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Short Communication

Lymphocyte-rich classical Hodgkin lymphoma

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Abstract

Lymphocyte-rich classical Hodgkin lymphoma accounts for a small fraction of all Hodgkin lymphomas.
Lymphocyte-rich classical Hodgkin lymphoma is a rare variant of classical Hodgkin lymphoma which resembles nodular lymphocyte predominance Hodgkin lymphoma, in terms of nodular growth and lymphocyte-richness, and mimics cHL, in terms of the immunophenotype of the tumour cells. Lymphocyte-rich classical Hodgkin lymphoma tumour cells have lost the B-cell phenotype, but express CD30 and the B-cell transcription program. As regards to genetics and cytogenetics findings please refer to the general features described in the CARDS related to nodular lymphocyte predominance Hodgkin lymphoma and classical Hodgkin lymphoma.

Keywords
Lymphocyte-rich classical Hodgkin lymphoma; LRCHL; Pathology; Phenotype; Clinics

Identity

Other names
Nodular lymphocyte-rich classical Hodgkin lymphoma
LRCHL
Nodular lymphocyte-rich classical Hodgkin disease

Clinics and pathology

Disease

Hodgkin lymphoma (HL) has been classified into classical HL (cHL) (Stein et al., 2008), which accounts for 95% of all cases, and the less common nodular lymphocyte predominant HL (NLPHL) (Poppema et al., 2008). A variant of cHL which resembles NLPHL, in terms of nodular growth and lymphocyte-richness, and mimics cHL, in terms of the immunophenotype of the tumour cells, was originally designated nodular lymphocyte-rich classic Hodgkin disease (Anagnostopoulos et al. 2000), now called lymphocyte-rich cHL (LRCHL). LRCHL displays histologic and clinical features intermediate between those of cHL and NLPHL (Nam-Cha et al., 2009; Anagnostopoulos et al., 2008; Swerdlow et al., 2016).

Phenotype/cell stem origin

Cell origin: LRCHL involves a clonal expansion of B lymphocytes which mimic those observed in the outer zone of germinal centers of lymphoid follicles (Nam-Cha et al., 2009). Tumour cells have partly lost the B-cell phenotype and coexpress CD30 and the B-cell transcription program.
Phenotype: The tumour cell phenotype, which is characterized by the expression of CD30, also shows the expression of CD20 and B-cell transcription factors.

The phenotype is the following (Nam-Cha et al., 2009):
MUM1/IRF4 + (100%)
PAX5 + (94%)
BOB1 + (62%)
CD15+ (56%)
OCT2 + (56%)
OCT1 + (50%)
BCL6 + (36%)
CD20+ (31%)

Cell microenvironment

LRCHL tumour cells reside in a microenvironment resembling expanded mantle zones, where numerous small B lymphocytes displaying a mantle cell phenotype (IgD+, CD20+) are admixed with meshworks of dendritic reticulum cells (CD21+, CD23+). LRCHL tumour cells are rosetted by CD4+, PD1+ T cells.

Epidemiology

LRCHL accounts for only a small fraction (3% to 5%) of all HLs (Younes et al., 2014), in similar frequency to NLPHL. The median age is similar to NLPHL and significantly higher than in other subtypes of cHL. There is a male predominance (Shimabukuro-Vornhagen, et al., 2005).

Pathology

Among the four histological subtypes of cHL, nodular sclerosis and mixed cellularity are the most common subtypes, whereas the lymphocyte-depleted and lymphocyte-rich subtypes are the less common (Stein et al., 2008).

LRCHL exhibits a nodular growth pattern.

The nodules are composed of small lymphocytes and may harbour germinal centers that are usually eccentrically located and relatively small or regressed.

The neoplastic cells, the Hodgkin Reed-Sternberg (HRS) cells, are predominantly found within the nodules, but consistently outside of the germinal centers.

The HRS cells show broad morphologic spectrum: a proportion of the HRS cells may resemble lymphocyte predominant (LP) cells or mononuclear lacunar cells.

However, the demonstration of an immunophenotype typical for classical HRS cells may permit their precise recognition as LRCHL tumour cells.

Other features

Virology

At variance with NLPHL the neoplastic cells in LRCHL appear to be permissive for an EBV infection. EBV infection is observed in LRCHL tumour cells less frequently than in mixed cellularity cHL but more frequently than in nodular sclerosis cHL (Carbone et al., 2016).

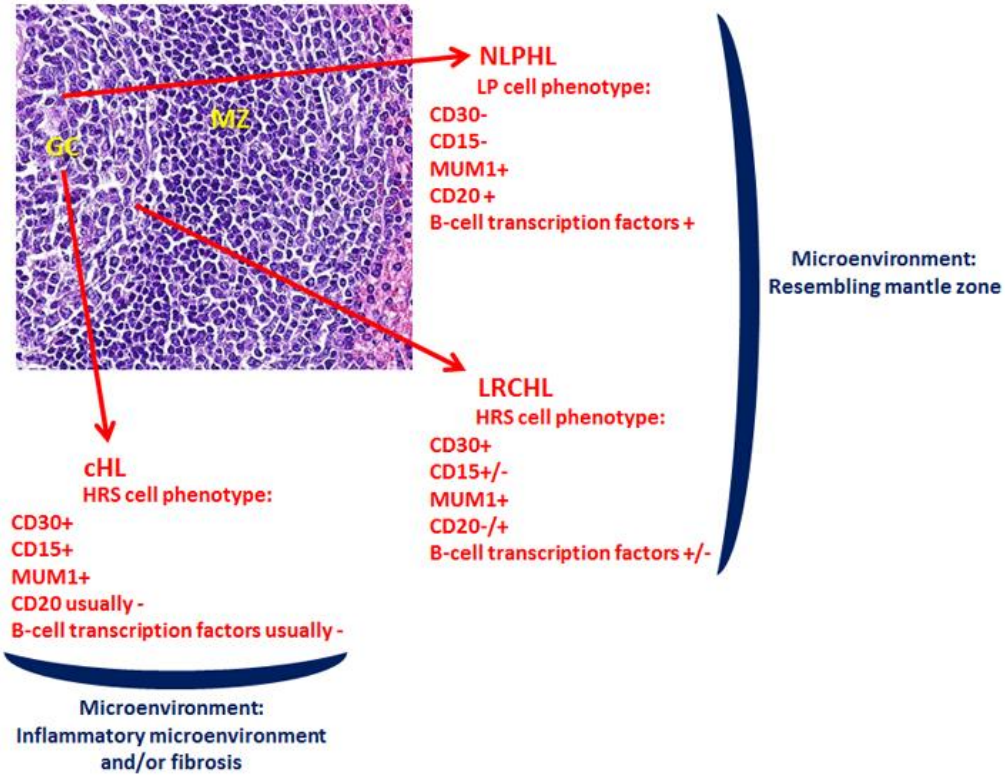

figure 1. The Figure shows that LRCHL displays histologic and phenotypic features intermediate between those of NLPHL and cHL. LRCHL may hypothetically be an early presentation of cHL in which tumour cells have lost the B-cell phenotype but coexpress CD30 and the B-cell transcription program (Younes et al., 2014).

It seems appropriate to mention here that the virologic characteristics of HL of the general population vary according to the immunocompetence status of the host and cHL subtype (IARC, 2012) as follows:
cHL of the general population
- Nodular sclerosis cHL, usually EBV negative
- Mixed cellularity cHL, usually EBV positive
- LRCHL, variably EBV positive
- Lymphocyte depletion cHL, variably EBV positive
- NLPHL usually EBV negative

Evolution

Clinically, patients with NLPHL and LRCHL show similar disease presentation but differ in the frequency of multiple relapses and prognosis after relapse. Patients with NLPHL and LRCHL differ from patients with cHL with nodular sclerosis or mixed cellularity, as they present with an earlier disease stage (Anagnostopoulos et al. 2000).

Prognosis

Most LRCHLs have a better prognosis than do other cHLs.

Genetics

See the pertinent sections within the CARDS describing the general features of NLPHL and cHL (Küppers, 2011; Carbone and Gloghini, 2016; Gloghini and Carbone, 2016).

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