

Leukaemia Section

Short Communication

T-cell/histiocyte rich large B-cell lymphoma

Antonino Carbone, Annunziata Gloghini

Department of Pathology Centro di Riferimento Oncologico Aviano (CRO), Istituto Nazionale Tumori, IRCCS, Aviano, Italy; acarbone@cro.it (AC); Department of Diagnostic Pathology and Laboratory Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; annunziata.gloghini@istitutotumori.mi.it (AG)

Published in Atlas Database: August 2016

Online updated version : <http://AtlasGeneticsOncology.org/Anomalies/TcellHistoRichLBcellINHLID1764.html>

Printable original version : <http://documents.irevues.inist.fr/bitstream/handle/2042/68244/08-2016-TcellHistoRichLBcellINHLID1764.pdf>

DOI: 10.4267/2042/68244

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2017 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Abstract

Although T-cell/histiocyte rich large B-cell lymphoma (THRLBCL) is an aggressive diffuse large B-cell lymphoma (DLBCL), its morphology can resemble nodular lymphocyte predominant Hodgkin lymphoma (NLPHL). These two entities are closely related: both diseases contain neoplastic cells with similar morphologic and immunophenotypic features but differ with respect to their architecture and the nature of the reactive background.

Due to the overlapping features between THRLBCL and NLPHL, it is sometimes impossible to distinguish these two entities; thus, "grey zone" lymphoma is used to define some of those cases.

Because of the morphologic and immunophenotypic similarities between THRLBCL and NLPHL, it is possible that these two entities may represent different stages of the same disease.

A possible biological relation of THRLBCL with NLPHL has been suggested. Overlapping recurrent genetic abnormalities (gain of 4q and loss of 19p) might be the genetic link between THRLBCL and NLPHL.

Keywords

THRLBCL; grey zone lymphoma; NLPHL

Clinics and pathology

Disease

T-cell/histiocyte rich large B-cell lymphoma (THRLBCL) is an aggressive diffuse large B-cell lymphoma (DLBCL) that morphologically can resemble nodular lymphocyte predominant Hodgkin lymphoma (NLPHL), a rare indolent type of Hodgkin lymphoma (HL). Interestingly, some studies suggest that THRLBCL and NLPHL are closely related, based on the overlap which occurs in the 'grey zone' between these two entities (Lim et al., 2002; Boudova et al., 2003; Vanhentenrijk et al.; 2006; Zhao et al., 2008; Hartmann et al., 2013). Due to the overlapping features between NLPHL and THRLBCL, it is sometimes impossible to distinguish these two entities; thus, "grey zone" lymphoma is used to define some of those cases (Rudiger et al., 1998; Boudova et al., 2003; Zhao et al., 2008).

Whereas the 2008 WHO monograph termed as "NLPHL, THRLBCL-like" cases of NLPHL that progress to a diffuse T-cell-rich pattern (De Wolf-Peeters C et al., 2008), the 2016 revision recommend the designation of "THRLBCL-like transformation of NLPHL" for those cases (Swerdlow et al., 2016).

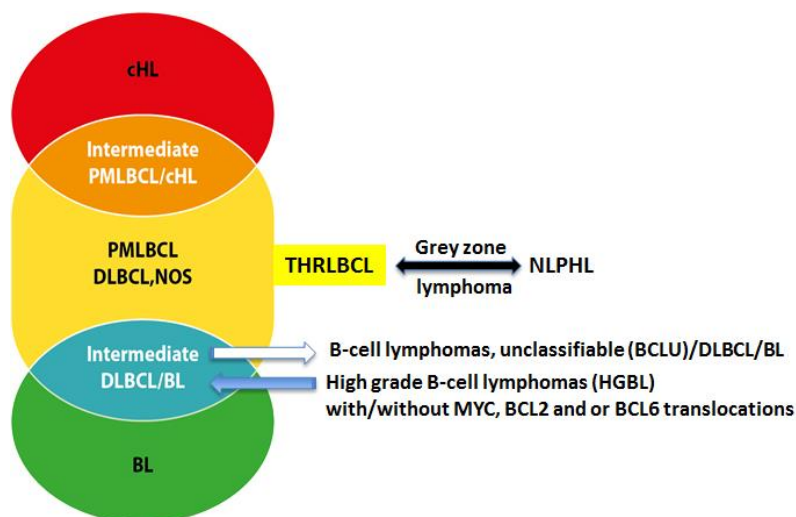


Figure 1. Borderline categories that do not clearly fit into one entity include the grey zone lymphoma between THRLBCL and NLPHL, and a category termed B-cell lymphoma, unclassifiable (BCLU), with features intermediate between diffuse large B-cell lymphoma (DLBCL) of the primary mediastinal type (PMLBCL) and classical Hodgkin lymphoma (cHL). Another unclassifiable category was created for cases showing features intermediate between DLBCL and Burkitt lymphoma (BL) with the newer recognized categories now termed high-grade B-cell lymphoma (HGBL) with and without MYC and BCL2 and/or BCL6 translocations

Epidemiology

THRLBCL usually affects middle aged men (Hartmann et al., 2015).

Pathology

THRLBCL and NLPHL diseases contain neoplastic cells with similar morphologic and immunophenotypic features but differ with respect to their architecture and the nature of the reactive background.

In the THRLBCL there are few large neoplastic B cells scattered in a background of non-neoplastic T cells with histiocytes (De Wolf-Peeters C et al., 2008; Carbone et al., 2010). The neoplastic cells may resemble centroblasts, immunoblasts, lymphocyte-predominant (LP) Hodgkin cells, or classic Hodgkin Reed-Sternberg (HRS) cells (Lim et al., 2002; Carbone et al., 2010). The pattern of involvement in lymph nodes is usually diffuse or may be vaguely nodular, in absence of aggregates of follicular dendritic reticulum cells (FDC).

Immunophenotype

Neoplastic cells of THRLBCL express CD45 and B-cell antigens, are strongly positive for BCL6, are negative for CD30 and CD15, and are not infected by EBV (Achten et al., 2002; Lim et al., 2002).

Background

Small B cells are virtually absent in THRLBCL, and T cells with a follicular helper T-cell phenotype (CD57 and/or PD1) are not numerous and do not form rosettes around the neoplastic B cells. Presence of granzyme B positive and Tia1 positive T cells is restricted to primary THRLBCL (Table 1).

The background in NLPHL is composed of large meshworks of FDC filled with B cells, histiocytes and numerous germinal center CD4 positive T cells. These T cells specifically express CD3, CD4, PD1,

and MUM1/IRF4. Tia1 and CD40L positive CD3 T cells are absent. PD1-ringing is a feature commonly seen in NLPHL (Carbone et al., 1995; Carbone et al., 2002; Poppema et al., 2008) (Table 1).

NLPHL may evolve to a completely diffuse T-cell-rich proliferation lacking any follicular dendritic cells which would be consistent with a THRLBCL.

	NLPHL	THRLBCL
Expression of molecular markers		
CD15	-	-
CD30	Usually -	-or +
EMA	+	Usually +
CD20	+	+
CD79a	+	+
IRF4	+	-or +
EBV	-	Usually -
Cell microenvironment		
T-cells	-or +	+
B-cells/B and T-cells	+	-
CD57 + rosetting T-cells	+ or -	-
CD40L + rosetting T-cells	-	-
MUM1 + rosetting T-cells	+	-
Histiocytes	-or +	+
DRCs meshworks	+	-

Table 1 Comparative expression of molecular markers and cell microenvironment. NLPHL: Nodular lymphocyte predominant Hodgkin lymphoma; THRLBCL: T-cell/histiocyte rich large B-cell lymphoma; EBV: Epstein-Barr virus; DRCs: Dendritic reticulum cells

Prognosis

This B-cell lymphoma is usually aggressive with a prognosis more close to DLBCL than NLPHL (Younes et al., 2014). The treatment outcomes of THRLBCL are similar to those of DLBCL. The addition of rituximab to CHOP seems to be helpful for the management of THRLBCL, as it is for DLBCL (Kim et al., 2014).

Genetics

Note

A biologic continuum has been supported by gene expression profiling (GEP) studies [(brune et al., 2008) that have demonstrated a surprisingly high similarity of LP cells to the tumor cells of THRLBCL, with deregulation of pro- or anti-apoptotic genes (CASP2, ATM, and TRAF5) and putative oncogenes. Comparative Genomic Hybridization (CGH) studies revealed a significantly higher number of genomic imbalances in NLPHL than in THRLBCL with only a few overlapping recurrent genetic abnormalities (gain of 4q and loss of 19p). These overlapping abnormalities might be the genetic link between NLPHL and THRLBCL (Rüdiger et al., 1998; Zhao et al., 2008). In conclusion, GEP and array CGH studies have shown similarities between NLPHL and THRLBCL, suggesting a relationship to each other, in spite of other major differences. (Hartman et al., 2015; Swerdlow et al., 2016).

References

- Achten R, Verhoef G, Vanuytsel L, De Wolf-Peeters C. Histiocyte-rich, T-cell-rich B-cell lymphoma: a distinct diffuse large B-cell lymphoma subtype showing characteristic morphologic and immunophenotypic features. *Histopathology*. 2002 Jan;40(1):31-45
- Brune V, Tiacci E, Pfeil I, Döring C, Eckerle S, van Noesel CJ, Klapper W, Falini B, von Heydebreck A, Metzler D, Bräuninger A, Hansmann ML, Küppers R. Origin and pathogenesis of nodular lymphocyte-predominant Hodgkin lymphoma as revealed by global gene expression analysis. *J Exp Med*. 2008 Sep 29;205(10):2251-68
- Carbone A, Gloghini A, Aiello A, Testi A, Cabras A. B-cell lymphomas with features intermediate between distinct pathologic entities. From pathogenesis to pathology. *Hum Pathol*. 2010 May;41(5):621-31
- De Wolf-Peeters C, Delabie J, Campo E, Jaffe ES, Delsol G.. T cell/histiocyte-rich large B-cell lymphoma. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele H, Vardiman JW (eds.) World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues, Lyon: IARC Press, 2008: 238-239.
- Hartmann S, Döring C, Vucic E, Chan FC, Ennishi D, Tousseyn T, de Wolf-Peeters C, Perner S, Wlodarska I, Steidl C, Gascoyne RD, Hansmann ML.. 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(3): 415-422.
- Kim YS, Ji JH, Ko YH, Kim SJ, Kim WS.. 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(3): 156-161.
- Lim MS, Beaty M, Sorbara L, Cheng RZ, Pittaluga S, Raffeld M, Jaffe ES.. T-cell/histiocyte-rich large B-cell lymphoma: a heterogeneous entity with derivation from germinal center B cells. *Am J Surg Pathol* 2002; 26(11): 1458-1466.
- Poppema S, Delsol G, Pileri SA, Stein H.. Nodular lymphocyte predominant Hodgkin lymphoma. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele H, Vardiman JW (eds.) World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues, Lyon: IARC Press, 2008: 323-325.
- Rüdiger T, Jaffe ES, Delsol G, deWolf-Peeters C, Gascoyne RD, Georgii A, Harris NL, Kadin ME, MacLennan KA, Poppema S, Stein H, Weiss LE, Müller-Hermelink HK.. Workshop report on Hodgkin's disease and related diseases ('grey zone' lymphoma). *Ann Oncol* 1998; 9 Suppl 5: S31-S38. (REVIEW)
- Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD, Jaffe ES.. The 2016 revision of the World Health Organization (WHO) classification of lymphoid neoplasms. *Blood* 2016; 127(20): 2375-2390. (REVIEW)
- Vanhentenrijk V, Vanden Bempt I, Dierickx D, Verhoef G, Wlodarska I, De Wolf-Peeters C.. Relationship between classic Hodgkin lymphoma and overlapping large cell lymphoma investigated by comparative expressed sequence hybridization expression profiling. *J Pathol* 2006; 210(2): 155-62.
- Younes A, Carbone A, Johnson P, Dabaja B, Ansell S, Kuruvilla L.. Hodgkin's lymphoma. De Vita VTJ, Lawrence TS, Rosenberg SA (eds). De Vita, Hellman, and Rosenberg's Cancer: Principles Practice of Oncology: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014.
- Zhao FX.. Nodular Lymphocyte-Predominant Hodgkin Lymphoma or T-cell/Histiocyte Rich Large B-cell Lymphoma: The Problem in "Grey Zone" Lymphomas. *Int J Clin Exp Pathol* 2008; 1(3): 300-305.

This article should be referenced as such:

Carbone A, Gloghini A. T-cell/histiocyte rich large B-cell lymphoma. *Atlas Genet Cytogenet Oncol Haematol*. 2017; 21(5):180-182.
