Author's response to reviews

Title: Relapsed angioimmunoblastic T-cell lymphoma with acquired expression of CD20: A case report and review of the literature

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Author's response to reviews: see over
The authors would like to thank the reviewers for their valuable comments. All points have been addressed and alterations made to the manuscript accordingly (all changes in the revised manuscript are highlighted in red color).

1. **Reply to reviewer comments Zhi Li:**

**Major Compulsory Revisions**

1. Is CD20-positivity in T-cell lymphomas an “acquired” expression of neoplastic T lymphocytes or an “aberrant” expression in T-cell lymphoma arising from circulating CD20 positive T cells? There remains controversial for the mechanism of CD20 expression in T-cell lymphomas, including CD20+ AITL, CD20+ NK/T-cell lymphoma and CD20+ peripheral T-cell lymphoma, NOS. The hypotheses of the nature of CD20-positive T cell lymphoma include circulating CD20 positive T cells undergoing neoplastic transformation, a marker of normal T cell activation, and an activation marker acquired after neoplastic transformation. The possible mechanism of CD20-positive in AITL should be discussed in the paper. **On pages 9 and 10 the possible mechanisms of CD20 expression have been expanded, including also the possibility of trogocytosis.**

2. If CD20-positive lymphoma described in this paper is an AITL-developed secondary B-cell lymphoma? It has been documented that the development of B-cell lymphoma can be a consequence of the disease progression of AITL. B-cell lymphoma can also coexist with AITL in same lymph node. Therefore, the differential diagnosis of secondary or coexistent B-cell lymphoma with AITL is important for pathologists even if cytogenetic abnormalities have been detected by PCR assay. The authors should provide an illustration to verify the co-expression of CD3 and CD20 in the same cell population with PD-1 or CXCL-13 positivity in serial sections. In addition, the key points of differential diagnosis of AITL-developed secondary B-cell lymphoma should also be summarized in discussion section. **Although AITL is known to progress / relapse as frank B-cell lymphoma, this could be excluded in the current case. B-cell clonality analysis in the initial biopsy as well as upon relapse did not detect a clonal B-cell population, whilst T-cell clonality analysis revealed an identical clone initially as well as upon relapse. This point has been clarified on pages 6 and 7 and has been added to the discussion on page 11.**

3. In figure 3C-E, it is difficult to distinguish reactive B-cells (CD20 and CD79a positive) from neoplastic T-cells (CD3 positive), please replace these figures. **Changes have been made to figure 3 (see revised form) with photos taken from a different area of the biopsies to more clearly show the staining pattern – in particular adding the data for PD-1 staining here in both the 2004 and 2011 biopsy (see also changes in the text, page 7, and figure legend, pages 18 and 19).**
2. Reply to reviewer comments Louisy Huang:

Minor Essential Revisions:

1. In the manuscript, the “FH” in the abbreviation of follicular T helper (TFH) is better to be placed in subscripts.
   Changes have been throughout the manuscript (new “$T_{FH}$” instead of “TFH”)

2. On the page 6 of the manuscript, there is a typing error: high endothelial “venules”.
   The typing mistake has been corrected (s. page 6).

Discretionary Revisions

1. On page 7, the authors compared the morphological features of biopsies in 2004 and 2011, and conclude that “there was no cytomorphological signs of progression”. Could the authors define the “cytomorphological signs of progression” more precisely in their manuscript?
   The term has been clarified i.e. pertaining to obvious signs of anaplasia (s. changes page 7).

2. On page 8, the authors mentioned that “CD20 expression may be acquired in T-cell lymphomas following activation of the T-cells, as has been demonstrated in stimulated lymph nodes from monkeys with simian immunodeficiency virus”. This is an interesting finding. In fact, the “lineage infidelity” also occurs in B-cell lymphomas as well as classical Hodgkin lymphomas, as previously demonstrated by the authors’ group. Is there any other possible mechanism involving the acquired expression of CD20 in T-cell lymphomas in addition to that mentioned in the manuscript? The authors are encouraged to discuss other potential mechanisms such as the role of trogocytosis in this “lineage infidelity”. 
   This valid point has been incorporated in the body of the discussion (page 8) and includes two new references (see references 15 and 16).