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CARACTERÍSTICAS CLÍNICAS E DESFECHOS TERAPÊUTICOS DOS PACIENTES COM LINFOMA PRIMÁRIO EXTRANODAL TRATADOS EM UM CENTRO DE REFERÊNCIA NO BRASIL

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Introdução: Linfomas primários extranodais (LPE) são linfomas não-Hodgkin (LNH) cujo envolvimento inicial e predominante ocorre fora dos linfonodos, afetando diversos órgãos e tecidos. Os subtipos mais frequentes são o linfoma de grandes células B (LGCB) e linfomas MALT (tecido linfoide associado à mucosa). Têm etiologia, prognóstico, comportamento clínico e perfis moleculares distintos dos LNH nodais. Dada a heterogeneidade clínica, influência geográfica e escassez de dados populacionais locais, é essencial investigar as características dos LPE no Brasil. **Objetivos:** O objetivo deste trabalho é caracterizar o perfil clínico e os desfechos terapêuticos dos pacientes com LPE tratados no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto (HCFMRP-USP). **Material e métodos:** Trata-se de uma coorte retrospectiva. Os dados clínicos, laboratoriais e epidemiológicos foram extraídos dos prontuários de todos pacientes consecutivos, ≥ 18 anos, com diagnóstico novo de LPE (conforme critérios da OMS), tratados no HCFMRP-USP de 2018-2024. Pacientes com acometimento extranodal secundário, recidiva extranodal, ou tratamento anterior foram excluídos. O estudo foi aprovado pelo CEP local. **Resultados:** Dos 472 pacientes com LNH acompanhados no período, 89 (18,8%) eram LPE. A mediana de idade foi 65,5 anos (22-89) e 47,2% eram mulheres. Os principais sítios de acometimento e desfechos terapeuticos observados foram: Estômago (22,5%): O LGCB foi o mais comum (50%), com 50% dos casos positivos para *H. pylori* na biópsia. Todos foram tratados com imunoquimioterapia, com resposta completa (RC) em 100% dos casos. Adicionalmente, 45% eram linfoma MALT, dos quais 66,7% eram *H. pylori* positivo na biópsia. A antibioticoterapia exclusiva foi o tratamento mais aplicado nos subtipos MALT (44,4%), com RC de 100%; Olhos (14,6%): linfoma MALT foi o mais frequente neste local (85%). Imunoterapia, imunoquimioterapia e radioterapia foram adotadas em igual proporção (30% cada) com RC observada em 33,3%, 66,7% e 100% dos casos, respectivamente; Intestinos (11,2%): LGCB foi o subtipo mais comum (70%) acometendo os intestinos, seguido do linfoma folicular (20%). Todos foram tratados com imunoquimioterapia (RC em 60%). Ossos (9%): LGCB foi o mais observado (87%). Imunoquimioterapia foi a modalidade mais utilizada (75%), com RC de 66,7%; Pele (7,9%): os subtipos histológicos encontrados foram MALT (4 casos), centrofolicular (2 casos), LGCB e plasmablástico (1 caso cada). Distintos tratamento foram empregados (locais ou sistêmicos). **Discussão e conclusão:** Nosso estudo demonstrou que o LPE corresponde a cerca de 20% dos LNH, em consonância com a literatura. O estômago é o principal sítio acometido, com alta prevalência de *H. pylori* (66,7% nos MALT e 50% nos LGCB). O LGCB foi o tipo mais frequente em estômago, intestinos e ossos, onde comumente se exige tratamento sistêmico, enquanto que o linfoma MALT foi mais comum em olhos e pele, com comportamento mais indolente e possibilidade de abordagem local. A imunoquimioterapia foi a estratégia mais utilizada de maneira geral, com RC entre 60% e 100% dos casos. Os resultados confirmam a heterogeneidade clínica e biológica dos LPE, com predomínio do acometimento gástrico e alta positividade para *H. pylori* nos linfomas MALT. A imunoquimioterapia é eficaz, com taxas elevadas de RC. Esses dados reforçam a importância de traçar o perfil dos LPE e fornecem subsídios para otimizar os resultados do tratamento desta neoplasia no Brasil. **Financiamento:** A presente pesquisa foi realizada com bolsa CNPq-PIBIC n° 2024-1215

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CD30 EXPRESSION IN DIFFUSE LARGE B-CELL LYMPHOMA AND PRIMARY MEDIASTINAL LYMPHOMA: FREQUENCY, ASSOCIATION WITH PROGNOSTIC FACTORS, AND IMPACT ON SURVIVAL

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Introduction: CD30 expression (ExpCD30) has been increasingly explored as a potential prognostic and therapeutic biomarker in non-Hodgkin lymphomas (NHL), particularly in diffuse large B-cell lymphoma (DLBCL) and primary mediastinal B-cell lymphoma (PMBCL). **Objectives:** We investigated the frequency of ExpCD30 and its association with National Comprehensive Cancer Network International Prognostic Index (NCCN-IPI), and cell of origin (Germinal Center [GC] vs. non-Germinal Center [NGC]), as well as its impact on survival in patients with DLBCL and PMBCL. **Material and methods:** This was a retrospective observational cohort study, approved by the Ethics Committee, which evaluated cases of DLBCL and PMBCL diagnosed between 2009 and 2016 at the Cancer Institute of the State of São Paulo. Adult patients eligible for curative treatment with viable histopathological material were included. CD30+ cases were tested for EBV by in situ hybridization, and EBV+ cases were excluded. ExpCD30 was analyzed as both a continuous and categorical variable. The classification into GC and NGC subgroups followed the Hans algorithm. The association between ExpCD30 and categorical variables, such as type of biopsy tissue, NCCN-IPI risk factors, and cell of origin, was assessed using the Chi-square. The primary outcomes were progression-free survival (PFS) and overall survival (OS), estimated using the Kaplan-Meier method. Statistical analyses included univariate and multivariate Cox regression, assessment of multicollinearity, and validation of the proportional hazards assumptions. ExpCD30 was retained in the final models regardless of p-value. A significance level of $p < 0.05$ was adopted. **Results:** A total of 301 patients were

included—279 with DLBCL and 22 with PMBCL. The overall frequency of CD30 positivity was 19.6%, with 19% in DLBCL and 27.3% in PMBCL. Among CD30+ cases, nodal biopsies were significantly more frequent (62.7%) than extranodal (37.3%), compared to 47.5% and 52.5% respectively in CD30-negative cases (p = 0.036). No significant associations were observed between ExpCD30 and NCCN-IPI risk category, or between ExpCD30 and cell of origin. ExpCD30 was not significantly associated with OS (p = 0.22) or PFS (p = 0.42). In multivariate models, the only independent predictor of worse outcomes was the presence of ≥ 4 NCCN-IPI risk factors, associated with poorer OS (HR 3.15, 95% CI: 1.99–5.01, p < 0.001) and PFS (HR 2.90, 95% CI: 1.90–4.42, p < 0.001). In the DLBCL subgroup, ExpCD30 was not significantly associated with GC vs. non-GC classification such as NCCN-IPI score. ExpCD30 did not impact OS (p = 0.35) or PFS (p = 0.70). Once again, having ≥ 4 NCCN- IPI risk factors remained the only significant prognostic factor in the multivariate analysis. Due to the small number of cases (n = 22), we were unable to conduct detailed statistical analyses in the PMBCL subgroup. **Discussion and conclusion:** Our cohort represents the third largest sample among previously published studies and is the first in Brazil and Latin America to evaluate CD30 expression in these specific lymphoma subtypes. Our findings are consistent with most of the studies published in the international literature. CD30 positivity was observed in approximately one-fifth of cases, more frequently in nodal biopsies, but showed no significant association with major prognostic factors or survival outcomes.

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CHARACTERISTICS AND TREATMENT PATTERNS OF PATIENTS WITH MANTLE CELL LYMPHOMA IN BRAZIL: A REAL-WORLD STUDY

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Introduction: Mantle cell lymphoma (MCL) is a non-Hodgkin lymphoma with an adverse prognosis, caused by an accumulation of malignant B-cells originating from the mantle zone of lymph nodes. There is limited evidence exploring patients (pts) with MCL and their treatment in Brazil. **Objectives:** This study aimed to describe the demographics, clinical characteristics and treatment patterns of pts with MCL across Brazil. **Material and methods:** Data were drawn from the Adelphi MCL Disease Specific Programme™, a cross-sectional survey with retrospective data collection from March-October 2022 in 8 countries including Brazil. Hematologists/hem-oncologists provided demographics, clinical characteristics and treatment data for six consecutively consulting pts with MCL in a 1:2 ratio of first-line (1L) to pre-treated (2L+), with ≥two of the 2L+ pts having received a Bruton's tyrosine kinase inhibitor (BTKi). All analyses were descriptive. **Results:** 37 physicians provided data on 244 pts with MCL in Brazil. Most physicians (85%, n = 29/34, known setting) practiced in a specialist center, and 12% (n = 4/34, known setting) in a university setting. Of the pts, 75% (n = 183/244) were male with median age (interquartile range) 65.0 (55.0-71.0) years and 19% (n = 46/244) had a caregiver. Most were covered by private healthcare plans (72%, n = 176/244), with 19% (n = 47/244) covered by the public healthcare system. Most pts had classical MCL (61%, n = 148/244), 12% (n = 30/244) blastoid/pleomorphic disease and one fifth indolent disease (22%, n = 53/244) as recorded by the treating physician. At diagnosis, 30%/35%/31% of pts had an ECOG performance status of 0/1/≥2. Using a simplified MCL international prognostic index (sMIPI) proxy, 55% (n = 101/182) were classed as low risk, 29% (n = 53/182) intermediate risk and 15% (n = 18/182) high risk at data collection. Overall, 50% received a BTKi, and 98% of 1L and 90% of 2L therapies were initiated post-2014 and post-2020, respectively. Stem cell transplant was received by 9% (n = 23/244) at 1L and by 2% (n = 3/160) at 2L. At 1L, 62% (n = 151/244) received chemoimmunotherapy (CIT), and 17% (n = 42/244) received a BTKi (monotherapy or combination), with R-CHOP the most common CIT (37%, n = 90/244) and ibrutinib the most common BTKi (12%, n = 29/244). Overall response rate (ORR) at 1L was 60% (n = 25/42) and 72% (n = 109/151) for BTKi-based treatment and CIT respectively, with a complete response rate (CRR) of 40% (n = 17/42) and 50% (n = 75/151) respectively. At 2L, 58% (n = 92/160) received a BTKi-based treatment (n = 67/92 ibrutinib, n = 25/92 acalabrutinib) and 15% (n = 24/160) received CIT with R-CHOP (n = 7/24) being the most common CIT. ORR was 53% (n = 49/92) for BTKi-based treatment and 75% (n = 18/24) for CIT, with 21% (n = 19/92) and 46% (n = 11/24) CRR, respectively. Unacceptable tolerability was reported as the reason for treatment cessation for one pt (n = 1/176) at 1L and 17% (n = 10/59) at 2L. **Discussion and conclusion:** Conclusions: Most pts were elderly males and classified as low risk or intermediate risk using a sMIPI proxy. Though one-fifth of pts were reported to have indolent disease at diagnosis, one-third had an ECOG score of ≥2 during treatment, indicating functional decline. Although our study set a quota for 2L+ pts treated with BTKi, observation of BTKi use in 1L was unexpected since BTKi was not approved in the 1L setting at data collection in Brazil; this could suggest unmet need for targeted treatment in the first-line setting at data collection.

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DESAFIO DIAGNÓSTICO EM LINFOMA PLASMABLÁSTICO: RELATO DE CASO EM PACIENTE IMUNOCOMPETENTE

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