COVID-19 AND POST-POLIOMYELITIS SYNDROME: COINCIDENCE?

Dilek AGIRCAN, Ozlem ETHEMOGLU, Tülin GESOGLU-DEMIR

Department of Neurology, Harran Faculty of Medicine, Harran University, Sanlıurfa, Turkey

English https://doi.org/10.18071/isz.75.0207 www.elitmed.hu

Although severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel virus, many central and peripheral nervous system manifestations associated with coronavirus disease-19 (COVID-19) infection have been reported. Beyond the neurologic manifestations, we may still have much to learn about the neuropathologic mechanism of SARS-CoV-2 infection. Here we report a case of post-poliomyelitis syndrome (PPS) related to COVID-19 and attempt to predict the possible pathophysiologic mechanism behind this association.

Keywords: *COVID-19, post-poliomyelitis syndrome, immune system, pathophysiology*

COVID-19 ÉS POST-POLIO SZINDRÓMA: VÉLETLEN EGYBEESÉS?

Agircan D, MD; Ethemoglu O, MD; Gesoglu-Demir T, MD
Ideggyogy Sz 2022;75(5–6):207–210.

Bár a súlyos heveny légúti szindrómát okozó koronavírus-2 (SARS-CoV-2) új vírus, az általa okozott koronavírus-19 betegség (Covid-19) már eddig is számos esetben járt együtt központi és perifériás idegrendszeri manifesztációval. A neurológiai manifesztációkon túl még a SARS-CoV-2-fertőzés neuropatológiai mechanizmusairól is sokat kell tanulnunk. Esetismertetésünkben bemutatjuk egy Covid-19-cel összekapcsolható post-polio szindróma kialakulását, és kísérletet teszünk az összefüggés hátterében feltételezhető patofiziológiás mechanizmus előrejelzésére.

Kulcsszavak: *COVID-19, post-polio szindróma, immunrendszer, patofiziológia*

Correspondent: Dilek AGIRCAN, MD, Assistant Professor, Osmanbey Kampüsü, Sanliurfa-Mardin Karayolu 18.Km, Haliliye, Sanlıurfa, Turkey 63290. Phone: 00 90 414 3444463, fax: 00 90 414 3183192.
E-mail: d_agircan@hotmail.com, dilekagircan@harran.edu.tr
https//:orcid.org/0000-0001-5055-1933

Érkezett: 2022. január 4. Elfogadva: 2022. április 18.

In 2019, coronavirus disease-19 (COVID-19) was first identified in Wuhan, China, and was recognized as a global pandemic by the World Health Organization (WHO) in 2020. Since then, many manifestations of central and peripheral nervous system involvement related to COVID-19 have been reported. Although there are no data showing motor neurons infected by coronaviruses, about 1% of coronavirus infections result in motor neuron infection, which may cause some motor dysfunction and paralysis[1]. In this report, we describe post-poliomyelitis syndrome (PPS) in an infected patient with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), for the first time.

Case report

A 45-year-old male with childhood-onset poliomyelitis was admitted to our hospital with progressive weakness, numbness and fatigability in his right lower limb lasting for 15 days. He tested posi-

Table 1. *EMG-findings of the patient at admission*

Muscle	Spontaneous act. Fib	PSW	Voluntary act. Amp	Dur	Poly	IP
Left gastroc caput med	0/10	0/10				0 act
Left tibialis anterior	0/10	0/10				0 act
Left rectus femoris	0/10	0/10				0 act
Left biceps	0/10	0/10	+	+	+	-
Left abd. pol. brevis	0/10	0/10	+	+	+	-
Left abd. digiti minimi	0/10	0/10	+	+	+	-
Left ext. dig. communis	0/10	0/10	+	+	+	-
Right biceps	0/10	0/10	+	+	+	-
Right gastroc caput med	3/10	4/10	+	+		-
Right rectus femoris	3/10	4/10	+	+		-
Right tibialis anterior	3/10	4/10	+	+		-
Right abd. pol. brevis	0/10	0/10	+	+	+	-
Right abd. digiti minimi	0/10	0/10	+	+	+	-
Right ext. dig. communis	0/10	0/10	+	+	+	-

tive for SARS-CoV-2 via an oropharyngeal swab and was quarantined for 10 days before admission. He did not see any physicians during these 10 days. In his medical history, after poliomyelitis, he developed weakness and atrophy of bilateral lower and upper limb muscles, more prominently in the lower extremities. Before COVID-19, he was able to walk on crutches, but later he used a wheelchair. When we retrospectively reviewed his medical records, it revealed that he had mild weakness in both upper limb muscles with the strength of -5/5, also paraparesis with 4/5 in the right lower limb and 1/5 in the left lower limb proximally and distally before Covid-19. In his neurologic examination, cranial nerves were intact. He had mild weakness in both upper limb muscles with the strength of -5/5, also paraparesis with 3/5 in the right lower limb and 1/5 in the left lower limb proximally and distally. Deep tendon reflexes were absent in the lower limbs and depressed in the upper limbs. The rest of the neurologic and systemic examination was normal. His laboratory tests showed a high level of hemoglobin A_{1c} and he was diagnosed as having diabetes mellitus by the endocrinology department. Other blood test results were normal including serum creatine kinase levels. Contrast-enhanced cranial magnetic resonance imaging (MRI) was normal. Cervical, thoracic, and lumbar spinal MRIs were done and lumbar MRI showed scoliosis. Nerve conduction studies (NCS) and electromyography (EMG) were performed. The motor NCS of the right peroneal and tibial nerves revealed low amplitude compound muscle action potential. Motor NCS of the left peroneal and tibial nerves were unobtainable. Motor NCS of the upper limbs and all sensory NCS were normal. In the EMG study, there were features of chronic denervations in muscles of both bilateral upper limb and the right lower limb, and there was no voluntary activity in the left lower limb. EMG also revealed signs of active denervations in right lower limb muscles **(Table 1)**. We offered to perform a lumbar puncture, but he didn't accept. We also excluded other conditions with EMG and imaging. At the 6th month follow-up examination, he had ongoing weakness with the strength of -3/5 in the right lower limb proximally and distally. His control EMG was the same as the previous. According to the clinical results and EMG findings, the patient was diagnosed as having PPS and was referred to physiotherapy.

Discussion

PPS refers to a clinical syndrome of new-onset muscle weakness, pain, and fatigue that may occur several decades after healing from acute poliomyelitis. Acute poliomyelitis results in lower motor neuron degeneration, and after the acute phase, reinnervation via distal axonal sprouting occurs in denervated muscle fibers. This compensatory mechanism continues as a denervation/reinnervation process until deterioration happens because of the overactivity of the surviving motor neurons. Aging, immune dysregulation, increased metabolic demand, premature dropout of muscle fibers and motor units, and the persistence of poliovirus are considered to be the decompensatory causes in the pathophysiology of PPS[2].

One hypothesis for the pathophysiology of PPS

is that the persistence of genetic viral materials has the potential to upregulate the transcription of cytokine genes and induce the production of cytokines, as a result dysregulating the inflammatory and immune system response. Inflammatory mediators such as interleukin- (IL) 2, IL-4, IL-10, interferon- (IFN) γ, and tumor necrosis factor- (TNF) α were detected in the cerebrospinal fluid (CSF) of patients with PPS. Also, inflammatory changes in the spinal cord and skeletal muscle biopsies have been reported in the literature. It is suggested that these cytokines may cause a smouldering inflammatory response and a sustained, inert neuronal dysfunction that can compromise the function or viability of already stressed and overactivated surviving motor neurons[3, 4].

COVID-19 can be a fatal syndrome characterized by severe acute respiratory syndrome caused by SARS-CoV-2. SARS-CoV-2 has 79.5% and 50% genetic resemblance to other coronaviruses such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), respectively. SARS-CoV-2 and other coronaviruses exhibit neurotropic characteristics. COVID-19 causes both peripheral and central nervous system involvement[5, 6].

Coronavirus infection leads to neuronal degeneration via several possible mechanisms such as direct infection, angiotensin-converting enzyme 2- (ACE 2) or immune-mediated, and hypoxia. Neuronal death by direct infection occurs in viral infections via several mechanisms such as cell lysis, oxidative stress, and mitochondrial dysfunction. Although there are no data showing motor neurons infected by coronaviruses, about 1% of coronavirus infections result in motor neuron infection causing some motor dysfunction and paralysis[7].

SARS-CoV-2 induces neuroinflammation and oxidative stress. Cytokine storm, caused by the overproduction of inflammatory factors after coronaviruses, induces neurodegeneration and neuronal dysfunction and is reported as the leading cause of death in patients with COVID-19. In addition, an important proinflammatory mediator, IL-6, which is elevated in COVID-19, can cause an immune response in the nervous system[8, 9].

The European Federation of Neurological Societies (EFNS) task force recommended the use of diagnostic criteria of PPS based on Halstead's definition from 1991 with emphasis on the new muscle weakness. Thereafter, the EFNS task force suggested that the criteria published by the March of Dimes in 2000 should be considered as universal criteria for PPS. In accordance with these criteria, the essential clinical feature for the diagnosis of PPS is new muscle weakness or muscle fatigability that should be persistent for at least 1 year. Although no objective test is available that can reliably and specifically diagnose PPS, needle EMG is helpful to document the evidence of motor neuron involvement or to determine or exclude other neurologic disorders that might mimic the new symptoms of PPS[10].

In the differential diagnosis of PPS, Guillain-Barré syndrome (GBS) is the most common cause of acute flaccid paralysis (AFP) in the post-poliomyelitis eradication era. After the initial progressive phase, patients with GBS reach a plateau phase that can last from days to weeks. 60–80% of patients with GBS are able to walk independently 6 months after disease onset, with or without treatment[11].

In this context our case has some limitations of the diagnosis of PPS. Although the patient has weakness for 6 months to date and on his control examination he had ongoing weakness and fatigue, this time duration is not enough to confirm the diagnosis as PPS. Even though a lumbar puncture could not be done as the patient didn't accept, Guillain-Barre syndrome was excluded in the differential diagnosis, because he had ongoing weakness and muscle fatigability for 6 months. After excluding GBS in the differential diagnosis, even if the 1-year period has not expired, the patient was diagnosed with PPS because of his progressive worsening for 6 months and his EMG being compatible with PPS.

To the best of our knowledge, this is the first case report of PPS related to COVID-19. A case report of a 23-year-old female patient with COVID-19 described steroid-responsive diffuse anterior horn cell disease[12]. Taking into account these two patients and the relation of PPS and COVID-19 with the inflammatory system, we thought that para-infectious dysregulation of the immune system caused by COVID-19 might trigger the decompensatory basis of PPS.

Conclusion

Regarding the antecedently reported neurologic manifestations of COVID-19, this is the first case of SARS-CoV-2 associated with PPS. The underlying mechanism of lower motor neuron degeneration related to COVID-19 is presumably the immunologic dysregulation. However, further studies with pathophysiologic data are necessary to support a causal relationship.

REFERENCES

1. *Guidon AC, Amato AA*. COVID-19 and neuromuscular disorders. Neurology 2020;94(22):959-69. https://doi.org/10.1212/WNL.0000000000009566
2. *Lo JK, Robinson LR*. Postpolio syndrome and the late effects of poliomyelitis. Part 1. pathogenesis, biomechanical considerations, diagnosis, and investigations. Muscle & Nerve 2018;58(6):751-9. https://doi.org/10.1002/mus.26168
3. *Gonzalez H, Khademi M, Andersson M, Wallström E, Borg K, Olsson T.* Prior poliomyelitis-evidence of cytokine production in the central nervous system. Journal of the Neurological Sciences 2002;205(1):9-13. https://doi.org/10.1016/S0022-510X(02)00316-7
4. *Melin E, Lindroos E, Lundberg IE, Borg K, Korotkova M*. Elevated expression of prostaglandin E2 synthetic pathway in skeletal muscle of prior polio patients. Journal of Rehabilitation Medicine 2014;46(1):67-72. https://doi.org/10.2340/16501977-1230
5. *Wang Y, Wang Y, Chen Y, Qin Q*. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. Journal of Medical Virology 2020;92(6):568-76. https://doi.org/10.1002/jmv.25748
6. *Li YC, Bai WZ, Hashikawa T.* The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. Journal of Medical Virology 2020;92 (6):552-5. https://doi.org/10.1002/jmv.25728
7. *Wu Y, Xu X, Chen Z, et al.* Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain, Behavior, and Immunity 2020;87:18-22. https://doi.org/10.1016/j.bbi.2020.03.031
8. *Payus AO, Lin CLS, Noh MM, Jeffree MS, Ali RA*. SARS-CoV-2 infection of the nervous system: A review of the literature on neurological involvement in novel coronavirus disease-(COVID-19). Bosnian Journal of Basic Medical Sciences 2020;20(3):283-92. https://doi.org/10.17305/bjbms.2020.4860
9. *Channappanavar R, Perlman S.* Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Seminars in Immunopathology 2017;39(5):529-39. https://doi.org/10.1007/s00281-017-0629-x
10. *Li Hi Shing S, Chipika RH, Finegan E, et al*. Post-polio Syndrome: More Than Just a Lower Motor Neuron Disease. Front Neurol 2019;10:773. https://doi.org/10.3389/fneur.2019.00773
11. *Fokke C, Van den Berg B, Drenthen J, et al.* Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain 2014;137(Pt 1):33-43. https://doi.org/10.1093/brain/awt285
12. *Nanda S, Handa R, Anand R, et al.* Curious case of steroid responsive diffuse anterior horn cell disease associated with COVID-19 infection. Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology 2021;42(8):3415-7. https://doi.org/10.1007/s10072-021-05163-9