



16. Bölüm

COVID-19 ve Periferik Sinir Sistemi Tutulumu

Tuğba ÖZEL¹

1. GİRİŞ

COVID-19 hastalarında nörolojik komplikasyonlar hastanede yatan hastalarda oldukça yaygındır (1-8). Hastanede yatan hastaların yüzde 80'den fazlasında hastalık seyri boyunca nörolojik semptomlar görülebilmektedir (8). Nörolojik komplikasyonların görülme sıklığı coğrafi konum ve hasta özelliklerine göre değişebildiği bildirilmiştir. Çin, Avrupa ve Amerika Birleşik Devletleri'nden bildirilen yayınlarda COVID-19 hastalarının yaklaşık üçte birinde nörolojik komplikasyonlar görüldüğü rapor edilmiştir (1, 3, 4, 8, 9).

Literatürde COVID-19' un hem santral sinir sistemi hem de periferik sinir sistemi ile ilgili semptom ve komplikasyonları bildirilmiştir. Bu bölümde COVID-19 ile ilişkili periferik sinir sistemine (PSS) ait semptom ve komplikasyonlar gözden geçirilecektir.

2. SARS-CoV-2 NÖROPATOGENEZİ

COVID-19 hastalarında nörolojik komplikasyonlar SARS-CoV-2 virüsünün doğrudan etkilerinden nörotropik etkisi ve enfeksiyona bağlı immün aracılı sistemik yanıt, akciğer hasarına bağlı hipoksemi, multiorgan yetmezliği ve kullanılan ilaçlar ile ilişkili olabilmektedir (9, 10). Literatürde, SARS-CoV-2 virüsünün sinir sistemini doğrudan invazyonunu destekleyen çalışmalar bulunmaktadır (11-13).

SARS-CoV-2, hücrelere giriş noktası olarak hücre zarına bağlı bir protein olan anjiyotensin dönüştürücü enzim 2'yi (ACE2) kullanır. ACE2, anjiyotensin II'yi

¹ Uzm. Dr., Akdeniz Üniversitesi Tıp Fakültesi Nöroloji ABD., tutmucze@gmail.com

KAYNAKLAR

1. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA neurology*. 2020;77(6):683-90.
2. Helms J, Kremer S, Merdji H. Neurologic Features in Severe SARS-CoV-2 Infection. *2020;382(23):2268-70*.
3. Montalvan V, Lee J, Bueso T, De Toledo J, Rivas K. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. *Clinical neurology and neurosurgery*. 2020;194:105921.
4. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, Sánchez-Larsen Á, Layos-Romero A, García-García J, et al. Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. *2020;95(8):e1060-e70*.
5. Koralnik IJ, Tyler KL. COVID-19: A Global Threat to the Nervous System. *Annals of neurology*. 2020;88(1):1-11.
6. Xiong W, Mu J. New onset neurologic events in people with COVID-19 in 3 regions in China. *2020;95(11):e1479-e87*.
7. Herman C, Mayer K, Sarwal A. Scoping review of prevalence of neurologic comorbidities in patients hospitalized for COVID-19. *Neurology*. 2020;95(2):77-84.
8. Liotta EM, Batra A. Frequent neurologic manifestations and encephalopathy-associated morbidity in COVID-19 patients. *2020;7(11):2221-30*.
9. Pezzini A, Padovani A. Lifting the mask on neurological manifestations of COVID-19. *Nature reviews Neurology*. 2020;16(11):636-44.
10. Kanberg N, Ashton NJ, Andersson LM, Yilmaz A, Lindh M, Nilsson S, et al. Neurochemical evidence of astrocytic and neuronal injury commonly found in COVID-19. *Neurology*. 2020;95(12):e1754-e9.
11. Al-Dalahmah O, Thakur KT, Nordvig AS, Prust ML, Roth W, Lignelli A, et al. Neuronophagia and microglial nodules in a SARS-CoV-2 patient with cerebellar hemorrhage. *Acta neuropathologica communications*. 2020;8(1):147.
12. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *The Lancet Neurology*. 2020;19(5):383-4.
13. Matschke J, Lütgehetmann M, Hagel C, Sperhake JP, Schröder AS, Edler C, et al. Neuropathology of patients with COVID-19 in Germany: a post-mortem case series. *The Lancet Neurology*. 2020;19(11):919-29.
14. Agarwal S, Jain R, Dogra S, Krieger P, Lewis A, Nguyen V, et al. Cerebral Microbleeds and Leukoencephalopathy in Critically Ill Patients With COVID-19. *Stroke*. 2020;51(9):2649-55.
15. Strawn WB, Ferrario CM, Tallant EA. Angiotensin-(1-7) reduces smooth muscle growth after vascular injury. *Hypertension (Dallas, Tex : 1979)*. 1999;33(1 Pt 2):207-11.
16. Ye M, Wysocki J, William J, Soler MJ, Cokic I, Battle D. Glomerular localization and expression of Angiotensin-converting enzyme 2 and Angiotensin-converting enzyme: implications for albuminuria in diabetes. *Journal of the American Society of Nephrology : JASN*. 2006;17(11):3067-75.
17. Lei Y, Zhang J, Schiavon CR, He M, Chen L, Shen H, et al. SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2. *Circulation research*. 2021;128(9):1323-6.
18. Pilotto A, Padovani A. Reply to the Letter "COVID-19-Associated Encephalopathy and Cytokine-Mediated Neuroinflammation". *Annals of neurology*. 2020;88(4):861-2.
19. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Seminars in immunopathology*. 2017;39(5):529-39.

20. Muccioli L, Pensato U, Cani I, Guarino M, Cortelli P, Bisulli F. COVID-19-Associated Encephalopathy and Cytokine-Mediated Neuroinflammation. 2020;88(4):860-1.
21. Huang KJ, Su IJ, Theron M, Wu YC, Lai SK, Liu CC, et al. An interferon-gamma-related cytokine storm in SARS patients. *Journal of medical virology*. 2005;75(2):185-94.
22. Hanafi R, Roger PA. COVID-19 Neurologic Complication with CNS Vasculitis-Like Pattern. 2020;41(8):1384-7.
23. Keller E, Brandi G, Winklhofer S, Imbach LL, Kirschenbaum D, Frontzek K, et al. Large and Small Cerebral Vessel Involvement in Severe COVID-19: Detailed Clinical Workup of a Case Series. *Stroke*. 2020;51(12):3719-22.
24. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*. 2020;277(8):2251-61.
25. Saniasiaa J, Islam MA. Prevalence of Olfactory Dysfunction in Coronavirus Disease 2019 (COVID-19): A Meta-analysis of 27,492 Patients. 2021;131(4):865-78.
26. Aragão M, Leal MC. Anosmia in COVID-19 Associated with Injury to the Olfactory Bulbs Evident on MRI. 2020;41(9):1703-6.
27. Li CW, Syue LS, Tsai YS, Li MC, Lo CL, Tsai CS, et al. Anosmia and olfactory tract neuropathy in a case of COVID-19. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi*. 2021;54(1):93-6.
28. Coolen T, Lolli V, Sadeghi N, Rovai A, Trotta N, Taccone FS, et al. Early postmortem brain MRI findings in COVID-19 non-survivors. 2020;95(14):e2016-e27.
29. Laurendon T, Radulesco T, Mugnier J, G rault M. Bilateral transient olfactory bulb edema during COVID-19-related anosmia. 2020;95(5):224-5.
30. Lin E, Lantos JE. Brain Imaging of Patients with COVID-19: Findings at an Academic Institution during the Height of the Outbreak in New York City. 2020;41(11):2001-8.
31. Kirschenbaum D, Imbach LL, Ulrich S, Rushing EJ, Keller E, Reimann RR, et al. Inflammatory olfactory neuropathy in two patients with COVID-19. *Lancet (London, England)*. 2020;396(10245):166.
32. Jang H, Boltz D, Sturm-Ramirez K, Shepherd KR, Jiao Y, Webster R, et al. Highly pathogenic H5N1 influenza virus can enter the central nervous system and induce neuroinflammation and neurodegeneration. *Proceedings of the National Academy of Sciences of the United States of America*. 2009;106(33):14063-8.
33. Doty RL. The olfactory vector hypothesis of neurodegenerative disease: is it viable? *Annals of neurology*. 2008;63(1):7-15.
34. Potter MR, Chen JH, Lobban NS, Doty RL. Olfactory dysfunction from acute upper respiratory infections: relationship to season of onset. *International forum of allergy & rhinology*. 2020;10(6):706-12.
35. Vaira LA, Salzano G, Petrocelli M, Deiana G, Salzano FA, De Riu G. Validation of a self-administered olfactory and gustatory test for the remotely evaluation of COVID-19 patients in home quarantine. *Head & neck*. 2020;42(7):1570-6.
36. Vellozzi C, Iqbal S, Broder K. Guillain-Barre syndrome, influenza, and influenza vaccination: the epidemiologic evidence. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2014;58(8):1149-55.
37. Alberti P, Beretta S, Piatti M, Karantzoulis A, Piatti ML, Santoro P, et al. Guillain-Barr  syndrome related to COVID-19 infection. *Neurology(R) neuroimmunology & neuroinflammation*. 2020;7(4).

38. Camdessanche JP, Morel J, Pozzetto B, Paul S, Tholance Y, Botelho-Nevers E. COVID-19 may induce Guillain-Barré syndrome. *Revue neurologique*. 2020;176(6):516-8.
39. Padroni M, Mastrangelo V, Asioli GM, Pavolucci L, Abu-Rumeileh S, Piscaglia MG, et al. Guillain-Barré syndrome following COVID-19: new infection, old complication? *Journal of neurology*. 2020;267(7):1877-9.
40. El Otmani H, El Moutawakil B, Rafai MA, El Benna N, El Kettani C, Soussi M, et al. COVID-19 and Guillain-Barré syndrome: More than a coincidence! *Revue neurologique*. 2020;176(6):518-9.
41. Virani A, Rabold E, Hanson T, Haag A, Elrufay R, Cheema T, et al. Guillain-Barré Syndrome associated with SARS-CoV-2 infection. *IDCases*. 2020;20:e00771.
42. Abu-Rumeileh S, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. 2021;268(4):1133-70.
43. Gutiérrez-Ortiz C, Méndez-Guerrero A. Miller Fisher syndrome and polyneuritis cranialis in COVID-19. 2020;95(5):e601-e5.
44. Dinkin M, Gao V, Kahan J, Bobker S, Simonetto M, Wechsler P, et al. COVID-19 presenting with ophthalmoparesis from cranial nerve palsy. *Neurology*. 2020;95(5):221-3.
45. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain-Barré Syndrome Associated with SARS-CoV-2. 2020;382(26):2574-6.
46. Wijdicks EF, Klein CJ. Guillain-Barré Syndrome. *Mayo Clinic proceedings*. 2017;92(3):467-79.
47. Tsai LK, Hsieh ST, Chao CC, Chen YC, Lin YH, Chang SC, et al. Neuromuscular disorders in severe acute respiratory syndrome. *Archives of neurology*. 2004;61(11):1669-73.
48. Kim JE, Heo JH, Kim HO, Song SH, Park SS, Park TH, et al. Neurological Complications during Treatment of Middle East Respiratory Syndrome. *Journal of clinical neurology (Seoul, Korea)*. 2017;13(3):227-33.
49. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet (London, England)*. 2020;395(10239):1763-70.
50. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. 2020;368:m1091.
51. Carfi A, Bernabei R, Landi F. Persistent Symptoms in Patients After Acute COVID-19. *Jama*. 2020;324(6):603-5.
52. Suwanwongse K, Shabarek N. Rhabdomyolysis as a Presentation of 2019 Novel Coronavirus Disease. *Cureus*. 2020;12(4):e7561.
53. Jin M, Tong Q. Rhabdomyolysis as Potential Late Complication Associated with COVID-19. *Emerging infectious diseases*. 2020;26(7):1618-20.
54. Manzano GS, Woods JK, Amato AA. COVID-19-Associated Myopathy Caused by Type I Interferonopathy. *The New England journal of medicine*. 2020;383(24):2389-90.
55. Guidon AC, Amato AA. COVID-19 and neuromuscular disorders. *Neurology*. 2020;94(22):959-69.
56. Goh Y, Beh DLL, Makmur A, Somani J, Chan ACY. Pearls & Oysters: Facial nerve palsy in COVID-19 infection. *Neurology*. 2020;95(8):364-7.
57. Decavel P, Petit C, Tatu L. Tapia syndrome at the time of the COVID-19 pandemic: Lower cranial neuropathy following prolonged intubation. *Neurology*. 2020;95(7):312-3.
58. Todisco M, Alfonsi E, Arceri S, Bertino G, Robotti C, Albergati M, et al. Isolated bulbar palsy after SARS-CoV-2 infection. *The Lancet Neurology*. 2021;20(3):169-70.
59. Cacciavillani M, Salvalaggio A, Briani C. Pure sensory neuralgic amyotrophy in COVID-19 infection. *Muscle & nerve*. 2021;63(1):E7-e8.

60. Siepmann T, Kitzler HH, Lueck C, Platzek I, Reichmann H, Barlinn K. Neuralgic amyotrophy following infection with SARS-CoV-2. 2020;62(4):E68-e70.
61. Madia F, Merico B, Primiano G, Cutuli SL, De Pascale G, Servidei S. Acute myopathic quadriplegia in patients with COVID-19 in the intensive care unit. *Neurology*. 2020;95(11):492-4.
62. Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, et al. The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings. *Brain : a journal of neurology*. 2020;143(10):3104-20.
63. Malik GR, Wolfe AR, Soriano R, Rydberg L, Wolfe LF, Deshmukh S, et al. Injury-prone: peripheral nerve injuries associated with prone positioning for COVID-19-related acute respiratory distress syndrome. *British journal of anaesthesia*. 2020;125(6):e478-e80.
64. Fernandez CE, Franz CK. Imaging Review of Peripheral Nerve Injuries in Patients with COVID-19. 2021;298(3):E117-e30.
65. Ottestad W, Seim M, Mæhlen JO. COVID-19 with silent hypoxemia. *Tidsskrift for den Norske lægeforening : tidsskrift for praktisk medicin, ny raekke*. 2020;140(7).
66. Tobin MJ, Laghi F, Jubran A. Why COVID-19 Silent Hypoxemia Is Baffling to Physicians. *American journal of respiratory and critical care medicine*. 2020;202(3):356-60.
67. Couzin-Frankel J. The mystery of the pandemic's 'happy hypoxia.' *Science (New York, NY)*. 2020;368(6490):455-6.
68. Lu Y, Li X, Geng D, Mei N, Wu PY, Huang CC, et al. Cerebral Micro-Structural Changes in COVID-19 Patients - An MRI-based 3-month Follow-up Study. *EClinicalMedicine*. 2020;25:100484.
69. Vanhorebeek I, Latronico N. ICU-acquired weakness. 2020;46(4):637-53.