

BÖLÜM 94

SEKONDER LÖKOENSEFALOPATİLER

Gülcan AKYÜZ YÜCEL¹
Hakkı AKBEYAZ²
Olca ÜNVER³

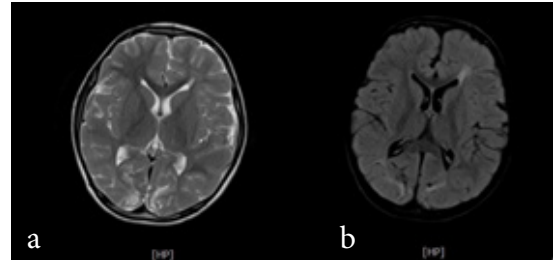
GİRİŞ

Etiyolojileri farklı olmasına rağmen; sekonder lökoensefalopatiler olarak gruplanan hastalıklarda da lökodistofilere benzer görüntüleme bulguları görülebilmektedir. Beyaz cevherde hipoksi ve perinatal etkilenmeler nedeni ile oluşan statik hasarlardan; çevresel, toksik, metabolik, hemodinamik bozukluklara bağlı akut gelişen ve geri dönüşümlü olabilen bazı durumlardan bu bölümde bahsedilecektir.¹

HİPOKSİK İSKEMİK LÖKOENSEFALOPATI

Hipoksik iskemik ensefalopati (HİE) hipoksi, boğulma, hava yolu tıkanıklığı veya kardiyopulmoner arrest gibi ani ve belirgin bir tetikleyici olaydan sonra gelişen lökoensefalopatinin genel bir tanımıdır. Aynı zamanda yenidoğanda; antenatal, perinatal veya postnatal olarak ortaya çıkan hipoksik iskemik olaylar, ensefalopatinin yaygın bir nedenidir.

HİE'nin diğer nedenleri arasında masif kanama veya kardiyak aritmilerin neden olduğu ciddi hipotansiyon ve karbon monoksit zehirlenmesinin neden olduğu hipoksemi yer alır. Hipoksi veya hipotansiyonun süresi ve şiddeti ve hastaya ait faktörler, nörolojik hasarın derecesini önemli bir düzeyde etkiler^{2,3} (**Resim 1**).



Resim 1. Prenatal hipoksi ve hipoglisemiye bağlı lökoensefalopatinin T2 ve FLAIR aksiyel kesitlerde MRI görüntüleri. Beş yaşında erkek hasta, hafif nöromotor gerilik, az görme ve nöbet şikayetleri ile başvurdu. Term asfiktik doğan hastanın yenidoğan yoğun bakım yatışında hipoglisemi öyküsü de mevcuttu.

PERİVENTRİKÜLER LÖKOMALAZİ

Periventriküler lökomalazi (PVL) veya periventriküler bölgeleri etkileyen prematüre beyaz cevher hasarı, en sık 30 gestasyon haftası veya 1500 gram altında doğum ağırlığı ile doğan bebeklerde görülür. Etkilenme derecesine göre serebral palsi, zihinsel yetersizlik ve görme yolları kusurları ile nitelenir.^{4,5}

Patolojisinde özellikle prematürelerde periventriküler alanda bulunan sulama alanlarındaki bozulmuş perfüzyondan kaynaklanan hipoksik-iskemik lezyonların bir sonucu olarak ortaya çıkar. Benzer şekilde enfeksiyon veya vaskülitin

¹ Uzm. Dr., Sancaktepe Şehit Profesör Dr. İlhan Varank Eğitim ve Araştırma Hastanesi, Çocuk Nörolojisi Kliniği
gulcan.akyuz@hotmail.com

² Arş. Gör., Marmara Üniversitesi Pendik Eğitim ve Araştırma Hastanesi Çocuk Nörolojisi Kliniği hakkakbeyaz@gmail.com

³ Doç. Dr., Marmara Üniversitesi Pendik Eğitim ve Araştırma Hastanesi Çocuk Nörolojisi Kliniği olcaymd@hotmail.com

İlaç veya toksin kaynaklı lökoensefalopati tablosunda hızlı tanının önemi büyüktür. Temel tedavi prensibi ajandan uzaklaşmak veya ajanın kesilmesidir. Ancak ilaçlar söz konusu olduğunda; ilacın devam etmesi veya kesilmesi, hastanın kliniği ve ilacın gerekliliği düşünülerek karar verilmelidir.

KAYNAKLAR

1. Victoria San Antonio Arce JCP, Alexis Arzimanoglou and Robert Ouvrier. *Aicardi's Diseases of the Nervous System in Childhood*. Arzimanoglou A, editor: Mac Keith Press; 2018.
2. Abend NS, Licht DJ. Predicting outcome in children with hypoxic ischemic encephalopathy. *Pediatr Crit Care Med*. 2008;9(1):32-9.
3. Jacinto SJ, Gieron-Korthals M, Ferreira JA. Predicting outcome in hypoxic-ischemic brain injury. *Pediatr Clin North Am*. 2001;48(3):647-60.
4. Volpe JJ. Neurobiology of Periventricular Leukomalacia in the Premature Infant. *Pediatric Research*. 2001;50(5):553-62.
5. Di Muzio B, Knipe, H. Periventricular leukomalacia. Reference article, *Radiopaedia.org*. 2022 [
6. van der Knaap MS, Vermeulen G, Barkhof F, Hart AA, Loeber JG, Weel JF. Pattern of white matter abnormalities at MR imaging: use of polymerase chain reaction testing of Guthrie cards to link pattern with congenital cytomegalovirus infection. *Radiology*. 2004;230(2):529-36.
7. Krakar G, Đaković I, Delin S, Bošnjak VM. Evolutive leukoencefalopathy in congenital cytomegalovirus infection. *J Child Neurol*. 2015;30(1):93-5.
8. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. *The New England journal of medicine*. 1996;334(8):494-500.
9. Ay H, Buonanno FS, Schaefer PW, Le DA, Wang B, Gonzalez RG, et al. Posterior leukoencephalopathy without severe hypertension: utility of diffusion-weighted MRI. *Neurology*. 1998;51(5):1369-76.
10. Ito Y, Arahata Y, Goto Y, Hirayama M, Nagamitsu M, Yasuda T, et al. Cisplatin neurotoxicity presenting as reversible posterior leukoencephalopathy syndrome. *AJNR American journal of neuroradiology*. 1998;19(3):415-7.
11. Brightman MW, Klatzo I, Olsson Y, Reese TS. The blood-brain barrier to proteins under normal and pathological conditions. *Journal of the neurological sciences*. 1970;10(3):215-39.
12. Kalimo H, Fredriksson K, Nordborg C, Auer RN, Olsson Y, Johansson B. The spread of brain oedema in hypertensive brain injury. *Medical biology*. 1986;64(2-3):133-7.
13. Gao B, Lyu C, Lerner A, McKinney AM. Controversy of posterior reversible encephalopathy syndrome: what have we learnt in the last 20 years? *Journal of neurology, neurosurgery, and psychiatry*. 2018;89(1):14-20.
14. Rabinstein AA, Mandrekar J, Merrell R, Kozak OS, Durosaro O, Fugate JE. Blood pressure fluctuations in posterior reversible encephalopathy syndrome. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2012;21(4):254-8.
15. Covarrubias DJ, Luetmer PH, Campeau NG. Posterior reversible encephalopathy syndrome: prognostic utility of quantitative diffusion-weighted MR images. *AJNR American journal of neuroradiology*. 2002;23(6):1038-48.
16. Stott VL, Hurrell MA, Anderson TJ. Reversible posterior leukoencephalopathy syndrome: a misnomer reviewed. *Internal medicine journal*. 2005;35(2):83-90.
17. Junna MR, Rabinstein AA. Tacrolimus induced leukoencephalopathy presenting with status epilepticus and prolonged coma. *Journal of neurology, neurosurgery, and psychiatry*. 2007;78(12):1410-1.
18. Lee VH, Wijdicks EF, Manno EM, Rabinstein AA. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. *Archives of neurology*. 2008;65(2):205-10.
19. Lysandropoulos AP, Rossetti AO. Postictal cortical visual impairment: a symptom of posterior reversible encephalopathy. *Epilepsy & behavior : E&B*. 2010;17(2):276-7.
20. Kastrup O, Gerwig M, Frings M, Diener HC. Posterior reversible encephalopathy syndrome (PRES): electroencephalographic findings and seizure patterns. *Journal of neurology*. 2012;259(7):1383-9.
21. Kozak OS, Wijdicks EF, Manno EM, Miley JT, Rabinstein AA. Status epilepticus as initial manifestation of posterior reversible encephalopathy syndrome. *Neurology*. 2007;69(9):894-7.
22. Oppenheim C, Logak M, Dormont D, Lehericy S, Manai R, Samson Y, et al. Diagnosis of acute ischemic stroke with fluid-attenuated inversion recovery and diffusion-weighted sequences. *Neuroradiology*. 2000;42(8):602-7.
23. Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. *Mayo Clinic proceedings*. 2010;85(5):427-32.
24. Mueller-Mang C, Mang T, Pirker A, Klein K, Prchla C, Prayer D. Posterior reversible encephalopathy syndrome: do predisposing risk factors make a difference in MRI appearance? *Neuroradiology*. 2009;51(6):373-83.
25. Kupferschmidt H, Bont A, Schnorf H, Landis T, Walter E, Peter J, et al. Transient cortical blindness and bioccipital brain lesions in two patients with acute intermittent porphyria. *Annals of internal medicine*. 1995;123(8):598-600.
26. Bakshi R, Bates VE, Mechtler LL, Kinkel PR, Kinkel WR. Occipital lobe seizures as the major clinical manifestation of reversible posterior leukoencephalopathy syndrome: magnetic resonance imaging findings. *Epilepsia*. 1998;39(3):295-9.
27. Datar S, Singh T, Rabinstein AA, Fugate JE, Hocker S. Long-term risk of seizures and epilepsy in patients with posterior reversible encephalopathy syndrome. *Epilepsia*. 2015;56(4):564-8.
28. Baldini M, Bartolini E, Gori S, Bonanni E, Cosottini M, Iudice A, et al. Epilepsy after neuroimaging normalization in a woman with tacrolimus-related pos-

- terior reversible encephalopathy syndrome. *Epilepsy & behavior* : E&B. 2010;17(4):558-60.
29. Gijtenbeek JM, van den Bent MJ, Vecht CJ. Cyclosporine neurotoxicity: a review. *Journal of neurology*. 1999;246(5):339-46.
 30. Hauben M. Cyclosporine neurotoxicity. *Pharmacotherapy*. 1996;16(4):576-83.
 31. Schwartz RB, Bravo SM, Klufas RA, Hsu L, Barnes PD, Robson CD, et al. Cyclosporine neurotoxicity and its relationship to hypertensive encephalopathy: CT and MR findings in 16 cases. *AJR American journal of roentgenology*. 1995;165(3):627-31.
 32. Rimkus Cde M, Andrade CS, Leite Cda C, McKinney AM, Lucato LT. Toxic leukoencephalopathies, including drug, medication, environmental, and radiation-induced encephalopathic syndromes. *Semin Ultrasound CT MR*. 2014;35(2):97-117.
 33. Koksel Y, Ozutemiz C, Rykken J, Ott F, Cayci Z, Oswood M, et al. "CHOICES": An acronym to aid in delineating potential causes of non-metabolic, non-infectious acute toxic leukoencephalopathy. *Eur J Radiol Open*. 2019;6:243-57.
 34. Beitinjaneh A, McKinney AM, Cao Q, Weisdorf DJ. Toxic leukoencephalopathy following fludarabine-associated hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2011;17(3):300-8.
 35. Luckman J, Zahavi A, Efrati S, Gilad G, Snir M, Michowitz S, et al. Difficulty in Distinguishing Posterior Reversible Encephalopathy Syndrome, Hypoxic-Ischemic Insult, and Acute Toxic Leukoencephalopathy in Children. *Neuropediatrics*. 2016;47(1):33-8.
 36. Abeyakoon O, Batty R, Mordekar S, Raghavan A, Sinha S, Griffiths PD, et al. The encephalopathic child. *Neuroradiol J*. 2011;24(4):483-502.
 37. Kumar Y, Drumsta D, Mangla M, Gupta N, Hooda K, Almast J, et al. Toxins in Brain! Magnetic Resonance (MR) Imaging of Toxic Leukoencephalopathy - A Pictorial Essay. *Pol J Radiol*. 2017;82:311-9.
 38. Filley CM. Toxic leukoencephalopathy. *Clin Neuropatharmacol*. 1999;22(5):249-60.
 39. McKinney AM, Kieffer SA, Paylor RT, SantaCruz KS, Kendi A, Lucato L. Acute toxic leukoencephalopathy: potential for reversibility clinically and on MRI with diffusion-weighted and FLAIR imaging. *AJR Am J Roentgenol*. 2009;193(1):192-206.
 40. Akiba T, Okeda R, Tajima T. Metabolites of 5-fluorouracil, alpha-fluoro-beta-alanine and fluoroacetic acid, directly injure myelinated fibers in tissue culture. *Acta Neuropathol*. 1996;92(1):8-13.
 41. Okeda R, Shibutani M, Matsuo T, Kuroiwa T, Shimokawa R, Tajima T. Experimental neurotoxicity of 5-fluorouracil and its derivatives is due to poisoning by the monofluorinated organic metabolites, monofluoroacetic acid and alpha-fluoro-beta-alanine. *Acta Neuropathol*. 1990;81(1):66-73.
 42. Shibutani M, Okeda R. Experimental study on subacute neurotoxicity of methotrexate in cats. *Acta Neuropathol*. 1989;78(3):291-300.
 43. McKinney AM, Short J, Truwit CL, McKinney ZJ, Kozak OS, SantaCruz KS, et al. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. *AJR Am J Roentgenol*. 2007;189(4):904-12.
 44. Filley CM, McConnell BV, Anderson CA. The Expanding Prominence of Toxic Leukoencephalopathy. *J Neuropsychiatry Clin Neurosci*. 2017;29(4):308-18.
 45. Iyer RS, Chaturvedi A, Pruthi S, Khanna PC, Ishak GE. Medication neurotoxicity in children. *Pediatric Radiology*. 2011;41(11):1455.
 46. Sandoval C, Kutscher M, Jayabose S, Tenner M. Neurotoxicity of intrathecal methotrexate: MR imaging findings. *AJNR Am J Neuroradiol*. 2003;24(9):1887-90.
 47. Fisher MJ, Khademian ZP, Simon EM, Zimmerman RA, Bilaniuk LT. Diffusion-weighted MR imaging of early methotrexate-related neurotoxicity in children. *AJNR Am J Neuroradiol*. 2005;26(7):1686-9.
 48. Gowan GM, Herrington JD, Simonetta AB. Methotrexate-induced toxic leukoencephalopathy. *Pharmacotherapy*. 2002;22(9):1183-7.
 49. Bernini JC, Fort DW, Griener JC, Kane BJ, Chappell WB, Kamen BA. Aminophylline for methotrexate-induced neurotoxicity. *Lancet*. 1995;345(8949):544-7.
 50. Lee EQ. Overview of neurologic complications of conventional non-platinum cancer chemotherapy. <https://www.uptodate.com/contents/overview-of-neurologic-complications-of-conventional-non-platinum-cancer-chemotherapy>.
 51. Reece DE, Frei-Lahr DA, Shepherd JD, Dorovini-Zis K, Gascoyne RD, Graeb DA, et al. Neurologic complications in allogeneic bone marrow transplant patients receiving cyclosporin. *Bone Marrow Transplant*. 1991;8(5):393-401.
 52. Bartynski WS, Zeigler Z, Spearman MP, Lin L, Shaddock RK, Lister J. Etiology of cortical and white matter lesions in cyclosporin-A and FK-506 neurotoxicity. *AJNR Am J Neuroradiol*. 2001;22(10):1901-14.
 53. Trullemans F, Grignard F, Van Camp B, Schots R. Clinical findings and magnetic resonance imaging in severe cyclosporine-related neurotoxicity after allogeneic bone marrow transplantation. *Eur J Haematol*. 2001;67(2):94-9.
 54. Ahmed A, Loes DJ, Bressler EL. Reversible magnetic resonance imaging findings in metronidazole-induced encephalopathy. *Neurology*. 1995;45(3 Pt 1):588-9.
 55. Heaney CJ, Campeau NG, Lindell EP. MR imaging and diffusion-weighted imaging changes in metronidazole (Flagyl)-induced cerebellar toxicity. *AJNR Am J Neuroradiol*. 2003;24(8):1615-7.
 56. Kim E, Na DG, Kim EY, Kim JH, Son KR, Chang KH. MR imaging of metronidazole-induced encephalopathy: lesion distribution and diffusion-weighted imaging findings. *AJNR Am J Neuroradiol*. 2007;28(9):1652-8.
 57. Dracopoulos A, Widjaja E, Raybaud C, Westall CA, Snead OC, 3rd. Vigabatrin-associated reversible MRI signal changes in patients with infantile spasms. *Epilepsia*. 2010;51(7):1297-304.
 58. Wheless JW, Carmant L, Bebin M, Conry JA, Chiron C, Elterman RD, et al. Magnetic resonance imaging abnormalities associated with vigabatrin in patients with epilepsy. *Epilepsia*. 2009;50(2):195-205.
 59. de Oliveira AM, Paulino MV, Vieira APF, McKinney AM, da Rocha AJ, Dos Santos GT, et al. Imaging Patterns of Toxic and Metabolic Brain Disorders. *Radiographics : a review publication of the Radiological Society of North America, Inc*. 2019;39(6):1672-95.