Chapter 14
The Diagnostic Approach to Bone Marrow Lymphoid Infiltrates

ABSTRACT

The diagnosis of lymphoid infiltrates in the bone marrow may be challenging for many reasons. The bone marrow is not often the primary site for most lymphoproliferative neoplasms, except leukemic and precursor subtypes but is a frequent site for dissemination, sometimes with the primary tumor not clinically evident. In addition, the overlapping morphology, subtle infiltration, transformation, and mimicking reactive conditions are further challenges. The approach to bone marrow evaluation varies with the clinicopathologic context, notably a clinically suspected lymphoma or staging and follow-up of lymphoma diagnosed in lymph nodes or extranodal sites. In any of these conditions, the exclusion of mimicking reactive and benign conditions is essential.

INTRODUCTION

Bone marrow involvement occurs in various subtypes of non-Hodgkin lymphoma (NHL) and, less frequently, in Hodgkin lymphoma (HL). Several diagnostic questions arise when a lymphoid infiltrate is detected in the bone marrow. These include distinguishing between neoplastic and benign processes, determining whether it is a primary or secondary involvement, and achieving a definitive diagnosis through bone marrow examination—a readily accessible site.

The Diagnostic Strategies Include

- Morphology and Ancillary Tests:

  - A combination of morphological assessment and an appropriate ancillary test panel often suffices for the primary diagnosis of most cases.
- Immunophenotyping plays a crucial role in the current diagnosis of lymphoid tumors.
- Genomic analysis is necessary for only a subset of entities.

The Clinical Presentations: Lymphoproliferative neoplasms may manifest in different ways:

- Primary Leukemic Cases: In these cases, both peripheral blood and bone marrow serve as primary diagnostic tissues.
- Primary Nodal or Extranodal Presentation: Some lymphomas initially present in nodal or extranodal tissues and subsequently involve the peripheral blood and bone marrow. Bone marrow examination becomes part of staging or therapy evaluation.

This chapter overviews the common diagnostic approach for bone marrow infiltration. Specimen types, applied techniques, and overlapping disorders are discussed. Additionally, the primary diagnosis of lymphoma and the role of marrow examination in staging and post-therapy follow-up, including challenging issues and differential diagnoses are explored.

THE DIAGNOSTIC APPROACH TO LYMPHOID BONE MARROW INFILTRATES

Lymphoid infiltrates in the bone marrow pose diagnostic challenges due to their diverse nature. While bone marrow involvement is common in some lymphoproliferative neoplasms, distinguishing between neoplastic and benign infiltrates remains crucial. (Alaggio et al., 2022).

The American Society of Clinical Oncology recommends an adequate excisional biopsy for the first assessment and staging of lymphoma. When accessible lymph nodes are unavailable or systemic manifestations are the primary presentation, the bone marrow becomes a valuable diagnostic site. (Fend & Kremer, 2007)

The morphologic Identification of the predominant cell type and pattern of involvement provides essential clues to diagnosis. Recognition of clinicopathologic features specific to each entity helps define sub-entities for differential diagnosis.

Trephine bone marrow biopsy and cytomorphology in aspirate smears complement the primary identification of the lymphoid infiltrate. Bone marrow assessment is part of staging or follow-up, and occasionally serves as a site for primary diagnosis (especially in low-grade B-cell lymphoma). Bone marrow biopsy remains a crucial alternative, especially in resource-constrained settings. Its concordance rate with lymph nodes makes it an acceptable choice for diagnosing lymphoma. Understanding the frequency and pattern of bone marrow involvement contributes to accurate diagnosis and optimal patient management.

Detecting bone marrow infiltration variably impacts prognosis and treatment options. Integrating clinicopathologic parameters and ancillary tests (including immunophenotyping, imaging, and clinical investigations) is crucial for a final diagnosis.

Bone Marrow Specimen Consideration in Lymphoma Diagnosis

The bone marrow biopsy (BMB) sample plays a crucial role in diagnosing lymphoma. Some essential considerations include: (*Phillips & Opie, 2018)*

1. **Specimen Adequacy** in terms of volume and quality. A minimum of 2 cm long core is recommended, free from aspiration or distortion artifacts with minimal cortical tissue.

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