**Burkitt lymphoma (BL)**

**Status: May 2020**

Inform yourself about the classification according to WHO criteria and the diagnosis of Burkitt lymphoma (BL) and learn more about the prognosis.

### Diagnostic recommendation

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<th>Method</th>
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<tr>
<td>Cytomorphology</td>
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<td>Immunophenotyping</td>
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<tr>
<td>Chromosome analysis</td>
<td>Heparin</td>
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<td>FISH</td>
<td>EDTA or Heparin</td>
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<td>Molecular genetics</td>
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*As test material for the FISH analysis we recommend unfixed, unstained smears*
Definition and characteristics

Burkitt lymphoma (BL) is a highly aggressive lymphoma and is characterized by an extraordinarily high cell division rate of 3 cells.

Burkitt lymphoma - Classification

According to the WHO, 3 clinical variants of BL are recognized: the endemic Burkitt lymphoma occurs in tropical regions, e.g., in Africa, and is associated with a tumour-inducing effect of EBV. There it is one of the most frequent tumour diseases in children between the ages of 4-7 years. The sporadic Burkitt lymphoma occurs in temperate climate zones (mainly USA and Western Europe), accounting for 1-2% of all lymphomas. The median age of the adults is 30 years, with men being affected twice as often as women. Immune deficiency-associated Burkitt lymphoma is more common in the setting of HIV infection than in other forms of immunosuppression. A leukemic form of Burkitt lymphoma is characterized by a bone marrow infiltration of more than 25% lymphocytic blasts in the bone marrow and is called Burkitt's leukemia (formerly "mature B-ALL").

A new provisional entity described in the WHO 2017 includes "Burkitt-like" lymphoma with 11q aberration. Burkitt-like lymphoma with 11q aberration is similar to Burkitt's lymphoma in morphology and gene expression profile, but differs from it cytogenetically, clinically (often nodal involvement) and molecularly.

Diagnostics of Burkitt lymphoma

Since there is no method that represents the sole gold standard in the diagnosis of Burkitt lymphoma or Burkitt's leukemia, an integrated diagnostic approach taking into account morphology, histology, immunophenotyping, and genetics is central. Due to the frequent involvement of the CNS, an additional cerebrospinal fluid (CSF) examination should be performed.

Cytomorphology

Unilateral bone marrow biopsy and cytology are highly recommended. The evaluation of the bone marrow smear allows to assess whether lymphoma infiltration exists or is possible. Cytomorphology and histology are also useful for evaluating the degree of lymphoma maturity.

Immunophenotyping

Unlike Burkitt lymphoma, the majority of medium-sized malignant cells are often found in the extended blastocyst gate (medium SSC, CD45+ low). Typical is an expression of CD19, CD20, CD79a and FMC7 with simultaneous expression of CD10 and often CD38 and IgM. CD23 and CD5 are negative. Differentiation from another B-lymphoblastic neoplasia is possible by lacking expression of immature markers (CD34, TdT) and by the presence of light chain expression.

Chromosome analysis

Burkitt's lymphoma is characterized by chromosomal changes affecting the MYC gene on chromosome 8. The most frequent translocation here is t(8;14)(q24;q32), which is associated with an IGH-MYC rearrangement. In rare cases, rearrangements with the locus of the immunoglobulin light chain lambda on chromosome 22 (t(22;8)(q11.2;q22)) or kappa on chromosome 2 (t(8;22)(q12;q11)) may also occur. Other characteristic aberrations include the gain of the long arm of chromosome 1 (t(1q), trisomy 7 and trisomy 12.

Although MYC rearrangements are characteristic for Burkitt lymphoma, they are not specific for this entity. They are also found in other mature B-cell neoplasms such as diffuse large B-cell lymphoma (DLBCL) or highly malignant B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangement (HG BL). The latter category (formerly known as "double hit lymphoma" or "triple hit lymphoma") show a variable morphology similar to DLBCL, Burkitt lymphoma and rarely follicular lymphoma. HG BL are mostly aggressive lymphomas with an unfavorable prognosis (see also further information on HGBL). Compared to other lymphomas with MYC rearrangement, the karyotypes in Burkitt lymphoma are less complex.

Instead of MYC rearrangement, Burkitt-like lymphoma shows proximal gains and losses of the telomere region of the long arm of chromosome 11. The smallest deleted region was described as region 11q24-1.1 and the smallest amplified region was described as region 11q23.2-23.3. The 1q gains typical for BL have not been observed in this new provisional entity, but an association with more complex karyotypes has been observed (Aukema et al. 2015, Salavenia et al. 2014).

FISH

Fluorescence in situ hybridization (FISH) plays a central role in the detection (Burkitt lymphoma) or exclusion (Burkitt-like) of a MYC rearrangement (q24). The use of FISH probes for the detection of a BCL6 and BCL2 rearrangement makes it possible to check whether a highly malignant B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangement is present. In addition, in addition to the classical chromosome analysis, "chromosome painting" with 5-3 colours or 24-colour FISH can be used to clarify or validate BL typical (e.g., trisomy 12) as well as complicated chromosomal aberrations.

Molecular genetics

While t(8;14) causes dysregulation of the MYC gene, mutations in TOC3, ID3 and CCND3 activate the TOC3 signaling pathway. The combination of both events plays an important role in the development of BL and leads to both increased proliferation and prolonged survival of BL cells. 70% of sporadic BLs show mutations in the TOC3 (also known as E2A) genes. In addition, mutations in the genes TP53 (60%), MYC (49%) and ID3 (36%) were found (Klaber et al. 2016). Further recurrent mutations were described in the genes CCND3, RHOA, SMARCA4 and ARID1A.
In contrast, Burkitt-like lymphoma with 11q change shows no mutations in the genes of the ID3-TCF3 pathway, TP53 or SMARCA4 (Wagener et al. 2019, Gonzalez-Farre et al. 2019). Instead, a GNA13 mutation is often found, which is otherwise associated with “germinal center B-cell (GCB) like” lymphomas.

**Prognosis of Burkitt lymphoma**

Since Burkitt’s lymphoma is an aggressively growing tumor with a proliferation rate of often 100%, early therapy is necessary. Intensive combination chemotherapy leads to a 5-year survival of 90% for adolescents, 84% for adults and 62% for elderly patients (Hölzer et al. 2014).

**References**

You can find the corresponding references here: