

Leukaemia Section

Review

DLBCL subtype: Extranodal lymphoma

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Abstract

The assessment of extranodal lymphomas poses considerable challenges to histopathologists in routine work, because of the breadth of lymphoma subtypes, the variation in morphology, immunophenotype, genetics and clinical features of these entities, the difficulties in differential diagnosis, and the different clinical significance of lymphomas with primary versus secondary involvement of extranodal sites. DLBCL-NOS is the more frequent extranodal lymphoma subtype, which has characteristic features. Here the clinicopathology of extranodal lymphomas will be discussed.

Clinics and pathology

Disease

Proposed definitions of extranodal lymphoma vary, according to purpose, from lymphomas restricted to a single extranodal site and its regional lymph nodes to lymphomas which may be more widespread but in which an extranodal organ is the presenting and predominant site of disease, to which therapy may be primarily aimed. Extranodal lymphomas are different from those of lymph nodes, representing approximately 25-50% of all non-Hodgkin lymphomas (only 2-5% of classical Hodgkin lymphomas present at extranodal sites) (d'Amore et al. 2008.). Most lymphomas are from the gastrointestinal (GI) tract, followed by skin,

Waldeyer's ring, central nervous system, salivary glands, orbit, lung, bone, sinonasal tract, thyroid gland, testes, breast and other sites. (d'Amore et al. 2008; Heckendorn, et al. 2015. Siddiqui et al. 2009.) Both the lymphoma subtype and the organ involved may influence the clinical behaviour and management of the lymphoma.

Both B- and T/NK-cell lymphomas can occur in extranodal sites, in which B-cell lymphomas are more common. At most of extranodal sites, DLBCL-NOS is the most frequent lymphoma subtype. Although sharing features typical of DLBCL-NOS at any site of destructive tumours composed of diffuse sheets of large atypical B cells with prominent nucleoli and a high proliferative rate, DLBCL arising at some extranodal sites has characteristic features. For example, DLBCL of the testis and DLBCL of the central nervous system (DLBCL-CNS) share characteristic deletions of chromosome 6p21.3 leading to loss of HLA genes, not seen in nodal DLBCL. Clinically, DLBCL-NOS of Waldeyer's ring and the GI tract have a better prognosis than DLBCL-NOS overall, while testicular DLBCL-NOS has a worse outcome with a tendency for spread or relapse to other extranodal sites, particularly the CNS, and a propensity for late relapse. (Bacon, et al. 2009. Swerdlow et al, 2008. Swerdlow et al, 2016.)

Phenotype/cell stem origin

DLBCL-NOS arising at some extranodal sites has characteristic features, which arising in bone often

DLBCL subtype: Extranodal lymphoma

has multilobated nuclei, and those of the testis and stomach are usually of non-germinal centre immunophenotype while those of the small intestine and Waldeyer's ring are more often of germinal centre phenotype. DLBCL almost always expresses pan-B-cell markers, such as CD20. Most are bcl-6+, many are bcl-2+, and a minority are CD10+ (Swerdlow et al, 2008. Ferry 2008).

Epidemiology

DLBCL is the most common extranodal lymphoma, and it is the most common lymphoma encountered in GI, the central nervous system, the eyes, the paranasal sinuses, Waldeyer ring, bone, heart, adrenals, and other sites. DLBCL is mainly found in older adults, with a median age in the seventh decade, but younger adults and children are occasionally affected. There is a slight male preponderance overall, but this varies among anatomic sites (Swerdlow et al, 2008. Ferry 2008).

Clinics

Patients usually present with a rapidly enlarging tumor mass at single or multiple extranodal sites.

DLBCL typically produces large, destructive lesions that may invade adjacent structures. Almost half of the patients have stage I or II disease. Most patients are asymptomatic but when symptoms are present they are highly dependent on the site of involvement. Extranodal DLBCL-NOS is relatively increased in frequency in immunosuppressed individuals (Swerdlow et al, 2008. Ferry 2008. Bacon et al. 2009).

Pathology

Microscopic examination reveals a diffuse proliferation of large cells with round, oval, irregular, or lobated nuclei, distinct nucleoli, and scant cytoplasm. In a few cases, neoplastic cells may be bizarre or anaplastic, and in occasional cases, they may show plasmacytoid differentiation. In some cases, there is a concomitant component of low-grade lymphoma or a history of low-grade lymphoma (marginal zone lymphoma, follicular lymphoma, etc) consistent with large-cell transformation.

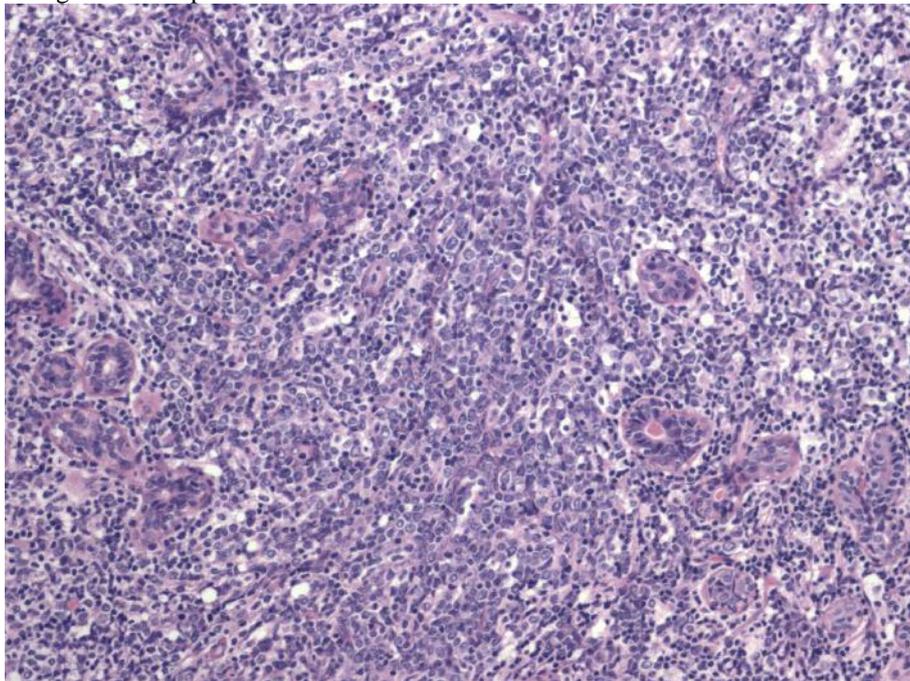


Figure 1. Primary DLBCL of the breast. Diffuse proliferation of lymphoid cells can be seen between ducts of the breast. Some ducts are distructed by the lymphoid cells, which are small to medium sized with sheets of large cells (HE staining).

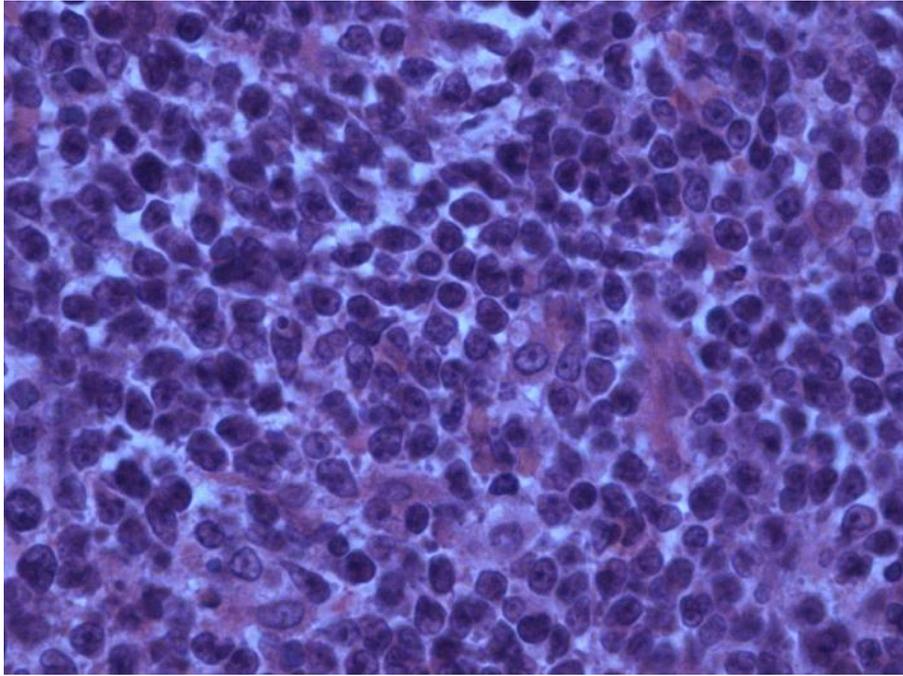


Figure 2. The lymphoid cells are large, with oval nuclei and distinct nucleoli. (HE staining).

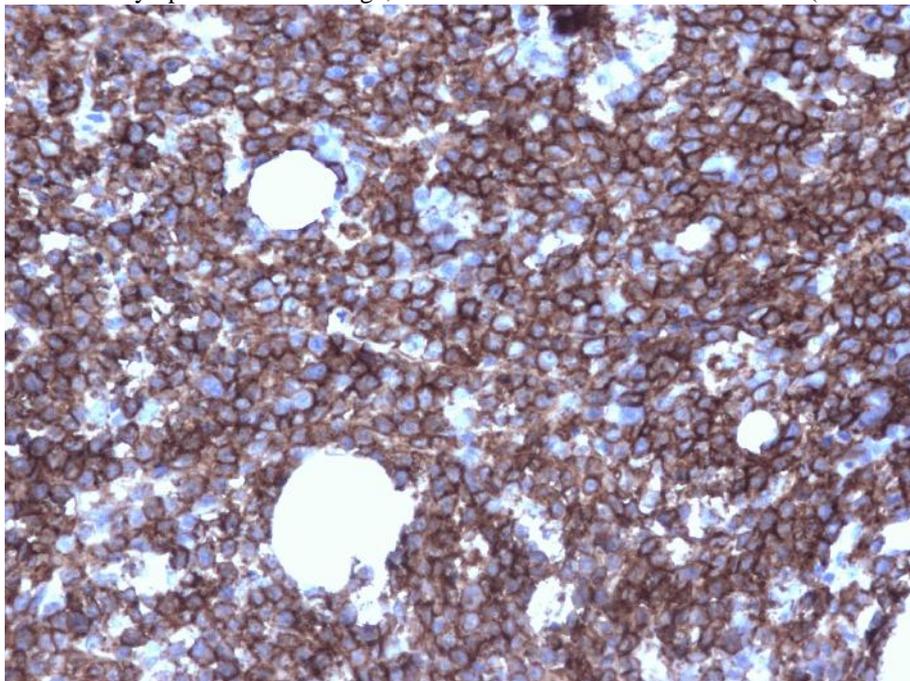


Figure3. The cells are positive for CD20.

Treatment

Both the lymphoma subtype and the organ involved may influence the clinical behaviour and management of the lymphoma. DLBCL are aggressive but potentially curable with multi-agent chemotherapy. The CHOP regimen has been the mainstay of therapy for several decades. The addition of the anti-CD20 monoclonal antibody rituximab to CHOP (R-CHOP) has led to a marked improvement in survival (Swerdlow et al,2008. Ferry, 2008. Bacon et al.2009). One study suggests

that anatomical location in B-NHL is governed by the differential expression of specific adhesion/motility molecules and provides implications for therapeutic strategies that aim to disrupt protective micro-environmental interactions (Middle et al. 2015.).

Prognosis

Clinically, DLBCL of Waldeyer's ring and the GI tract have a better prognosis than DLBCL overall, while testicular DLBCL has a worse outcome with a tendency for spread or relapse to other extranodal

sites, particularly the CNS, and a propensity for late relapse (Swerdlow, et al, 2008. Bacon, et al. 2009).

Cytogenetics

Cytogenetics morphological

There is emerging evidence of differences and similarities in somatic genetic abnormalities between DLBCL-NOS arising at different sites. For example, DLBCL-NOS of the testis and DLBCL-CNS (both tumours of immune privileged sites) share characteristic deletions of chromosome 6p21.3 leading to loss of HLA genes, not seen in nodal DLBCL (Swerdlow et al, 2008. Bacon et al. 2009).

References

Bacon CM.. Extranodal lymphomas. Diagnostic histopathology, 2009,16(2):82-98.

Ferry JA. Extranodal lymphoma Arch Pathol Lab Med 2008 Apr;132(4):565-78

Heckendorn E, Auerbach A. Pathology of Extranodal Lymphoma Radiol Clin North Am 2016 Jul;54(4):639-48

Middle S, Coupland SE, Taktak A, Kidgell V, Slupsky JR, Pettitt AR, Till KJ. Immunohistochemical analysis indicates that the anatomical location of B-cell non-Hodgkin's lymphoma is determined by differentially expressed chemokine receptors, sphingosine-1-phosphate receptors and integrins Exp Hematol Oncol 2015 Apr 1;4:10

Siddiqui MT, Pitelka LA, Gattuso P. Extranodal lymphomas: review of clinicopathologic and cytologic features Diagn Cytopathol 2009 Mar;37(3):220-9

Swerdlow SH, Webber SA, Chadburn A, et al.. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon : IARC press; 2008: 343-349. ISBN:978-92-832-2431-0

d'Amore F, de Nully Brown P, Weisenberger D.. Epidemiology of extranodal lymphomas. In: Cavalli F, Stein H, Zucca E, eds. Extranodallymphomas, pathology and management. London: Informa Healthcare,2008: 14e23.

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