

Leukaemia Section

Short Communication

Follicular dendritic cell in lymphomas of follicular origin

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Abstract

B-cell lymphomas of presumed follicular origin include follicular lymphoma (FL), mantle cell lymphoma (MCL) and marginal zone lymphoma (MZL). Within the microenvironment of all these follicle-derived lymphomas tumor cells show a strict topographical and functional relationship with FDCs, together with reactive lymphoid and stromal cells. The FDC patterns, as described for FL and MCL, are reminiscent of the distribution pattern of FDC meshwork seen in the GC or the mantle zone of the secondary lymphoid follicle, respectively.

Keywords

Lymphomas; Follicular lymphoma; Mantle cell lymphoma; Marginal zone Lymphoma; Follicular dendritic cells

Identity

Other names

Follicular dendritic cell patterns in the microenvironment of b-cell lymphomas of follicular origin

Clinics and pathology

Follicular dendritic cell: main features and functions

Follicular dendritic cells (FDCs) are stromal cells of mesenchymal origin, located in the peripheral lymphoid tissues, particularly in the B-cell-

dependent areas, i.e. in lymphoid primary follicles (primary FDCs) or in secondary follicles (secondary FDCs) (Allen et al., 2008; Rezk et al., 2013). The lymphoid follicle is a structure made of B and T lymphoid cells within a meshwork of FDCs. In the secondary lymphoid follicle, rounded collections of cohesive FDCs are seen in the germinal center (GC), whereas irregularly shaped meshworks of poorly cohesive FDCs are evident in the mantle zone (Tsunoda et al., 1999). Therefore, the patterns of FDC distribution, usually recognizable in secondary lymphoid follicles, include a tight/dense meshwork pattern with a polarized FDC meshwork pattern in the GC, and an expanded FDC meshwork with extension into the mantle zones (Rezk et al., 2013). Classic FDC immunophenotype includes the expression of CD21, CD23, and CD35. Other markers reported to be highly sensitive but not specific to FDCs include S-100 protein (Carbone et al., 1986), clusterin (Grogg et al., 2004) and podoplanin (Yu et al. 2007). FDC's main functions comprise: histoarchitecture organization of lymphoid follicles, antigen trapping and presentation, organization of apoptotic "waste" removing, and self-immunity prevention. Organizing functions of FDCs are chemokine dependent (Carbone and Gloghini 2014).

B-cell lymphomas of follicular origin: classification

B-cell lymphomas of presumed follicular origin include follicular lymphoma (FL), mantle cell lymphoma (MCL) and marginal zone lymphoma

(MZL). Within the microenvironment of all these follicle-derived lymphomas tumor cells show a strict topographical and functional relationship with FDCs, together with reactive lymphoid and stromal cells (Carbone et al. 2009; Rezk et al., 2013). The FDCs are thought to represent newly generated cells arising during lymphoma growth and progression, although they remain non-neoplastic bystander cells (Jin et al., 2011). The FDC patterns, as described for FL and MCL, (Manconi et al., 1988; Gloghini and Carbone 1993) are reminiscent of the distribution pattern of FDC meshwork seen in the GC or the mantle zone of the secondary lymphoid follicle, respectively (Carbone et al., 1988). The FDC patterns shown by FL and the other lymphomas of follicular origin have recently been reviewed (Rek et

al., 2013).

Disease

Follicular Lymphoma

FLs are derived from GC B cells and usually express BCL2 as a result of the characteristic t(14;18)(q32;q21) IGH/ BCL2 translocation. A pathologic diagnosis requires immunohistologic detection of neoplastic B cells that show positive staining for BCL2 and CD10. The FDC meshwork usually form a well-developed "spherical" dendritic meshwork with a sharp outline highlighting an attenuated mantle zone (Figure 1). Other patterns that can be seen include contracted/distorted/disintegrated FDC meshworks (Rezk et al., 2013; Carbone and Gloghini 2014).

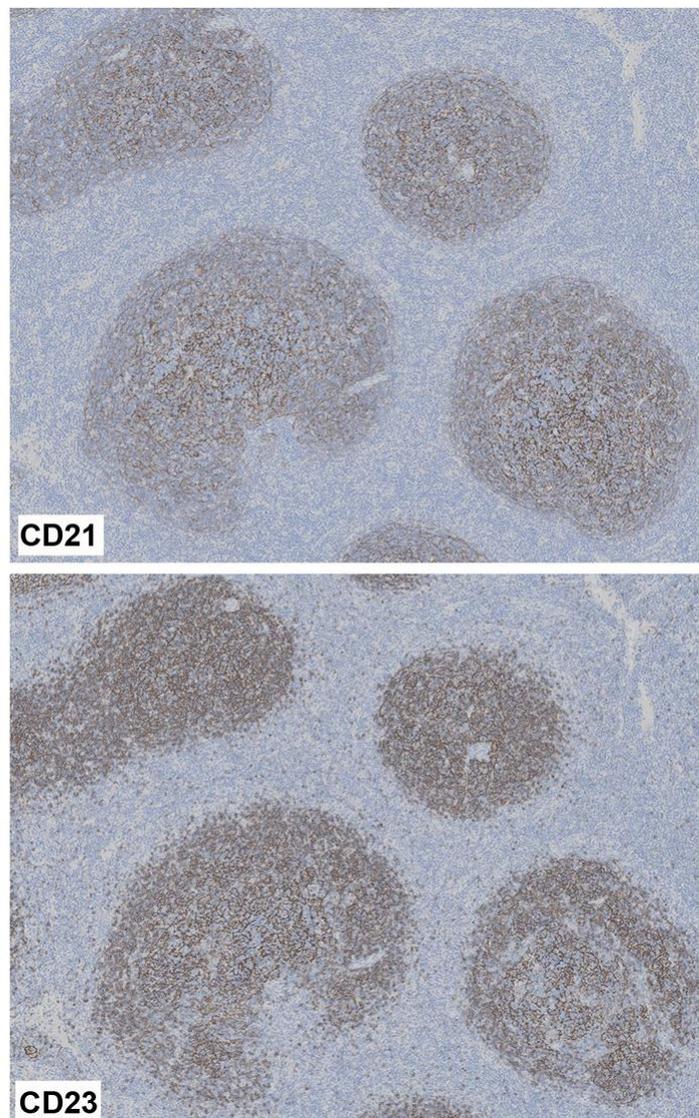


Figure 1. Follicular lymphoma. In this figure a follicular lymphoma shows a nodular pattern. Within the nodules, follicular dendritic cells form a spherical meshwork stained by CD21 and CD23.

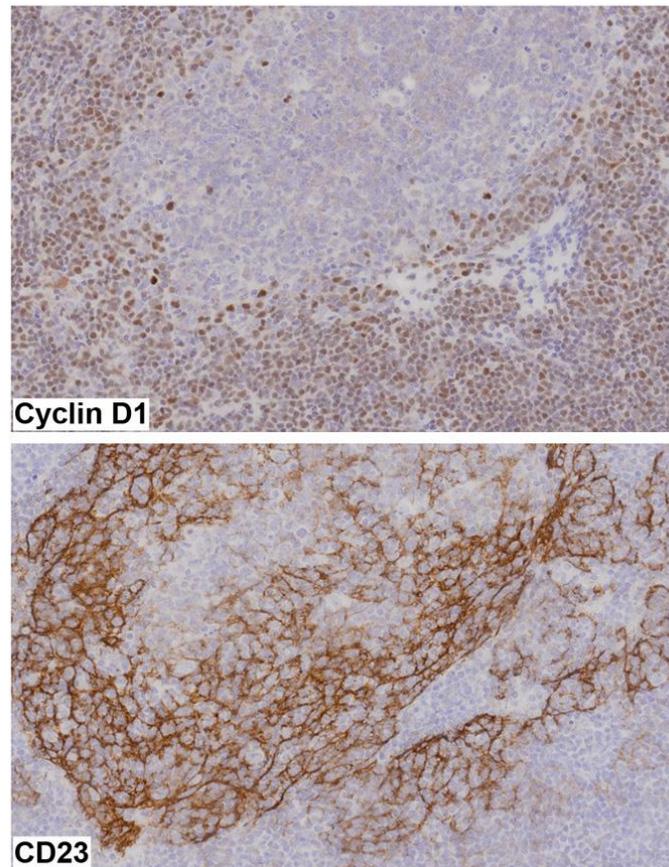


Figure 2. Mantle cell lymphoma (MCL) with mantle zone pattern. In this MCL, cyclin D1+ tumor cells involve the mantle zone of a secondary follicle where the CD23+ follicular dendritic cell meshwork is fragmented.

Disease

Mantle Cell Lymphoma

MCL is a B-cell neoplasm that usually carries the characteristic t(11;14)(q13;q32) translocation that juxtaposes the protooncogene CCND1, which encodes cyclin D1, at chromosome 11q13, to the Ig heavy-chain gene at chromosome 14q32.25 The typical antigen profile in this lymphoma includes the coexpression of CD5 and CD20 in the absence of CD3, CD10, and CD23 expression. Several growth patterns may be observed in MCL. They include a nodular growth pattern with residual GCs, a nodular growth pattern without residual GCs, a nodular growth pattern due to the colonization of reactive GCs, and a diffuse pattern with or without residual GCs (Campo et al., 2011). The t(11;14) translocation is the primary event of the B lymphocyte transformation that is followed by colonization and expansion of the mantle cell area of the lymphoid follicles (Figure 2).

When there is a nodular growth pattern with residual GCs, obviously the reactive GCs have preserved tight FDC meshworks, whereas neoplastic zones show a disrupted and fragmented FDC meshwork. Conversely, as the expansion of the neoplastic mantle zones continue outward, MCL neoplastic nodules with absent FDC meshworks and negative

staining for CD21 and CD23 are formed (Carbone and Gloghini 2014).

Disease

Marginal Zone Lymphoma

MZL is a B-cell lymphoma that is supposed to derive from the marginal zone. It encompasses 3 distinct entities known as mucosa-associated lymphatic tissue (MALT) lymphoma, nodal MZL (NMZL), and splenic MZL (SMZL) (Cook et al., 2017; Campo et al., 2017).

Among these B-cell lymphomas, early lesions may be observed within the subsets of NMZL and SMZL with tumor cells growing inside an attenuated mantle zone and often around a residual GC. Immunohistochemical studies show that in all MZL entities neoplastic B cells express CD20, CD43, and BCL2, but not CD3, CD5, CD10, and CD23 (Carbone et al. 1986; Rezk et al., 2013).

The FDC meshwork is variably distorted and disintegrated when there is a follicular colonization (Rez et al., 2013; Carbone and Gloghini, 2014; Cook et al., 2017; Campo et al., 2017). The presence of remnants of FDC meshwork suggests colonized follicles (Rez et al., 2013; Carbone and Gloghini, 2014). The FDC meshwork is more evident in cases with a nodular/follicular pattern (Figure 3).

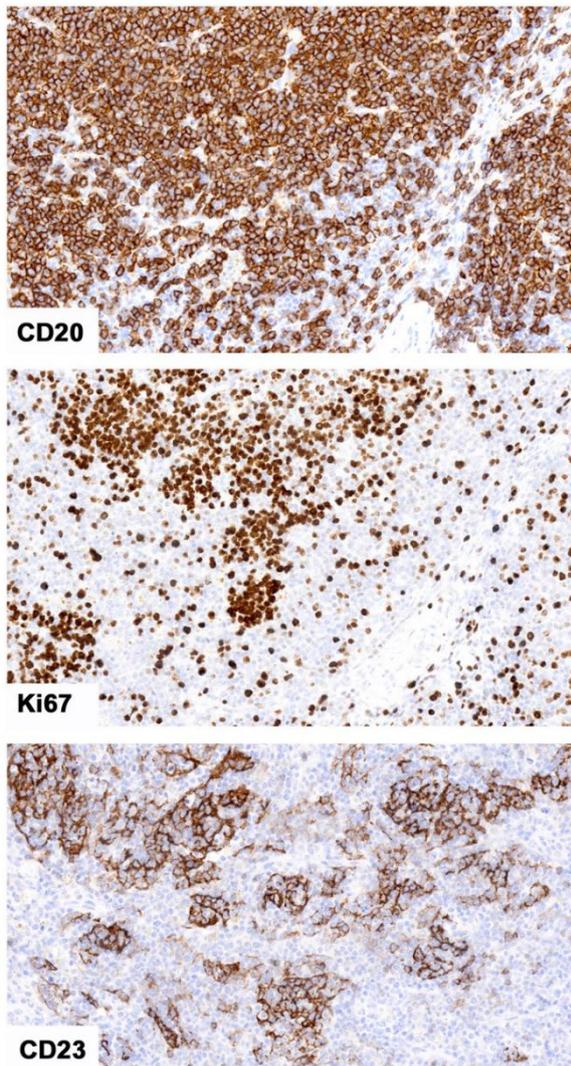


Figure 3. Marginal zone lymphoma with follicular colonization. The CD20+ neoplastic cells invade and colonize the germinal center. These neoplastic cells show a low proliferative index by MIB1/Ki67. The germinal center is still recognizable, but the CD23+ follicular dendritic cell meshwork is fragmented and disrupted.

To be noted

Conclusions: The microenvironmental FDC patterns seen in the CD21 and CD23 stains contribute to the definition of the early stages of B-cell lymphomas of follicular origin. The FDC patterns recognizable include a "spherical" pattern in FLs, a "mantle zone" pattern in MCL and a "centrifugal" pattern in MZL. These FDC patterns are easily recognizable the lymphoma is in its early stage and still maintains a follicular/nodular pattern of growth.

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