Bölüm 8

KRONİK NÖROLOJİK HASTALIKLARDA PERİFERİK İNFLAMASYON BİYOBELİRTEÇLERİNİN YERİ VE ÖNEMİ

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GİRİŞ

Platelet/lenfosit (PLR), monosit/lenfosit (MLR), nötrofil/lenfosit (NLR), C-Reaktif protein ve C-Reaktif protein/albümin (CAR) oranı düzeyleri periferik inflamasyonun biyobelirteci olarak, kolay ulaşılabilir, ucuz ve basit testler olmaları nedeniyle son yıllarda farklı hastalık gruplarında sık olarak kullanılmaya başlanmıştır.

Kronik nörolojik hastalıklarda ilgili parametreler, IL-6, IL-1β ve TNF-α gibi inflamatuvar sitokinlerle karşılaştırıldığında daha kolay ulaşılabilir olmaları nedeniyle prognostik ve trombo-inflamatuvar biyobelirteçler olarak sık kullanılmaya başlanılmıştır [1-5].

NLR başta olmak üzere, PLR, MLR çalışmalarda periferik inflamasyonun biyobelirteci olarak tanımlanmıştır [2-4]. NLR, farklı hastalıklarda prognozun bir göstergesi olarak sıkça kullanılmaktadır. Daha yüksek NLR değerlerinin akut iskemik inme, kardiyak bozukluklar ve kanser hastalarında daha kötü prognozun bağımsız bir öngörücüsü olduğu gösterilmiştir [4-7]. Benzer şekilde, artan PLR'nin, akut inme ve kanserli hastalarda kötü prognozu belirlemede kullanılabileceği bildirilmiştir [7,8].

Bu çalışmada, Alzheimer Hastalığı (AH) ve Parkinson Hastalığı (PH) başta olmak üzere kronik nörolojik hastalıklarda, NLR, MLR, PLR, CRP ve CAR düzeylerinin değerlendirildiği çalışmaların taranması ile ilgili hastalıkların etiyolojisinde periferik inflamasyonun yeri ve öneminin değerlendirilmesi amaçlanmıştır.

ALZHEİMER TİPİ DEMANS TANILI HASTALARDA PERİFERİK İNFLAMASYON BİYOBELİRTEÇLERİ

Demans, kronik, progresif seyirli bir hastalıktır. Yaşla ilişkili unutkanlık, hafif kognitif yetmezlik gibi daha basit tablolardan hafif, orta, ağır demans evrelerine kadar değişik oranda bilişsel ve günlük yaşam aktivitesi kaybı ile karakterizedir [9].

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roz ve optik nöropati tanılılarda Bisgaard ve ark., myasteni gravis tanılı hastalarda Yang ve ark. serum NLR düzeylerinin yüksek olduğunu bildirmişlerdir [55,56].

Benzer şekilde Huang ve ark. Guillain-Barré sendromu tanılı hastalarda NLR ve MLR düzeylerinin sağlıklı kontrollerden daha yüksek olduğunu ve hastalık prognozunda bu verinin önemli olabileceğini bildirmişlerdir [2].

Özdemir ve ark. konvulsif status epileptikuslu hastalarda serum albümin düzeylerinin anlamlı derecede düşük olduğunu ve NLR' nin akut dönemde anlamlı olarak daha yüksek olduğunu bildirmişlerdir [57].

ÖNERİLER

NLR, MLR, PLR, CRP ve CAR düzeyleri AH ve PH başta olmak üzere kronik nörolojik hastalıkların değerlendirilmesinde kolay ulaşılabilir, az maliyetli parametreler olmaları nedeniyle önemlidirler.

Kronik nörolojik hastalıkların tanı ve tedavisine katkıları olabileceği hipotezine dayanarak ilgili hastalıklarda periferik inflamasyon biyobelirteçlerinin değerlendirileceği geniş populasyonlu, prospektif çalışmalara ihtiyaç vardır.

KAYNAKLAR

1. Akıl E, Bulut A, Kaplan İ, Özdemir HH, Arslan D, Aluçlu MU. The increase of carcinoembryonic antigen (CEA), high-sensitivity C-reactive protein, and neutrophil/lymphocyte ratio in Parkinson's disease. Neurol Sci. 2015 Mar; 36(3): 423-8. doi:10.1007/s10072-014-1976-1.
2. Huang Y, Ying Z, Quan W, Xiang W, Xie D, Weng Y, et al. The clinical significance of neutrophil-to-lymphocyte ratio and monocyte-to-lymphocyte ratio in Guillain–Barré syndrome, Int J Neurosci. 2018; 128:8, 729-735, DOI: 10.1080/00207454.2017.1418342.
3. Ozdemir HH. Analysis of the albumin level, neutrophil-lymphocyte ratio, and platelet-lymphocyte ratio in Guillain-Barré syndrome. Arq Neuropsiquiatr. 2016 Sep;74(9):718-722. doi: 10.1590/0004-282X20160132
4. Akıl E, Akıl MA, Varol S, Özdemir HH, Yücel Y, Arslan D et al. Echocardiographic epicardial fat thickness and neutrophil to lymphocyte ratio are novel inflammatory predictors of cerebral ischemic stroke. J Stroke Cerebrovasc Dis. 2014;23(9):2328-34. doi:10.1016/j.jstrokecerebrovasdis.2014.04.028
5. Park MG, Kim MK, Chae SH, Kim HK, Han J, Park KP. Lymphocyte-to-monocyte ratio on day 7 is associated with outcomes in acute ischemic stroke. Neurol Sci. 2018 Feb;39(2):243-249. doi: 10.1007/s10072-017-3163-7.
6. Qun S, Tang Y, Sun J, Liu Z, Wu J, Zhang J, et al. Neutrophil-To-Lymphocyte Ratio Predicts 3-Month Outcome of Acute Ischemic Stroke. Neurotox Res. 2017 Apr;31(3):444-452. doi: 10.1007/s12640-017-9707-z.
7. Auezova R, Ryskeldiev N, Doskaliyev A, Kuanyshev Y, Zhetpisbaev B, Aldiyarova N et al. Association of preoperative levels of selected blood inflammatory markers with prognosis in gliomas. Onco Targets Ther. 2016 Oct 11;9:6111-6117.
8. Altintas O, Altintas MO, Tasal A, Kucukdagli OT, Asil T. The relationship of platelet-to-lymphocyte ratio with clinical outcome and final infarct core in acute ischemic stroke patients who have undergone endovascular therapy. Neurol Res. 2016;38(9):759–765.
9. Koca E, Taşkapılıoğlu Ö, Bakar M. Caregiver Burden in Different Stages of Alzheimer's Disease.

Arch Neuropsychiatry 2017; 54: 82-6.

10. Kuyumcu ME, Yesil Y, Ozturk ZA, Kizilarslanoğlu C, Etgül S, Halil M, et al. The Evaluation of Neutrophil-Lymphocyte Ratio in Alzheimer's Disease. Dement Geriatr Cogn Disord 2012;34:69-74

11. Saleem M, Herrmann N, Swardfager W, Eisen R, Lanktot KL. İnflammatory markers in mild cognitive impairment: a meta analysis. J Alzheimer's Dis 2015;47(3):669-679

12. Cankurtaran M, Yesil Y, Kuyumcu ME, Ozturk ZA, Yavuz BB, Halil M, et al. Altered levels of homocysteine and serum natural antioxidants links oxidative damage to Alzheimer's disease. J Alzheimers Dis. 2013; 33 (4): 1051–1058.

13. Alexiou A, Soursou G, Yarla NS, Ashraf G.. Proteins commonly linked to autism spectrum disorder and Alzheimer's disease. Curr Protein Pept Sci. 2018; 19(9):876-880.

14. Rembach A, Watt AD, Wilson WJ, Rainey- Smith S, Ellis K, Rowe CC, et al. An increased neutrophil lymphocyte ratio in Alzheimer's disease is a function of age and is weakly correlated with neocortical amyloid accumulation. J Neuroimmunol. 2014;273:65–71. doi:10.1016/j.jneuroim. 2014.05.005.

15. Kalelioglu T, Yuruyen M, Gultekin G, Yavuzer H, Öztürk Y, Kurt M, et al. The neutrophil and platelet to lymphocyte ratios in people with subjective, mild cognitive impairment and early Alzheimer's disease Psychogeriatrics. 2017 Nov;17(6):506-508. doi: 10.1111/psyg.12260.

16. Iwamoto N, Nishiyama E, Ohwada J, Arai H. Demonstration of CRP immunoreactivity in brains of Alzheimer's disease: immunohistochemical study using formic acid pretreatment of tissue sections.Neurosci Lett. 1994 Aug 15; 177 : 23–6.

17. Bredesen DE. Metabolic profiling distinguishes three subtypes of Alzheimer's disease. Aging (Albany NY) 2015 Aug; 7(8): 595–600.

18. Luan YY, Yao YM. The Clinical Significance and Potential Role of C-Reactive Protein in Chronic Inflammatory and Neurodegenerative Diseases. Front Immunol. 2018 Jun 7;9:1302

19. Nadrowski P, Chudek J, Skrzypek M, Puzianowska-Kuznicka M, Mossakowska M, Wiecek A, et al. Associations between cardiovascular disease risk factors and IL-6 and hsCRP levels in the elderly. Exp Gerontol. 2016 Dec 1; 85:112–7.

20. Taheri S, Baradaran A, Aliakbarian M, Mortazavi M. Level of inflammatory factors in chronic hemodialysis patients with and without cardiovascular disease. J Res Med Sci. 2017 April 26 ;22:47. doi: 10.4103/jrms.JRMS_282_15.

21. Towfighi A, Cheng EM, Ayala-Rivera M, McCreath H, Sanossian N, Dutta T, et al. Randomized controlled trial of a coordinated care intervention to improve risk factor control after stroke or transient ischemic attack in the safety net: secondary stroke prevention by uniting community and chronic care model teams early to end disparities (SUCCEED). BMC Neurol. 2017 17(1):24. doi: 10.1186/s12883-017-0792-7.

22. Mancinella A, Mancinella M, Carpinteri G, Bellomo A, Fossati C, Gianturco V, et al. Is there a relationship between high C-reactive protein (CRP) levels and dementia? Arch Gerontol Geriatr. 2009;49 Suppl 1:185-94.

23. Kalia LV, Lang AE. Parkinson's disease. Lancet. 2015; 386(9996): 896–912. doi: 10.1016/S0140-6736(14)61393-3.

24. Torun Ş, Uysal M, Gücüyener D, Özdemir G. Parkinson's disease in Eskişehir, Turkey. Eur J Neurol 1995; 2(suppl 1): 44-45.

25. Blesa J, Trigo-Damas I, Quiroga-Varela A, Jackson-Lewis VR. Oxidative stress and Parkinson's disease. Front Neuroanat. 2015; 9: 91 doi: 10.3389/fnana.2015.00091.

26. Kaur K, Gill JS, Bansal PK, Deshmukh R. Neuroinflammation - A major cause for striatal dopaminergic degeneration in Parkinson's disease. J Neurol Sci. 2017 Oct 15;381:308-314. doi: 10.1016/j.jns.2017.08.3251.

27. Pankratz N, Foroud T. Genetics of Parkinson Disease. NeuroRx. 2004 Apr; 1(2): 235–242. Doi: 10.1602/neurorx.1.2.235.

28. Gallagher DA, Schapira AH. Etiopathogenesis and treatment of Parkinson's disease. Curr Top Med Chem. 2009;9(10):860-8.

29. Sanjari Moghaddam H, Ghazi Sherbaf F, Mojtahed Zadeh M, Ashraf-Ganjouei A, Aarabi MH. Association Between Peripheral Inflammation and DATSCAN Data of the Striatal Nuclei in Different Motor Subtypes of Parkinson Disease. Front Neurol. 2018 Apr 16;9:234. doi: 10.3389/fneur.2018.00234.

30. Uçar AC, Gökçe Çokal B, Ünal Artık HA, İnan LE, Yoldaş TK. Comparison of neutrophil-lymphocyte ratio (NLR) in Parkinson's disease subtypes. Neurol Sci. 2017; 38:287. Doi: https://doi.org/10.1007/s10072-016-2758-8.

31. Kutluk K. İskemik İnme; Yozbatıran N. Rehabilitasyon, Nobel Tıp Kitabevi, İstanbul, 2004; 237-52.

32. Köklü E, Yüksel İÖ, Arslan Ş, Bayar N, Çağırcı G, Gencer ES, et al. Is Elevated Neutrophil-to-Lymphocyte Ratio a Predictor of Stroke in Patients with Intermediate Carotid Artery Stenosis? J Stroke Cerebrovasc Dis. 2016 Mar; 25 (3): 578-84. doi: 10.1016/ j.jstrokecerebrovasdis.2015.10.031.

33. Akboğa YE, Bektas H, Anlar O. Usefulness of platelet lymphocyte and neutrophil to lymphocyte ratios in predicting the presence of serebral venous sinüs thrombosis and in-hospital majör adverse cerebral events. J Neurol Sci. 2017 Sep15: 380:226-229.

34. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, spesial considerations and epidemiology. Sleep Med. 2003 Mar;4(2): 101-19.

35. Yeh P, Walters AS, Tsuang JW. Restless legs syndrome: a comprehensive overview on its epidemiology, risk factors, and treatment. Sleep Breath. 2012;16(4):987–1007.

36. Alsafadi S, Abaalkhail B, Wali SO, Aljammali K, Alotaiby B,Zakaria I, Sabbahi H. Risk factors of primary and secondary restless legs syndrome among a middle-aged population in Saudi Arabia: A community-based study. Ann Thorac Med. 2018;13(3):175-181.

37. Hwang IC, Na KS, Lee YJ, Kang SG. Higher Prevalence of Hypertension among Individuals with Restless Legs Syndrome: A Meta-Analysis. Psychiatry Investig. 2018;15(7):701-709.

38. Cho CH, Kim L, Lee HJ. Individuals with Restless Legs Syndrome Tend to have Severe Depressive Symptoms: Findings from a Community-Based Cohort Study. Psychiatry Investig. 2017;14(6):887-893.

39. Varım C, Acar BA, Uyanık MS, Acar T, Alagöz N, Nalbant A, et al. Association between the neutrophil-to-lymphocyte ratio, a new marker of systematic inflammation, and restless legs syndrome. Singapore Med J 2016;57(9):514-516. doi: 10.11622/smedj.2016154.

40. Tak AZA, Şengül Y. Evaluation of Inflammation with Neutrophil-to-lymphocyte Ratio and Platelet-to-lymphocyte Ratio in Restless Legs Syndrome. Turk J Neurol. 2018; 24(3): 259-263.

41. Trotti LM, Rye DB, De Staercke C, Hooper WC, Quyyumi A, Bliwise DL. Elevated C-reactive protein is associated with severe periodic leg movements of sleep in patients with restless legs syndrome. Brain Behav Immun. 2012 Nov;26(8):1239-43. doi: 10.1016/j.bbi.2012.06.003.

42. Higuchi T, Abe M, Mizuno M, Yamazaki T, Suzuki H, Moriuchi M, et al. Association of restless legs syndrome with oxidative stress and inflammation in patients undergoing hemodialysis. Sleep Med. 2015 Aug;16(8):941-8. doi: 10.1016/j.sleep.2015.03.025.

43. Benediktsdottir B, Janson C, Lindberg E, Arnardottir ES, Olafsson I, Cook E, et al. Prevalence of restless legs syndrome among adults in Iceland and Sweden: Lung function, comorbidity, ferritin, biomarkers and quality of life. Sleep Med. 2010;11:1043–1048. doi: 10.1016/j.sleep.2010.08.006

44. Berger K, von Eckardstein A, Trenkwalder C, Rothdach A, Junker R, Weiland SK. Iron metabolism and the risk of restless legs syndrome in an elderly general population--the MEMO-Study. J Neurol. 2002; 249:1195–1199. DOI: 10.1007/s00415-002-0805-2

45. Neves PD, Graciolli FG, Oliveira IB, Bridi RA, Moysés RM, Elias RM. Effect of Mineral and Bone Metabolism on Restless Legs Syndrome in Hemodialysis Patients. J Clin Sleep Med. 2017;13(1):89-94. doi:10.5664/jcsm.6396

46. Gade K, Blaschke S, Rodenbeck A, Becker A, Anderson-Schmidt H, Cohrs S. Uremic restless legs syndrome (RLS) and sleep quality in patients with end-stage renal disease on hemo-

dialysis: potential role of homocysteine and parathyroid hormone. Kidney Blood Press Res. 2013;37(4-5):458-63. doi: 10.1159/000355727.

47. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013 Jul;33(9):629-808. doi: 10.1177/0333102413485658.

48. Kelman L. The premonitory symptoms (prodrome): a tertiary care study of 893 migraineurs. Headache 2004;44(9):865-872.

49. Charles A. The pathophysiology of migraine: implications for clinical management. Lancet Neurol. 2018 Feb;17(2): 174-182. doi: 10.1016/S1474-4422(17)30435-0.

50. Ramachandran R. Neurogenic inflammation and its role in migraine. Semin Immunopathol. 2018 May;40(3):301-314. doi: 10.1007/s00281-018-0676-y.

51. Zeller JA, Lindner V, Frahm K, Baron R, Deuschl G. Platelet activation and platelet-leucocyte interaction in patients with migraine. Subtype differences and influence of triptans. Cephalalgia. 2005;25:536–541.

52. Varol S, Akıl E, Çevik MU. Investigation of mean platelet volume and platelet count in the blood of patients with migraine. Turk J Neurol. 2013; 19(3): 90-92 | DOI: 10.4274/Tnd.88156.

53. Karabulut KU, Egercioglu TU, Uyar M, Ucar Y. The change of neutrophils/lymphocytes ratio in migraine attacks: A case-controlled study. Ann Med Surg (Lond). 2016 Jul 27;10:52-6. doi: 10.1016/j.amsu.2016.07.023.

54. Eryigit U, Altunayoglu Cakmak V, Sahin A, Tatli O, Pasli S, Gazioglu G, Karaca Y. The diagnostic value of the neutrophil-lymphocyte ratio in distinguishing between subarachnoid hemorrhage and migraine. Am J Emerg Med. 2017 Sep;35(9):1276-1280. doi: 10.1016/j.ajem.2017.03.063).

55. Bisgaard AK, Pihl-Jensen G, Frederiksen JL.The neutrophil-to-lymphocyte ratio as disease actvity marker in multiple sclerosis and optic neuritis. Mult Scler Relat Disord. 2017 Nov;18:213-217. doi: 10.1016/j.msard.2017.10.009.

56. Yang DH, Qian MZ, Wei MM, Li J, Yu MM, Lu XM, et al. The correlation of neutrophil-to-lymphocyte ratio with the presence and activity of myasthenia gravis. Oncotarget. 2017 Jun 16;8(44):76099-76107. doi: 10.18632/oncotarget.18546.

57. Ozdemir HH, Akil E, Acar A, Tamam Y, Varol S, Cevik MU, et al. Changes in serum albumin levels and neutrophil–lymphocyte ratio in patients with convulsive status epilepticus, Int J Neurosci. 2017; 127:5, 417-420. Doi: 10.1080/00207454.2016.118760