To the editor:

Phenotype of neoplastic cells in angioimmunoblastic T-cell lymphoma is consistent with activated follicular B helper T cells

We read the letter by Grogg et al., recently published in Blood, with great interest. The authors demonstrated that CD10+ T cells in angioimmunoblastic T-cell lymphoma (AITL) coexpress CXCL13 and proposed that AITL is a neoplasm of germinal center (GC) T-helper cells.

We have hypothesized that neoplastic T cells may be related to follicular B helper T (Tfh) cells, since CD10+ atypical T cells were found to be in intimate contact with the expanded meshwork of proliferating follicular dendritic cells (FDCs), a characteristic of AITL. Therefore, we have performed consecutive double immunolabeling to analyze expression of some known Tfh cell functional antigens (CXCR5, CD154/CD40L, CD134/OX40, and CD57) in the CD10+ T cells in 20 paraffin-embedded AITL cases. Since Kim et al. and Chhtanova et al. established that CXCL13 is highly up-regulated in Tfh cells, expression of this antigen was also investigated; the same has also been done by Grogg et al.

In 18 of 20 cases, the expression of CD10 on 5% to 30% of T cells strongly correlated with CXCL13 production. The remaining 2 cases exhibited CXCL13+ atypical T cells without apparent CD10 expression. The neoplastic T cells, as defined by CD10 as well as CXCL13 expression, revealed a CXCR5+CD40L+CD154+CD57− immunophenotype (Figure 1), which is most consistent with GC outer-zone Tfh cells. All cases displayed comitant...

Cancer revealed only one additional lymphoma with the t(2;12)(p12;p13), which was also diagnosed as typical MCL. Unfortunately, gene expression profiling was not available in the cases presented here. Nevertheless, the typical morphologic and immunophenotypic features of our cases indicate that rare cyclin D1-negative MCLs exist, in which deregulation of cyclin D2 due to a t(2;12)(p12;p13) substitutes for t(11;14)–driven cyclin D1 expression.

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expression of CXCL13 and CXCR5 in neoplastic T cells, again pointing to a T<sub>FH</sub> phenotype. Coexpression of the CXCR5 chemokine receptor and its ligand CXCL13 suggests an autocrine loop, possibly contributing to the survival of neoplastic T cells. All cases demonstrated coexpression of CD154 in the majority of the neoplastic T cells. This antigen plays a crucial role in GC formation and provides survival signals to follicular B cells. Each case showed significant but variable numbers (10%-100%) of neoplastic T cells. This antigen may be retained in B follicles. One case coexpressed CD57 in a significant proportion of neoplastic cells, while the remaining cases displayed only a minute fraction of CD57<sup>+</sup> cells that may reflect the residual normal T<sub>FH</sub> cells. Since proliferating FDCs expressed CXCL13 and are known to express CD40<sup>L</sup> (receptor for CD154) and OX40L, our data suggest a selective cross-talk between FDCs and neoplastic T cells.

Our observations not only fully support the notion of Grogg et al. but extend it by a more detailed analysis, establishing that the phenotype of the neoplastic cells (as shown here) is consistent with activated T<sub>FH</sub> cells localized at the boundary between the mantle zone and the GC light zone. These findings provide direct explanations for some peculiar features of AITL, including B-cell hyperactivation and hypergamaglobulinemia despite gradual reduction of follicular B-cell mass, as well as the follicular outgrowths of FDCs as a result of stimulation by neoplastic T<sub>FH</sub> cells. Further investigations will be needed to explain loss of follicular B cells, a phenomenon that occurs in advanced cases and may be caused by a disarrayed dialogue between neoplastic T<sub>FH</sub> cells and non-neoplastic B cells.

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References


To the editor:

Immune thrombocytopenic purpura does not exhibit a disparity in prevalence between African American and white veterans

Ethnic, racial, and geographic differences influence virtually all human disease, and certain conditions exhibit well-established differences between Africans and Europeans. Once such differences are identified, it is important to examine them, because etiologic, genetic, and therapeutic heterogeneity may be present. In addition, ethnic disparities of all types may be accompanied by

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