Burkitt's lymphoma (BL)

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

Diagnostic recommendation

Method	Anticoagulant	Recommendation
Cytomorphology	EDTA	mandatory
Immunophenotyping	EDTA or Heparin	mandatory
Chromosome analysis	Heparin	optional
FISH	EDTA or Heparin	mandatory*
Molecular genetics	EDTA or Heparin	optional

*As test material for the FISH analysis we recommend unfixed, unstained smears

Definition and characteristics of Burkitt's lymphoma

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

Burkitt's lymphoma - Classification

According to the WHO, 3 clinical variants of Burkitt's lymphoma (BL) are recognized: the endemic Burkitt's lymphoma is 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 tumor diseases in children between the ages of 4-7 years. The sporadic Burkitt's 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. Immunodeficiency-associated Burkitt's lymphoma is more common in the setting of HIV Infection than in other forms of immunosuppression. A leukemic form of Burkitt's 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's lymphoma

Since there is no method that represents the sole gold standard in the diagnosis of Burkitt's lymphoma or Burkitt's leukemia, an integrated diagnostic approach taking into account morphology/histology, immunophenotype 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 cytomorphology is 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.

Cytomorphology often shows a characteristic phenotype with medium-sized blast forms, which are conspicuous by a deep basophilic cytoplasm with characteristic vacuolisation.

Immunophenotyping

In immunophenotyping, the mostly medium-sized malignant cells are often found in the extended blastocyst gate (medium SSC, CD45+-low). Typical is an expression of CD19, CD20, CD79b 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 (IGL-*MYC*/t(8;22)(q24;q11)) or kappa on chromosome 2 (IGK-*MYC*/ t(2;8)(p12;q24)) may also occur. Other characteristic aberrations include the gain of the long arm of chromosome 1 (+1q), trisomy 7 and trisomy 12.

Although *MYC* rearrangements are characteristic for Burkitt's 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 (HGBL). The latter category (formerly known as "double hit lymphoma" or "triple hit lymphoma") show a variable morphology similar to DLBCL, Burkitt's lymphoma and rarely follicular lymphoma. HGBL 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's 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-ter and the smallest amplified region was described as region 11q23.2- 23.3. The 1q gains typical for Burkitt's lymphoma (BL) have not been observed in this new provisional entity, but an association with more complex karyotypes has been observed (Aukema et al. 2015, Salaverria et al. 2014).

FISH

Fluorescence in situ hybridization (FISH) plays a central role in the detection (Burkitt's lymphoma) or exclusion (Burkitt-like) of a *MYC* rearrangement (8q24). 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 1-3 colours or 24-colour FISH can be used to clarify or validate Burkitt's lymphoma 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 *TCF3*, *ID3* and *CCND3* activate the *TCF3* signaling pathway. The combination of both events plays an important role in the development of Burkitt's lymphoma and leads to both increased proliferation and prolonged survival of Burkitt's lymphoma (BL) cells. 70% of sporadic BLs show mutations in the *TCF3* (also known as *E2A*) genes. In addition, mutations in the genes

TP53 (60%), *MYC* (49%) and *ID3* (36%) were found (Haberl 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's 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:
https://www.mll.com/en/diagnostic-offer/mature-b-cell-neoplasms/burkitts-lymphoma-bl.html#references