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Short Communication

Lymphocyte depletion classical Hodgkin lymphoma

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Abstract

The lymphocyte depletion classical Hodgkin lymphoma (LDCHL) is the less common subtype of cHL. In LDCHL, Hodgkin and Reed-Sternberg (HRS) cells grow within a background depleted in reactive lymphocytes. LDCHL subtype accounts for only a small fraction of all HL cases in Western countries. It also occurs in people with HIV/AIDS. The HRS cells show the same immunophenotype as in the other subtypes of cHL.

Keywords
Lymphocyte depletion; classical Hodgkin Lymphoma; Hodgkin Lymphoma; LDCHL.

Identity

Other names
Lymphocyte depletion Hodgkin Lymphoma
Lymphocyte-depleted classical Hodgkin lymphoma
Lymphocyte depletion Hodgkin disease.

Clinics and pathology

Disease

Hodgkin Lymphoma (HL) includes classical Hodgkin lymphoma (CHL) which accounts for 95% of all cases (Stein et al. 2008). Lymphocyte depletion classical Hodgkin lymphoma (LDCHL) is the less common subtype of cHL (Benharroch et al., 2008). LDCHL is a subtype of cHL rich in Hodgkin and Reed-Sternberg (HRS) cells. These cells reside within a background depleted in non-neoplastic lymphocytes. In the past few decades, a fraction of these cases have been reclassified into different non-Hodgkin lymphoma entities (Benharroch et al., 2008).

Phenotype/cell stem origin

LDCHL involves a clonal expansion of germinal center B-cell derived lymphocytes which mimic those observed in the other subtypes of cHL.

Epidemiology

LDCHL accounts for only a small fraction, less than 1%, of all HL cases in Western countries. There is a male predominance. The median age ranges from 30 to 40 years. LDCHL is often seen in people infected with HIV and more often in developing countries (IARC, 2012).
People with HIV/AIDS are at increased risk of HL in the highly active antiretroviral therapy era. In HIV-infected people cHL is presently the most common non-AIDS defining cancer (Carbone et al., 2014).

Clinics

Patients affected by LDCHL present with an advanced stage (III-IV stage) and with B symptoms more often than those affected by the other subtypes. LDCHL usually involves retroperitoneal lymph-nodes and extranodal sites including abdominal organs and bone-marrow (Younes et al., 2014).

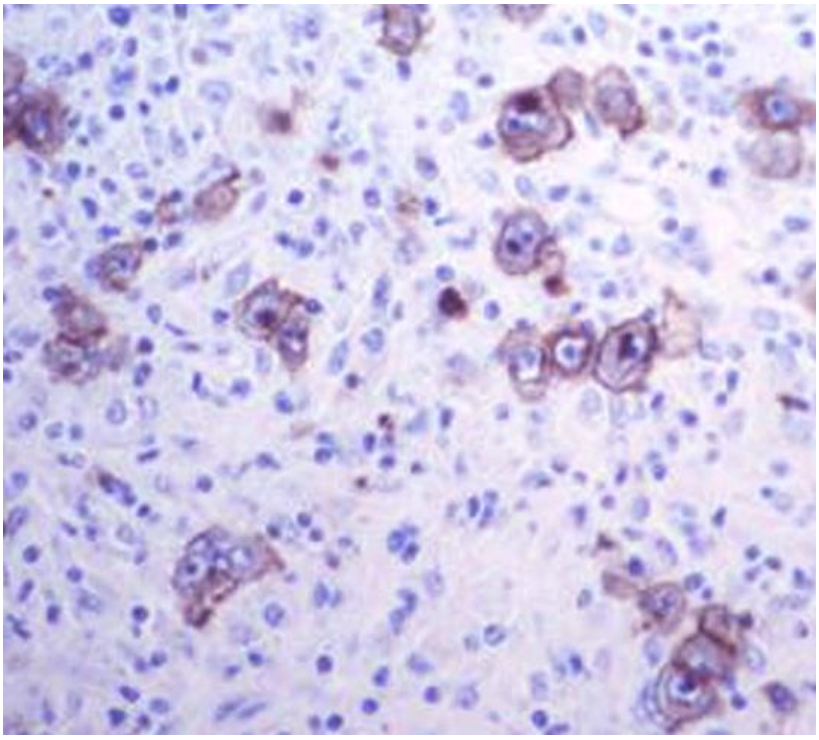

Figure 1. Involvement of lymph node by HIV-associated classic Hodgkin lymphoma (cHL) of the lymphocyte depletion subtype. Large Hodgkin Reed-Sternberg (HRS) cells with multiple nuclei and prominent nucleoli are present. HRS cells express the typical phenotype with intense staining for CD30.

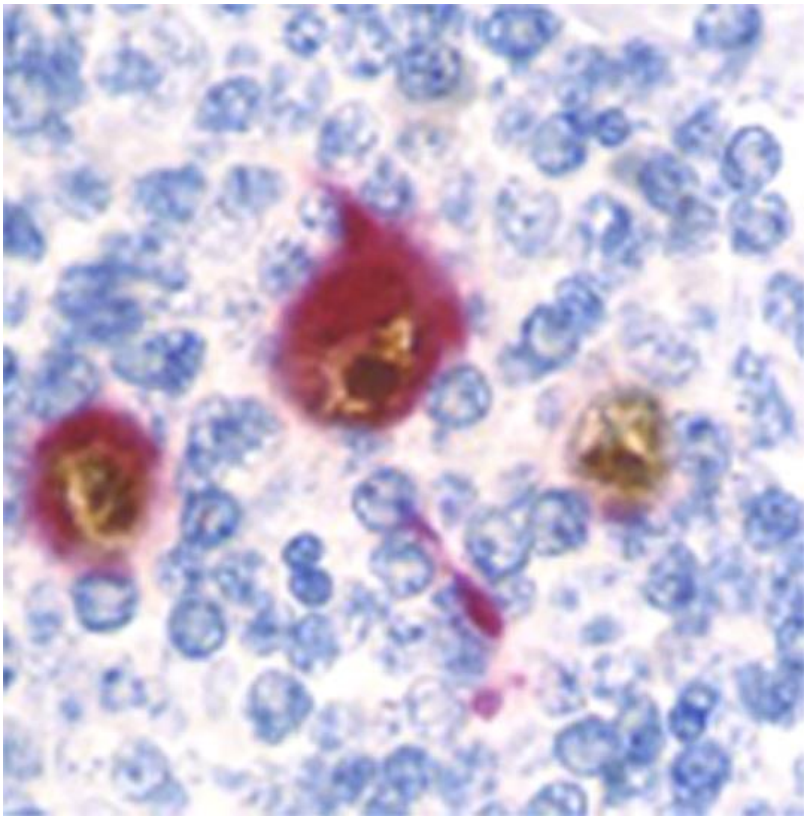

Figure 2. Involvement of lymph node by HIV-associated classic Hodgkin lymphoma (cHL) of the lymphocyte depletion subtype. Large Hodgkin Reed-Sternberg (HRS) cells are Epstein-Barr virus-infected as demonstrated by EBER in situ hybridization (brown) with latent membrane protein 1 expression (red).

Pathology

A consistent feature is the predominance of HRS cells in relation to the cell density of the background. The HRS cells are pleomorphic with a sarcomatous appearance. A proportion of HRS cells may resemble anaplastic forms of tumour cells observed in some large cell non-Hodgkin lymphoma. The background is characterized by diffuse fibrosis and depletion in reactive lymphocytes.

Phenotype

The HRS cells show the same immunophenotype as in the other subtypes of CHL (Carbone and Gloghini, 2016); the immunophenotype is the following: CD30+, CD15 usually+, MUM1/IRF4+, PAX5 usually+, CD20-/+

Other features

Virology

Tumour tissue is characterized by an unusual large proportion of HRS cells infected by EBV. EBV is found in nearly all cases of LDCHL occurring in patients infected by HIV. EBV infected tumour cells contain LMP1 which can activate critical signaling pathways including NF-kB.

It seems appropriate to mention here that the virologic characteristics of HL vary according to the immunocompetence status of the host and cHL subtype (IARC, 2012; Swerdlow et al., 2008) as follows:

cHL of the general population
- NS cHL, usually EBV negative
- MC cHL, usually EBV positive
- LRCHL, variably EBV positive
- LD cHL, variably EBV positive

Immunodeficiency-associated cHL
- HIV-associated cHL, EBV positive
- Post-transplant cHL, EBV positive
- Iatrogenic (methotrexate), variaby EBV positive

Etiology

LMP1 expression is observed in virtually all HIV associated LDCHL cases: it suggests that EBV play an etiological role in the pathogenesis of these tumours.

Cell microenvironment

HRS cells are usually seen in a microenvironment where several histiocytoid cells are admixed with few small lymphocytes. These lymphocytes predominantly express the CD3+, CD4+, CD8-/+, CD20- phenotype.

It has been recognized that EBV has the capability to modulate the tumour microenvironment (Dolcetti, 2015; Dolcetti et al., 2016).

Treatment

The combination of cART with better supportive therapy has made standard ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine), used for LDCHL occurring in the general population, feasible in patients with HIV-associated Hodgkin lymphoma (Carbone et al., 2014).

Prognosis

Most patients affected by LDCHL have a worse prognosis than do patients affected by other cHL subtypes (Younes et al., 2012).

Poor prognosis have been observed in patients affected by HIV-associated LDCHL. The outcome of HIV-associated cHL has dramatically improved since the introduction of cART with intensive chemotherapy regimens (Carbone et al., 2014).

Genetics

Due to the small number of LDCHL cases analysed for genetics/cytogenetics characteristics and to the reclassification of cases into different lymphoma categories, the previously described genetics and cytogenetics findings are not unquestionably acknowledged.

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