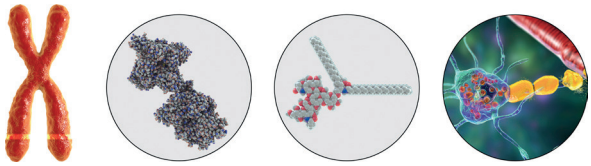

BÖLÜM 11

PROGRESİF MULTİFOKAL LÖKOENSEFALOPATİ VE NÖROLOJİK ENFEKSİYONLARA BAĞLI DEMYELİNİZAN HASTALIKLAR

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GİRİŞ

Progresif multifokal lökoensefalopati (PML), merkezi sinir sistemini multifokal tutan ciddi bir enfeksiyöz demiyelinizan hastalıktır. Polyomaviridae ailesinden bir DNA virüsü olan nörotropik özellikte 'JC (John Cunningham) virüs' tarafından oluşturulur. PML, özellikle hücresel immünitenin (sitotoksik T hücre) baskılandığı durumlarda latent JC virüsün reaktivasyonu ile ortaya çıkar (1).

JCV VE PML PATOGENEZİ

PML esas olarak immünkompromize kişi hastalığıdır. Çalışılan popülasyona göre değişmekle birlikte normal popülasyonun %70-90'ında serumda JC virüse karşı antikorlar pozitif saptanmıştır (2). Ancak kişi eğer immunkompetan ise bu kişilerde JC virüs ilişkili bir hastalık tablosu oluşması beklenmez. Virüs çoğu bireyde böbreklerde ve lenfoid organlarda latent kalır (3).

JCV'nin nörotropizmini nerede nasıl kazandığının mekanizması bilinmemektedir. Böbrekler, kemik iliği, dolaşımdaki lenfositler ve beyin viral replikasyonun meydana gelebileceği yerler olarak öngörülmektedir, ancak elde net veri yoktur. Reaktive olan virüslerin SSS'ne penetrasyonu hematojen yolla olmaktadır, bazı kaynaklara göre ise virüsün SSS'de olduğu ve burada reaktivasyonun

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DİĞER VİRAL DEMYELİNİZAN HASTALIKLAR

HIV enfeksiyonu, mikroglial nodül veya çok çekirdekli dev hücreli ensefalit, yaygın lökoensefalopati ve vakuolar miyelopati dahil olmak üzere bir dizi beyaz cevher anormalliğine neden olabilir. Ek olarak, yüksek düzeyde aktif antiretroviral tedavi alan AIDS'li hastalarda zaman zaman PML'ye bağlı olmayan şiddetli inflamatuar demiyelinizasyon gelişebilir (39-41). Lenfositlerin ve makrofajların yoğun perivasküler inflamatuar infiltratı vardır. En azından ara sıra makrofajlar (bildirilen bazı vakalarda çoğu) HIV için immünopozitiftir. Viral RNA genellikle bol miktarda bulunur.

Kızamık virüsüne bağlı subakut sklerozan panensefalit, perivasküler inflamasyona ve beyaz cevherin (aynı zamanda gri cevherin) gliozuna neden olur. Bu, miyelinli liflerin yamalı veya yoğun kaybı ile ilişkili olabilir. Akson kaybı genellikle miyelin kaybıyla orantılıdır, ancak özellikle ciddi şekilde etkilenen beyaz maddenin kenarlarına doğru aksonlar bazen nispeten korunur. Kızamık virüsü intranükleer inklüzyon cisimcikleri görülebilir, ancak seyrek olma eğilimindedir. Çoğu durumda klinik ve serolojik bulgular tanısaldır ve viral RNA PCR ile tespit edilebilir (42).

KAYNAKLAR

1. Saji AM, Gupta V. Progressive Multifocal Leukoencephalopathy. 2020.
2. Shackelton LA, Rambaut A, Pybus OG, Holmes EC. JC virus evolution and its association with human populations. Journal of virology. 2006;80(20):9928-33.
3. Kartau M, Sipilä JO, Auvinen E, Palomäki M, Verkkoniemi-Ahola A. Progressive multifocal leukoencephalopathy: current insights. Degenerative neurological and neuromuscular disease. 2019;9:109.
4. Cortese I, Reich DS, Nath A. Progressive multifocal leukoencephalopathy and the spectrum of JC virus-related disease. Nature Reviews Neurology. 2021;17(1):37-51.
5. Grebenciucova E, Berger JR. Progressive multifocal leukoencephalopathy. Neurologic clinics. 2018;36(4):739-50.
6. Scarpazza C, Signori A, Prosperini L, Sormani MP, Cosottini M, Capra R, et al. Early diagnosis of progressive multifocal leucoencephalopathy: longitudinal lesion evolution. Journal of Neurology, Neurosurgery & Psychiatry. 2019;90(3):261-7.
7. Berger JR, Aksamit AJ, Clifford DB, Davis L, Koralnik IJ, Sejvar JJ, et al. PML diagnostic criteria: consensus statement from the AAN Neuroinfectious Disease Section. Neurology. 2013;80(15):1430-8.

8. Bernal-Cano F, Joseph J, Koralnik I. Spinal cord lesions of progressive multifocal leukoencephalopathy in an acquired immunodeficiency syndrome patient. Journal of neurovirology. 2007;13(5):474-6.
9. Murayi R, Schmitt J, Woo JH, Berger JR. Spinal cord progressive multifocal leukoencephalopathy detected premortem by MRI. Journal of neurovirology. 2015;21(6):688-90.
10. Moll N, Rietsch A, Ransohoff A, Cossoy M, Huang D, Eichler F, et al. Cortical demyelination in PML and MS: similarities and differences. Neurology. 2008;70(5):336-43.
11. Wüthrich C, Koralnik IJ. Frequent infection of cortical neurons by JC virus in patients with progressive multifocal leukoencephalopathy. Journal of Neuropathology & Experimental Neurology. 2012;71(1):54-65.
12. Lima MA, Drislane FW, Koralnik IJ. Seizures and their outcome in progressive multifocal leukoencephalopathy. Neurology. 2006;66(2):262-4.
13. Giovannoni G, Marta M, Davis A, Turner B, Gnanapavan S, Schmierer K. Switching patients at high risk of PML from natalizumab to another disease-modifying therapy. Practical neurology. 2016;16(5):389-93.
14. Kleinschmidt-DeMasters B, Tyler KL. Progressive multifocal leukoencephalopathy complicating treatment with natalizumab and interferon beta-1a for multiple sclerosis. New England Journal of Medicine. 2005;353(4):369-74.
15. Langer-Gould A, Atlas SW, Green AJ, Bollen AW, Pelletier D. Progressive multifocal leukoencephalopathy in a patient treated with natalizumab. New England Journal of Medicine. 2005;353(4):375-81.
16. Sriwastava S, Kataria S, Srivastava S, Kazemlou S, Gao S, Wen S, et al. Disease-modifying therapies and progressive multifocal leukoencephalopathy in multiple sclerosis: A systematic review and meta-analysis. Journal of Neuroimmunology. 2021;360:577721.
17. Bloomgren G, Richman S, Hotermans C, Subramanyam M, Goelz S, Natarajan A, et al. Risk of natalizumab-associated progressive multifocal leukoencephalopathy. New England Journal of Medicine. 2012;366(20):1870-80.
18. Dwyer CM, Jokubaitis VG, Stankovich J, Baker J, Haartsen J, Butzkueven H, et al. High rates of JCV seroconversion in a large international cohort of natalizumab-treated patients. Therapeutic advances in neurological disorders. 2021;14:1756286421998915.
19. Sørensen PS, Bertolotto A, Edan G, Giovannoni G, Gold R, Havrdova E, et al. Risk stratification for progressive multifocal leukoencephalopathy in patients treated with natalizumab. Multiple Sclerosis Journal. 2012;18(2):143-52.
20. Kuesters G, Plavina T, Lee S, Campagnolo D, Richman S, Belachew S, et al. Anti-JC virus (JCV) antibody index differentiates risk of progressive multifocal leukoencephalopathy (PML) in natalizumab-treated multiple sclerosis (MS) patients with no prior immunosuppressant (IS) use: an updated analysis (P4. 031). AAN Enterprises; 2015.
21. Plavina T, Subramanyam M, Bloomgren G, Richman S, Pace A, Lee S, et al. Anti–JC virus antibody levels in serum or plasma further define risk of natalizumab-associated progressive multifocal leukoencephalopathy. Annals of neurology. 2014;76(6):802-12.

22. Berger JR, Cree BA, Greenberg B, Hemmer B, Ward BJ, Dong VM, et al. Progressive multifocal leukoencephalopathy after fingolimod treatment. Neurology. 2018;90(20):e1815-e21.
23. Jordan AL, Yang J, Fisher CJ, Racke MK, Mao-Draayer Y. Progressive multifocal leukoencephalopathy in dimethyl fumarate-treated multiple sclerosis patients. Multiple Sclerosis Journal. 2022;28(1):7-15.
24. Baber U, Bouley A, Egnor E, Sloane JA. Anti-JC virus antibody index changes in rituximab-treated multiple sclerosis patients. Journal of Neurology. 2018;265(10):2342-5.
25. Prezioso C, Grimaldi A, Landi D, Nicoletti CG, Brazzini G, Piacentini F, et al. Risk Assessment of Progressive Multifocal Leukoencephalopathy in Multiple Sclerosis Patients during 1 Year of Ocrelizumab Treatment. Viruses. 2021;13(9):1684.
26. Toorop AA, van Lierop ZY, Strijbis EE, Teunissen CE, Petzold A, Wattjes MP, et al. Mild progressive multifocal leukoencephalopathy after switching from natalizumab to ocrelizumab. Neurology-Neuroimmunology Neuroinflammation. 2021;8(1).
27. Zanghì A, Gallo A, Avolio C, Capuano R, Lucchini M, Petracca M, et al. Exit strategies in natalizumab-treated RRMS at high risk of progressive multifocal leukoencephalopathy: a multicentre comparison study. Neurotherapeutics. 2021;18(2): 1166-74.
28. Van Lierop Z, Toorop A, Coerver E, Willemse E, Strijbis E, Kalkers N, et al. Ocrelizumab after natalizumab in JC-virus positive relapsing remitting multiple sclerosis patients. Multiple Sclerosis Journal–Experimental, Translational and Clinical. 2021;7(2):20552173211013831.
29. Patel A, Sul J, Gordon ML, Steinklein J, Sanguinetti S, Pramanik B, et al. Progressive multifocal leukoencephalopathy in a patient with progressive multiple sclerosis treated with ocrelizumab monotherapy. JAMA neurology. 2021;78(6):736-40.
30. Bartsch T, Rempe T, Leypoldt F, Riedel C, Jansen O, Berg D, et al. The spectrum of progressive multifocal leukoencephalopathy: a practical approach. European Journal of Neurology. 2019;26(4):566-e41.
31. Aksamit AJ. Progressive multifocal leukoencephalopathy. Viral Infections of the Human Nervous System. 2013:65-86.
32. Whiteman M, Post M, Berger J, Tate L, Bell M, Limonte L. Progressive multifocal leukoencephalopathy in 47 HIV-seropositive patients: neuroimaging with clinical and pathologic correlation. Radiology. 1993;187(1):233-40.
33. Sahraian M, Radue EW, Eshaghi A, Besliu S, Minagar A. Progressive multifocal leukoencephalopathy: a review of the neuroimaging features and differential diagnosis. European Journal of Neurology. 2012;19(8):1060-9.
34. Post MJD, Yiannoutsos C, Simpson D, Booss J, Clifford DB, Cohen B, et al. Progressive multifocal leukoencephalopathy in AIDS: are there any MR findings useful to patient management and predictive of patient survival? American Journal of Neuroradiology. 1999;20(10):1896-906.

35. Honce JM, Nagae L, Nyberg E. Neuroimaging of natalizumab complications in multiple sclerosis: PML and other associated entities. Multiple sclerosis international. 2015;2015.
36. Manenti G, Altobelli S, Nezzo M, Antonicoli M, Vasili E, Neroni L, et al. Early magnetic resonance detection of natalizumab-related progressive multifocal leukoencephalopathy in a patient with multiple sclerosis. Case reports in radiology. 2013;2013.
37. Wattjes MP, Wijburg MT, Vennegoor A, Witte BI, de Vos M, Richert ND, et al. MRI characteristics of early PML-IRIS after natalizumab treatment in patients with MS. Journal of Neurology, Neurosurgery & Psychiatry. 2016;87(8):879-84.
38. De Mercanti SF, Gned D, Matta M, Iudicello M, Franchin E, Clerico M. Atypical multiple sclerosis lesions or progressive multifocal Leukoencephalopathy lesions: that is the question. Journal of Investigative Medicine High Impact Case Reports. 2020;8:2324709620939802.
39. Gray F, Chrétien F, Vallat-Decouvelaere AV, Scaravilli F. The changing pattern of HIV neuropathology in the HAART era. Journal of Neuropathology & Experimental Neurology. 2003;62(5):429-40.
40. Corral I, Quereda C, García-Villanueva M, Casado J-L, Pérez-Elías M-J, Navas E, et al. Focal monophasic demyelinating leukoencephalopathy in advanced HIV infection. European neurology. 2004;52(1):36-41.
41. Langford TD, Letendre SL, Marcotte TD, Ellis RJ, McCutchan JA, Grant I, et al. Severe, demyelinating leukoencephalopathy in AIDS patients on antiretroviral therapy. AIDS (London, England). 2002;16(7):1019.
42. Rocke Z, Belyayeva M. Subacute Sclerosing Panencephalitis. 2020.