Update on Burkitt Lymphoma

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KEYWORDS

• Burkitt lymphoma • MYC • TCF3 • CCND3 • ID3 • Risk-adapted • Endemic • Sporadic

KEY POINTS

- While Burkitt lymphoma (BL) is highly curable with short duration, intensive therapies in children these are poorly tolerated in middle-aged and older adults and immunosuppressed patients.
- Some novel less intensive approaches that maintain high cure rates while significantly decreasing treatment-related toxicity compared with traditional strategies are promising.
- There have been great strides in the molecular elucidation of BL that have provided several new targets for novel drug development in the disease.

INTRODUCTION

Burkitt lymphoma (BL), first described by Denis Burkitt in African children over 50 years ago, is a rare and highly aggressive B-cell lymphoma.[1] In Burkitt's initial paper, he reported unusual jaw tumors associated with a specific distribution pattern of anatomic sites in a group of 38 Ugandan children. This endemic variant, which was the first to be described, occurs in equatorial Africa and some other specific regions of the world, peaks in incidence in 4- to 7-year–old children, and has a predilection for males (**Table 1**). Two other epidemiologic variants are recognized. Sporadic BL typically affects children and young adults, presents worldwide, and is the most common variant in the Western world. Immunodeficiency-associated BL occurs in association with human immunodeficiency virus (HIV) infection and is approximately 1000 times more common in HIV-infected individuals compared with HIV-negative counterparts. Over recent years, the understanding of the biology of BL has advanced significantly with the identification of novel mutations that cooperate with *MYC*, and there has also

The authors have no conflicts of interest.

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Hematol Oncol Clin N Am 30 (2016) 1333–1343
http://dx.doi.org/10.1016/j.hoc.2016.07.009 **hemonc.theclinics.com**
0889-8588/16/Published by Elsevier Inc.

Table 1
Comparison of endemic, sporadic, and human immunodeficiency virus-associated Burkitt lymphoma

	Endemic	Sporadic	HIV-Associated
Epidemiology	Equatorial Africa and Papua, New Guinea Geographic association with malaria	Worldwide	Worldwide
Incidence	5–10 cases per 100,000 population	2–3 cases per million population	6 per 1000 AIDS cases
Age and Gender	Malignancy of childhood Peak Incidence: 4–7 y Male:female ratio of 2: 1	Malignancy of childhood and young adults Median age: 30 y Male:female ratio of 2–3:1	Malignancy of adults Median age: 44 y Associated with higher CD4 counts >100/mm^3
EBV association	100%	25%–40%	25%–40%
Genomics	*MYC* mutation 100%; *ID3* and/or *TCF3* mutations 40%; *CCND* mutations 1.8%	*MYC* mutation 100%; *ID3* and/or *TCF3* mutations 70%; *CCND* mutations 38%	*MYC* mutation 100%; *ID3* and/or *TCF3* mutations 67%; *CCND* mutations 67%
Clinical Presentation	Jaw and facial bones in approximately 50%; Also involves mesentery and gonads Increased risk of CNS dissemination	Abdomen most common presentation often involving the ileo-cecal region Other extranodal sites include bone marrow, ovaries, kidneys, and breasts Increased risk of CNS dissemination	Nodal presentation most common with occasional bone marrow Increased risk of CNS dissemination

been therapeutic progress with the development of less toxic strategies that maintain the high cure rates of historical high-dose, intensive strategies.

PATHOBIOLOGY OF BURKITT LYMPHOMA

The pathobiology of BL is unique and distinct from that of other aggressive B-cell lymphomas. BL is characterized by an extremely high proliferation fraction and a high fraction of apoptosis, and this accounts for its starry sky appearance at low magnification under the microscope. The cells are intermediate in size, have little pleomorphism, and contain basophilic cytoplasm that contains small vacuoles and characteristically round nuclei with little variation in size and shape. The nuclear chromatin is granular and contains small nucleoli with frequent mitoses. Biologically, BL is derived from a germinal center B cell, and the cells are positive for CD10, BCL6, CD20, CD79a, and CD45. The cells are negative for terminal deoxynucleotidyl transferase (TdT) as well as BCL2. The growth fraction as measured by Ki67 staining approaches 100%. Epstein-Barr virus (EBV) is virtually always detected in endemic BL and is