Lymph node status (Core and Non-core)

If lymph nodes are NOT received, this element should not be reported.

The presence or absence of nodal metastasis is an important N category criterion in the American Joint Commission on Cancer (AJCC)/Union for International Cancer Control (UICC) staging systems.[1,2]

Regional lymph nodes are the most common site of initial metastasis in patients with cutaneous melanoma. Among patients with regional lymph node metastasis, the majority have clinically occult disease that is detected by the technique of lymphatic mapping and sentinel lymph node biopsy. Patients without clinical or radiographic evidence of regional lymph node metastases but who have microscopically documented nodal metastases (usually detected by lymphatic mapping and sentinel node biopsy) are defined as "clinically occult" whereas nodal metastases detected by palpation or radiological imaging are defined as “clinically apparent”.[1] Patients with "clinically occult" metastases are designated (as in the prior edition) as N1a, N2a, or N3a based on the number of tumour-involved nodes unless microsatellites, satellites, or in-transit metastases are present.[1] Patients who present with clinical evidence of regional disease are assigned as N1b, N2b, or N3b based on the number of nodes involved. If at least one node was clinically evident, and there are additional involved nodes detected only on microscopic examination, the total number of involved nodes (e.g., both those clinically apparent and those detected only on microscopic examination of a complete lymphadenectomy specimen) should be recorded for N categorization.[1] If a node is “clinically apparent” it is not, strictly speaking, a sentinel node.

If a lymph node is received but it is not specifically stated that it is a sentinel node then it should be reported as a non-sentinel node. Any additional relevant microscopic comments should be recorded.

Extranodal extension (ENE) is an adverse prognostic factor in melanoma patients. It is defined as the presence of a nodal metastasis extending through the lymph node capsule and into adjacent tissue, which may be apparent macroscopically but must be confirmed microscopically. Matted nodes (defined as two or more nodes adherent to one another through involvement by metastatic disease, identified at the time the specimen is examined macroscopically in the pathology laboratory) often suggest the presence of ENE but the latter must be confirmed microscopically.[3]

Sentinel lymph nodes

Tumour-harbouring status of the sentinel lymph nodes (SLN) is the strongest predictor of outcome for clinically localized primary cutaneous melanoma patients.[4-8]

There are a number of potential pitfalls in the microscopic examination of SLNs.[9] The most common diagnostic problem is distinguishing nodal nevus cells from a melanoma metastasis. This can usually be resolved by careful assessment of the location, morphologic features, and immunohistochemical staining characteristics of the cells and, in some instances, comparing the cytology of the nodal melanocytes with the cells of the primary invasive melanoma. Nodal nevi are usually located in the fibrous capsule and trabeculae of lymph nodes (but may rarely occur within the nodal parenchyma) and consist of small cytologically bland cells that are devoid of mitotic activity and, on immunohistochemistry, show strong diffuse positivity for S-100 and Melan-A, minimal staining for HMB-45, and a low (<2%) Ki-67 proliferative index. In contrast, melanoma deposits in SLNs are typically located in the subcapsular sinus or parenchyma and often comprise large, cytologically atypical cells with variably prominent nucleoli, mitotic activity, HMB-45 positivity, and Ki-67 positivity (variable but usually >2%).[10,11] Other cells that may be found within lymph nodes and that are positive for S-100 include interdigitating (antigen presenting dendritic) cells, nerves, and, occasionally, macrophages. These can usually be distinguished from melanoma cells on the basis of

their location, size, shape, nuclear and cytoplasmic characteristics, distribution within the node, and immunohistochemical profile.[12] Positive Melan-A/MART-1 staining of small numbers of cells in the intraparenchymal portion of lymph nodes from patients without a history of melanoma has been reported, and in our view caution should be exercised to not overinterpret isolated Melan-A/MART-1-positive (or HMB-45-positive) cells in SLNs as melanoma in the absence of other corroborative evidence (such as cytologic atypia, mitotic activity, or immunohistochemical positivity for HMB-45 and an increased high Ki-67/MIB-1 index).[13] In our experience, the occurrence of such cells has become a more frequent diagnostic problem in recent years, presumably reflecting the utilization of more sensitive antibodies and immunohistochemical techniques.[14,15] These cells could represent nevus cells, macrophages passively carrying melanoma-associated antigens, or some other cell type carrying antigens that cross-react with Melan-A/MART-1. Similarly, weak positive staining for HMB-45 is sometimes observed in pigment-laden macrophages and nevus cells. For a node to be interpreted as positive for melanoma, the immuno-positive cells in question should be morphologically consistent with being melanoma cells.

Histologic parameters of melanoma deposits in SLNs have been shown to be predictive of the presence or absence of tumour in non-SLNs and clinical outcome.[16-30] If there are only a small number of metastatic melanoma cells in the subcapsular sinus of the SLN, the patient's prognosis is very good and the chance of finding additional metastases in a completion lymph node dissection specimen is very small. However, if there are multiple large deposits of melanoma cells that extend deeply into the central part of an SLN, the prognosis is much worse, and the chance of finding additional metastases in non-SLNs in a completion lymph node dissection specimen is much higher. SLN parameters predictive of non-SLN status and survival include the size of metastases, tumour penetrative depth (also known as maximal subcapsular depth and centripetal thickness and defined as the maximum distance of melanoma cells from the nearest inner margin of the lymph node capsule), the location of tumour deposits in the SLN, the percentage cross-sectional area of the SLN that is involved, and the presence of extracapsular spread. However, the power of individual features of melanoma metastases in SLNs to predict tumour in non-SLNs, as well as survival, reported in some studies has not been reported by others. The determination of some of these parameters may not always be reliable, because tumour deposits are often irregularly shaped, the limits of tumour deposits can be difficult to discern, and tumour burden is to some degree dependent on sectioning protocols, as more extensive sectioning may reveal additional tumour deposits or demonstrate a greater dimension of deposit(s) in the deeper sections.[31]

It is recommended that guidelines provided for the measurement of the maximum dimension of the largest sentinel node metastasis in the AJCC melanoma staging system[1] be used. The single largest maximum dimension (measured in millimetres to the nearest 0.1 mm using an ocular micrometre) of the largest discrete metastatic melanoma deposit in sentinel nodes should be measured and recorded. To be considered a discrete deposit, the tumour cells must be in direct continuity with adjacent tumour cells. In some instances, multiple small tumour aggregates may be disbursed within a lymph node and separated by lymphoid cells. In this circumstance, the size of the largest discrete single deposit (not the nodal area over which the multiple deposits are contained) should be recorded. The measurement may be made either on H&E-stained sections or on sections stained immunohistochemically."[32]

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