



Bölüm 37

COVID-19'A HİSTOPATOLOJİK YAKLAŞIM

Gökçen GÖKÇE¹



GİRİŞ

Dünya Sağlık Örgütü (WHO)'nın 2020 yılının Şubat ayında COVID-19 olarak tanımladığı mevcut koronavirüs hastalığının etkeni, Beta-koronavirüs (β -CoV) ailesi üyesi şiddetli akut solunum sendromu koronavirüs-2 (SARS-CoV-2)'dir. İlk olarak 2019 yılının Aralık ayında Çin'e bağlı Wuhan şehrinde ortaya çıkmasıyla birlikte virüsün insanı enfekte etme durumu ve hastalık yetisinin yüksekliği binleri aşan sayıda insan yaşamının sonlanmasına sebep olmuştur ve 2020 yılının Mart ayında WHO tarafından pandemi olarak ilan edilmiştir(1,2). SARS-CoV-2, günümüzde kadar insanlarda enfeksiyona neden olan yedinci koronavirüs ailesi üyesidir. Çin kaynaklı Şiddetli Akut Solunum Sendromu Coronavirüsü (SARS-CoV) ve Orta Doğu kaynaklı Orta Doğu Solunum Sendromu Coronavirüsü (MERS-CoV) yakın zamanda salgın oluşturan diğer koronavirüs ailesi üyeleridir. Her üç örnek hayvan kaynaklıdır ve insan yaşamını ciddi derecede etkileyebilecek hastalık oluşturma potansiyeline sahiptir (3,4). SARS-CoV-2, hayvanlar ve insanlar arasındaki etkileşimin sıklığı, insandan insana geçiş durumu ile ani ve ölümcül bir hastalık tablosu oluşturmaktadır(1,5,6). Klinik

belirtileri arasında ateş, halsizlik, öksürük, balgam, kaslarda yaygın ağrı ve nefes darlığı yer alır ve bulaştırıcılığının çok yüksek olması sebebiyle hastalığın erken teşhisi, tedavinin en önemli adımini oluşturmaktadır(6,7). Yakın zaman itibarıyle teşhis ve tedavisinde CRISPR tabanlı yöntemler kullanılmaktadır. Nükleik asit amplifikasyon testleri (NAAT), sekans analizleri, viral kültürler ve seralojik yöntemler ise tanıda kullanılan metodlar arasındadır. SARS-CoV-2, diğer hücrelere girmek için bir reseptör olarak olarak konakçı hücre transmembran karboksipeptidaz angiotensin converting enzim 2 (ACE2)'yi kullanır. Bu işlem, viral proteinin hücre girişi için tip II transmembran serin proteaz (TMPRSS2)'ye dayanır. Hedef hücrelerde hem ACE2 hem de TMPRSS2 ekspresyonunun viral enfeksiyon için önemli olduğu düşünülmektedir. SARS-CoV-2, çoğunlukla insanlarda hafif veya şiddetli solunum yolu hastalıkları ile ilişkilendirilmekle birlikte bulguları değişken klinik derecelerde görülebilmektedir (1,5,8-10). SARS-CoV-2'ye bağlı COVID-19, dünya çapındaki sağlık sistemleri için büyük bir zorluk teşkil etmekte ve ileri yaş, diyabet, hipertansiyon, kalp ve damar hastalıkları, immün yetmezlik, kronik akciğer hastalıkları, kanser, kronik böbrek hasta-

¹ Arş. Gör. Dr., Ankara Üniversitesi Tıp Fakültesi Histoloji-Embriyoloji AD, gkgkcn@hotmail.com

topatolojik değişimleri daha iyi ifade edebilmek adına daha çok sayıda vaka üzerinde çalışılmasıının literatüre büyük katkılar sağlayacağı düşünülmektedir.

KAYNAKLAR

- Chams N, Chams S, Badran R, Shams A, Araji A, Raad M, et al. COVID-19: A Multidisciplinary Review. *Front Public Health.* 2020;8:383.
- Gao Z, Xu Y, Sun C, Wang X, Guo Y, Qiu S, et al. A systematic review of asymptomatic infections with COVID-19. *J Microbiol Immunol Infect.* 2021;54(1):12-6.
- Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. *Nat Med.* 2020;26(4):450-2.
- Zhang XY, Huang HJ, Zhuang DL, Nasser MI, Yang MH, Zhu P, et al. Biological, clinical and epidemiological features of COVID-19, SARS and MERS and AutoDock simulation of ACE2. *Infect Dis Poverty.* 2020;9(1):99.
- V'Kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. *Nat Rev Microbiol.* 2021;19(3):155-70.
- Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *Jama.* 2020;324(8):782-93.
- Sarma P, Prajapati M, Avti P, Kaur H, Kumar S, Medhi B. Therapeutic options for the treatment of 2019-novel coronavirus: An evidence-based approach. *Indian journal of pharmacology.* 2020;52(1):1-5.
- Bourgonje AR, Abdulle AE, Timens W, Hillebrands JL, Navis GJ, Gordijn SJ, et al. Angiotensin converting enzyme 2 (ACE2), SARS CoV 2 and pathophysiology of coronavirus disease 2019 (COVID 19). *The Journal of Pathology.* 2020.
- Pawlik L, Śpiołek E, Fichna J, Tarasiuk A. [Characteristics of SARS-CoV-2 and potential pharmacological treatment]. *Postepy biochemii.* 2020;66(2):83-90.
- Pagliaro P, Penna C. ACE/ACE2 ratio: a key also in 2019 coronavirus disease (Covid-19)? *Frontiers in Medicine.* 2020;7.
- Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. *Am J Emerg Med.* 2020;38(7):1504-7.
- Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. *American Journal of Physiology-Endocrinology and Metabolism.* 2020;318(5):E736-E41.
- Scheen AJ. [Obesity and risk of severe COVID-19]. *Revue medicale suisse.* 2020;16(695):1115-9.
- Metawea MI, Yousif WI, Moheb I. COVID 19 and liver: An A-Z literature review. *Dig Liver Dis.* 2021;53(2):146-52.
- Becker RC. Covid-19 treatment update: follow the scientific evidence. *Journal of thrombosis and thrombolysis.* 2020;50(1):43-53.
- Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty.* 2020;9(1):45.
- Siddiqi HK, Libby P, Ridker PM. COVID-19 - A vascular disease. *Trends in cardiovascular medicine.* 2021;31(1):1-5.
- Gavriatopoulou M, Korompoki E, Fotiou D, Ntassis-Stathopoulos I, Psaltopoulou T, Kastritis E, et al. Organ-specific manifestations of COVID-19 infection. *Clin Exp Med.* 2020;20(4):493-506.
- Mohamadian M, Chiti H, Shoghli A, Biglari S, Parsamanesh N, Esmaeilzadeh A. COVID-19: Virology, biology and novel laboratory diagnosis. *J Gene Med.* 2021;23(2):e3303.
- Samudrala PK, Kumar P, Choudhary K, Thakur N, Wadekar GS, Dayaramani R, et al. Virology, pathogenesis, diagnosis and in-line treatment of COVID-19. *Eur J Pharmacol.* 2020;883:173375.
- Alsharif W, Qurashi A. Effectiveness of COVID-19 diagnosis and management tools: A review. *Radiography (Lond).* 2021;27(2):682-7.
- Tang YW, Schmitz JE, Persing DH, Stratton CW. Laboratory Diagnosis of COVID-19: Current Issues and Challenges. *J Clin Microbiol.* 2020;58(6).
- Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. *Postgrad Med J.* 2021;97(1147):312-20.
- Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol.* 2021;19(3):141-54.
- Ke Z, Oton J, Qu K, Cortese M, Zila V, McKeane L, et al. Structures and distributions of SARS-CoV-2 spike proteins on intact virions. *Nature.* 2020;588(7838):498-502.
- Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *Nature.* 2020;581(7807):215-20.
- Flower TG, Buffalo CZ, Hooy RM, Allaire M, Ren X, Hurley JH. Structure of SARS-CoV-2 ORF8, a rapidly evolving immune evasion protein. *Proceedings of the National Academy of Sciences of the United States of America.* 2021;118(2).
- Awadasseid A, Wu Y, Tanaka Y, Zhang W. SARS-CoV-2 variants evolved during the early stage of the pandemic and effects of mutations on adaptation in Wuhan populations. *International journal of biological sciences.* 2021;17(1):97-106.
- Verdeccia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med.* 2020;76:14-20.
- Seyed Hosseini E, Riahi Kashani N, Nikzad H, Azadbakht J, Hassani Bafrani H, Haddad Kashani H. The novel coronavirus Disease-2019 (COVID-19): Mechanism of action, detection and recent therapeutic strategies. *Virology.* 2020;551:1-9.
- Bianchi M, Borsetti A, Ciccozzi M, Pasarella S. SARS-CoV-2 ORF3a: Mutability and function. *Int J Biol Macromol.* 2021;170:820-6.
- Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients disc-

- harged from hospital: a cohort study. Lancet (London, England). 2021;397(10270):220-32.
33. Echeverría-Esnal D, Martín-Ontiyuelo C, Navarrete-Rouco ME, De-Antonio Cuscó M, Ferrández O, Horcajada JP, et al. Azithromycin in the treatment of COVID-19: a review. Expert Rev Anti Infect Ther. 2021;19(2):147-63.
 34. Lindsley AW, Schwartz JT, Rothenberg ME. Eosinophil responses during COVID-19 infections and coronavirus vaccination. J Allergy Clin Immunol. 2020;146(1):1-7.
 35. Magadum A, Kishore R. Cardiovascular Manifestations of COVID-19 Infection. Cells. 2020;9(11).
 36. Topol EJ. COVID-19 can affect the heart. Science (New York, NY). 2020;370(6515):408-9.
 37. Sun J, Aghemo A, Forner A, Valenti L. COVID-19 and liver disease. Liver Int. 2020;40(6):1278-81.
 38. Wu J, Song S, Cao HC, Li LJ. Liver diseases in COVID-19: Etiology, treatment and prognosis. World J Gastroenterol. 2020;26(19):2286-93.
 39. Ma C, Cong Y, Zhang H. COVID-19 and the Digestive System. Am J Gastroenterol. 2020;115(7):1003-6.
 40. Amin M. COVID-19 and the liver: overview. Eur J Gastroenterol Hepatol. 2021;33(3):309-11.
 41. Akoumianakis I, Filippatos T. The renin-angiotensin-aldosterone system as a link between obesity and coronavirus disease 2019 severity. Obesity Reviews. 2020;21(9):e13077.
 42. Kudose S, Batal I, Santoriello D, Xu K, Barasch J, Peleg Y, et al. Kidney Biopsy Findings in Patients with COVID-19. J Am Soc Nephrol. 2020;31(9):1959-68.
 43. Greco A, Buccheri S, D'Arrigo P, Calderone D, Agnello F, Monte M, et al. Outcomes of renin-angiotensin-aldosterone system blockers in patients with COVID-19: a systematic review and meta-analysis. European heart journal Cardiovascular pharmacotherapy. 2020;6(5):335-7.
 44. Kaneko N, Kuo HH, Boucau J, Farmer JR, Allard-Chamard H, Mahajan VS, et al. Loss of Bcl-6-Expressing T Follicular Helper Cells and Germinal Centers in COVID-19. Cell. 2020;183(1):143-57.e13.
 45. Remmelink M, De Mendonça R, D'Haene N, De Clercq S, Verocq C, Lebrun L, et al. Unspecific post-mortem findings despite multiorgan viral spread in COVID-19 patients. Crit Care. 2020;24(1):495.
 46. Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, et al. Extrapulmonary manifestations of COVID-19. Nat Med. 2020;26(7):1017-32.
 47. Prilutskiy A, Kritselis M, Shevtsov A, Yambayev I, Vadlamudi C, Zhao Q, et al. SARS-CoV-2 Infection-Associated Hemophagocytic Lymphohistiocytosis. Am J Clin Pathol. 2020;154(4):466-74.
 48. Rongioletti F, Ferrelí C, Sena P, Caputo V, Atzori L. Clinicopathologic correlations of COVID-19-related cutaneous manifestations with special emphasis on histopathologic patterns. Clin Dermatol. 2021;39(1):149-62.
 49. Gianotti R, Recalcati S, Fantini F, Riva C, Milani M, Dainese E, et al. Histopathological Study of a Broad Spectrum of Skin Dermatoses in Patients Affected or Highly Suspected of Infection by COVID-19 in the Northern Part of Italy: Analysis of the Many Faces of the Viral-Induced Skin Diseases in Previous and New Reported Cases. Am J Dermatopathol. 2020;42(8):564-70.
 50. Catalá Gonzalo A, Galván Casas C. COVID-19 and the Skin. Actas Dermosifiliogr (Engl Ed). 2020;111(6):447-9.
 51. Gottlieb M, Long B. Dermatologic manifestations and complications of COVID-19. Am J Emerg Med. 2020;38(9):1715-21.
 52. Andina D, Belloni-Fortina A, Bodemer C, Bonifazi E, Chiriac A, Colmenero I, et al. Skin manifestations of COVID-19 in children: Part 3. Clin Exp Dermatol. 2021;46(3):462-72.
 53. Andina D, Belloni-Fortina A, Bodemer C, Bonifazi E, Chiriac A, Colmenero I, et al. Skin manifestations of COVID-19 in children: Part 2. Clin Exp Dermatol. 2021;46(3):451-61.
 54. Sharps MC, Hayes DJL, Lee S, Zou Z, Brady CA, Almoghrabi Y, et al. A structured review of placental morphology and histopathological lesions associated with SARS-CoV-2 infection. Placenta. 2020;101:13-29.
 55. Resta L, Vimercati A, Cazzato G, Mazzia G, Cicinelli E, Colagrande A, et al. SARS-CoV-2 and Placenta: New Insights and Perspectives. Viruses. 2021;13(5).
 56. Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, et al. [Pregnancy with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases]. Zhonghua Bing Li Xue Za Zhi. 2020;49(5):418-23.
 57. Alshaikh B, Cheung PY, Soliman N, Brundler MA, Yusuf K. Impact of Lockdown Measures during COVID-19 Pandemic on Pregnancy and Preterm Birth. Am J Perinatol. 2021.
 58. Bradley BT, Maioli H, Johnston R, Chaudhry I, Fink SL, Xu H, et al. Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series. Lancet (London, England). 2020;396(10247):320-32.