Reviewer’s report

Title: Transformation of nodular lymphocyte predominant Hodgkin lymphoma into "LP type" diffuse large B cell lymphoma

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Reviewer: Maria Claudia N Nogueira Zerbini

Reviewer’s report:

The authors present 33 cases of NLPHL with a DLBCL component, concomitant in the same biopsy (26 cases) or in temporally distinct biopsies (7 cases). Two patients with simultaneous presentation of NLPHL and DLBCL had a past history of NLPHL. Using clinical, morphological and immunophenotypic features (using the antibodies anti-: CD20, CD79a, CD19, CD3, EMA, J-chain, CD75, CD10, BCL2, BCL6, CD30, CD15, MUM1, IgD, JAK2 and STAT6) and EBER/ISH – the authors look for common features between the two neoplasms which could identify the origin of DLBCL from a NLPHL (‘LP-type’ DLBCL). A group of patients with conventional DLBCL (41 cases) is used for comparison with those 33 patients in order to confirm the relevance of these findings.

The result of the analysis shows that the DLBCL originating in NLPHL exhibits quite variable characteristics, which does not allow a clear distinction from conventional DLBCL in the absence of representative areas of NLPHL. The authors present suggestions as to the origin of DLBCL from NLPHL: the axillary, abdominal and splenic location, the precise delimitation of the large cells sheets and the immunohistochemical expression of EMA and/or the J-chain component by neoplastic cells.

COMMENTS

1. The objectives are not clearly defined and the title does not match the findings described, since it has not been possible to characterize a specific type of DLBCL that justifies the designation ‘LP type’ for DLBCL associated with NLPHL.

2. The design work is interesting and the methodology used is appropriate, applying available techniques to most pathology laboratories: immunohistochemistry and morphology. The paper does not use complementary molecular methods, but concludes that these would probably be necessary for the characterization of a possible variant of DLBCL originating in NLPHL.

3. The immunohistochemical panel is broad, but would necessarily have to add markers of follicular dendritic cells (CD21 + CD23).

4. The number of cases is interesting and deserves a detailed descriptive analysis, performed in a clearer and more organized way, complemented by comparison with the findings of other published series.

5. The additional files are relevant, although not defined as objective the comparison between the two groups of patients, with synchronous evolution to
DLBCL with those of subsequent evolution to DLBCL.

6. References are pertinent and updated.

RECOMMENDATIONS

1. The manuscript cannot be accepted in its current version. A detailed review defining precisely the objectives, the title and the results is recommended. The strong point of this study is the sample size and use of a broad panel of markers selected in an interesting way.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.