Primary mediastinal B-cell lymphoma (PMBL)

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Abstract

Review on primary mediastinal B-cell lymphoma, with data on clinics, and the genes involved.

Keywords
primary mediastinal B-cell lymphoma; diffuse large B-cell lymphoma

Identity

Other names
Thymic large B-cell lymphoma
Primary mediastinal (thymic) large B-cell lymphoma
Mediastinal Large B-cell lymphoma

Clinics and pathology

Disease
PMBL is a subtype of diffuse large B-cell lymphoma (DLBCL) that arises in the thymus. It accounts for 2-4% on non-Hodgkin lymphoma and 10% of DLBCL. It is epidemiology, clinically and biologically distinct from the other subtypes of DLBCL. Similar to nodular sclerosis Hodgkin lymphoma (NSHL) arising in the mediastinum, it is likely derived from thymic B cells (Dunleavy et al., 2015).

Phenotype/cell stem origin
An origin from medullary thymic B cells has been proposed for this disease. PMBL has a B-cell phenotype and express CD20 and pan B-cell markers such as CD79a, CD 45, CD 19 and CD22, but tumor cells do not express surface immunoglobulin, therefore, monoclonality cannot be established by Κ and λ staining. B-cell transcription factors including PAX-5, OCT2 and BOB1 are typically strongly expressed. CD23 expression is present in almost 66% of cases; CD30 is expressed in 78% whereas CD 15 is usually negative, although one third of patients are positive. High expression of BCL2 and PD1 has been described (Bledsoe et al., 2016). CD21 and class I and/or II histocompatibility molecules have been claimed to be absent. Bcl-2 protein seems to be generally expressed, while fragmentary data are available concerning the occurrence of some molecules, such as CD10, MUM1/IRF4, PAX5/BSAP (B-cell Specific Activating Protein), Bcl-6.

Epidemiology
Typically presents in adolescents and young adults with a median age of 35 years and a female predominance with a male:female ratio of 1:2. (Gaulard et al., 2008).

Clinics
PMBL is an aggressive disease manifested by a localized, bulky mediastinal mass, often with pleural and pericardial effusions. Symptoms at diagnosis are caused by the mediastinal mass, and complications such as superior vena cava syndrome are common at presentation. Regional lymph nodes may be involved, but spread to distant nodal sites is uncommon. Less frequent, the disease involves extranodal sites, including the lung, kidneys, gastrointestinal organs or brain.

Pathology
Morphologically, the thymic B-cells are medium to large cells having round or lobulated nuclei and abundant cytoplasm. In most cases,
 compartamentalizing sclerosis is observed, and sometimes tumor cells can resemble Hodgkin/Reed Sternberg cells. The nodal architecture is typically diffuse, with occasional cases showing focal nodularity, and necrosis is sometimes seen.

**Treatment**

In making decisions about the initial treatment one must consider the long-term complications of mediastinal radiation in this population of patients who are predominantly young women. R-CHOP followed by radiation has been effective in low-risk patients. In high-risk disease and high rate of primary refractory disease DA- EPOCH-R without radiation is the best treatment option, followed or not of autologous stem cell transplantation.

**Prognosis**

Although the international prognosis index (IPI) is useful in DLBCL, its use in PMBL could be limited by the young age distribution and its typical mediastinal presentation. Lactate dehydrogenase level, male sex, performance status and advanced-stage disease may be useful predictors of survival.

**Genetics**

NoteAmong the most common genetic alterations in PMBL are abnormalities on chromosome 9p and 2p. The 9p region encodes JAK2, which then activates the STAT6 through phosphorylation. This STAT 6 phosphorylated can transcriptionally repress BCL6. Also in 9p region, CD274 and PDCD1LG2 (programmed death ligands (PDLs) 1 and 2 respectively) are rearranged at a frequency of 20%. Gains or amplifications of REL may be seen at 2p. One third of cases may have gains in chromosome X. New two recurrent mutations have been identified; one of these is the recurrent somatic coding-sequence mutation in the PTPN1 gene (also found in Hodgkin lymphoma cases) and the recurrent point mutation in the XPO1 (exportin 1 gene or CRM1), which results in the Glu571Lys missense substitution, in refractory/relapsed PMBL (Jardin et al., 2016). The XPO1 mediate the translocation of numerous RNAs and cellular regulatory proteins, including tumor suppressor proteins (TP53, BRCA1, NPM1, APC and FOXO).

**References**


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