Pathologic Quiz Case

Supraclavicular Lymphadenopathy in a 30-Year-Old Man

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A 30-year-old previously healthy white man presented to his primary care physician with a 1-year history of increasing pruritus. The pruritus initially began in the lower extremities and then became generalized. He had been prescribed topical and intramuscular steroids without improvement of his symptoms. He had recently noted early satiety after eating, as well as increasing dyspnea. On admission, a chest radiograph demonstrated a large right pleural effusion, as well as left-sided deviation of the mediastinum. Computed tomographic scans of the chest and abdomen revealed a large solid mediastinal or lung mass that impinged on the trachea (Figure 1) and an enlarged nodular spleen, but no other lesions. Physical examination was remarkable for an enlarged right supraclavicular lymph node and splenomegaly.

Thoracentesis of the right hemithorax was performed. No malignant cells were identified in the pleural fluid. Fine-needle aspiration biopsy of the supraclavicular lymph node was also performed, which revealed a heterogeneous population of lymphoid cells with an occasional atypical cell present. Immunophenotypic analysis by flow cytometry failed to demonstrate any aberrant or monoclonal immunophenotypes. There was a predominance of positivity for T-lymphocyte–related antigens.

Excisional biopsy of the lymph node revealed a 4 × 2 cm, firm, tan-gray, well-encapsulated lymph node. Cut surfaces of the lymph node were tan and homogeneous. Microscopic examination of hematoxylin-eosin–stained sections demonstrated subtotal effacement of the lymph node structure by thick bands of fibrotic tissue. Loosely cohesive aggregates of enlarged atypical cells were seen admixed with eosinophils, plasma cells, and histiocytes. The atypical cells had enlarged multilobate nuclei with irregular nuclear outlines. The chromatin was vesicular, and prominent nucleoli were visible in some of the cells. The cytoplasm was amphophilic and wispy (Figure 2). Immunohistochemistry of the atypical cells demonstrated positivity for CD15 (Leu-M1) with prominent Golgi localization (Figure 3) and CD30 (Ber-H2). Reactions for CD45 (leukocyte common antigen), CD3, CD45RO (UCHL-1), and epithelial membrane antigen were negative in the cells of interest. Additionally, pan-B-cell markers, including CD20 (L26), CD45RA (MB1), and MB2, were negative and there was no light-chain restriction in the atypical cells. Reactions for cytokeratin and S100 protein (Figure 4) were also negative.

What is your diagnosis?
Pathologic Diagnosis: Syncytial Variant of Nodular Sclerosing Hodgkin Disease

The syncytial variant of nodular sclerosing Hodgkin disease is an unusual form of Hodgkin disease characterized microscopically by the more typical features of nodular sclerosis, as well as the presence of cohesive aggregates of atypical mononuclear Reed-Sternberg cell variants. Although relatively uncommon, the syncytial variant is important to recognize to prevent misdiagnosis as carcinoma, thymoma, germ cell tumors, melanoma, or non-Hodgkin lymphoma.

Hodgkin disease is a lymphoma with a bimodal peak incidence occurring in the ages between 15 and 35 years, and 55 years and older. It is one of the most common malignancies to appear in young adults. The disease usually presents with painless lymphadenopathy, usually limited to one or more contiguous groups of lymph nodes, especially in the neck, axilla, or the mediastinum. Dissemination to the spleen or bone marrow may also occur. The presence of the B category of constitutional symptoms, including fever, night sweats, pruritus, and weight loss, is more commonly seen in older patients and in those with disseminated disease. Prognosis for Hodgkin disease is most closely linked to the stage of the disease rather than the histologic subtype.

Traditionally, Hodgkin disease has been divided into 4 subtypes based on differences in the appearance of the neoplastic cells, as well as the components of the background. The subtypes include nodular sclerosing, lymphocyte predominance, lymphocyte depletion, and mixed cellularity. The nodular sclerosing form is the most common subtype, accounting for about 60% of the total number of cases. The classic presentation is a mediastinal or supraclavicular mass. Gross examination usually reveals a moderately firm, tan lymph node that may have distinctive nodules on cut surfaces. Microscopically, it is characterized by the presence of dense bands of birefringent collagen, which separate the lymph node into distinct “nodules.” The lacunar cell variant of the Reed-Sternberg cell is the most common variant identified in nodular sclerosis. It is characterized by a multilobate nucleus with or without prominent nucleoli and amphophilic cytoplasm. The cells are often found isolated from other cells in small lacunae. The lacunae are caused by a combination of retraction artifact and peripheral cytoplasmic clearing of the neoplastic cells. In contrast with the classic form, the syncytial variant of nodular sclerosing Hodgkin disease is characterized by large aggregates of lacunar cells, which are present within the nodules. The location of the individual cells in small lacunae is a feature that is helpful in differentiating this disease from other malignancies. The background cells in the nodules are small mature lymphocytes of predominantly T-cell type, plasma cells, macrophages, and eosinophils. Although Reed-Sternberg cells or variants are required for the diagnosis of Hodgkin disease, they are not entirely pathognomonic and may be encountered in other malignancies.

The presence of infiltration of lymph node sinuses by tumor cells, phagocytosis of neutrophils by tumor cells, and marked anaplasia or the presence of spindle-shaped tumor cells are more common in carcinoma than Hodgkin disease.

Immunohistochemical stains are essential in establishing the correct diagnosis of the syncytial variant of nodular sclerosing Hodgkin disease. Positive Golgi localization staining of the neoplastic cells for CD15 is thought to be characteristic of Hodgkin disease. Additionally, positive staining for CD30 and negative staining for CD45 (leukocyte common antigen) are present. Immunohistochemical stains for cytokeratin and S100 demonstrate lack of staining in the neoplastic cells, which is useful in excluding carcinomas, thymomas, germ cell tumors, and melanomas. Additional studies that can be performed to exclude other large cell lymphomas include gene rearrangement studies and studies to identify the anaplastic lymphoma kinase gene (ALK).

In conclusion, the syncytial variant of nodular sclerosing Hodgkin disease is an uncommon entity, which may histologically resemble a diverse group of malignancies. Careful consideration of the clinical history, as well as the presence of lacunar Reed-Sternberg cells in nodules surrounded by dense collagenous fibrosis, should suggest the diagnosis. Immunohistochemical stains that are positive for CD15 and CD30, and negative for CD45 (leukocyte common antigen), epithelial membrane antigen, CD3, cytokeratin, and S100 are essential for exclusion of other malignancies.

References