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Case Report
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Extranodal Natural Killer/T-Cell Lymphoma, Nasal Type Mimicking Classic Hodgkin Lymphoma

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Abstract

Introduction: Extranodal Natural Killer/T-Cell lymphoma of the nasal type has unique histologic, immunohistochemical, flow cytometric, and chromogenic *in situ* hybridization characteristics. It can be associated with nasal obstruction and regional lymph node involvement. Histologic presentation may mimic classic Hodgkin lymphoma when large, atypical cells with irregular nuclear contours, prominent nucleoli, and bi-/multi-nucleation resembling Reed-Sternberg cells are present in conjunction with positive CD30 immunohistochemical stain. Although reduced expression of B cell markers such as PAX5 is typical in classic Hodgkin lymphoma, a completely negative stain, as in our patient, is rare. This discrepancy along with the clinical presentation of predominant lymph node enlargement significantly contributed to the initial erroneous diagnosis of classic Hodgkin lymphoma.

Case Report: Herein we describe a case of a 33-year-old Hispanic male with newly diagnosed Extranodal Natural Killer-/T-Cell Lymphoma (ENTKL), nasal type. His initial diagnosis of classic Hodgkin lymphoma rendered on a cervical lymph node biopsy was amended upon subsequent discovery of classic diagnostic findings of ENTKL on microscopic evaluation of specimens excised to treat nasal obstruction interfering with chemotherapy.

Conclusion: This case emphasizes the need to further investigate medical history and evaluate symptoms on a multi systemic level when eliciting differential diagnoses in suspected lymphoma patients. A more comprehensive approach can increase diagnostic accuracy when deceiving histologic findings are present. Diagnostic accuracy is essential for treatment effectiveness and for its potential to improve disease progression and patient outcomes.

Keywords: Extranodal natural killer-/t-cell lymphoma; Nasal type; Classic Hodgkin lymphoma; PAX5

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Introduction

Extranodal Natural Killer/T-Cell Lymphoma (ENTKL) can present in the upper aerodigestive tract with patients suffering from obstruction, epistaxis, and midline destructive lesions. Although regional lymph node involvement is not uncommon, primary involvement of lymph nodes is rare and usually lacks angiodestruction and necrosis. The absence of these classically diagnostic findings can present a challenge when neoplastic lymphocytes with deceiving morphology are present. Herein we describe a case of a 33-year-old Hispanic male who presented with a neck mass. Classic Hodgkin lymphoma was initially rendered on a cervical lymph node biopsy, and the patient was treated with systemic chemotherapy. Two months later, the patient underwent septoplasty with turbinate reduction for nasal obstruction and inflammation, which interfered with corona virus testing necessary for hospital admission prior to cancer treatment. Subsequent evaluation of resected surgical specimens revealed a diagnosis of extranodal natural killer/T-cell lymphoma, nasal type.

Case Presentation

The patient is a 33-year-old Hispanic male who presented to otolaryngology with a large, progressively enlarging left neck mass underneath the sternocleidomastoid. The patient first noticed the mass one year prior. Review of systems was positive for epistaxis and nasal congestion but negative for fever, chills, sweats, or weight loss. Pertinent physical exam findings included a large conglomeration of the left supraclavicular and parotid lymph nodes, in addition to shotty right cervical and axillary lymphadenopathy. There was no inguinal adenopathy. The patient reported a

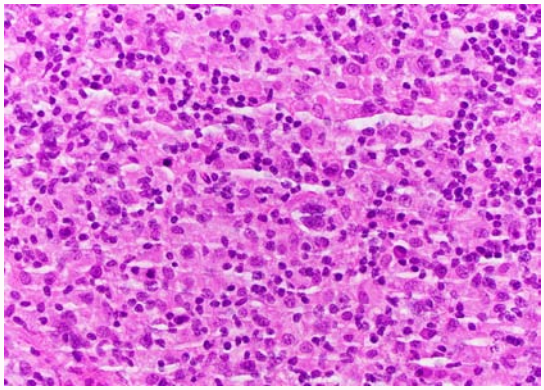

Figure 1: Hematoxylin and eosin stain, 40x. Lymph node section containing large, atypical multinucleated lymphocytes resembling Reed-Sternberg cells surrounded by mixed inflammatory infiltrate.

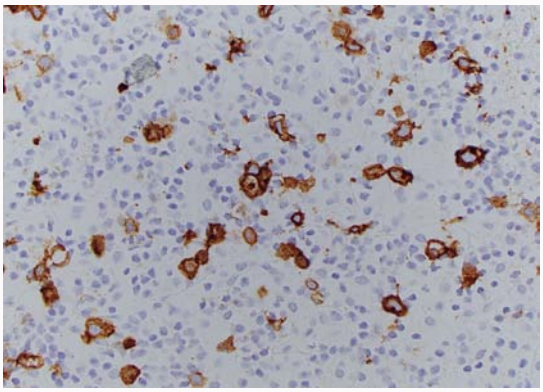

Figure 2: CD30 Immunohistochemical stain, 40x. Lymph node section with positive antibody expression in cell membranes and Golgi areas of neoplastic cells.

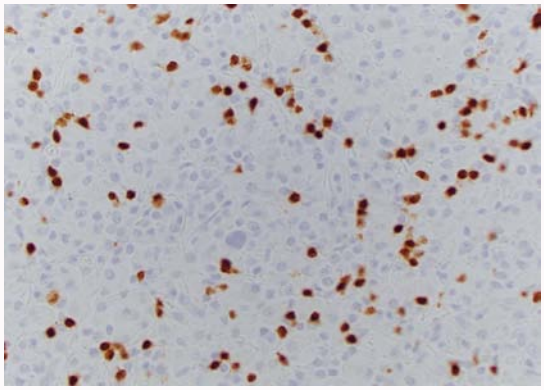

Figure 3: PAX5 Immunohistochemical stain, 40x. Lymph node section with absent nuclear expression on large, atypical lymphocyte.

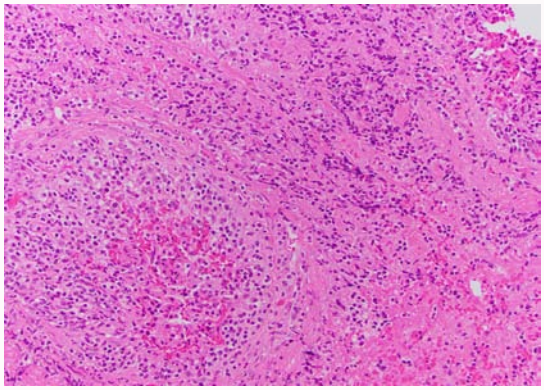

Figure 4: Hematoxylin and eosin, 20x. Paranasal section with extensive angiodestruction accompanied by diffuse, vaguely nodular and atypical lymphoid infiltrate with moderate clear cytoplasm.

past history of recurrent bilateral tonsillitis and light smoking. Family history was significant for a brother with cancer of unspecified type. Computed tomography of the neck was significant for extensive left cervical lymphadenopathy.

The patient subsequently underwent incisional cervical lymph node biopsy, but the extensive mass was not completely excised due to significant potential for neurovascular complication. Lymphoma workup, including flow cytometry, was initiated. Tissue sections showed a lymph node effaced by a diffuse proliferation of many histiocytes and small lymphocytes with intermixed plasma cells and rare granulocytic cells. Scattered large, atypical lymphocytes with irregular nuclear contours, prominent eosinophilic nucleoli, and occasional bi-/multi-nucleation resembling Reed-Sternberg cells were present (Figure 1). No nodules or bands of collagen fibrosis were seen but mummified cells and a pseudo granulomatous appearance were noted. Giemsa and acid fast bacilli special stains were negative for fungal or mycobacterial organisms, respectively. Immunohistochemistry showed positivity for CD30 (Figure 2) and MUM-1 but negative stains for PAX5 (Figure 3), CD20, CD79a and CD15. In situ hybridization results were positive for Epstein-Barr virus. Flow cytometric analysis showed no evidence of a monoclonal B-cell or phenotypically abnormal T-cell population. Classic Hodgkin lymphoma, mixed cellularity type was diagnosed and treatment with AAVD (brentuximab vedotin, doxorubicin, vinblastine, dacarbazine) was initiated. Computed Positron Emission Tomography (PET) prior to therapy demonstrated extensive cervical lymphadenopathy, left worse than right, with multiple bilateral pulmonary nodules, left hilar lymph nodes and soft tissue thickening of the left nasal mucosa.

Four months after initial presentation, the patient underwent septoplasty with turbinate reduction to treat progressively worsening nasal obstruction and inflammation aggravated *via* COVID swabs necessary for hospital admission prior to chemotherapy. Resected specimens of the left nasal septum, inferior turbinate and ethmoid sinus were negative for acid fast bacilli and fungal organisms. Examination of hematoxylin and eosin stain morphology demonstrated respiratory epithelium with extensive necrosis and ulceration accompanied by a diffuse, vaguely nodular and angiocentric atypical lymphoid infiltrate with evidence of angioinvasion and angiodestruction (Figure 4). The mucosal glands appeared to have evidence of clear-cell change. The atypical infiltrate was composed of a mixture of predominantly small and medium-sized atypical lymphocytes and a few intermixed larger cells. No Reed-Sternberg or Hodgkin-like cells were identified, and there was no significant increase in eosinophils. The atypical cells had irregular nuclear contours, dispersed to vesicular chromatin, predominantly inconspicuous but variably prominent nucleoli and a moderate amount of clear cytoplasm. A few scattered mitotic figures were seen. Interestingly, no large CD30+ Reed-Sternberg-like cells were present.

Following microscopic examination, immunohistochemical stains were performed to evaluate the lymphoid infiltrate more accurately. Large, atypical lymphocytes were positive for CD2 (Figure

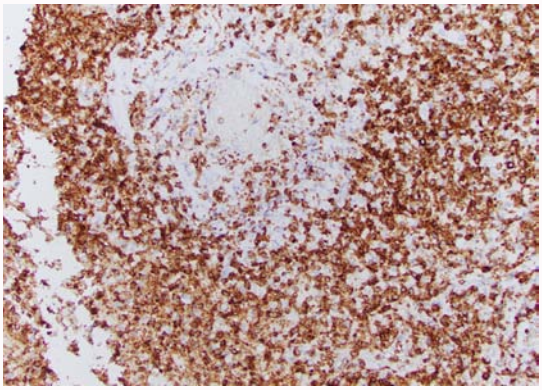

Figure 5: CD2 Immunohistochemical stain, 20x. Paranasal section with intact antibody expression on large, atypical lymphocytes.

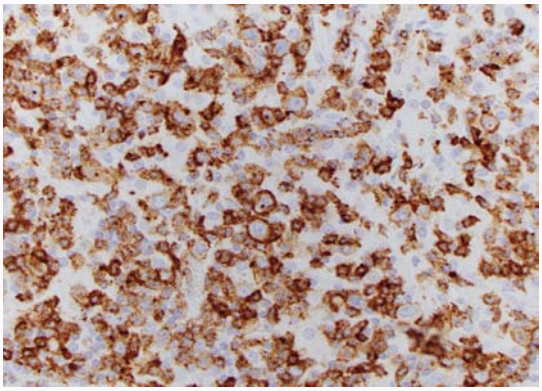

Figure 6: CD2 Immunohistochemical stain, 40x. Lymph node section with intact antibody expression on cell membranes of large, atypical lymphocytes.

5), CD56, CD7 (diminished), and cytotoxic markers granzyme B and TIA-1. Possible staining for CD3 and CD5 was present but difficult to differentiate from background normal T cells. Epstein Barr virus chromogenic in situ hybridization was notably positive. Although the presence of possible CD3 and CD5 expression raised the possibility of a cytotoxic T-cell lineage, a natural killer cell lineage was favored due to negative T-cell clonality testing.

The initial lymph node specimen was subsequently re-evaluated with a panel of natural killer and T-cell Immunohistochemistry markers, including CD2 (Figure 6) and results showed a similar phenotype to the paranasal specimens. The morphologic and immunophenotypic findings supported the diagnosis of extranodal natural killer/T-cell lymphoma, nasal type. Therefore, the patient's diagnosis was subsequently amended to extranodal natural killer/T-cell lymphoma and treatment with P-GELOX (pegaspargase, gemcitabine and oxaliplatin) was initiated.

Six months later, follow-up PET scan status-post treatment showed recurrent left cervical lymphadenopathy, enlargement of the porta hepatis lymph nodes, and positivity in the right proximal femur. The patient was not a candidate for transplant and palliative radiation therapy to the right femur was recommended to minimize fracture risk while systemic therapy options were determined.

Discussion

The misleading finding, which prompted the initial diagnosis of classic Hodgkin lymphoma in the initial cervical lymph node biopsy, was the presence of scattered large, CD30-positive, Reed-Sternberg-like atypical lymphocytes with irregular nuclear contours, prominent eosinophilic nucleoli, and occasional bi-/multi-nucleation. Classic Hodgkin lymphoma is a monoclonal B cell lymphoid neoplasm composed of Hodgkin (large cells with single nuclei and prominent nucleoli) and Reed-Sternberg (large cells with binucleated and very prominent nucleoli) lymphocytes in a variable inflammatory background.

The majority of classic Hodgkin lymphoma cases show positivity for CD30 and reduced expression of most B-cell antigens such as CD20, CD79a and PAX5 in atypical lymphocytes. In contrast, immunohistochemical evaluation of this patient's cervical lymph node was positive for CD30 but completely negative for CD20, CD79a, and PAX5 in atypical lymphocytes. Complete absence of PAX5 in Hodgkin cells is rare; however, cases have been documented [1]. This fact, combined with the misleading Hodgkin-like morphology of neoplastic cells, were the key components that supported the erroneous initial diagnosis of classic Hodgkin lymphoma. Although Epstein-Barr virus infection is present in up to 40% of cases [2], it is of minimal diagnostic value due to presence in multiple different etiologies. Classic Hodgkin lymphoma typically presents in the cervical or mediastinal lymph nodes and has a favorable prognosis in early-stage disease.

Extranodal natural killer/T-cell lymphoma is a predominantly extranodal lymphoma of either natural killer or T-cell lineage. Its common location in the paranasal sinuses prompted further workup as a potential diagnosis in this case. Additional immunohistochemical stains of both the original lymph node and paranasal sections supported the amended diagnosis by demonstrating positivity for CD2 and CD56 in large, atypical cells. Although CD30 is positive in 50% to 70% of cases [3], the patient's paranasal resection specimens lacked the large CD30+ Hodgkin-like cells. This interesting finding was possibly attributed to recently administered brentuximab vedotin therapy for the initial diagnosis of classic Hodgkin lymphoma. Classic features of extranodal natural killer/T-cell lymphoma include Epstein-Barr virus infection, necrosis, cytotoxic immunophenotype and angioinvasion. Its cytological presentation is very broad with cells often having irregularly folded nuclei that may be elongated. Chromatin is granular and large cells may have vesicular nuclei. There is moderate pale to clear cytoplasm and mitotic figures are easily found. A heavy admixture of small lymphocytes, plasma cells, histiocytes and eosinophils can mimic an inflammatory process. Extensive pseudoepitheliomatous hyperplasia of the overlying epithelium can result in mass formation, as evidenced in this patient's nasal obstruction. Prognosis is historically poor; although, outcomes have improved with intense chemotherapy and radiotherapy.

The Prognostic Index of Natural Killer Lymphoma may be useful to predict survival in patients treated with non-anthracycline-based chemotherapy. It was developed *via* a retrospective analysis of 527 patients and identified adverse prognostic factors including age >60 years, stage III or IV disease, distant lymph node involvement, non-nasal type disease, and detection of Epstein Barr virus *via* reverse transcriptase polymerase chain reaction [4]. It has been argued that using the Ann Arbor lymphoma staging system is in effective for this diagnosis due to consistently poor survival in patients classified as early stage and studies demonstrating worse outcomes for extranasal tumors [5,6]. As a response, a proposal for a new staging system that classifies tumors via their proximity to the nasal cavity and nasopharynx was created by the Chinese Southwest Oncology Group

and Asia Lymphoma Study Group (CA system) and published in 2020 [7].

The atypical presentation of this case emphasizes the need to further investigate medical history and symptoms on a multisystemic level when eliciting differential diagnoses in suspected lymphoma patients. It demonstrates the responsibility for pathologists to conduct additional comprehensive workup of seemingly unrelated anatomic sites when deceiving histologic findings are present and ancillary studies are inconclusive. The importance for oncologists and surgeons to continuously monitor for treatment effectiveness and residual disease is also represented. These tasks are essential to increase the diagnostic accuracy necessary for optimal patient outcomes, particularly when multiple etiologies are within consideration.

References

1. Vali Betts E, Dwyre DM, Wang HY, Rashidi HH. PAX5-negative classical hodgkin lymphoma: A case report of a rare entity and review of the literature. Case Rep Hematol. 2017;2017:7531729.
2. Massini G, Siemer D, Hohaus S. EBV in Hodgkin lymphoma. Mediterr J Hematol Infect Dis. 2009;1(2):e2009013.
3. Hu B, Oki Y. Novel immunotherapy options for extranodal NK/T-Cell lymphoma. Front Oncol. 2018;8:139.
4. Kim SJ, Yoon DH, Jaccard A, Chng WJ, Lim ST, Hong H, et al. A prognostic index for natural killer cell lymphoma after non-anthracycline-based treatment: a multicentre, retrospective analysis. Lancet Oncol. 2016;17(3):389-400.
5. Jhuang JY, Chang ST, Weng SF, Pan ST, Chu PY, Hsieh PP, et al. Extranodal natural killer/T-cell lymphoma, nasal type in Taiwan: A relatively higher frequency of T-cell lineage and poor survival for extranasal tumors. Hum Pathol. 2015;46(2):313-21.
6. Vazquez A, Khan MN, Blake DM, Sanghvi S, Baredes S, Eloy JA. Extranodal natural killer/T-Cell lymphoma: A population-based comparison of sinonasal and extranasal disease. Laryngoscope. 2014;124(4):888-95.
7. Hong H, Li Y, Lim ST, Liang C, Huang H, Yi P, et al. A proposal for a new staging system for extranodal natural killer T-cell lymphoma: A multicenter study from China and Asia Lymphoma Study Group. Leukemia. 2020;34(8):2243-8.