



Observations on hematogones with light chain restriction.

ARTICLE INFO

Keywords

Light chain restriction
Reactive processes

ABSTRACT

Light-chain restricted hematogones (LCR HGs) detected by flow cytometry (FC) may, occur in bone marrow mimicking involvement by a B-cell lymphoma. This phenomenon can present a diagnostic pitfall and negatively impact patient management, and may occur in other organs, including lymph nodes. For this reason, it is recommended to utilize, in case of LCR in lymph node, one additional morphological, phenotypical or molecular criteria for the diagnosis of lymphoma on cytological samples.

Dear Editor, we read with great interest the article by El Hussein S. et al: Hematogones with light chain restriction: A potential diagnostic pitfall when using flow cytometry analysis to assess bone marrow specimens, recently published on Leukemia Research [1]. The Authors describe the possible occurrence of light-chain restricted hematogones (LCR HGs) detected by flow cytometry (FC), which can mimic bone marrow involvement by a B-cell lymphoma. The Authors stress that this phenomenon can present a diagnostic pitfall and negatively impact patient management, as misinterpretation may upgrade disease stage in patient suffering from B-cell non-Hodgkin lymphoma (NHL). The Authors also reported that this phenomenon may occur in other organs too [2]. We fully agree with their conclusions and we would like to add some additional comments. Some years ago, we observed LCR in a lymph node cell suspension, processed by FC, in a HIV positive patient who had suffered from a follicular lymphoma (FL). The case was considered a relapse of FL but the histological control revealed a florid follicular hyperplasia [3]. We also recently described one false-positive cytological diagnosis due to LCR that turned out to be a case of progressively transformed germinal centers without IGH rearrangement at histology [4]. Checking on the literature we found similar cases showing LCR with or without CD10 positivity, without IGH gene rearrangement or t(14;18), described in different organs and different samples [2–9]. The common aspect of this heterogeneous group of cases was the clinical data, in almost all the corresponding patients, of immunodepression, as is the case in the series of El Hussain et al [1], or autoimmune diseases [2–9]. These clones, at FC analysis and, mainly in extra-nodal sites, did not seem to exceed 20% of the gated B-cells. Therefore, we called them “microclones” [5] and supposed that, in cases in which there is an impairment of the immune system either for autoimmune stimulation, or for a compensation for defective T-cell response, small clones of monotypic B-cell may produce LCR. The possible occurrence of LCR in non-lymphomatous processes has been one of the reasons for which a recent proposal for the performance, classification, and reporting of lymph node fine-needle aspiration cytopathology (the Sydney system) [4,10] adopted the criteria proposed for clonality assessment of lymphomas by the EuroClonality/BIOMED-2 guidelines [11], but recommends also to utilize, in case of LCR in lymph node FNAC, additional morphological, phenotypical or molecular criteria for the diagnosis of

lymphoma on cytological samples.

Source of Funding

The authors have disclosed that they have no relationships with, or financial interest in, any commercial companies pertaining to this article.

Declaration of Competing Interest

All authors do not have any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work

Acknowledgements

No Acknowledgements need to be made.

References

- [1] S El Hussein, W Wang, SA Wang, H Fang, S Garces, M Tashakori, KA Lyapichev, L Qiu, X Wang, S Loghavi, LJ Medeiros, P Challagundla, JL Jorgensen, Hematogones with light chain restriction: A potential diagnostic pitfall when using flow cytometry analysis to assess bone marrow specimens, *Leuk Res. Sep 8 (111) (2021)*, 106704.
- [2] S. Matsubayashi, H. Tamai, T. Morita, S. Fukata, F. Matsuzuka, T. Suzuki, K. Kuma, S. Nagataki, R. Volpe, Hashimoto's thyroiditis manifesting monoclonal lymphocytic infiltration, *Clin. Exp. Immunol.* 79 (1990) 170–174.
- [3] I Cozzolino, E Vigliar, LV Sosa Fernandez, C Selleri, S Pepe, M Vitale, M Triggiani, P Zeppa, Non lymphomatous clonal B-Cell populations in enlarged lymph nodes in acquired immunodeficiency syndrome, *Infez Med* 20 (2) (2012) 35–42. Suppl.
- [4] A. Caputo, V. Ciliberti, A. D'Antonio, A. D'Ardia, R. Fumo, V. Giudice, L. Pezzullo, F. Sabbatino, P. Zeppa, Real-world experience with the Sydney System on 1458 cases of lymph node fine needle aspiration cytology, *Cytopathology: official journal of the British Society for Clinical Cytology* 33 (2) (2022) 166–175, <https://doi.org/10.1111/cyt.13079>.
- [5] P. Zeppa, I. Cozzolino, A.L. Peluso, G. Troncone, A. Lucariello, M. Picardi, C. Carella, F. Pane, A. Vetrani, L. Palombini, Cytologic, flow cytometry, and molecular assessment of lymphoid infiltrate in fine-needle cytology samples of Hashimoto thyroiditis, *Cancer* 117 (2009) 174–184.
- [6] S.J. Kussick, M. Kalnoski, R.M. Brazier, B.L. Wood, Prominent clonal B-cell populations identified by flow cytometry in histologically reactive lymphoid proliferations, *Am J Clin Pathol*; 121 (2004) 464–472.

<https://doi.org/10.1016/j.lrr.2022.100316>

Received 23 November 2021; Received in revised form 11 February 2022; Accepted 11 April 2022

Available online 13 April 2022

2213-0489/© 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

- [7] P. Bhargava, J.A. Parker, B.J. Dezube, Pitfalls of diagnosis based on abnormal flow cytometry and [(18)F] fluorodeoxyglucose positron emission tomography, *Clin Lymphoma Myeloma* 8 (13) (2008) 117–120.
- [8] E. Vigliar, I. Cozzolino, M. Picardi, A.L. Peluso, L.V. Fernandez, A. Vetrani, G. Botti, F. Pane, C. Selleri, P. Zeppa, Lymph node fine needle cytology in the staging and follow-up of cutaneous lymphomas, *BMC Cancer* 14 (2014) 8. Jan 6.
- [9] E. Vigliar, A. Caleo, M. Vitale, V. Di Crescenzo, A. Garzi, P. Zeppa, Early cytological diagnosis of extranodal stage I, primary thyroid non-Hodgkin lymphoma in elderly patients. Report of two cases and review of the literature, *BMC Surg* 13 (2) (2013) S49. Suppl.
- [10] M.A. Al-Abbadi, H. Barroca, B. Bode-Lesniewska, M. Calaminici, N.P. Caraway, D. F. Chhieng, I. Cozzolino, M. Ehinger, A.S. Field, W.R. Geddie, R.L. Katz, O. Lin, L. J. Medeiros, S.E. Monaco, A. Rajwanshi, F.C. Schmitt, P. Vielh, P. Zeppa, A Proposal for the Performance, Classification, and Reporting of Lymph Node Fine-Needle Aspiration Cytopathology: The Sydney System, *Acta Cytol* 64 (2020) 306–322.
- [11] A.W. Langerak, P.J. Groenen, M. Brüggemann, K. Beldjord, C. Bellan, L. Bonello, E. Boone, G.I. Carter, M. Catherwood, F. Davi, M.H. Delfau-Larue, T. Diss, P. A. Evans, P. Gameiro, R.Garcia Sanz, D. Gonzalez, D. Grand, A. Håkansson, M. Hummel, H. Liu, L. Lombardia, E.A. Macintyre, B.J. Milner, S. Montes-Moreno, E. Schuurin, M. Spaargaren, E. Hodges, J.J. van Dongen, EuroClonality/BIOMED-2 guidelines for interpretation and reporting of Ig/TCR clonality testing in suspected lymphoproliferations, *Leukemia* 26 (10) (2012) 2159–2171.

Angela D'Ardia, Valeria Ciliberti, Pio Zeppa*, Alessandro Caputo
*University of Salerno - Baronissi Campus: Universita degli Studi di Salerno,
Campus Baronissi Via Allende Baronissi (SA), Salerno, Italy*

* Corresponding author.
E-mail address: pzeppa@unisa.it (P. Zeppa).