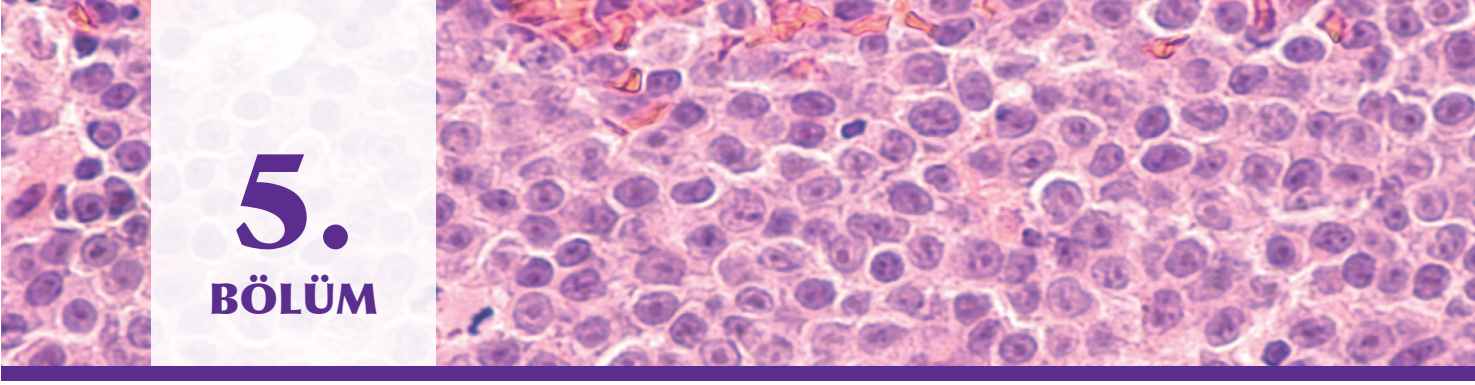

5. BÖLÜM

T-HÜCRE/HİSTİYOSİTTEN ZENGİN BÜYÜK B-HÜCRELİ LENFOMA

Sibel CANGİ [1]

TANIM

T-hücre/histiyositten zengin büyük B-hücreli lenfoma (THZBBHL) ilk defa 2008 Dünya Sağlık Örgütü (DSÖ) sınıflamasında ayrı bir antite olarak yer alan agresif bir lenfomadır (1). Diffüz büyük B-hücreli lenfomanın (DBBHL) nadir bir varyantı olup, seyrek neoplastik büyük B-hücreleri ile belirgin reaktif T-hücreleri ve histiyositlerden meydana gelmektedir (1-3). Tüm DBBHL'ların %10'unu oluşturmaktadır (4).

Nodüler lenfosit baskın Hodgkin lenfoma (NLBHL) ile benzer morfolojik ve immünohistokimyasal birçok özelliğe sahiptir ve bu nedenle bazı olgularda ayırıcı tanı yapmak oldukça zordur. Her iki antitenin de histolojik özelliklerini gösteren bazı olguların varlığı nedeniyle, THZBBHL'nın NLBHL'dan progrese bir hastalık formu olduğu varsayılmıştır (5, 6). Yoğun T-hücrelerinin ve örtüşen özelliklerin varlığı, olguların bir kısmının, sıklıkla T-hücreli lenfoma veya NLBHL olarak, yanlış tanı almasına neden olmaktadır (7).

ETİYOLOJİ

THZBBHL'larda tanımlanmış herhangi bir etiyolojik faktör bulunmamaktadır. Zemindeki zengin T-hücre infiltrasyonunun malign hücreler ve histiyositler tarafından üretilen IL-4 ile ilişkili olabileceği düşünülmektedir (8). Diğer hücrelere oranla daha az sayıda neoplastik hücre varlığının ise, sitotoksik CD8 pozitif T-hücre aracılığıyla tümör hücrelerinin apoptozise uğramasıyla kısmen açıklanabileceği göz önünde bulundurulmaktadır (9).

Olguların bir bölümü patogenetik olarak NLBHL ile ilişkilidir (10, 11). Bazı olguların daha öncesinde NLBHL öyküsü mevcuttur (2), fakat bu olgular sıklıkla THZBBHL yerine NLBHL'nın diffüz büyümesi olarak yorumlanırlar ve ayırıcı tanı oldukça zordur.

KLİNİK ÖZELLİKLER

Hastalık özellikle orta yaşlı bireylerde görülmekle birlikte çocukluk çağında da görülebilmektedir. Pediatrik olgularda daha çok lokal hastalık olma eğilimindedir (12, 13). Erkeklerde görülme sıklığı daha fazladır (12, 14-16). Hastalar genellikle ateş, halsizlik, splenomegali ve/veya hepatomegali ile klinik bulgu vermektedirler. Tanı anında, olguların neredeyse yarısı ileri evrede ve orta-yüksek IPI (International Prognostic Index) skoruna sahiptir. Hastalık mevcut kemoterapi rejimlerine sıklıkla dirençlidir (4).

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B-hücrelerinde olduğu gibi CD20 ile heterojen boyanma göstermektedirler (49).

THZBBHL, zemindeki hafif atipi gösteren aktive T-hücreleri nedeniyle, periferal T-hücreli lenfoma ile de karıştırılabilmektedir. Bu olgularda immün reaksiyon ve morfoloji arasında dikkatli korelasyon gerekmektedir. Periferal T-hücreli lenfomada, T-hücreleri daha belirgin derecede sitolojik atipi göstermektedirler ve bu atipi değişken boyutlardaki lenfoid hücreleri içermektedir. Lenfoid infiltrat içerisindeki daha büyük hücreler, THZBBHL'da olduğu gibi, belirgin biçimde ayrı bir popülasyon olarak dikkat çekmez ve küçük atipik hücrelerle bir geçiş göstermektedir. İmmünfenotipik olarak, büyük atipik hücreler pan-B-hücre belirteçlerinden daha çok pan-T-hücre belirteçlerini eksprese etmektedirler. Bununla birlikte, bazı periferal T-hücreli lenfomalarda, özellikle anjioimmünoblastik T-hücreli lenfomada, sıklıkla EBV ilişkili reaktif büyük B-hücre proliferasyonu eşlik ettiğinden tanıda karışıklığa neden olabilmektedir (50-53).

KAYNAKLAR

1. Swerdlow SH, Campo E, Harris NL, et al. (2008). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: IARC Press.
2. De Jong D, Van Gorp J, Sie-Go D, et al. T-cell rich B-cell non-Hodgkin's lymphoma: a progressed form of follicle centre cell lymphoma and lymphocyte predominance Hodgkin's disease. Histopathology. 1996;28:15-24.
3. Rodriguez J, Pugh WC, Cabanillas F. T-cell-rich B-cell lymphoma. Blood. 1993;82:1586-1589.
4. Swerdlow, SH, Campo, E, Harris, NL, et al. (2017). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Revised 4th ed. Lyon: IARC Press.
5. Rüdiger T, Gascoyne RD, Jaffe ES, et al. Workshop on the relationship between nodular lymphocyte predominant Hodgkin's lymphoma and T cell/histiocyte-rich B cell lymphoma. Ann Oncol. 2002;13:44-51.
6. Carbone A, Gloghini A, Aiello A, et al. B-cell lymphomas with features intermediate between distinct pathologic entities. From pathogenesis to pathology. Hum Pathol. 2010;41:621-631.
7. Ohgami RS, Zhao S, Natkunam Y. Large B-cell lymphomas poor in B cells and rich in PD-1+ T cells can mimic T-cell lymphomas. Am J of Clin Pathol. 2014;142:150–156.
8. Macon WR, Cousar JB, Waldron JA Jr, et al. Interleukin-4 may contribute to the abundant T-cell reaction and paucity of neoplastic B cells in T-cell-rich B-cell lymphomas. Am J Pathol. 1992;141:1031-1036.
9. Felgar RE, Steward KR, Cousar JB, et al. T-cell- rich large-B-cell lymphomas contain non-activated CD8+ cytolytic T cells, show increased tumor cell apoptosis, and have lower Bcl-2 expression than diffuse large-B-cell lymphomas. Am J Pathol. 1998;153:1707- 1715.
10. Boudova L, Torlakovic E, Delabie J, et al. Nodular lymphocyte-predominant Hodgkin lymphoma with nodules resembling T-cell/histiocyte-rich B-cell lymphoma: differential diagnosis between nodular lymphocyte-predominant Hodgkin lymphoma and T-cell/histiocyte-rich B-cell lymphoma. Blood. 2003;102:3753-3758.
11. Hartmann S, Döring C, Jakobus C, et al. Nodular lymphocyte predominant Hodgkin lymphoma and T cell/histiocyte rich large B cell lymphoma–endpoints of a spectrum of one disease? PLoS One. 2013;8(11):e78812.
12. Lones MA, Cairo MS, Perkins SL. T-cell-rich large B-cell lymphoma in children and adolescents: a clinicopathologic report of six cases from the Children's Cancer Group Study CCG-5961. Cancer. 2000;88(10):2378–2386.
13. Tiemann M, Riener MO, Claviez A, et al. Proliferation rate and outcome in children with T-cell rich B-cell lymphoma: a clinicopathologic study from the NHL-BFM-study group. Leuk Lymphoma. 2005;46(9):1295–1300.
14. Achten R, Verhoef G, Vanuytsel L, et al. T-cell/histiocyte-rich large B-cell lymphoma: a distinct clinicopathologic entity. J Clin Oncol. 2002;20:1269- 1277.
15. Lim MS, Beaty M, Sorbara L, et al. T-cell/histiocyte-rich large B-cell lymphoma: a heterogeneous entity with derivation from germinal center B cells. Am J Surg Pathol. 2002;26:1458-1466.
16. Greer JP, Macon WR, Lamar RE, et al. T-cell-rich B-cell lymphomas: diagnosis and response to therapy of 44 patients. J Clin Oncol. 1995;13:1742-1750.
17. 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.
18. Skinnider BF, Connors JM, Gascoyne RD. Bone marrow involvement in T-cell-rich B-cell lymphoma. Am J Clin Pathol. 1997;108:570-578.
19. Barber NA, Loberiza FR Jr, Perry AM, et al. Does functional imaging distinguish nodular lymphocyte-predominant Hodgkin lymphoma from T-cell/histiocyte-rich large B-cell lymphoma? Clin Lymphoma Myeloma Leuk. 2013;13:392-397.
20. Ramsay AD, Smith WJ, Isaacson PG. T-cell-rich B-cell lymphoma. Am J Surg Pathol. 1988;12:433-43.
21. Nam-Cha SH, Roncador G, Sanchez-Verde L, et al. PD-1, a follicular T-cell marker useful for recognizing nodular lymphocyte-predominant Hodgkin lymphoma. Am J Surg Pathol. 2008;32:1252-1257.
22. Dogan A, Burke JS, Goteri G, et al. Micronodular T-cell/histiocyte-rich large B-cell lymphoma of the spleen: histology, immunophenotype, and differential diagnosis. Am J Surg Pathol. 2003;27:903-911.
23. Ng CS, Chan JK, Hui PK, et al. Large B-cell lymphomas with a high content of reactive T cells. Hum Pathol. 1989;20:1145-1154.

24. Krishnan J, Wallberg K, Frizzera G. T-cell-rich large B-cell lymphoma. A study of 30 cases, supporting its histologic heterogeneity and lack of clinical distinctiveness. Am J Surg Pathol. 1994;18:455-465.
25. Macon WR, Williams ME, Greer JP, et al. T-cell-rich B-cell lymphomas. A clinicopathologic study of 19 cases. Am J Surg Pathol. 1992;16:351-363.
26. Rudiger T, Ott G, Ott MM, et al. Differential diagnosis between classic Hodgkin's lymphoma, T-cell-rich B-cell lymphoma, and paragranuloma by paraffin immunohistochemistry. Am J Surg Pathol. 1998;22:1184-1191.
27. Fraga M, Sanchez-Verde L, Forteza J, et al. T-cell/histiocyte-rich large B-cell lymphoma is a disseminated aggressive neoplasm: differential diagnosis from Hodgkin's lymphoma. Histopathology. 2002;41:216-229.
28. Achten R, Verhoef G, Vanuytsel L, et al. Histiocyte-rich, T-cell-rich B-cell lymphoma: a distinct diffuse large B-cell lymphoma subtype showing characteristic morphologic and immunophenotypic features. Histopathology. 2002;40:31-45.
29. Kraus MD, Haley J. Lymphocyte predominance Hodgkin's disease: the use of bcl-6 and CD57 in diagnosis and differential diagnosis. Am J Surg Pathol. 2000;24:1068-1078.
30. Nicolae A, Pittaluga S, Abdullah S, et al. EBV-positive large B-cell lymphomas in young patients: a nodal lymphoma with evidence for a tolerogenic immune environment. Blood. 2015;126:863-872.
31. Baddoura FK, Chan WC, Masih AS, et al. T-cell-rich B-cell lymphoma. A clinicopathologic study of eight cases. Am J Clin Pathol. 1995;103:65-75.
32. Osborne BM, Butler JJ, Pugh WC. The value of immunophenotyping on paraffin sections in the identification of T-cell rich B-cell large-cell lymphomas: lineage confirmed by JH rearrangement. Am J Surg Pathol. 1990;14:933-938.
33. Brauninger A, Kuppers R, Spieker T, et al. Molecular analysis of single B cells from T-cell-rich B-cell lymphoma shows the derivation of the tumor cells from mutating germinal center B cells and exemplifies means by which immunoglobulin genes are modified in germinal center B cells. Blood. 1999;93:2679-2687.
34. Wlodarska I, Nooyen P, Maes B, et al. Frequent occurrence of BCL6 rearrangements in nodular lymphocyte predominance Hodgkin lymphoma but not in classical Hodgkin lymphoma. Blood. 2003;101(2):706-710.
35. Braeuninger A et al. Hodgkin and Reed–Sternberg cells in lymphocyte predominant Hodgkin disease represent clonal populations of germinal center-derived tumor B cells. Proc Natl Acad Sci U S A. 1997;94(17):9337–9342.
36. Franke S, Wlodarska I, Maes B, et al. Lymphocyte predominance Hodgkin disease is characterized by recurrent genomic imbalances. Blood. 2001;97(6):1845–1853.
37. Hartmann S, Doring C, Vucic E, et al. Array comparative genomic hybridization reveals similarities between nodular lymphocyte predominant Hodgkin lymphoma and T cell/histiocyte rich large B cell lymphoma. Br J Haematol. 2015;169:415-422.
38. Mitterer M, Pescosta N, McQuain C, et al. Epstein-Barr virus related hemophagocytic syndrome in a T-cell rich B-cell lymphoma. Ann Oncol. 1999;10:231-234.
39. Hartmann S, Tousseyn T, Döring C, et al. Macrophages in T cell/histiocyte rich large B cell lymphoma strongly express metal-binding proteins and show a bi-activated phenotype. Int J Cancer. 2013;133:2609-18.
40. Bouabdallah R, Mounier N, Guettier C, et al. T-cell/histiocyte-rich large B-cell lymphomas and classical diffuse large B-cell lymphomas have similar outcome after chemotherapy: a matched-control analysis. J Clin Oncol. 2003;21:1271-1277.
41. Kim YS, Ji JH, Ko YH, et al. Matched-pair analysis comparing the outcomes of T cell/histiocyte- rich large B cell lymphoma and diffuse large B cell lymphoma in patients treated with rituximab-CHOP. Acta Haematol. 2014;131:156-161.
42. Tousseyn T, De Wolf-Peeters C. T cell/histiocyte-rich large B-cell lymphoma: an update on its biology and classification. Virchows Arch. 2011;459:557-563.
43. National Comprehensive Cancer Network. (2018) NCCN Clinical practice guidelines in Oncology- B-cell lymphomas. Vol. Version 1.2018-February 15, 2018. NCCN.
44. Aki H, Tuzuner N, Ongoren S, et al. T-cell-rich B-cell lymphoma: a clinicopathologic study of 21 cases and comparison with 43 cases of diffuse large B-cell lymphoma. Leukemia Research. 2004;28:229-236.
45. El Weshi A, Akhtar S, Mourad WA, et al. T-cell/histiocyte-rich B-cell lymphoma: clinical presentation, management and prognostic factors: report on 61 patients and review of literature. Leuk Lymphoma. 2007;48:1764–1773.
46. Jaffe ES, Harris NL, Stein H, et al. (2001). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: IARC Press. 47: Chittal SM, Brousset P, Voigt JJ, et al. Large B-cell lymphoma rich in T-cells and simulating Hodgkin's disease. Histopathology. 1991;19(3):211-220.
48. McBride JA, Rodriguez J, Luthra R, et al. T-cell-rich B large-cell lymphoma simulating lymphocyte-rich Hodgkin's disease. Am J Surg Pathol. 1996;20(2):193-201.
49. Chan ACL, Chan JKC. (2017). Diffuse large B-cell lymphoma. Elaine S. Jaffe, et al. (Ed.), Hematopathology içinde (s. 415-445). Philadelphia: Elsevier.
50. Higgins JP, van de Rijn M, Jones CD, et al. Peripheral T-cell lymphoma complicated by a proliferation of large B cells. Am J Clin Pathol. 2000;114(2):236-247.
51. Zettl A, Lee SS, Rudiger T, et al. Epstein-Barr virus-associated B-cell lymphoproliferative disorders in angioimmunoblastic T-cell lymphoma and peripheral T-cell lymphoma, unspecified. Am J Clin Pathol. 2002;117(3):368-379.
52. Quintanilla-Martinez L, Fend F, Moguel LR, et al. Peripheral T-cell lymphoma with Reed-Sternberg-like cells of B-cell phenotype and genotype associated with Epstein-Barr virus infection. Am J Surg Pathol. 1999;23:1233-1240.
53. Ho JW, Ho FC, Chan AC, et al. Frequent detection of Epstein-Barr virus-infected B cells in peripheral T-cell lymphomas. J Pathol. 1998;185:79-85.