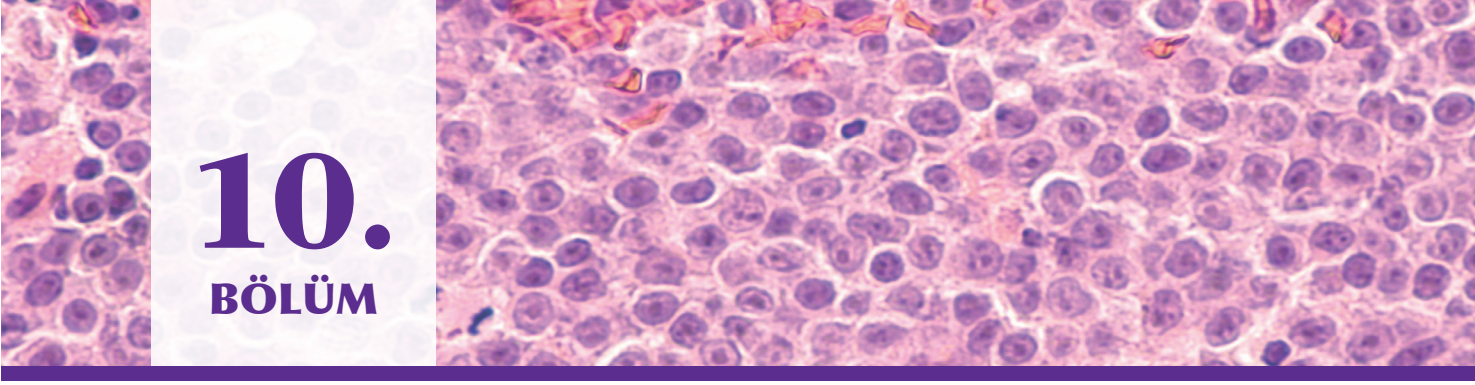

10.
BÖLÜM

# BURKITT LENFOMA

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## GİRİŞ

Burkitt lenfoma (BL), ilk olarak 1958 yılında Dennis Burkitt tarafından Afrikalı çocuklarda yüz ve abdomen bölgesinde gelişen bir sarkom olarak tanımlanmıştır (1). 1960 yılında ise O'Conor ve Davies, hızlı büyüyen bu lezyonların sarkom olmadığını, lenfoma olduğunu bildirmiştir (2).

Burkitt lenfoma, olgun germinal merkez ya da postgerminal merkez B hücrelerinden kaynaklanan, agresif seyreden ve tedavi edilebilen bir lenfomadır (3). Sıklıkla ekstranodal bölge tutulumu ile ya da akut lösemi formunda prezente olur (4). Çok hızlı büyüme kapasitesine sahip olan bu tümör, *MYC* onkogen rearanjmanı göstermesi ile karakterizedir. BL'da en sık görülen kromozomal translokasyon olan t(8;14)(q24;q32) translokasyonu, *MYC* onkogeninin bulunduğu 8. kromozomun uzun kolu ile 14. kromozomun Ig ağır zincir bölgesi ile ilişkilidir (5).

2016 Dünya Sağlık Örgütü (DSÖ) hematopoetik ve lenfoid doku tümörlerinin sınıflandırılması kitapçığında, daha önceden BL'nın da içinde bulunduğu agresif B hücreli lenfomalar morfolojik ve genetik özellikleri baz alınarak tekrardan sınıflandırılmıştır. BL kendine has immunofenotipik özellikleri ve c-myc overekspresyonu göstermesi ile diğerlerinden ayrılmış, BL benzeri özellikler sergileyen diğer lenfomalar; 'Burkitt'e benzer 11 q anomalisi olan lenfoma', 'Yüksek dereceli B-hücreli lenfoma, *MYC*, *BCL*-2 ve/veya *BCL*-6 re-aranjmanı içeren' ve 'Yüksek dereceli B hücreli lenfoma, sınıflandırılamayan' olarak yeniden sınıflandırılmıştır (6).

## EPİDEMİYOLOJİ

BL, coğrafik dağılımı, klinik, morfolojik, genetik ve biyolojik özelliklerine göre farklılık gösteren 3 epidemiyolojik varyanta sahiptir; endemik (Afrika tipi) BL, sporadik BL, immünyetmezlik-ilişkili BL (6).

Endemik BL, Afrika'nın tropikal bölgelerinde ve Papua Yeni Gine'de saptanan ve özellikle çocuklarda görülen subtiptir (7). Endemik BL'nın insidansı ekvotaral Afrika'da 18 yaş altı her 100.000 çocukta 4-5'tir (8). Bu bölgedeki çocukluk çağı tümörlerinin %50'sinden, çocukluk çağı lenfomalarının %90'ından sorumlu olan BL, en sık 4-7 yaş arası çocuklarda görülmektedir (4, 9). Erkeklerde kadınlara göre 2 kat daha sıktır (4, 9). Olguların hemen tamamında (>%95) Epstein-Barr virüs (EBV) pozitifliği görülmekte ve

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## KAYNAKLAR


1. Burkitt D. A sarcoma involving the jaws in African children. Br J Surg. 1958;46:218-223.
2. O'Conor GT, Davies JN. Malignant tumors in African children. With special reference to malignant lymphoma. J Pediatr. 1960;56:526-535.
3. Casulo C, Friedberg JW. Burkitt lymphoma- a rare but challenging lymphoma. Best Pract Res Clin Haematol. 2018;31:279-284.
4. Swerdlow SH, Campo E, Harris NL, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th Edition. . Lyon, France: IARC press; 2017.
5. Dunleavy K, Little RF, Wilson WH. Update on Burkitt Lymphoma. Hematol Oncol Clin North Am. 2016;30:1333-1343.
6. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127:2375-2390.
7. Molyneux EM, Rochford R, Griffin B, et al. Burkitt's lymphoma. Lancet. 2012;379:1234-1244.
8. Orem J, Mbidde EK, Lambert B, et al. Burkitt's lymphoma in Africa, a review of the epidemiology and etiology. Afr Health Sci. 2007;7:166-175.
9. Saleh K, Michot JM, Camara-Clayette V, et al. Burkitt and Burkitt-Like Lymphomas: a Systematic Review. Curr Oncol Rep. 2020;22:33.
10. Orazi A, Weiss LM, Foucar K, et al. Knowles' Neoplastic Hematopathology (Third Edit.)

. Lippincott Williams & Wilkins (LWW); 2013.

11. Sant M, Allemani C, Tereanu C, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. Blood. 2010;116:3724-3734.
12. Dozzo M, Carobolante F, Donisi PM, et al. Burkitt lymphoma in adolescents and young adults: management challenges. Adolesc Health Med Ther. 2017;8:11-29.
13. Smith A, Howell D, Patmore R, et al. Incidence of haematological malignancy by sub-type: a report from the Haematological Malignancy Research Network. Br J Cancer. 2011;105:1684-1692.
14. Morton LM, Wang SS, Devesa SS, et al. Lymphoma incidence patterns by WHO subtype in the United States, 1992-2001. Blood. 2006;107:265-276.
15. Kalisz K, Alessandrino F, Beck R, et al. An update on Burkitt lymphoma: a review of pathogenesis and multimodality imaging assessment of disease presentation, treatment response, and recurrence. Insights Imaging. 2019;10:56.
16. Shiels MS, Pfeiffer RM, Hall HI, et al. Proportions of Kaposi sarcoma, selected non-Hodgkin lymphomas, and cervical cancer in the United States occurring in persons with AIDS, 1980-2007. JAMA. 2011;305:1450-1459.
17. Barta SK, Samuel MS, Xue X, et al. Changes in the influence of lymphoma- and HIV-specific factors on outcomes in AIDS-related non-Hodgkin lymphoma. Ann Oncol. 2015;26:958-966.
18. Guech-Ongey M, Simard EP, Anderson WF, et al. AIDS-related Burkitt lymphoma in the United States: what do age and CD4 lymphocyte patterns tell us about etiology and/or biology? Blood. 2010;116:5600-5604.
19. de Martel C, Franceschi S. Infections and cancer: established associations and new hypotheses. Crit Rev Oncol Hematol. 2009;70:183-194.
20. Dittmer DP. Not like a wrecking ball: EBV fine-tunes MYC lymphomagenesis. Blood. 2014;123:460-461.
21. Moormann AM, Snider CJ, Chelimo K. The company malaria keeps: how co-infection with Epstein-Barr virus leads to endemic Burkitt lymphoma. Curr Opin Infect Dis. 2011;24:435-441.
22. Quintana MDP, Smith-Togobo C, Moormann A, et al. Endemic Burkitt lymphoma - an aggressive childhood cancer linked to Plasmodium falciparum exposure, but not to exposure to other malaria parasites. APMIS. 2020;128:129-135.
23. Magrath IT. African Burkitt's lymphoma. History, biology, clinical features, and treatment. Am J Pediatr Hematol Oncol. 1991;13:222-246.
24. Falini B, Fizzotti M, Pileri S, et al. Bcl-6 protein expression in normal and neoplastic lymphoid tissues. Ann Oncol. 1997;8 Suppl 2:101-104.
25. Mbulaiteye SM, Anderson WF, Ferlay J, et al. Pediatric, elderly, and emerging adult-onset peaks in Burkitt's lymphoma incidence diagnosed in four continents, excluding Africa. Am J Hematol. 2012;87:573-578.
26. Armitage JO, Weisenburger DD. New approach to classifying non-Hodgkin's lymphomas: clinical features of the major histologic subtypes. Non-Hodgkin's Lymphoma Classification Project. J Clin Oncol. 1998;16:2780-2795.
27. Mbulaiteye SM, Biggar RJ, Bhatia K, et al. Sporadic childhood Burkitt lymphoma incidence in the United States during 1992-2005. Pediatr Blood Cancer. 2009;53:366-370.
28. Hoelzer D, Walewski J, Dohner H, et al. Improved outcome of adult Burkitt lymphoma/leukemia with rituximab and chemotherapy: report of a large prospective multicenter trial. Blood. 2014;124:3870-3879.
29. Gabarre J, Raphael M, Lepage E, et al. Human immunodeficiency virus-related lymphoma: relation between clinical features and histologic subtypes. Am J Med. 2001;111:704-711.
30. Haralambieva E, Rosati S, van Noesel C, et al. Florid granulomatous reaction in Epstein-Barr virus-positive nonendemic Burkitt lymphomas: report of four cases. Am J Surg Pathol. 2004;28:379-383.
31. Hollingsworth HC, Longo DL, Jaffe ES. Small noncleaved cell lymphoma associated with florid epithelioid granulomatous response. A clinicopathologic study of seven patients. Am J Surg Pathol. 1993;17:51-59.
32. Roithmann S, Toledano M, Tourani JM, et al. HIV-associated non-Hodgkin's lymphomas: clinical characteristics and outcome. The experience of the French Registry of HIV-associated tumors. Ann Oncol. 1991;2:289-295.
33. Barth TF, Muller S, Pawlita M, et al. Homogeneous immunophenotype and paucity of secondary genomic aberrations are distinctive features of endemic but not of sporadic Burkitt's lymphoma and diffuse large B-cell lymphoma with MYC rearrangement. J Pathol. 2004;203:940-945.

34. Lai YY, Li Y, Shi Y, et al. [Characteristics of 11 patients with acute myeloid leukemia accompanied with karyotype aberration t(6;9)]. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2012;20:1293-1296.
35. Naresh KN, Ibrahim HA, Lazzi S, et al. Diagnosis of Burkitt lymphoma using an algorithmic approach--applicable in both resource-poor and resource-rich countries. Br J Haematol. 2011;154:770-776.
36. Tapia G, Lopez R, Munoz-Marmol AM, et al. Immunohistochemical detection of MYC protein correlates with MYC gene status in aggressive B cell lymphomas. Histopathology. 2011;59:672-678.
37. Ambrosio MR, Piccaluga PP, Ponzoni M, et al. The alteration of lipid metabolism in Burkitt lymphoma identifies a novel marker: adipophilin. PLoS One. 2012;7:e44315.
38. Bell A, Rickinson AB. Epstein-Barr virus, the TCL-1 oncogene and Burkitt's lymphoma. Trends Microbiol. 2003;11:495-497.
39. Rodig SJ, Vergilio JA, Shahsafaei A, et al. Characteristic expression patterns of TCL1, CD38, and CD44 identify aggressive lymphomas harboring a MYC translocation. Am J Surg Pathol. 2008;32:113-122.
40. Haralambieva E, Boerma EJ, van Imhoff GW, et al. Clinical, immunophenotypic, and genetic analysis of adult lymphomas with morphologic features of Burkitt lymphoma. Am J Surg Pathol. 2005;29:1086-1094.
41. Lin CW, O'Brien S, Faber J, et al. De novo CD5+ Burkitt lymphoma/leukemia. Am J Clin Pathol. 1999;112:828-835.
42. Navid F, Mosijczuk AD, Head DR, et al. Acute lymphoblastic leukemia with the (8;14)(q24;q32) translocation and FAB L3 morphology associated with a B-precursor immunophenotype: the Pediatric Oncology Group experience. Leukemia. 1999;13:135-141.
43. Amato T, Abate F, Piccaluga P, et al. Clonality Analysis of Immunoglobulin Gene Rearrangement by Next-Generation Sequencing in Endemic Burkitt Lymphoma Suggests Antigen Drive Activation of BCR as Opposed to Sporadic Burkitt Lymphoma. Am J Clin Pathol. 2016;145:116-127.
44. Aukema SM, Theil L, Rohde M, et al. Sequential karyotyping in Burkitt lymphoma reveals a linear clonal evolution with increase in karyotype complexity and a high frequency of recurrent secondary aberrations. Br J Haematol. 2015;170:814-825.
45. Maria Murga Penas E, Schilling G, Behrmann P, et al. Comprehensive cytogenetic and molecular cytogenetic analysis of 44 Burkitt lymphoma cell lines: secondary chromosomal changes characterization, karyotypic evolution, and comparison with primary samples. Genes Chromosomes Cancer. 2014;53:497-515.
46. Scholtysik R, Kreuz M, Klapper W, et al. Detection of genomic aberrations in molecularly defined Burkitt's lymphoma by array-based, high resolution, single nucleotide polymorphism analysis. Haematologica. 2010;95:2047-2055.
47. Toujani S, Dessen P, Ithzar N, et al. High resolution genome-wide analysis of chromosomal alterations in Burkitt's lymphoma. PLoS One. 2009;4:e7089.
48. Haralambieva E, Schuuring E, Rosati S, et al. Interphase fluorescence in situ hybridization for detection of 8q24/MYC breakpoints on routine histologic sections: validation in Burkitt lymphomas from three geographic regions. Genes Chromosomes Cancer. 2004;40:10-18.
49. Hummel M, Bentink S, Berger H, et al. A biologic definition of Burkitt's lymphoma from transcriptional and genomic profiling. N Engl J Med. 2006;354:2419-2430.
50. Jaffe ES, L.; HN, al. VJWe. Hematopathology. St. Louis: Elsevier Saunders; 2010.
51. Leucci E, Cocco M, Onnis A, et al. MYC translocation-negative classical Burkitt lymphoma cases: an alternative pathogenetic mechanism involving miRNA deregulation. J Pathol. 2008;216:440-450.
52. Onnis A, De Falco G, Antonicelli G, et al. Alteration of microRNAs regulated by c-Myc in Burkitt lymphoma. PLoS One. 2010;5.
53. Dave SS, Fu K, Wright GW, et al. Molecular diagnosis of Burkitt's lymphoma. N Engl J Med. 2006;354:2431-2442.
54. Lenze D, Leoncini L, Hummel M, et al. The different epidemiologic subtypes of Burkitt lymphoma share a homogenous micro RNA profile distinct from diffuse large B-cell lymphoma. Leukemia. 2011;25:1869-1876.
55. Piccaluga PP, De Falco G, Kustagi M, et al. Gene expression analysis uncovers similarity and differences among Burkitt lymphoma subtypes. Blood. 2011;117:3596-3608.
56. Love C, Sun Z, Jima D, et al. The genetic landscape of mutations in Burkitt lymphoma. Nat Genet. 2012;44:1321-1325.
57. Richter J, Schlesner M, Hoffmann S, et al. Recurrent mutation of the ID3 gene in Burkitt lymphoma identified by integrated genome, exome and transcriptome sequencing. Nat Genet. 2012;44:1316-1320.
58. Sander S, Calado DP, Srinivasan L, et al. Synergy between PI3K signaling and MYC in Burkitt lymphomagenesis. Cancer Cell. 2012;22:167-179.
59. Schmitz R, Young RM, Ceribelli M, et al. Burkitt lymphoma pathogenesis and therapeutic targets from structural and functional genomics. Nature. 2012;490:116-120.
60. Giulino-Roth L, Wang K, MacDonald TY, et al. Targeted genomic sequencing of pediatric Burkitt lymphoma identifies recurrent alterations in antiapoptotic and chromatin-remodeling genes. Blood. 2012;120:5181-5184.
61. Wagener R, Aukema SM, Schlesner M, et al. The PCBP1 gene encoding poly(rC) binding protein I is recurrently mutated in Burkitt lymphoma. Genes Chromosomes Cancer. 2015;54:555-564.
62. Abate F, Ambrosio MR, Mundo L, et al. Distinct Viral and Mutational Spectrum of Endemic Burkitt Lymphoma. PLoS Pathog. 2015;11:e1005158.