

5 Lymph Nodes

Metastatic spread to lymph nodes carries profound treatment and prognostic implications for patients with carcinomas, melanomas, or any other malignant neoplasm with metastatic potential. Accordingly, assessment of lymph node specimens is every bit as important as evaluating a neoplasm at its primary site.

Lymph Node Dissections

A general approach to sampling lymph nodes is described in Chapter 1, and the organ-specific approach to the dissection of regional lymph nodes is detailed in each organ-specific chapter. In this chapter we review a few general guidelines that can be broadly applied when it comes to evaluating lymph nodes for metastatic disease.

Lymph nodes are easiest to appreciate in the fresh state before subtle distinctions in tissue density are obscured by tissue fixation. Submersion of specimens in certain clearing agents may be helpful in eliminating the bulk of adipose tissue, but this is an unnecessary and time-consuming step that does not improve on meticulous examination of the fresh tissues. When appropriate, the anatomic levels of the lymph nodes should be maintained and separately reported in the surgical pathology report (e.g., colectomy specimens and neck dissection specimens). In cases where important anatomic landmarks do not accompany the specimen, it may not be possible to identify levels without the help of the submitting surgeon.

Although tedious, the objective of any lymph node dissection for metastatic disease is nothing

less than detection and processing of every lymph node contained in the specimen. There is practically no role for representative nodal sampling when searching for metastatic spread. Each lymph node identified should be submitted for microscopic examination. If tumor is grossly visible, a section that includes the tumor suffices. If tumor is not grossly visible, the lymph node should be sectioned in 3- to 4-mm slices and all of the sections submitted for microscopic evaluation. You can slice the lymph node along its long or short axis, but longitudinal sections are generally preferable, as this minimizes the number of slices. No single cassette should contain slices from more than one lymph node unless colored inks are used to distinguish different lymph nodes. For these nonsentinel lymph node dissections, one hematoxylin and eosin (H&E)-stained section per tissue block is adequate.

Sentinel Lymph Node Biopsy

As noted above, the standard pathologic practice for the evaluation of nonsentinel lymph nodes is to examine microscopically one section from each lymph node using the simple H&E technique. Although this approach may be practical for evaluating large numbers of lymph nodes, most pathologists would concede that such limited analysis consistently underestimates the true incidence of occult nodal metastases. Recent improvements in our clinical ability to identify the lymph nodes most likely to harbor metastases

have facilitated the accurate staging of cancers. The sentinel lymph node strategy is particularly appealing because the surgical removal of just one or several selected lymph nodes permits a more comprehensive pathologic search for small and localized metastatic deposits.

Methods for detecting tumor cells in sentinel lymph nodes have become increasingly sophisticated and sensitive, ranging from routine histologic examination of serial sections to reverse transcriptase-polymerase chain reaction-based methods for detecting a single tumor cell among a sea of lymphocytes. Outside of routine H&E staining, however, most detection methods are investigational, and currently there is no agreement as to an optimal detection protocol. Given the diversity of the processing and examination of sentinel lymph node biopsies among laboratories, you should be familiar with the protocol details specific to your own institution. At the same time, there are generic guidelines that are widely applicable across institutions and assorted tumor types.

The sentinel lymph node biopsy specimen should be carefully examined to determine the number of lymph nodes. The size of each should be recorded. Each lymph node should be processed separately. Each node is serially sectioned along the longitudinal or transverse plane into 3- to 4-mm slices. Small lymph nodes that cannot be easily sectioned should be submitted in toto. Examine the cut surface of each slice for the presence of grossly visible tumor nodules.

Your gross assessment of the lymph node dictates the degree of sectioning by the histopathology laboratory. If tumor is visualized grossly, routine H&E staining of a single level is sufficient to document the presence of tumor and its possible extension beyond the lymph node capsule. If tumor is not grossly visible, the lymph node slices should be sectioned at multiple levels. There is currently no standard to guide the extent of tissue sectioning. At a minimum, one section from each of three levels of the tissue block should be obtained for routine H&E staining. Regardless of whether immunohistochemistry is part of a specific protocol, the histopathology laboratory should place intervening unstained sections on sialinated slides in an effort to minimize loss of potentially diagnostic material and provide a source of unstained sections should the need for immunohistochemistry arise.

Handling Radioactive Specimens Obtained by Sentinel Lymphadenectomy

The process of clinical lymphatic mapping and the identification of sentinel lymph nodes relies on nodal uptake of radioactive tracers. Fortunately for pathology personnel, the amount of radiation associated with sentinel lymphadenectomies is low. Even with frequent handling of these specimens, radiation exposure usually does not approach statutory exposure limits. Given the exceedingly low radiation exposure, most authorities now agree that quarantining these specimens does not enhance the safety of pathology personnel and only serves to delay the final diagnosis. Accordingly, sentinel lymph node biopsies should be processed immediately on receipt from the operating room using customary universal precautions. Nonetheless, if you have a question about a particular specimen, you should call your institution's radiation safety officer.

Sentinel Lymph Node Biopsy for Evaluating Metastatic Disease

1. Record the number of lymph nodes and their dimensions.
2. Serial section each lymph node along its longitudinal or transverse plane into 3- to 4-mm slices.
3. If a metastatic implant is grossly visible, have the histopathology laboratory cut and stain one representative section to document the presence of tumor.
4. If a metastatic implant is not grossly visible, have the histopathology laboratory cut multiple sections from at least three levels. At least one section from each level should be stained with H&E. Additional unstained sections should be stored on treated slides for future immunohistochemical studies as needed.

Important Issues to Address in Your Surgical Pathology Report

- What procedure was performed?
- How many lymph nodes from each anatomic level harbor metastatic tumor, and how many lymph nodes from each level were microscopically examined?
- What is the size of the largest metastatic implant?

- Does the metastasis extend beyond the nodal capsule into the surrounding perinodal fat? (This is particularly important to note for metastatic squamous cell carcinomas of the head and neck and metastatic carcinomas of the breast.)
- For sentinel lymph node biopsies, was the metastasis detected by routine histopathology, immunohistochemistry, molecular-genetic analysis, or some combination of these techniques?