ambulatorial. Durante o seguimento foi disponibilizado laudo de biópsia de medula óssea com possível infiltração por neoplasia linfoproliferativa T e assim pausado protocolo HLH 94 para tratamento específico. **Conclusão:** Visto a raridade da HLH não há ensaios clínicos em adultos determinando tratamento e o mesmo é baseado principalmente no estudo prospectivo pediátrico HLH 94. O diagnóstico deve ser prontamente aventado em caso de síndromes febris associadas a citopenias e hiperferritininemia e o tratamento precoce é fundamental para redução de mortalidade.

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LOW MOLECULAR DIVERSITY AND GENOTYPIC-PROGNOSTIC ASSOCIATIONS IN FOLLICULAR LYMPHOMA (FL): IDENTIFICATION OF NEW BIOLOGICAL MARKERS BY LARGE-SCALE GENE MICROARRAY

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Introduction: FL has heterogeneous biological behavior, variable clinical outcomes, and a natural history marked by histological transformation (HT). The management of FL and its outcomes are highly dependent on staging (CS) and tumor burden (TB). The identification of new molecular biomarkers is crucial, not only to understand FL's biology, but also, can guide better prognostic stratification, and determine new therapeutic targets. This study aims to outline the GEP in tissue samples from FL categorized by CS and TB using a large-scale gene microarray platform with subsequent expansion by RT-qPCR. **Methods:** This study involved 219 FL cases. FL patients were categorized into early-stage disease (I/II) (ES), advanced-stage (AS) (III/IV) with low tumor burden (LTB), and AS with high tumor burden (HTB) according to GELF criteria. The experimental phase involved 126 FFPE samples. Firstly, 42 samples (12 ES, 11 AS-LTV, 12 AS-HTV, 6 control lymph nodes and 1 control HELA) were submitted to the array using the *Clariom D Array Human* platform. The identification of differentially expressed genes (DEGs) between the 4 groups used the *Transcriptome Analysis Console* by the eBay ANOVA method. Bidimensional PCA sought to identify discriminatory DEGs clusters. A comparison between pairs was subsequently performed. The 7 most discriminatory DEGs were selected for a cohort expansion by RT-qPCR. **Results:** According to CS and TB, 14.6% of FL cases were categorized as ES, 17.8% as AS-LTB, and 67.6% as AS-HTB. With a median follow-up of 80.7 months, the median OS was 208.2, 130.5, and 126.3 months for ES, AS-LTB, and AS-HTB,$p = 0.249$. The median PFS was 113.3, 110.7, and 59.5 months, for the same groups, $p = 0.018$. The array identified 135,750 genes comparisons between the control, ES, AS-LTB, and AS-HTB. PCA analysis was not able to identify discriminatory DEGs clusters among the 4 groups. Pairwise comparative analysis identified 1913 DEGs among the 4 groups. Of these, 1759 (91.9%) were DEGs between FL and healthy controls, but only 218 (11.3%) were DEGs among the 3 different FL subgroups, evidencing a low molecular diversity in FL when categorized by CS and TB. In the cohort expansion by qRT-PCR, 7 pre-selected DEGs based on the microarray were tested, including the genes *GNG7*, *ITGAM*, *AZN1*, *TIMD4*, *IL7R*, *PTGS2*, and *MTTL10*. The comparison between the median expression of these genes among the 3 FL's groups showed that the expression of the *ILR7* was downregulated with the progression of the disease, with marked hypoexpression in AS-HTB patients. These data may suggest downregulation of *IL7R* gene in the FLs natural history. We found that hypoexpression of the *GNG7* ($p = 0.024$) and *PTGS2* ($p = 0.090$) were associated with higher rates of disease progression/relapse, and hypoexpression of the *GNG7* ($p = 0.006$) was associated with a higher probability of HT, highlighting the potential prognostic impact of these molecular biomarkers. Finally, we established phenotypic-genotypic associations, as hypoexpression of *ITGAM* was associated with higher rates of B-symptoms ($p = 0.017$) and bulky disease ($p = 0.026$), as well as hypoexpression of *IL7R* was correlated with a higher probability of bulky ($p = 0.025$) and extranodal involvement ($p = 0.016$). **Conclusion:** Although CS and TB are strong determinants of the prognostic heterogeneity of FL, this study did not find high molecular diversity by this categorization. We observed a relatively homogeneous GEP with low biological diversity in FL presenting different disease evolution phases. Moreover, new molecular biomarkers potentially implicated in FLs natural history, prognostication and specific clinical phenotypes were revealed.

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OUTCOMES AND TOXICITY PROFILE IN ELDERLY DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS (DLBCL): A REAL-WORLD AND COMPARATIVE STUDY INVOLVING THREE DIFFERENT DOSE-MODULATED ANTHRACYCLINE-BASED IMMUNOCHEMOTHERAPY REGIMENS IN LATAM

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Introduction: DLBCL commonly affects the older population. Elderly patients often present high-risk molecular profile, lower tolerability to chemotherapy, and poor outcomes. In this setting, attenuated therapeutic regimens, such as R-miniCHOP and R-miniCHOP of the elderly, have emerged for this fragile population. Albeit its relevance, response rates, clinical outcomes, and toxicities of these regimens remain