Coexistence of Ankylosing Spondylitis and Amyotrophic Lateral Sclerosis: Case Report

Ankilozan Spondilit ve Amyotrofik Lateral Skleroz Birlikteliği

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ABSTRACT Although neurological symptoms are not common in Ankylosing spondylitis (AS), myelopathy, atlantoaxial joint subluxation, vertebral fractures, dislocation, the cauda equina syndrome, root lesions, intraspinal ligament ossification and foraminal stenosis can be observed. Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterised by the involvement of the central and peripheral motor neurons. This case study presents a patient who was initially considered to have cervical myelopathy that can develop during the course of the disease due to causes such as intraspinal ligament ossification but was finally diagnosed with ALS based on electroneuromyography. In rheumatic diseases such as AS, symptoms such as weakness, atrophy, numbness, tingling or cramps may be observed as a result of the neurological and musculoskeletal involvement. These symptoms may be confused with those related to neurological diseases including ALS, which can complicate the diagnosis. In rheumatic diseases, ALS may accompany the disease as well as occurring as a complication of the drug therapy. In patients, it must be kept in mind that concurrent neurological diseases may be seen and these diagnoses should be done cautiously.

Key Words: Ankylosing spondylitis; amyotrophic lateral sclerosis; rehabilitation

ÖZET Ankilozan spondilitte (AS) nörolojik komplikasyonlar sık olmamakla birlikte miyelopati, antanyo-aksiyel eklem subluksasyonu, vertebra fraktürü, dislokasyon, cauda equina sendromu, kök lezyonları, intraspinal ligament ossifikasyonları, foraminal stenoz olarak sıralanabilir. Amyotrofik lateral skleroz (ALS) santral ve periferik motor nöronların tutulumu ile karakterize nörodejeneratif bir hastalıktır. Bu olguda intraspinal ligament ossifikasyonları gibi nedenlere bağlı hastalık seyri sırasında gelişebilen servikal miyelopati düşünülen ancak elektronöromiyografide ALS tanısı alan bir AS hastası sunulmaktadır. AS gibi romatolojik hastalıklarda nörolojik ve kas iskelet sistemi tutulumlarına bağlı güçsüzlük, atrofi, uyuşma, karıncalanma, kramp gibi bulgular gözlenebilmektedir. Bu semptomlar ile ALS gibi nörolojik hastalıkların bulguları karışabilir, bu da tanının konulmasını zorlaştırabilir. Romatolojik hastalıklarda, ALS hastalığa eşlik edebileceği gibi kullanılan ilaçların komplikasyonu olarak da karşımıza çıkabilir. Bu hastalarda eş zamanlı nörolojik hastalıkların da görülebileceği unutulmamalı ve tanıda dikkatli olunmalıdır.

Anahtar Kelimeler: Ankilozan spondilit; amyotrofik lateral skleroz; rehabilitasyon

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Ankylosing spondylitis (AS) is a chronic, inflammatory and rheumatic disease primarily involving the axial vertebra and the peripheral joints. Although neurological symptoms are rare in AS, myelopathy, atlantoaxial joint subluxation, vertebral fractures, dislocation, the cauda equina syndrome, root lesions, intraspinal ligament ossification and foraminal stenosis can be observed.[1]

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterised by the involvement of the central and peripheral motor neurons. The condition may lead to progressive muscle weakness, dysarthria or dysphagia due to the loss of the pyramidal and anterior motor neurons. Although familial tendencies have been reported, 90% of the cases are sporadic and of unknown etiology. In sporadic cases, the mean age of onset is 60-65 and the condition is more common among males. The incidence of ALS is 1-3 per 100,000 people. The patient's history, and neurological and electrophysiological examinations play an important role in the diagnosis.[2]

In this case study, we would like to present a patient who had AS for 22 years and presented with weakness in the upper extremity. Although cervical myelopathy that can develop during the course of the disease due to causes such as intraspinal ligament ossification was initially considered, the patient was finally diagnosed with ALS based on electroneuromyography (EMG).

CASE REPORT

A 44-year old male patient had been diagnosed with AS 22 years ago. Subsequently, he presented with bilateral numbness in his arms, weakness, hoarseness and difficulty swallowing that had started approximately four months ago and progressed gradually. The patient's file revealed that he had presented to our hospital for examination 5 years ago with the diagnosis of AS, but had not returned for his routine follow-up. His personal history and family history was uneventful. In terms of systemic complaints, he reported malaise and fatigue for the last 4 months. The musculoskeletal examination revealed thoracic kyphosis. The cervical anteflexion was 10 degrees, while the bilateral flexion was 5, lateral rotation was 5, and retroflexion was 0 degree. The lumbar modified Schober was measured as 2 cm and the chest expansion was 1.5 cm. The peripheral joints were normal. There was no tenderness in the sacroiliac joints and the Mennel and Gaenslen tests were negative. The BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) score was 2.2, the BASFI (Bath Ankylosing Spondylitis Functional Index) was 6.2, and the BASMI (Bath Ankylosing Spondylitis Metrology Index) score was 9. During his neurological examination, the deep tendon reflexes in the bilateral upper and lower extremities were hyperactive, Hoffman's sign was bilaterally positive and clonus was observed. Speech disturbance, atrophy in the interosseous muscles of the hand, and fasciculation in the limbs and the tongue were observed. While the muscle tone was normal in the lower extremities, it was observed as +3/5 strength proximally and 3/5 strength distally in the upper left extremity and 4/5 strength proximally and +3/5 strength distally in the upper right extremity. The patient was independently ambulant, could walk without support and perform his daily activities independently.

His erythrocyte sedimentation rate was 27 mm/h and C-reactive protein level was 27.9 mg/l. He was on 2x500 mg/day of sulfasalazine (SLZ). His hemogram, biochemistry results, thyroid function tests, and vitamin B12 and protein electrophoresis results were normal. His tumor markers (prostate-specific antigen, carcinoembryonic antigen, carbohydrate antigen 19-9, carbohydrate antigen 15-3, alpha-fetoprotein) and brucella agglutination tests were negative.

The patient's pelvic radiographic evaluation was consistent with bilateral grade 4 sacroiliitis. The cervical and thoracic radiographic evaluation demonstrated vertebral squaring and bamboo spine. The cervical and cranial magnetic resonance imaging did not indicate any findings that explain the weakness in the upper extremities.

The electrophysiological examination revealed diffuse involvement of the active anterior horn motor neurons in the upper and lower extremities. The needle EMG indicated diffuse fasciculation in the lower and upper extremities, fibrillation, positive sharp waves, increased motor unit potential, and reduced interference patterns. The nerve conduction study and needle EMG are shown in Table 1, 2, 3.

TABLE 1: Sensory nerve conduction study.

Nerves	Amplitude (2-4 µV)	Velocity (m/s)
R Median Digit II	24.3	42.1
L Median Digit II	24.7	45.3
R Ulnar Digit V	53.2	37.1
L Ulnar Digit V	61.2	43.7
R Sural	12.1	40

R; Right, L; Left

TABLE 2: Motor nerve conduction study.

Nerves	Amplitude(2-4 mV)	Velocity(m/s)
L Median -APB		
1.	2,6	
2.	3,3	52,7
R Median-APB		
1.	2,7	
2.	2,0	55,7
L Ulnar-ADM		
1.	1,5	
2.	1,5	44,6
3.	1,4	41,1
R Ulnar-ADM		
1.	4,3	
2.	3,5	51,2
3.	2,9	34,0
R Tıbıal-AH		
1.	6,2	
2.	5,7	44,1
R Common Peroneal-EDB		
1.	4,1	
2.	3,7	43,1
3.	3,7	42,2

APB; Abductor pollicis brevis, ADM; Abductor digiti minimi, AH; Abductor hallucis, EDB; Extensor digitorum brevis.

The patient was diagnosed with ALS based on the clinical examination, EMG and laboratory tests and started on a regimen with 2x50 mg/day of riluzole. The patient was admitted to our clinic and started on the neurological rehabilitation program.

DISCUSSION

Coexistence of AS and ALS is very rarely observed. There is only one patient with coexistence of AS and ALS reported in the literature. In that case report, a 57-year-old patient started infliximab therapy since he was resistant to NSAIDs. After the 4th infliximab infusion, the patient presented to the clinic with cramps in both upper and lower extremities. The examination revealed diffuse fasciculation, motor deficits in bilateral extremities and increase in deep tendon reflexes. He was diagnosed with ALS based on the electrophysiological assessment. It is thought that the tumor necrosis factor-

TABLE 3: Needle EMG.

	Spontaneous	MUAP	Recruitment						
	IA	Fib	PSW	Fasc	H.F.	Amp	Dur	Poly	Pattern
R.Abductor Pollicis Brevis	N	1+	2+	None	None	2+	1+	1+	2-
R.First Digitorum İnterosseus	N	1+	2+	None	1+	2+	2+	N	2-
L.Abductor Pollicis Brevis	N	1+	2+	None	None	2+	2+	N	2-
L.abductor digiti minimi	N	1+	2+	None	None	2+	2+	N	2-
L. Extensor indicis	N	2+	2+	None	1+	2+	1+	N	2-
R. Deltoid	N	None	None	None	None	2+	N	N	1-
R.Biceps	N	None	None	None	None	2+	1+	N	1-
R.Triceps	N	None	1+	+1	None	2+	2+	N	1-
L.Cervical Paraspinal	N	1+	None	None	None	2+	N	N	N
L.Thoracal Paraspinal	N	1+	None	None	None	2+	N	N	N
R. Tibialis Anterior	N	1+	None	+2	1+	2+	1+	N	1-
R.Vastus Medialis	N	1+	None	+2	1+	2+	1+	N	1-

IA; Introduction activity, Fib; Fibrillation, PSW; Positive sharp waves, Fasc; Fasciculation, HF; High frequency, Amp; Amlitude, Dur; Duration, Poly; Polyphase.

α (TNF-α) is responsible for the apoptosis of motor neurons in ALS. TNF-α blockers are thought to have a neuroprotective effect in the treatment of ALS. However, as in this case, the neurotoxic and neuroprotective balance of TNF-α is assumed to be disturbed by the use of TNF-α blockers. The probable neuroprotective effect of TNF-α has been suggested to be disturbed by TNF-α blockers, leading to demyelinising diseases including ALS.[3] Our patient was not receiving TNF-α blockers; he was on an irregular therapy with 1 g/day of SLZ. No clear information about the duration of the SLZ therapy could be obtained from the patient. Interestingly, a literature study has demonstrated that the systemic administration of SLZ reduces neuronal damage after transient cerebral and retinal ischemia in rats. It is thought that SLZ blocks the N-methyl-D-aspartate (NMDA)-mediated neuronal death through a different mechanism than its anti-inflammatory effect.[4]

Although the number of the studies focusing on the neurological complications in AS is limited, in a study conducted on 24 patients, neurological findings were observed in 25% of the patients. These included radiculopathy (16.7%), myelopathy (8.3%), and posterior (8.3%) and anterior (4.2%) longitudinal ligament calcification.[1] The compression and inflammation of the calcified ligament is thought to be the main cause of the neurological complications. However, vasculitis can also lead to neuronal damage. In AS, an erosive and inflammatory disease, structural changes in the spinal canal including new bone formation, ossification, syndesmophytes, and joint fusion may also lead to the compression of the cord and the spinal canal.[5-7] Since these complications are primarily considered in patients with AS, rarely observed neurological diseases such as ALS may be overlooked.

In the literature, there are 7 patients in whom ALS developed while on therapy with TNF-α blockers for rheumatoid arthritis (RA).[8-11] ALS has been considered to develop as a neurological complication of TNF-α blockers in these RA patients. All these 7 patients have been reported to have symmetrical and erosive RA causing severe functional disturbances and all but one have been reported to be positive in terms of RF. In 5 of the 7 patients, the neurological symptoms were observed either after the first dose of infliximab or after an increase in the dose.

In rheumatic diseases including AS or RA, weakness, atrophy, numbness, tingling or cramps may be observed as a result of the neurological and musculoskeletal involvement. These symptoms may be confused with those related to neurological diseases including ALS, which can complicate the diagnosis. It must be borne in mind that ALS may accompany rheumatic diseases as well as occurring as a complication of the drug therapy.

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