FİZİKSEL TIP VE REHABİLİTASYON BİLİMLERİ DERGİSİ
Journal of Physical Medicine and Rehabilitation Sciences J PMR Sci. 2022;25(3):346-54

ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH DOI: 10.31609/jpmrs.2022-90845

Increased Cases of Acute Polyneuropathy in COVID-19 Pandemic: What Awaits Neurologists?

COVID-19 Pandemisinde Artmış Akut Polinöropati Vakaları: Nörologları Neler Bekliyor?

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ABSTRACT Objective: Severe acute respiratory syndrome coronavirus disease-2019 (COVID-19) primarily affects the respiratory system but central and peripheral neurological manifestations have been increasingly recognized and reported. Our aim is to shed light on the relationship between COVID-19 and polyneuropathy. **Material and Methods:** The study consisted of patients with acute polyneuropathy that developed after the COVID-19 infection. All patients were confirmed serologically with polymerase chain reaction positivity. In 16 patients, acute polyneuropathy was diagnosed with an electrophysiological, laboratory findings and neurological examination. All patients underwent etiological studies to exclude possible causes of polyneuropathy. **Results:** The average age of the patients was 64.3 (29-83) years; most cases were female (13 vs 3). The interval between the onset of symptoms of COVID-19 and the first symptoms of acute polyneuropathy ranged from 11 to 63 (mean: 21.5) days. On electroneuromyography, there was acute motor-sensory axonal neuropathy in 8 patients, 6 patients had acute motor axonal neuropathy and 2 patients had acute inflammatory demyelinating polyneuropathy findings. Five patients accepted lumbar puncture; on analysis of the cerebrospinal fluid (CSF), 2 patient had normal protein level and the others showed an albuminocytological dissociation, increased protein in the CSF without increase in cell count, characteristic of the Gullain-Barré syndrome (GBS). **Conclusion:** This article; indicates the awareness of the possible causal association between acute polyneuropathy and COVID-19, and recommends long-term follow-up of COVID-19 patients for neurologic complications.

Keywords: Guillain-Barré syndrome; COVID-19; acute polyneuropathy

ÖZET Amaç: Şiddetli akut solunum yolu sendromu koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)], öncelikle solunum sistemini etkiler, ancak merkezî ve periferik nörolojik bulgular giderek daha fazla tanınmakta ve literatürde sunulmaktadır. Amacımız, COVID-19 polinöropati ilişkisine ışık tutmaktır. **Gereç ve Yöntemler:** Çalışma, COVID-19 enfeksiyonundan sonra gelişen akut polinöropatili hastalardan oluşuyordu. Tüm hastalarda tanı polimeraz zincir reaksiyonu pozitifliği ile kesinleşti. On altı hastada elektrofizyolojik, laboratuvar bulguları ve nörolojik muayene ile akut polinöropati tanısı kondu. Tüm hastalara polinöropatinin olası nedenlerini dışlamak için etiyolojik araştırmalar yapıldı. **Bulgular:** Hastaların yaş ortalaması 64,3'tü (29-83 yıl); vakaların çoğu kadındı (13 kadın, 3 erkek). COVID-19 semptomlarının başlangıcı ile akut polinöropatinin ilk semptomları arasındaki süre 11 ile 63 gün (ortalama: 21,5 gün) arasında değişmekte idi. Elektronöromiyografide 8 hastada akut motor-duyusal aksonal nöropati, 6 hastada akut motor aksonal nöropati ve 2 hastada akut inflamatuar demiyelinizan polinöropati bulguları saptandı Beş hasta lomber ponksiyonu kabul etti; beyin omurilik sıvısı analizinde 2 hastada normal protein seviyesi diğerlerinde albüminositolojik disosiasyon saptandı. **Sonuç:** Bu makale; akut polinöropati ile COVID-19 arasındaki olası nedensel ilişkinin farkındalığı, nörolojik komplikasyonlar açısından COVID-19 hastalarının daha uzun süreli takibinin gerektiğini göstermektedir.

Anahtar Kelimeler: Guillain-Barré sendromu; COVID-19; akut polinöropati

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) continues to spread around the world by mutation. In the literature, symptoms of the central and peripheral nervous system associated with SARS-CoV-2 infection are increasingly being reported.[1,2] Along with new mutations, new neurological

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Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

Received: 25 Apr 2022 ***Received in revised form:*** 31 May 2022 ***Accepted:*** 02 Jun 2022 ***Available online:*** 13 Jun 2022

complications began to be reported both in the acute period and in the post-coronavirus disease (COVID) period. Acute polyneuropathy is a condition that can develop after respiratory tract and/or gastrointestinal tract infections and can be fatal due to a delay in treatment.

In this case series, a prospective analysis of patients with COVID-19 associated GBS was conducted, which determined the demographic and clinical characteristics of polyneuropathy symptoms, including laboratory tests and electrophysiological findings, in order to elucidate the possible underlying pathophysiology.

MATERIAL AND METHODS

The study consisted of patients with acute polyneuropathy that developed after the COVID-19 infection. We examined 16 patients who had acute polyneuropathy after the COVID-19. All patients were confirmed serologically with COVID-19 polymerase chain reaction (PCR) positivity. The patients had not been vaccinated in the pre-COVID period. All of our patients were hospitalized at the infection diseases department in the COVID-19 process and treated but none of our patients had an intensive care process. During this process, there were no motor and/or sensory neurological signs that would suggest polyneuropathy. Disease activity was mild to moderate. There were no treatments given for COVID-19 that could cause polyneuropathy. The patients had been given symptomatic, supportive treatments.

The study consisted of patients with acute polyneuropathy that developed after the COVID-19 infection. The patients were evaluated in terms of factors that play a role in the etiology of polyneuropathy and no other risk factors were found. Concomitant risk factors were excluded. Exclusion criteria from the study are the presence of one of the factors playing a role in the etiology of polyneuropathy: diabetes mellitus, thyroid disorders, renal failure, previous spinal cord surgery, spinal and/or plexus injuries, electrolyte disorders, cancer diagnosis or patients under antineoplastic therapy cases diagnosed with familial or inflammatory polyneuropathy. All patients underwent electroneuromyography (ENMG) by the same neurologist. There were no pathological evidence to explain acute paraparesis on the brain and spinal cord imaging of the patients.

In the serological tests studied for any infective disorder other than COVID-19 that may cause acute polyneuropathy, no findings suggesting a different pathogen were detected. The study was a prospective study approved by Hitit University School of Medicine Ethics Committee (date: October 13, 2021, no: 500) and conducted by following STROBE guidelines and the Declaration of Helsinki. All participants gave their informed consent for this study.

RESULTS

We examined 16 patients who had acute polyneuropathy after the onset of COVID-19. Most cases were female (13 vs 3). The average age was 64.3 (29-83) years. The interval between the onset of polyneuropathy symptoms of COVID-19 and the first symptoms of acute polyneuropathy ranged from 11 to 63 (mean: 21.5) days.

Pneumoniac findings on thorax tomography had been detected in 10 patients in the acute period of COVID-19 infection however none of them needed extensive care.

Characteristics of the patients, symptoms of acute polyneuropathy, CSF, and ENMG findings, and abnormal findings detected in routine blood tests are given in Table 1. One of the common neurological symptoms of polyneuropathy was acute weakness, mostly in the lower extremities. Although the neurological examination findings of the patients were summarized in the table, distal limb weakness was dominant in all patients with pathological findings in the motor system examination. The symptoms of acute polyneuropathy were lower-limb weakness and paraesthesia in 12 patients whereas generalized, flaccid tetraparesis was in 3 patients. Except for pure sensory symptoms, no motor findings were detected in one patient. On ENMG, there was motor sensory axonal neuropathy (MSAN) in 8 patients, 6 patients had motor axonal neuropathy (MAN) and 2 patients had inflamatory demiyelinating polyneuropathy (IDP) findings.

Five patients accepted lumbar puncture; CSF analysis of 3 patients revealed albumino-cytological

TABLE 1: Clinical electrophysiological and laboratory findings of patients.

Age/sex	Days between COVID-19 symptoms and GBS onset	Neurological examaination	Chest radipgraphic features	GBS symptoms GBS/clinical)	GBS electrophysiologic subtype	CSF findings	Previous comorbidities	Blood fndings
1.75/M	15 days after	Proximal and distal lower limb weakness (2/5 MSM), hypoactive deep tendon refexes in upper limb and absent in lower limb	Yes	Progression of limb weakness and inability to walk loss of ambulation, AMAN	MAN	Normal total protein (56.61 mg/ dL)	HT	Ferritin 1079 ng/mL lymphopenia 0.6x9×109/L thrombocytopenia (140×109/L)
2.74/FM	17 days after	Hypoaesthesia, paraparesis (4/5 MSM) paraesthesia in the lower limb	Yes	Hypoaesthesia,weakness paraesthesia in the lower limb AMSAN	MSAN	Increased total protein (78.39 mg/ dL)	HT	Ferritin 247 ng/mL lymphopenia 0.22x9×109/L thrombocytopenia (102×109/L)
3.80/FM	19 days after	Paraparesis (3/5 MSM), pain in the lower limb and hyporefexia at the lower limb	No	Lower limb weakness, and difficulty walking AMAN	MAN		HT	Ferritin 466 ng/mL lymphopenia 0.77x9×109/L
4.80/FM	12 days after	Paraparesis (2/5 MSM) paresthesia pain and arerefexia at the lower limb/hyporeflexia in the upper limb	Yes	Progressive ascending paraesthesia of distal lower limb,loss of ambulation AMSAN	MSAN		HT	Ferritin 597 ng/mL lymphopenia 0.44x9×109/L thrombocytopenia (143×109/L)
5.70/FM	16 days after	Paraparesis (1/5 MSM), and arerefexia at the lower limb	Yes	Flaccid paraparesis, arefexia a tlower limb and loss of ambulation AMAN	MAN		HT	Ferritin 487.2 ng/mL
6.83/FM	16 days after	Lower limb weakness (4/5 MSM), hypoactive deep tendon refexes in upper limb and absent in lower limb	Yes	lower limb paraesthesia and paraparesis,difficulty walking AMSAN	MSAN		HT	Ferritin 910 ng/mL lymphopenia 0.56x9×109/L thrombocytopenia (124×109/L)

Continue →

TABLE 1: Clinical electrophysiological and laboratory findings of patients (*Continued*).

7.82/FM	12 days after	Lower limb weakness (3/5 MSM), hypoactive and absent in lower limb	Yes	lower limb paraparesis difficulty walking AMAN	MAN	Increased total protein (91.05 mg/ dL)	HT	Ferritin 986 ng/mL
8.57/FM	18 days after	Tetraparesis (3/5 MSM), generalized arefexia, hypoesthesia in the 4 limbs	No	Ascendant weakness, tetraparesis, generalized, sensory loss. weakness in four limbs AMSAN	MSAN	Normal total protein (47.12 mg/ dL)	No comorbid diseases	Ferritin 906.2 ng/mL
9.75/FM	11 days after	Flaccid paraparesis (3/5 MSM),paresthesia generalized arefexia	Yes	Paraparesis, generalized, sensory loss AMSAN	MSAN		HT	Ferritin 1,015 ng/mL lymphopenia 0.96x9×109/L thrombocytopenia (117×109/L)
10.72/FM	17 days after	Ascending weakness, paraparesis (2/5 MSM) and paresthesia hypoactive deep tendon refexes in upper limb and absent in lower limb	Yes	Lower limb paraesthesia and weakness AMSAN	MSAN		No comorbid diseases	Ferritin 1,402 ng/mL lymphopenia 1.02x9×109/L
11. 67/M	63 day	Ascending weakness, paraparesis (4/5 MSM) hypoactive deep tendon refexes in lower limb	Yes	Lower limb weakness, and difficulty walking AMAN	MAN		No comorbid diseases	Lymphopenia 0.29x9×109/L thrombocytopenia (248×109/L) ferritin 1,718 ng/mL
12. 68/M	30	Tetraparesis (4/5 MSM), generalized hypoactive deep tendon reflexes, hypoesthesia in the 4 limbs	Yes	Ascendant weakness, tetraparesis generalized, sensory loss. weakness in four limbs AIDP	Sensoriel predominant IDP		No comorbid disease	Ferritin 1,219 ng/mL lymphopenia 0.94x9×109/L thrombocytopenia (141×109/L)
13. 49/FM	35	Tetraparesis (2/5 MSM), generalized areflexia, hypoesthesia in the 4 limbs	No	Ascendant weakness Tetraparesis, generalized, sensory loss. weakness in four limbs AMAN	MAN	Increased total protein (82,08 mg/ dL)	No comorbid disease	Lymphopenia 1x9×109/L ferritin 2,320 ng/mL
14. 33/FM	15	Lower limb weakness (4/5 MSM), hypoactive reflexes in lower limbs	No	Paraparesis, generalized, sensory loss AMSAN	MSAN		No comorbid disease	N
15. 36/FM	18	Generalized hyporefexia, paraparesis (4/5 MSM) and hypoesthesia in the lower limb	No	Sensory and motor loss in lower limbs AMSAN	MSAN		No comorbid disease	Ferritin 2,491 ng/mL lymphopenia 0.94x9×109/L
16. 29/FM	60	Generalized areflexia, hypoesthesia in the 4 limbs	No	Sensory loss in four limbs AIDP	Sensoriel predominant IDP		No comorbid disease	N

Ferritin: 13-150 ng/mL; Platelet: 150-450X109/L; Lymphocyte: 1.26-3.35 9x109/L; CSF Protein: 40-70 ng/mL.

COVID: Coronavirus disease; GBS: Guillain-Barré syndrome; CSF: Cerebrospinal fluid; MSM: Motor muscle strength; AMAN: Acute motor axonal neuropathy; MAN: Motor axonal neuropathy; HT: Hypertension; AMSAN: Acute motor sensory axonal neuropathy; MSAN: Motor sensory axonal neuropathy; AIDP: Acute inflamatory demiyelinating polyneuropathy; IDP: Inflamatory demiyelinating polyneuropathy.

dissociation. While the blood tests of 2 patients during the acute COVID-19 period were within normal limits, the abnormal findings of the other patients are summarized in the table. None of the patients had features of myopathy. There were no symptoms of autonomic dysfunction in the patients during the GBS period.

As treatment; intravenous immunoglobulin 0.4 g/kg was administered for 5 days. We found a regression in the complaints and symptoms of the patients after intravenous immuglobulin. The follow-up and rehabilitation processes of the patients are still ongoing. We shared our experience with our COVID-19 case series, which developed GBS as a neurological complication.

DISCUSSION

GBS is an inflammatory disease of the peripheral nervous system, characterized by rapidly progressive, symmetrical, and typically ascending weakness of the upper and lower extremities sensory symptoms. Three electrophysiological subtypes of GBS are: acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor-sensory axonal neuropathy (AMSAN). GBS diagnosis is based on anamnesis, clinical findings, electrophysiological and CSF results.[3-6]

GBS occurs with an approximate incidence of 0.16-3 cases per 100,000 annually in the general population but, incidence of GBS in COVID-19 patients is unknown, as a potential association remains uncertain. An increasing number of reported case series of COVID-19 infection are presented with GBS in the literature.[7,8]

Peripheral and central nervous system damage in COVID-19 has been postulated to be the consequence of 2 different mechanisms: hematogenous or trans-neuronal dissemination to the central nervous system in relation with viral neurotropism, and abnormal immune-mediated response causing secondary neurological involvement. The first mechanism is supposed to be responsible for the most common neurological symptoms developed by patients with COVID-19 (e.g., hypogeusia, hyposmia, headache, vertigo, and dizziness). In contrast, the second can lead to severe complications during or after the course of the illness, either dysimmune (e.g., myelitis, encephalitis, GBS) or induced by cytokine overproduction (hypercoagulable state and cerebrovascular events).[9-11] Since the onset of the COVID-19 pandemic, there have been articles of the possible link between GBS and the COVID-19 infection.[12] Clinically, acute flask paresis of the limbs was observed in most cases of GBS associated with COVID-19.[13] The majority of GBS associated with COVID-19 documented up to date had a several disease process with respiratory failure and of demyelating type after a short latency period from COVID-19, also, axonal variants were also commonly reported.[13,14] As reported in the review by Aladawi et al, the first case of GBS due to COVID-19 was seen in 2020 in China, where the infection was first observed.[14] In this report identified a total of 109 GBS cases with an average latency period between the arboviral symptoms and neurologic manifestations for confirmed COVID-19 cases as 12 days. The most commonly reported GBS variants were classical sensorimotor GBS, followed by paraparetic GBS, Miller Fischer syndrome, facial diplegia with paresthesia, pharyngeal-cervical-brachial GBS, and pure sensory GBS. CSF analysis was performed in 86 cases. In the CSF analysis of 86% of these cases, albumino-cytological dissociation was shown. The predominant EMG variant of GBS was AIDP, 37% of the cases required intensive care, and 30% required mechanical ventilation, and the mortality rate was 5.5%. The male to female ratio was 2.5:1. In this series, the duration between arboviral and neurological symptoms, the latency period was highly variable including cases even GBS manifestations preceded COVID-19 arboviral symptoms. Thus, though the authors have considered a post-infectious immunepathogenesis rather than direct neuronal damage or a para-infectious mechanism considering the average 12 days latency period; the morbidity due to direct viral damage is a possibility at least in some of the cases.[14] The argument could be whether the GBS is para-infectious or post-infectious.[14] GBS is known to be post-infectious following several types of infections and causality can only be proven through large epidemiological studies for COVID-19.

In our series, the mean time between the onset of COVID-19 symptoms and the first symptoms of acute polyneuropathy was 21.5 days. The increased latency period favoured the post-infectious autoimmune nature of GBS in our patients. There was a female preponderance and as given in the table, the majority of our patients did not have any major respiratory involvement thus none of them needed extensive care. As reported in many countries, COVID-19 mortality is higher in men as well as disease morbidity. Thus there could be a selection bias as more severe cases, probably males could be missed or decerased during the peak active pandemic period. Consistent with the literature, paraparesis was present in 12 patients, tetraparesis in 3, and pure sensory symptoms in 1 patient, however, mortality from COVID-19 and GBS was not observed in our series. The excess of the female gender, the high incidence of MAN and MSAN in our cases could be related to cultural, genetic and socioeconomic differences affecting the immunogenicity of COVID-19 and development of GBS as epidemiologic studies involving certain populations might introduce bias in reporting results. One should always consider the variations between different populations as well as changing viral characteristics with mutations as well as acquired viral immunity through immunization or acquired after infection. Classically observed polyneuropathy cases may change the spectrum in the future. May the mutated virus play a role in the development of a different spectrum of neurological complications? This issue can be clarified with long-term, more comprehensive and etiopathogenesis-oriented studies.

A systematic review pointed to a significantly increased number of patients with GBS after the COVID-19 pandemic, with higher prevalence among older patients than with younger ones.[15] In our case series, 11 cases were over 60 years old, 4 cases were between 30-60 years old, and one of our cases was under 30 years old. Consistent with the literature, most of our patients were middle-aged or aged. While the mean time between GBS and COVID-19 was 21.5 days in our case series, a case report of GBS developing approximately 100 days later was reported.[16] There were no laboratory and electrophysiological findings suggesting myopathy in our patients.

The polyneuropathy of GBS is considered to be related to cross-immunity between peripheral nerve components and bacterial products. In case of viral infections, the “molecular mimicry” and related autoantibodies have not been well documented supporting the possibility of direct viral damage and/or neurotoxicity effecting some group of patients. SARS-CoV-2 has well-known neurotropism recognized by hyposmia and could enter the nervous system via terminals of the olfactory nerve and the olfactory epithelium that express angiotensin converting enzyme-2 (ACE2). Molecular mimicry between SARS-CoV-2 and various human organs and tissues have been hypothesized as a potential trigger of multi-organ autoimmunity in COVID-19.[17-19] For example, the study by Lucchese and Flöel, sequence analysis of the 41 human proteins associated with immune-mediated neuropathies revealed that SARS-CoV-2 contained two immunologically-related hexapeptides with the human heat shock proteins 90 and 60 respectively.[20] These authors hypothesized that SARS-CoV2 infection may trigger an adaptive immune response in which T cell-B cell interactions result in the production-specific antibodies similar to ganglioside-peptide sequences or structure, resulting in loss of self-tolerance.[20] The gangliosides located on the membranes of neurons and the schwann-cells, which form the myelin sheath, act as receptors for antiganglioside antibodies, promoting neutralization of neurons complement inhibitory activity, which turns them into targets for autoimmune-mediated destruction of myelin sheaths or axons.[20] Thus, antiganglioside antibodies in GBS could be biomarkers of axonal injury rather demyelination, as they directly target the neuronal membrane gangliosides. About 50 to 85% of previously reported cases with GBS or its variants have anti-ganglioside antibodies in their serum. However, there is limited data on the presence of antiganglioside antibodies in the patients with COVID-19 related GBS. Dufour et al. reported the first case with COVID-19 related GBS with positive GM1 antibody.[21] However, in the review by Aladawi et al. that consisted of 109 GBS cases 86% of the patients were antiganglioside antibodies negative and

not surprising as most of their cases were demyelinating variant of GBS. Antiganglioside tests could be possibly positive in axonal variants. Therefore, further studies are necessary to confirm the presence of antiganglioside antibodies in COVID-19 related GBS.[14] Unfortunately, we could not detect antiganglioside antibody and interleukin-6 (IL-6) levels in our case series.

The role of neuroinflammation and the effect of cytokine storms caused by SARS-CoV-2 infection on the nervous system have been discussed. In COVID-19 patients, an increase has been observed in cytokines such as IL-1b, IL-6, IL-17, tumour necrosis factor alpha, and interferon-g, along with other chemokines. Many of the same cytokines have been implicated in the pathogenesis of typical GBS, the cytokine storm in COVID-19 may play a primary role in the development and progression of GBS.[22] However, the role of cytokines in COVID-19 related GBS needs further investigation.[23-25]

Coronaviruses are thought to cause GBS in certain patients either directly through neuroinvasive capacity (ACE2 receptors on neuronal tissues) or indirectly through the response of the immune system.[26,27] The data indicate that SARS-CoV-2 can cause an immune reaction with an increased level of IL-6 which stimulates the inflammatory cascade and damages tissues. Therefore, inflammatory factors may play an important role in the organ dysfunctions of patients with COVID-19 infection. The actual data indicate that SARS-CoV-2 is capable of causing an excessive immune reaction with an increased level of cytokines as IL-6, which are produced by activated leukocytes and stimulate the inflammatory cascade. IL-6 plays an important role in multiple organ dysfunctions, which are often fatal for patients with COVID-19.[28-31] In the literature, although polyneuropathy was found to be more common in men, we had only three male patients in our series of 16 cases.[32] In our case series, IDP cases were observed less frequently than the other 2 subtypes. Studies that are more comprehensive and include inflammatory markers will add new dimensions to the acute polyneuropathy COVID-19 relationship, which we shed light on with our case series. COVID-19 causes an exaggerated immune response with persistent fevers, elevated inflammatory markers, and elevated proinflammatory cytokines. COVID-19 associated immune dysregulation increases the risk of immune-mediated conditions such as GBS.[33] In our case series, IL levels were not studied in the acute period of COVID-19. Therefore, we think that high ferritin levels only in the acute period can be associated with complications in the post-COVID period. It should also be considered that prospective studies will be needed to examine long-term complications in patients who have had a cytokine storm.

Common patient characteristics in this series besides COVID-19 were increased ferritin levels. Ferritin is a key mediator of immune dysregulation, especially under hyperferritinemia, via immune suppressive and pro-inflammatory effects. It can be thought that patients with hyper ferritinemia will experience more severe COVID-19 related complications.[34,35] Laboratory findings in patients with severe COVID-19 showed data consistent with cytokine storm involving elevated inflammatory markers, including ferritin, which has been associated with critical and life-threatening illness.[33] The height of ferritin detected during the COVID-19 period also requires more caution in terms of polyneuropathy that may develop. An important question regarding the pathophysiology of GBS following COVID-19 is whether it reflects a para-infectious response related to the acute inflammation or a true post-infectious immune-mediated response.[27,36] The case would give credence to the hypothesis that it is the immune response to COVID-19 and not the virus itself or the acute vascular changes that underly the pathophysiology of long COVID-19 syndrome.[37] Although the interval between COVID-19 and GBS was 21.5 days on average.

In our series clinically, there were no symptoms of autonomic dysfunction in the patients during the GBS period. Considering that further tests were not conducted. This could be attributed to long latency period of our patients. In the review by Abu-Rumeileh et al., autonomic disturbances were reported in 16.7% of GBS cases associated with COVID-19.[32] However, Milovanovic et al detected significant cardiovascular autonomic neuropathy in COVID-19 patients during the early phase of infection when

compared to controls even an increased risk of sudden cardiac death.[38]

CONCLUSION

Our knowledge about the COVID-19 pandemic is still very limited as the disease is still evolving with new mutants and continuing efforts for vaccination and new treatment models. Accordingly, there is limited data to yield any conclusion about the short and long term consequences. There are also racial and socioeconomic differences among countries that reflect the immune response, disease course, complications and mortality rates. We add to the literature 16 cases of GBS related to COVID-19 infection supporting the SARS-Cov-2 virus could be a triggering factor of GBS. The high number of women in our case series and the presence of motor axonal and motor-sensory axonal electrophysiological findings in the ENMG examination were not compatible with the literature. With this case series, we can suggest that acute polyneuropathy occurring after COVID-19 should be addressed from this perspective. In addition to classical GBS cases, whether there will be an increase in AMAN and AMSAN cases should be examined with detailed studies. Therefore, with more comprehensive studies, new targets should be determined for both etiology and treatment in post-COVID period GBS. Studies assisted by histopathological evidence could show us the fate of patients with axonal neuropathy, which occurs acutely but can be reflected in the chronic period. However, more cases with epidemiological data should be studied and future investigations should be carried out in this regard. Awareness of the possible causal association between acute polyneuropathy and COVID-19, recommends long-term follow-up of COVID-19 patients for neurologic complications. Finally, it is recognized that research on the relationship between COVID-19 and the nervous system surely would not be limited to the current period but would also serve basis for providing knowledge and treatment for future pandemics.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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