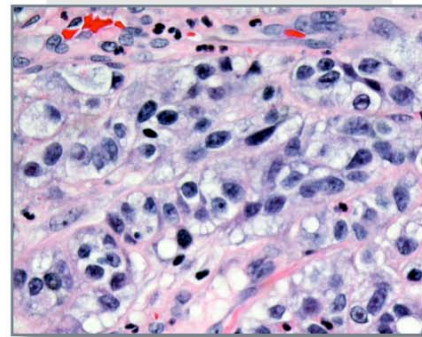
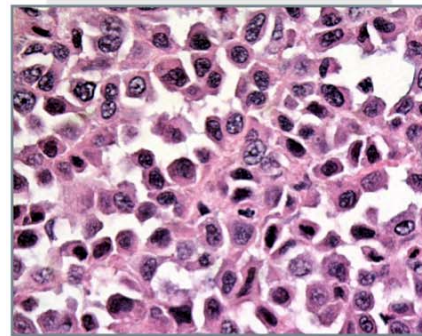


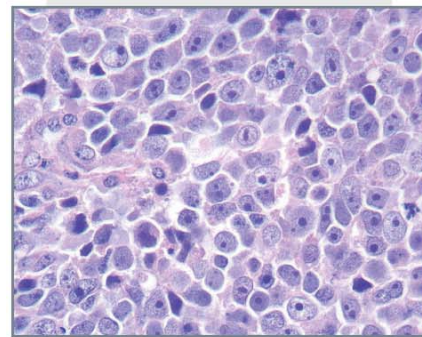
H&E - A



H&E - B



H&E - C



H&E - D

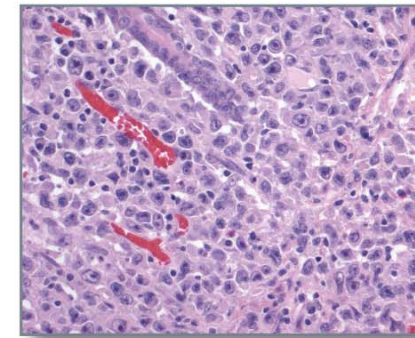
Large cell undifferentiated malignant neoplasms generally, but not always, present as lymph node-based processes, usually suggesting the differential diagnosis of metastatic carcinoma, metastatic melanoma, or high-grade lymphoma (e.g., anaplastic large cell lymphoma (ALCL), or diffuse large B cell lymphoma). However, this category of tumors may include more uncommon entities such as sarcomas with epithelioid features (e.g., angiosarcoma, malignant peripheral nerve sheath tumor, epithelioid sarcoma) and germ cell tumors, depending upon the histologic and clinical settings.

Histologic clues about the nature of the tumor can be minimal at best or deceiving at worst. Look at the four H&E images to the left. All represent large cell undifferentiated malignancies. Histologic clues might suggest the diagnosis of carcinoma in specimen A - but immunohistochemistry (IHC) studies demonstrate the tumor to represent lymphoma. The morphology of specimen B might suggest poorly differentiated adenocarcinoma, but IHC demonstrates it to represent melanoma. The poorly cohesive nature of the tumor in specimen C might suggest large cell lymphoma, but IHC studies demonstrate it to represent carcinoma. Finally, the tumor in specimen D is demonstrated by IHC to represent malignant germ cell tumor.

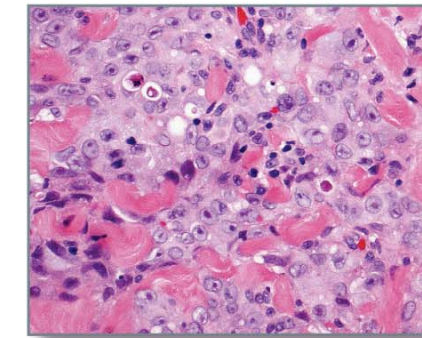
As illustrated in the heat map below, a basic panel of antibodies to CD45, cytokeratin, and S100 (or, perhaps, a melanoma-restricted antigen such as the HMB-45-defined gp100 protein) can be used in the initial analysis of these tumors. But it must be remembered that among large cell undifferentiated malignancies, there are many exceptions to the general rule. For example, cytokeratin, generally considered a marker of epithelial differentiation, can be expressed in a significant subset of metastatic melanomas as well as angiosarcomas, particularly those with epithelioid histologic features. And while CD45 shows a very high specificity for hematolymphoid processes, a number of these malignancies (e.g., classical Hodgkin's lymphoma, ALCL, granulocytic sarcoma, plasmacytoma) may be CD45 negative, and other markers are required to positively identify these tumors (see Hematopathology section). Note the relative lack of utility of antibodies to vimentin in this clinicopathologic setting.

	Cytokeratins	Vimentin	Melanoma-specific antigen	CD45
Carcinoma				
Lymphoma	Heatmap content available in the printed Pathology Reference Guide			
Melanoma				
Sarcoma				

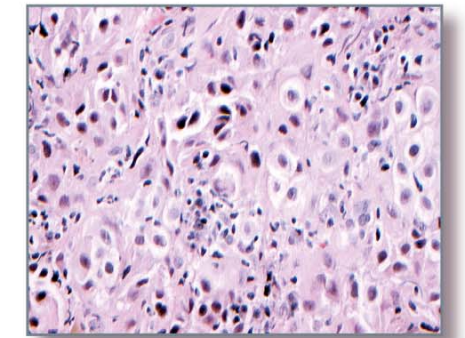
In each of these large cell undifferentiated malignancies (E, F and G) the diagnosis of carcinoma was entertained. However, the correct diagnosis was arrived at using a limited panel of immunostains. None of the three tumors demonstrated the strong, uniform cytokeratin expression characteristic of carcinoma. In tumor E, presenting in the colon, residual colonic glands are identified and the tumor is confirmed as lymphoma by documenting CD45 expression (see below). In tumor F, the diagnosis is confirmed as epithelioid angiosarcoma by demonstrating CD31 expression (see below). In tumor G, while there is some cytokeratin expression, it is in the 'anomalous' pattern that can be seen in melanoma, a diagnosis confirmed by demonstrating the presence of gp100 (identified with antibody HMB-45; see below).



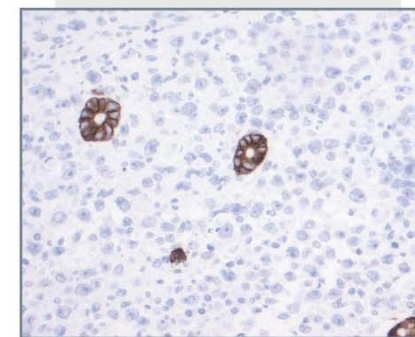
H&E - E



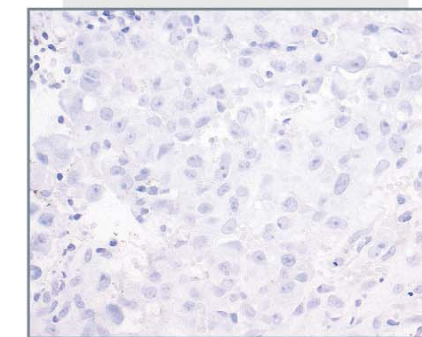
H&E - F



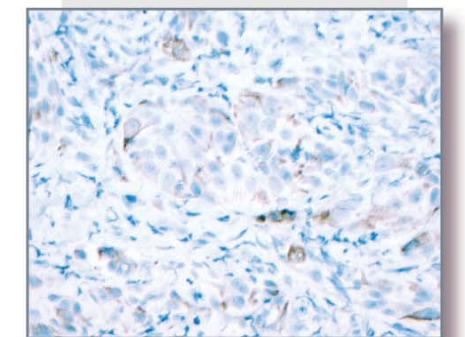
H&E - G



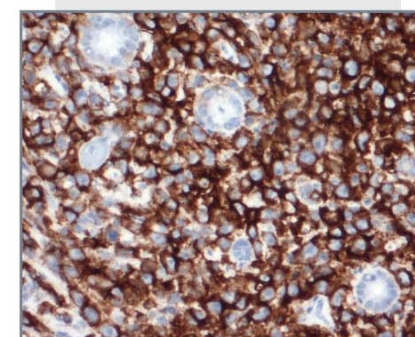
CYTOKERATINS [OSCAR]



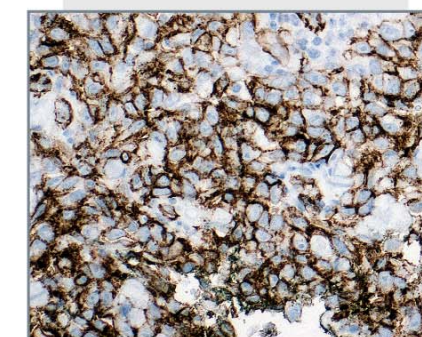
OSCAR



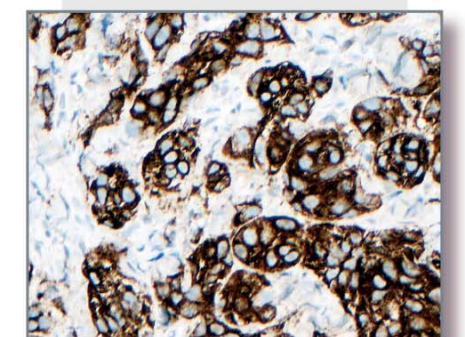
OSCAR



CD45
Expression of CD45 confirms the diagnosis of malignant lymphoma



CD31
Expression of CD31 confirms the diagnosis of angiosarcoma



gp100 [HMB-45]
Expression of gp100 confirms the diagnosis of melanoma

Almost always positive	Usually positive	Not helpful	Usually negative	Almost always negative

See introduction to heat maps page 15