

Chapter 12

Mature B Cell Lymphoproliferation and Lymphomas: Diagnostic Approach

ABSTRACT

Most mature B cell lymphomas arise as clonal expansions corresponding to differentiation pathway stages with few exceptions. Many immunologic, toxic, and genetic factors predispose to lymphoma development. B-cell lymphomas are the most frequent types, often widely disseminated, involving the bone marrow and hemopoietic system. Many reactive conditions simulate lymphomatous infiltrates and need special diagnostic consideration, including viral and immunological reactions. The diagnosis should integrate clinicopathologic features, imaging, comprehensive hematologic examination, immunophenotyping, cytogenetics, molecular profile, and risk stratification. This comprehensive assessment also helps with treatment selection and potential targeted therapy.

INTRODUCTION

Mature B-cell lymphomas, arising from neoplastic clonal expansions along the B-cell differentiation pathway, are intricately linked to the immune system. While most follow well-defined stages, exceptions like hairy cell leukemia (HCL) challenge this norm. These lymphomas exhibit lineage heterogeneity, aberrant phenotypes, and even lineage plasticity.

In the realm of lymphoma, mature B-cell variants dominate, with distinct diagnostic entities. Among adults, follicular lymphoma (FL), diffuse large B-cell lymphoma (DLBCL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and multiple myeloma (MM) prevail. In pediatric cases, Burkitt-like lymphoma (BL), lymphoblastic lymphoma (LBL/L), and large B-cell lymphoma (LBCL) are common, while FL and marginal zone lymphoma (MZL) remain less frequent.

At diagnosis, most mature B-cell lymphomas have already disseminated widely. Unlike T-cell lymphomas, extra-nodal presentation is more frequent, and B symptoms or mediastinal involvement are less common (except for lymphoblastic lymphoma and mediastinal LBCL).

Mature B Cell Lymphoproliferation and Lymphomas

Diagnostic challenges arise due to reactive conditions mimicking lymphomatous infiltrates, including viral infections and autoimmune lymphoproliferative disorders (LPDS). To navigate this complexity, an integrated approach is essential:

1. **Pathogenic Mechanisms:** Understanding the underlying processes driving lymphomagenesis.
2. **Clinicopathologic Features:** Detailed assessment of clinical presentation, physical findings, and medical history.
3. **Diagnostic Criteria:** Incorporating morphologic, immunophenotypic, and genetic information.
4. **Staging and Risk Stratification:** Evaluating disease extent and prognosis.
5. **Treatment Strategies:** Tailoring therapeutic approaches based on subtype and patient factors.
6. **Therapeutic Response Criteria:** Monitoring treatment effectiveness.

The main mature B-cell lymphoma subtypes, guided by the International Consensus Conference (ICC, 2022) and the 5th WHO classification (2022):

1. **Small Lymphocyte Lymphomas/Leukemias:** Characterized by small, mature lymphocytes.
2. **Splenic B-cell lymphomas and Leukemias:** Involving the spleen and related tissues.
3. **Lymphoplasmacytic and Plasma Cell Neoplasms:** Including paraprotein-related disorders.
4. **Follicular Lymphoma (FL):** Indolent lymphoma with nodal and extra-nodal involvement.
5. **Mantle Cell Lymphoma (MCL):** Aggressive lymphoma arising from mantle zone B-cells.
6. **Large Cell and High-Grade Mature B-cell lymphoid Neoplasms:** Encompassing diverse aggressive variants

SMALL LYMPHOCYTE LYMPHOMAS/LEUKEMIAS

Chronic Lymphocytic Leukemia (CLL)

Chronic lymphocytic leukemia (CLL) is the most prevalent chronic leukemia in the elderly, with a median presentation age of 72 with 10% presenting before 55 years. An inherited genetic susceptibility is associated with a six to ninefold higher risk in family members (*Eichhorst, 2021*).

The initial diagnostic workup and follow-up of CLL as recommended by the ESMO Clinical Practice guideline (2020) include the following items in Table 1. (*Eichhorst et al., 2021*).

Table 1. Diagnostic and staging work-up of CLL (*Eichhorst et al., 2021*)

	Initial Staging at Diagnosis	Pre-Treatment Evaluation	End Of Therapy Staging	Follow-Up
History, physical examination, and performance status	+	+	+	+
Complete blood count and differential	+	+	+	+
Serum chemistry, immunoglobulins & direct antiglobulin test	–	+	+	+
Cytogenetics (FISH) & molecular genetics for <i>TP53</i> mutation or <i>del(17p)</i>	(+)	+	–	–
IGHV mutational status	(+)	+	–	–

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