Peripheral T-Cell Lymphoma With Aberrant Expression of CD30, CD15, and CD20

Case Report

A 72-year-old male presented with slowly growing submental and inguinal lymph nodes for the previous 3 months. A biopsy of the submental lymph node was performed, and flow cytometric analysis showed a predominant population of cells positive for CD3, CD5, dim CD7, and CD20 and negative for CD4, CD19, and surface immunoglobulin. The lymph node architecture was effaced by atypical cells of varying size arranged in cords and large sheets. These cells had irregular nuclear contours, vesicular chromatin, and occasional prominent nucleoli. Rare bizarre cells and occasional Reed-Sternberg-like cells were seen (Fig 1A). Mitotic figures were abundant. The background contained small lymphocytes and histiocytes, but no eosinophils or neutrophils were appreciated. According to immunohistochemistry, the neoplastic cells were positive for CD20 (Fig 1B), CD2 (subset), CD3 (Fig 1C), CD5, CD30 (subset; Fig 1D), CD15 (subset; Fig 1D inset), MUM1, and CD45. The cells were negative for CD79a, PAX5 (Fig 1B inset), CD4, CD8, TIA1, granzyme B, CD56, ALK1, and in situ hybridization for Epstein-Barr virus (EBV) –encoded RNA. Molecular studies for immunoglobulin gene rearrangement

showed a polyclonal rearrangement pattern (Figs 2A and 2B; PC, polyclonal; IGH, immunoglobulin heavy chain gene; FR2, framework 2; FR3, framework 3). T-cell gene rearrangement studies showed two intense peaks consistent with a clonal process (Fig 2C; TRG, T-cell receptor gamma gene rearrangement). A diagnosis of peripheral T-cell lymphoma (PTCL) with aberrant expression of CD30, CD15, and CD20 was rendered.

The patient was treated with 6 cycles of R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone) and a follow-up positron emission tomography scan (5 months) showed no evidence of residual disease. However, 4 months later, he relapsed with recurrent disease in the skin. Interestingly, the neoplastic cells had become CD4 positive but negative for CD20, likely as a result of therapy with rituximab. This case highlights pitfalls in the accurate diagnosis of PTCL as the expression of CD20 might lead one to suspect a B-cell neoplasm, whereas the expression of CD30 and CD15 point toward diagnosis of classical Hodgkin's lymphoma (cHL).

Discussion

PTCLs are histologically and clinically diverse and can be nodal or extranodal. Because of the marked variability of these

Fig 1.

Fig 2.

lesions in routine hematoxylin and eosin–stained sections, immunophenotypic and sometimes molecular studies are required for accurate diagnosis. At a minimum, there must be demonstration of some T-cell–associated antigens, but in some cases, the immunophenotype may be ambiguous. For example, PTCL with aberrant expression of CD20¹ and more rarely CD79a have been described.^{2,3}

The differential diagnosis of PTCL also includes cHL. Hodgkin's and Reed-Sternberg cells (HRS) in cHL characteristically express CD30 and CD15 with variable staining for CD20. However, CD30 and CD15 have also been reported to be positive in rare cases of PTCL. In a report by Barry et al,⁴ some patients had disease with morphologic features resembling cHL whereas others were more in keeping with PTCL. The present patient's disease would be more consistent with the latter group in that the infiltrate was composed of sheets of atypical cells with marked cytologic atypia. Although, in focal areas, occasional large cells with Hodgkin's-like morphology could be appreciated, the inflammatory background (neutrophils and eosinophils) typical for cHL was not seen. Additional features that did not support a diagnosis of cHL were the atypia in the background T cells as well as the clonal T-cell receptor gene rearrangement studies.

Quintanilla-Martinez et al⁵ also reported patients with PTCL that mimicked cHL by a different mechanism. These contained HRS-like cells with a B-cell phenotype and genotype interspersed among the neoplastic cells. In contrast to our patient, the HRS-like cells were positive for EBV, demonstrated by expression of LMP1 or EBV-encoded RNA.

Another pitfall in the differential diagnosis of PTCL is aberrant expression of T-cell–associated antigens in cHL, as reported by

Tzankov et al.⁶ CD2 was expressed most often, but fewer patients expressed CD4, CD3, CD5, and CD8. The authors noted that the HRS cells were PAX5-positive and the lesions lacked clonal T-cell gene rearrangement, arguing against a diagnosis of PTCL. However, recent studies have shown that no marker has absolute lineage specificity. Feldman et al⁷ reported four patients with anaplastic large-cell lymphoma with weak expression of PAX5 mediated by extra copies of the *PAX5* gene in the tumor cells.⁷ We have also encountered similar findings with one patients with primary cutaneous anaplastic large-cell lymphoma and one patient with anaplastic large-cell lymphoma (unpublished data) with weak expression of PAX5 according to immunostaining.

Treatment for PTCL has included high-dose chemotherapy (eg, CHOP [cyclophosphamide, doxorubicin, vincristine, and prednisone]), radiation, and autologous hematopoietic stem-cell transplant. The addition of rituximab for tumors expressing CD20 has given mixed results.^{1,8} Rahemtullah et al¹ reported nine on patients with T-cell lymphoma with aberrant CD20 expression. Three of the patients were treated with chemotherapy with rituximab and two developed recurrent disease. Given the rarity of CD20-expressing PTCL, it has been impossible to determine the clinical use of rituximab in such situations in a clinical trial setting.

We present the first case, to our knowledge, of PTCL with aberrant expression of CD30, CD15, and CD20. This case highlights potential pitfalls in diagnosis, given that some of the features suggested a B-cell lymphoma or cHL. The integration of an extensive immunoprofile with molecular studies was needed to arrive at an accurate diagnosis.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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