PERONEAL PALSY ASSOCIATED WİTH COVID-19: A CASE REPORT

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ABSTRACT

There are many publications in the literature on neurological involvement in COVID-19 disease. This article described the unilateral peroneal nerve palsy which developed in a 53-year-old male patient while undergoing COVID-19 treatment, along with the current literature and neurological involvement mechanisms of SARS-CoV-2. This is the first case report that describes peroneal nerve palsy associated with SARS-CoV-2.

Keywords: *COVID-19, SARS-CoV-2, Peroneal nerve palsy.*

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Introduction

COVID-19 is a disease in which the clinical features caused by the SARS-CoV-2 virus may vary from asymptomatic infection to respiratory failure. SARS-CoV-2 binds to the cell membrane protein angiotensin-converting enzyme 2 (ACE2) to enter human cells. ACE-2 receptors are broadly expressed in the nasal mucosa, respiratory tract epithelium, lung parenchyma, lymphoid tissue, gastrointestinal tract, urinary tract, reproductive organs, vascular endothelium, and brain. Although COVID-19 mainly affects respiratory and immune systems, other systems like the cardiovascular, gastrointestinal tract, urinary, reproductive system, and nervous system are not spared[(2)].

Suggested pathways of neurological involvement are both direct and indirect. In the literature, cases of stroke, Guillain barre syndrome, encephalitis, myelitis, and cranial neuropathy associated with SARS-CoV-2 infection have been described. This report describes the clinical features of the first case of 2019-nCoV infection with unilateral foot drop.

Case description

A 53-year-old male patient was admitted to the physical therapy and rehabilitation outpatient clinic with the complaint of left foot weakness. His history was unremarkable except for the COVID-19 diagnosed by PCR test 2 weeks ago. During the COVID-19 disease process, he had no complaints other than fever, cough, widespread muscle pain, weakness, fatigue, loss of taste, and smell. During this period, the patient was given and 5 days of favipiravir treatment and 2 weeks of home isolation for COVID-19. When he was in home quarantine, he noticed that his foot was stuck to the floor while walking on the 5th day of his treatment. He had assumed that the weakness was due to muscle pain, and he applied

to the outpatient clinic with the symptom of a weak foot at the end of the quarantine period. At the outpatient clinic, the patient had no symptoms other than the loss of smell and weakness in the foot. The patient had no disease other than anxiety disorder in his medical history, and he had been using escitalopram 10 mg/day for 6 months. The patient had no history of trauma, previous surgery, weight loss, prolonged sitting, or squatting.

At admission, the patient's vital signs were normal; he had no fever. In the posture analysis, the patient had a steppage gait. Physical examination revealed a height of 1.76 m, a weight of 83 kg, and a body mass index of 26.8 kg/m^2. Muscle strength of left ankle dorsiflexion and left toe dorsiflexion was 1/5; left ankle eversion was 2/5. Other upper-lower extremity muscle strengths were normal. There was mild hypoesthesia in the dorsum of the left foot. The straight leg raising test was negative. The range of motion of all lower extremity joints was normal. The patient's deep tendon reflexes were normoactive. Foot plantar reflex was flexor.

In the laboratory investigations of the patient, complete blood count, sedimentation, C-reactive protein, liver, kidney, and thyroid function tests, creatinine kinase, coagulation panel, anti-nuclear antibody, vitamin b12, folate, blood glucose and HgA1c levels were normal. Laboratory results of the patient during the COVID process were as follows; Wbc: 9.7 10 ^ 3 / uL (4.5--9.5) Sedimentation: 32 mm / hour (0-20), Crp: 4.1 mg / L (0-2), D-dimer: 12 mg / L (<0.50), Ferritin: 883 μg / L (23-336).

Nerve/sites	Latency Ms	Peak amp uV	Distance Cm	Velocity m/s
R MEDIAN DİGİT II				
Wrist	2,45	31,0	13	53.1
L MEDIAN DİGİT II				
Wrist	2,19	30,2	13	59,4
R ULNAR DİGİT V				
Wrist	1,77	21,6	11	62,1
L ULNAR DİGİT V				
Wrist	1,98	17,6	11	55,6
L SURAL Lat malleolus				
Calf	2,6	5,7	12	54,6
R SURAL Lat malleolus				
Calf	2,5	5,6	12	58,8

Table 1: Clinical characteristics of patients.

Brain and brain diffusion-weighted magnetic resonance imaging for the etiology of drop foot revealed normal findings. Lumbar magnetic resonance imaging had no findings other than L3-L4 bulging. There was no pathology causing a mass effect on magnetic resonance imaging of the left knee. The patient's CSF examination was normal. Arterial and venous lower extremity doppler ultrasonography were normal. Median, ulnar, tibial, and sural motor and sensory nerve conduction studies were normal in the electrophysiological evaluation. Right common peroneal and bilateral tibial nerve F wave responses were within normal limits. Compound muscle action potential (CMAP) could not be obtained from the extensor digitorum brevis and tibialis anterior muscles of the left common peroneal nerve. In the needle EMG, denervation findings were detected in the left tibialis anterior and left peroneus longus muscles (Table 1-3). The electrophysiological findings indicated a lesion behind the fibular head of the peroneal nerve.

Nerve/Sites	Latency ms	Amp mV	Distance Cm	Velocity m/s
L MEDIAN-APB				
Wrist	2,97	9,9		
Elbow	7,34	8,3	23	52,6
R MEDIAN-APB				
Wrist	3,13	12,7		
Elbow	7,71	9,8	23	50,2
L ULNAR-ADM				
Elbow	2,24	9,8		
Wrist	7,03	9,0	26	54,3
R ULNAR-ADM				
Wrist	2,29	10,4		
Elbow	6,93	9,3	24	51,8
L COMM PERONEAL EDB				
Ankle	NR	NR	NR	
Fib Head	NR	NR	NR	NR
L COMM PERONEAL Tibialis Anterior				
Fibula Head	NR	NR	NR	
Knee	NR	NR	NR	NR
R COMM PERONEAL EDB				
Ankle	4,69	2,0	31	
Fib Head	11,67	1,8	31	44,4
L TIBIAL(KNEE)-AH				
Ankle	5,16	7,6		
Knee	15,73	7,5	45	42,6
R TIBIAL(KNEE)-AH				
Ankle	5,73	8,2		
Knee	15,694	6,6	45	44,1

Table 2: Motor nerve conduction study.
NR: no response, APB: Abductor pollicis brevis, ADM: Abductor digiti minimi,AH: Abductor hallucis.

We assumed the clinical picture might be associated with SARS-CoV-2. An exercise program and ankle stabilizing orthosis were given to the patient. Since he did not want a physical therapy program due to his anxiety disorder, he was given

a home program, including a range of motion and strengthening exercises. When the patient was re-evaluated at 3rd week control, ankle dorsiflexion strength increased to 3/5, toe dorsiflexion strength to 3/5, and foot eversion strength to 4/5.

	Spontaneous				MUAP			Recruitment
	IA	Fib	PSW	Fasc	Amp.	Dur.	PPP	Pattern
L TIB ANTERIOR	N	2+	2+	None	1+	1+	1+	Discrete
L BICEPS FEMORIS SHORT HEAD	N	N	None	None	N	N	N	N
L GASTROCNEMIUS MED	N	None	None	None	N	N	N	N
L VAST LATERALIS	N	None	None	None	N	N	N	N
L PERONEUS LONGUS	N	1+	2+	None	N	1+	1+	Discrete
L VASTUS MEDIALİS	N	N	None	None	N	N	N	N
L ADDUKTOR LONGUS	N	N	None	None	N	N	N	N
L GLUTEUS MEDİUS	N	N	None	None	N	N	N	N

Table 3: Needle EMG.
L: left, N: Normal, IA: insertional activity, Fib: fibrillation, PSW: positive sharp wave, MUAP: motor unit action potential Amp: amplitude, Dur: duration, PPP: polyphasic

Discussion

The SARS-CoV-2 virus infects cells by interacting with the spike protein and ACE-2 receptor protein on the human cell surface. ACE-2 is expressed in many tissues in the body, including neural tissues.

Neurological findings were detected in 36.4% of patients with COVID-19 in a case series[3]. Various hypotheses have been presented in the literature regarding the fact that the SARS-CoV-2 is a neurotrophic virus. Regarding pathophysiology of neural involvement, the point most emphasized by the researchers is ACE-2-related direct infection by the virus. The presence of ACE-2 protein in neural tissues suggests that the virus can directly damage the nerve tissue. Also, the decrease in ACE-2 level and ACE-1-mediated binding of the SARS-CoV-2 virus to the ACE-2 receptor cause neuroinflammation, neuronal apoptosis, and neurodegeneration[4]. Genomic sequencing and isolation of SARS-CoV-2 in autopsy studies of patients with encephalitis support the opinion that it causes neural invasion[5]).

Due to the presence of ACE-2 in vascular endothelial tissue, it may cause neural damage by disrupting the microcirculation in neural tissues. On the other hand, it was thought that SARS-CoV-2 could enter the systemic circulation by passing through the cribriform plate of the ethmoid bone[6]. The absence of virus particles in non-neuronal areas in the infected brain tissue supports the view of the hematogenous spread of the virus[7].

According to another hypothesis, SARS-CoV-2 can invade peripheral nerve terminals and reach the central nervous system by slowly traveling through the synapse-connected path. In this context, it has been demonstrated that the virus can access the brain through the olfactory nerve by intranasal administration of SARS-CoV and MERS-CoV viruses in mice[7].

It is thought that the virus reaching the gastrointestinal tract can perform neuronal invasion and transport through the enteric nervous system and sympathetic afferent neurons. Moreover, the autoimmune inflammation triggered by the infection can affect the central and peripheral nervous system[8].

The cases of Guillain Barre syndrome associated with COVID-19 were also reported in the literature. In our case, the unilateral peroneal palsy and the normal protein level in the CSF examination excluded Guillen Barre syndrome diagnosis.

The absence of polyneuropathy findings in the EMG and normal blood tests for systemic diseases excluded the diagnosis of peroneal palsy due to systemic diseases. In the patient's detailed history, there was no mechanical factors to cause peroneal nerve damage such as trauma, surgery, prolonged sitting, squatting, and crossing legs. The normal creatine kinase level and the presence of a conduction block in the peroneal nerve in electrophysiological evaluation excluded myositis diagnosis.

The presence of the ACE-2 receptor in neural tissues and the fact that the virus; can directly invade neural tissue by hematogenous route can cause neural damage via vascular endothelial damage, microvascular thrombosis, and immune response-mediated neural damage, suggested that the peroneal nerve damage may be due to SARS-CoV-2 infection in our case. High levels of D-dimer and ferritin at the time of admission and the absence of anticoagulant therapy suggested that there may be both microvascular and immune response-mediated neural damage[9].

Peripheral motor neuropathy cases associated with SARS-CoV and MERS-CoV[10], peripheral unilateral facial paralysis cases due to SARS-CoV-2 infection[11] and ,COVID-19 case presenting with peripheral motor neuropathy[12] have been presented in the literature.

Detailed differential diagnosis of our case supports the idea that direct or indirect neural damage by SARS-CoV-2 causes drop foot. We see that our case will shed light on new studies and that more detailed studies are needed in this regard. We believe that the first case of isolated peripheral nerve involvement may shed light on the underlying mechanisms of SARS-CoV-2 infection.

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