C5-C6 roots innervated muscles	CSM
Patient 3	M	60	DM	4	Paraesthesia and loss of muscle strength in both hands, gait disorder	Intrinsic muscle atrophy of both hands, loss of muscle strength in both hands, exaggerated DTR in both lower extremities	C3-T1 levels syrinx cavity	Chronic neurogenic MUPs and positive spikes and fibrillations in bilateral C4-C5-C6-C7-C8-T1 roots innervated muscles	Syringomyelia
Patient 4	F	67		0.5	Paraesthesia and loss of muscle strength in both legs, gait disorder	Mild spasticity and exaggerated DTR in both lower extremities and gait disorder	C4-C5, C5-C6, C6-C7 protrusions and spinal cord compressions	Chronic neurogenic MUPs and positive spikes and fibrillations in C5-C6-C7 roots innervated muscles	CSM
Patient 5	F	54		2	Paraesthesia and loss of muscle strength in both hands	Mild weakness and hypoesthesia in both upper extremities, atrophy of intrinsic muscles in both hands	C4-C5 and C5-C6 paracentral bulging, spinal cord compression, C5-C6 myelomalacia	Chronic neurogenic MUPs and positive spikes and fibrillation in bilateral C5-C6 root innervated muscles.	CSM
Patient 6	M	78		3	Paraesthesia and loss of muscle strength in the left hand	Intrinsic muscle atrophy of the left hand	C3-C7 syrinx cavity in the spinal cord	Positive spikes and fibrillations in left C3-C7 roots innervated muscles	Syringomyelia

C: Cervical; CKD: Chronic kidney disease; CSM: Cervical spondylotic myelopathy; DM: Diabetes Mellitus; DTR: Deep tendon reflex; F: Female; HT: Hypertension; M: Male; MRI: Magnetic resonance imaging; MUP: Motor unit potentials.

Table 3. Continue.

Patient 7	M	78	DM	8	Paraesthesia and loss of muscle strength in the right hand	Intrinsic muscle atrophy of the right hand	C3-C4, C4-C5, C5-C6, C6-C7 bulging, right C6-C7 nerve root compression	Positive spikes and fibrillations in right C6-C7 roots innervated muscles	CSM
Patient 8	F	51		5	Paraesthesia and loss of muscle strength in the left hand	Hypoesthesia in the left arm and intrinsic muscle atrophy of the left hand	C5-C7 syrinx cavity in the spinal cord	Fibrillations in C5-C6-C7 innervated muscles on the left and chronic neurogenic MUPs in the same muscles	Syringo-myelia
Patient 9	F	62	HT, CKD	0.5	Paraesthesia and loss of muscle strength in the right hand	Intrinsic muscle atrophy of the right hand	C4-C6 syrinx cavity in the spinal cord	Fibrillations in C5-C6 innervated muscles on the right and neurogen-ic MUPs in the same muscles	Syringo-myelia
Patient 10	M	61	HT	1	Paraesthesia and loss of muscle strength in both hands and legs, gait disor-der	Mild weakness in both upper extremities, intrin-sic muscle atrophy of both hands, spasticity and ex-aggerated DTR in both lower extremities	C3-C4, C4-C5, C5-C6, C6-C7 disc compressions, myelomalacia at the C4-C7 level	Fibrillations and posi-tive spike activities in muscles with bilateral C4-C5-C6-C7 innerva-tion and thinning in the same muscles, chronic neurogenic MUPs	CSM

C: Cervical; CKD: Chronic kidney disease; CSM: Cervical spondylotic myelopathy; DM: Diabetes Mellitus; DTR: Deep tendon reflex; F: Female; HT: Hypertension; M: Male; MRI: Magnetic resonance imaging; MUP: Motor unit potentials.

DISCUSSION AND CONCLUSION

ALS is characterised by the widespread degeneration of lower and upper motor neurons, which typically leads to death (often from respiratory failure) approximately 3 years after symptoms first appear.[10] The disease is 90–95% sporadic and 3–10% familial. In Europe, the annual incidence is 2.1/100,000.[11] Although genetics, glutamate excitotoxicity, viral infections, autoimmunity, and heavy metal intoxication, such as lead, mercury, and aluminium, are thought to be implicated in the pathogenesis of the disease, the exact cause remains unknown. The diagnosis of the disease relies on an in-depth medical history and neurological examination results. There is no definitive test for an ALS diagnosis.[12] A confirmed diagnosis typically takes 1–2 years from the onset of symptoms. CSM and syringomyelia are two conditions that are often mistaken for ALS. Early diagnosis often leads to more favourable outcomes for patients.

Wu et al. reported that myelopathy was more common in men, especially those working in physically demanding jobs. They also found that CSM was more common in older and male patients.[13] Similarly, the proportion of male patients was also higher in our study. Degenerative changes in the spine in CSM lead to the compression of the nerve roots and spinal cord, causing symptoms both at and below the site of compression. Patients typically present with motor deficits due to damage to both upper and lower motor neurons. In addition to motor dysfunction, patients with CSM often experience a variety of sensory deficits related to the compression of specific sensory pathways.[14]

In our study, all patients reported sensory complaints. Lower motor neuron symptoms, such as upper extremity weakness, muscle atrophy, fasciculations, hyporeflexia, and hypotonia, are common at the affected vertebral level in CSM. In addition, 75% of patients have difficulty with fine motor skills, such as writing or buttoning, due to weakness of the intrinsic hand muscles.[15,16] Of our patients, eight had a loss of strength in the upper extremities, including intrinsic hand muscle weakness. Gait dysfunction is seen in most cases of CSM and is a differentiating characteristic.[16] In our study, four patients had this symptom. Lower extremity symptoms, such as clonus, are less sensitive (11%) but highly specific (96%) to CSM.[17] Clonus was observed in two of our patients. Cervical spine MRI is considered the definitive diagnostic tool for CSM.[18] In our study, all patients underwent both cervical spine MRI and concentric needle EMG for differential diagnosis.

Syringomyelia manifests as a disorder due to the disturbed circulation of cerebrospinal fluid (CSF) within the spinal cord, resulting in a fluid-filled cavity, or syrinx, within the spinal cord parenchyma or central canal.[19] The clinical manifestations of syringomyelia vary widely. Patients often present with pain, weakness, and atrophy, especially in the hands and arms, along with sensory disturbances in the upper extremities and spasticity or stiffness in the lower extremities.[20,21] A significant number of patients are in the 20 to 50-year range. The increased use of MRI for the routine evaluation of back and neck pain has led to more frequent diagnoses of syringomyelia.[22] In a study by Bogdanov et al. of 103 patients (35 females and 68 males) with syringomyelia, all participants had symptoms of syringomyelia. Bilateral segmental sensory deficits in the trunk and upper extremities were found in 35 (34%) patients, whereas unilateral deficits were observed in 58 (56%) patients. Upper limb weakness or atrophy was bilateral in 36 (35%) patients, unilateral in 45 (44%), and absent in 22 (21%). Pain was reported in 24 (23%) patients.[23] In our study, of the four patients with syringomyelia, three had unilateral upper extremity weakness and atrophy, while one patient had bilateral symptoms. In our study, the patients sent to our clinic with an initial diagnosis of ALS were ultimately diagnosed with CSM or syringomyelia after a thorough evaluation of clinical symptoms, neurological examination findings, concentric needle EMG, and spinal MRI findings.

In conclusion, the findings suggest that careful consideration of the combined clinical signs, physical examination findings, EMG, and MRI results is critical when evaluating patients with a preliminary diagnosis of ALS. Given the overlapping age range and symptom presentation, conditions such as CSM and syringomyelia should be carefully considered as potential differential diagnoses. Due to the small cohort and retrospective nature of the study, it underscores the requirement for further research with larger groups. The study's main limitations include being at a single institution with a limited number of patients. Furthermore, the small sample size precluded the opportunity to make reliable comparisons of the clinical and radiological features of CSM and syringomyelia.

Ethics Committee Approval: The study was approved by the Sakarya University Faculty of Medicine Ethical Committee (Date:10.07.2020, decision No: E.6172), and conducted in compliance with the Helsinki Declaration.

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept - NUC; Supervision - NUC; Materials - NUC; Data Collection and/or Processing - NUC; Analysis and/or Interpretation - NUC; Writing - NUC.

Peer-review: Externally peer-reviewed.

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