DIAGNOSIS OF BURKITT LYMPHOMA AND RELATED HIGH-GRADE B-CELL NEOPLASMS

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KEYWORDS

• Burkitt lymphoma • MYC • Epstein-Barr virus • High-grade B-cell lymphoma unclassifiable
• Diffuse large B-cell lymphoma • Acute lymphoblastic lymphoma

ABSTRACT

Burkitt lymphoma (BL) is an aggressive B-cell neoplasm with an extremely short doubling time that mainly affects children and young adults. Despite having several characteristic features, none is entirely specific for BL and the differential diagnosis may include diffuse large B-cell lymphoma (DLBCL), B lymphoblastic leukemia/lymphoma, and B-cell lymphoma unclassifiable with features intermediate between DLBCL and BL. We outline a practical approach to establish a diagnosis of BL and distinguish it from other high-grade B-cell malignancies. We pay particular attention to B-cell lymphomas with features intermediate between DLBCL and BL, a new diagnostic category in the 2008 World Health Organization classification system that provides a framework for categorizing challenging cases not meeting diagnostic criteria for either "classic" BL or DLBCL.

Pathologic Key Features OF BURKITT LYMPHOMA

1. Morphology is characterized by a diffuse proliferation of small to medium-sized monomorphous cells with round nuclei, finely clumped chromatin, multiple small paracentric nucleoli, and scant deeply basophilic cytoplasm. Numerous mitoses and apoptotic histiocytes give the tumor a characteristic "starry-sky" pattern on low magnification.
2. Slight nuclear pleomorphism, nuclear membrane irregularities, or nucleolar prominence is acceptable, particularly in immunodeficiency-associated cases, provided other key immunophenotypic and genetic criteria are met.
3. The immunophenotype of BL is CD10 strongly positive, BCL6-positive, BCL2-negative (or occasionally weakly positive), and a Ki-67 proliferation index greater than 95%.
4. The main genetic feature of BL is the presence of a *MYC* translocation, present in 95% of cases. This is most often an *IGH-MYC* translocation, or less commonly, *IGK-MYC* or *IGL-MYC* translocation.

BURKITT LYMPHOMA

OVERVIEW

The pathogenesis of BL appears to be multifactorial, as evidenced by its occurrence in different populations and clinical settings and its varying association with Epstein-Barr virus (EBV) infection; the 3 clinical variants of BL are described in **Table 1**. The vast majority of cases of endemic BL are EBV positive and their geographic distribution closely parallels that of holoendemic malaria. Evidence suggests that endemic BL may result from polyclonal B-cell activation and reactivation of latently

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Table 1
Clinical variants of Burkitt lymphoma

Clinical Variant	Age of Onset and Incidence	Male:Female Ratio	Geographic Distribution	Sites of Disease	EBV Association
Endemic BL	Mainly children, peak incidence 4–7 years Most common childhood malignancy in equatorial Africa	2:1	Equatorial Africa and Papua New Guinea	Commonly extranodal: jaws, orbit or other facial bones (50% of cases); also ileocecal region, omentum, gonads, kidneys, long bones, thyroid, salivary glands and breasts	>90% of cases
Sporadic BL	Children and young adults (median age of adult patients 30 years) 1%–2% of all lymphomas in Western Europe and North America and 30%–50% of childhood lymphomas	2–3:1 in adults, higher in children	Worldwide	Commonly extranodal: ileocecal region (most frequent site); also ovaries, kidneys, breasts. Nodal presentation more common in adults. Jaw tumors, Waldeyer ring and mediastinal disease rare	15%–30% of cases
Immunodeficiency-associated BL	HIV+ adults and patients with congenital or iatrogenic immunodeficiency	Males more commonly affected	Worldwide	Nodal and bone marrow involvement more common than Endemic or Sporadic BL	25%–40% of cases

Abbreviations: EBV, Epstein-Barr virus; HIV, human immunodeficiency virus.
Data from Refs.[2,8,11,12]