2 TRIAGING LYMPH NODES

In this chapter, we will:

1. Encapsulate a basic approach to the diagnosis of lymphoid disorders, using a combination of histologic and immunohistochemical (IHC) findings, with an emphasis on the latter.
2. Expand on IHC evaluation in a variety of other challenging circumstances in hematopathology.

This serves as an overview, with some expansion in areas where more clarification is in order. Subsequent chapters provide a more in-depth approach to B- and T-cell lymphoproliferative disorders as well as benign conditions.

The stepwise evaluation of a lymph node specimen includes:

1. Determination of adequacy and assessment of pre-analytic artifacts.
2. Basic histologic evaluation to determine a general pattern and generate a differential diagnosis.
3. Performance of appropriate ancillary tests (IHC, cytogenetics, flow cytometry, molecular studies) to render a diagnosis (Schematic, Fig. 2-1).

Based on clinical information and tissue site, the evaluation may be altered to address a site-specific or history-specific diagnosis.

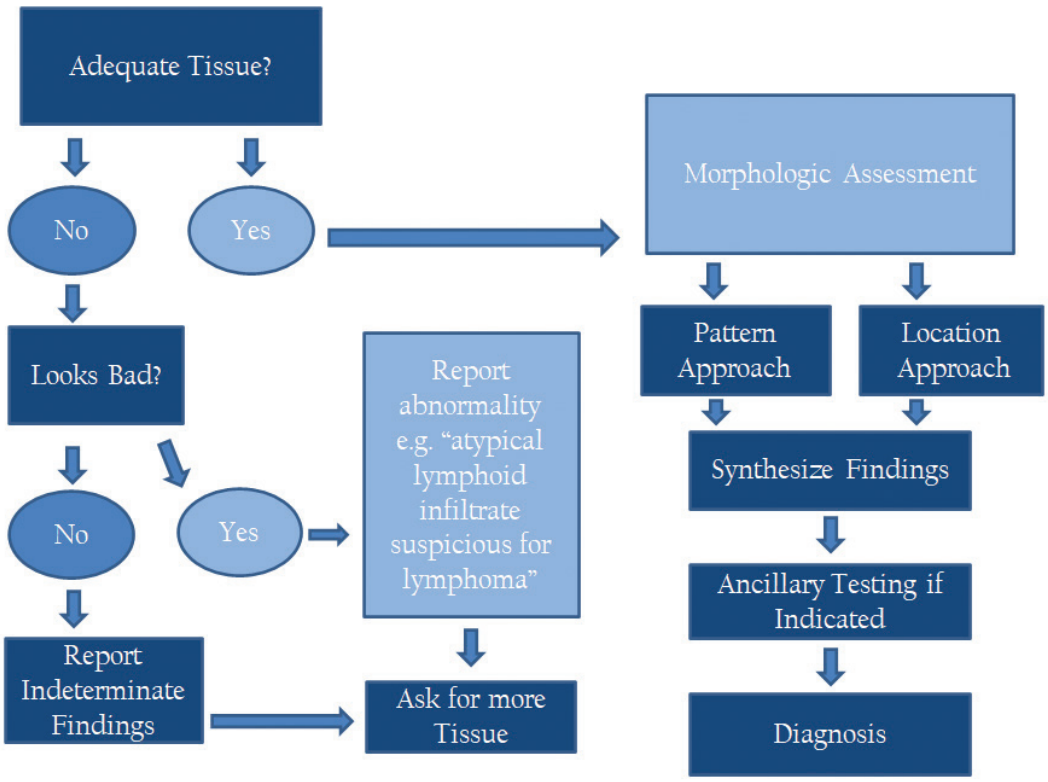

FIGURE 2-1. APPROACH TO LYMPH NODE SPECIMENS

Flow chart illustrating potential approach to lymph node specimens.

TISSUE ADEQUACY AND BIOPSY SIZE

In all cases, the primary assessment is one of sample adequacy. Tissue necrosis, crush artifact, and a variety of pre-analytic artifacts may prevent diagnostic evaluation. In these cases, it is appropriate to state that the sample is non-diagnostic and, if possible, make a statement about the possible cause(s) of inadequacy.

It is an obvious statement that tissue size can affect diagnosis. We see a variety of tissue types and sizes of samples, with an increasing reliance of small samples including needle core biopsies. In some cases, a small sample may be just as diagnostic as a larger sample. However, much of lymph node pathology is based on evaluating overall morphologic "pattern" and small samples may preclude architectural evaluation. In these cases, it is appropriate to employ the terminology of "atypical," explain that there is a suspicion for lymphoma (or other disorder), and that an excisional sample would be necessary for a more complete diagnosis. Without stating this latter point, follow-up may lead to more, non-diagnostic small biopsies (Schematic, Fig. 2-1).

GENERAL PATTERNS

In evaluating lymph nodes (or other tissues with suspicion of a hematolymphoid disorder), most processes can be put into general histologic patterns that correspond to potential broad diagnoses or approaches (Table 2-1)(1,2).

We propose a simpler grouping of four "approaches." Although each approach has a name of the most common type of lymphoma considered, it is not the only possible diagnosis for the pattern or evaluation approach. These named approaches are:

1. Small B-cell lymphoma approach
2. Hodgkin lymphoma approach
3. Large B-cell lymphoma approach
4. T-cell lymphoma approach

Each individual approach can be used in a number of circumstances, based both on histologic findings as well as general or clinically driven differential diagnoses (summarized in Table 2-2). They can also be combined if there is a differential diagnosis that overlaps with more than one category. Specific modifications of these approaches can be made based on location or circumstance (Discussed further below).

Small B-cell Pattern

This approach is used when the lymphoid tissue has one of the following characteristics:

- Relatively benign appearance to exclude low-grade lymphoma
- Normal appearing or atypical follicles
- Proliferations of small blue nodules/primary follicles (Fig. 2-2)
- Diffuse proliferations of small dark blue lymphocytes
- Features typical or suggestive of small B-cell lymphomas

In this case, "small B-cell lymphomas" include: chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), follicular lymphoma (FL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL) and lymphoplasmacytic lymphoma (LPL).

The most useful immunohistochemical stains for this approach are: CD3, CD20, CD5, cyclin D1, BCL2, BCL6, LEF1 and Ki67.

CD3 and CD20 are cornerstones to the diagnosis of lymphoid disorders. The combination allows evaluation of the number and distribution of T- and B-cells, respectively. The combination of these stains should account for 90%+ of cells in a normal lymph node. Lack of staining for one or the other, or a massive predominance of one stain or the other could suggest a lymphoproliferative disorder.

CD5 is expressed in most T-cells. Dim or negative expression in T-cells could be an indication of a T-cell lymphoproliferative disorder. Co-expression of CD5 in abnormal B-cell proliferations is usually indicative of a B-cell lymphoma; however, a small but variable subset of normal B-cells do express CD5. These are referred to as B1 cells and are innate-like B-cells, which arise from an antigen independent pathway (6). Their relation to CD5+ B-cell lymphomas is unclear (7). When an increase CD5+ B-cell population is encountered, the most common diagnoses to be considered would be CLL/SLL or MCL. Rare cases of MZL or LPL will also express