diagnóstico de Linfoma de células T paniculite subcutâneo. Biópsia de medula óssea não demonstrou infiltração. **Discussão:** O LCTPS é um linfoma de células T raro, representa menos que 1% de todos os Linfomas não-Hodgkin e, em geral, apresenta-se como nódulos subcutâneos ou placas endurecidas, sendo ulcerações pouco frequentes. Locais de acometimento são variáveis e não há, na literatura, estabelecimento de epidemiologia para acometimento mamário. O diagnóstico se baseia em achados clínicos, biópsia de pele e exames laboratoriais, sendo análise imunofenotipica essencial. Como muitas vezes tais lesões apresentam características inflamatórias importantes, isso acaba atrasando o diagnóstico, o que aconteceu com a paciente. **Conclusão:** Estabelecer diagnóstico pode ser desafiador, pois a condição pode assumir formas diferentes na pele e, no caso, a paciente abriu quadro com alterações restritas às mamas. O diagnóstico só foi possível após segunda biópsia, que necessitou de ampla amostra para evidenciar células neoplásicas e, após, análise imunohistoquímica. Frequentemente, o LCTPS apresenta curso agressivo, na ausência de manifestações sistêmicas e disseminação incomum para sítios extracutâneos. A raridade dessa neoplasia dificulta a escolha da estratégia terapêutica. A paciente foi submetida a três linhas de quimioterapia, incluindo antraciclina, mas com respostas efêmeras, seguidas de progressão da doença com acometimento ósseo difuso e de Sistema Nervoso Central. Deparando-se com quadro de paniculite, o LCTPS é considerado entre os diagnósticos diferenciais.

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WHOLE BRAIN RADIOTHERAPY IS AN EFFECTIVE AND SAFE STRATEGY TO CONSOLIDATE PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA PATIENTS IN MIDDLE-INCOME COUNTRIES: A REAL-LIFE EXPERIENCE FROM BRAZIL

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Introduction: Primary central nervous system lymphoma (PCNSL) is a rare and aggressive B-cell malignancy. Although potentially curable, its prognosis remains dismal. Its treatment is based on high-doses of methotrexate (HD-MTX) and rituximab, followed by consolidation therapy with whole-brain radiotherapy (WB-RT) or autologous stem cell transplantation (ASCT). Currently, there is no consensus about the best consolidation strategy, but better outcomes with ASCT are achieved with conditioning regimens based on thiotepa, a high-cost drug, with restricted use in resource-constrained settings. Additionally, Latin American data on clinical outcomes, prognostic factors, and therapeutic management in PCNSL are virtually unknown. **Methods:** This is a retrospective, observational and single-center study, involving 47-Brazilian patients with PCNSL treated at the University of São Paulo from January 2000 to December 2021. We aimed to assess outcomes, determine predictors of survival and compare responses, as well as toxicities in patients consolidated with chemotherapy alone (HIDAC) versus chemotherapy plus WB-RT. **Results:** The median age at diagnosis was 59 years (24-88 years), and 53.1% (25/47) were male. LDH ≥ UVN occurred in 44.7% (21/47), ECOG ≥ 2 in 67.6% (32/47), and 34.1% (16/47) had multifocal disease. Hemiparesis was the main clinical presentation, observed in 48.9% (23/47), 51.1% (24/47) had an intermediate or high-risk *IELSG* prognostic score, and 57.6% (19/33) had an ABC-like phenotype detected by IHC. Up-front therapy involved MPV+/-R followed by WB-RT plus HIDAC in 48.9% (23/47), MPV+/-R followed by HIDAC in 36.1% (17/47), WB-RT alone in 8.5% (4 /47) and steroids +/- intrathecal chemotherapy in 6.5% (3/47). With a median follow-up of 24.4 months (95% CI: 10.2-41.0), estimated 5-year OS and PFS were 45.5% (95% CI: 32.1-64.7) and 36.4% (95% CI: 23.0-57.1), respectively. Among 40 patients treated with HD-MTX-based induction, estimated 2-year OS was 85.8% (95% CI: 72.2-100) for those consolidated with WB-RT plus HIDAC versus only 41.5% (95% CI: 21.7- 79.7) for those consolidated with HIDAC alone ($p < 0.001$). Hematologic and non-hematologic adverse events were not significant, and severe cognitive decline occurred in only 6.3% (3/47) of cases, all of them received WB-RT. In univariate analysis, age < 60 years [HR: 0.46, $p = 0.05$], Hb > 120 g/L [HR 0.84, $p = 0.06$] and consolidation with WB-RT [HR 0.20, $p < 0.001$] were associated with increased OS, however, LDH ≥ UVN [HR 2.03, $p = 0.02$], hypoalbuminemia < 3.5 g/dL [HR 3.39, $p = 0.009$], ECOG ≥ 2 [HR 9.35, $p = 0.04$], Karnofsky < 70 points [HR 2.43, $p = 0.05$] and an Intermediate- or high-risk Barcelona score [HR 4.39, $p = 0.01$] were associated with decreased OS. **Conclusion:** Combined consolidation therapy (CCT) based on WB-RT plus HIDAC was associated with increased OS in PCNSL compared to isolated consolidation therapy (ICT) based on HIDAC alone. Here, severe late neurotoxicity was uncommon with this approach. These data support that WB-RT may be an effective and safe alternative to ASCT for consolidation therapy in PCNSL, particularly in resource-constrained settings, where access to thiotepa for pre-ASCT conditioning is not universal.

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AGE 75 YEARS, CLINICAL STAGE III/IV, NEUTROPHILIA AND HIGH LYMPHOCYTE/MONOCYTE RATIO PREDICT DECREASED OVERALL SURVIVAL IN ELDERLY PATIENTS WITH DLBCL, NOS OLDER THAN 70 YEARS

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin's lymphoma, with a

wide clinical and biological diversity, as well as a heterogeneous prognosis. It especially affects the elderly population, with an increasing incidence with advancing age. The DLBCL of elderly (≥ 60 years) and very-elderly (≥ 80 years) patients has numerous particularities, including high-risk molecular-genetic findings, greater association with Epstein-Barr (EBV) virus infection, lower tolerability to conventional immunochemotherapy, and poor clinical outcomes. Therefore, alternative therapeutic strategies have emerged for these patients, including immunochemotherapy in reduced doses and regimens without anthracyclines. Based on this premisse, the current study aims to describe clinical and laboratory characteristics, assess outcomes, determine survival predictors and compare responses and toxicities in a large cohort of elderly patients with DLBCL, NOS older than 70 years. **Methods:** This is a retrospective, observational and single-center study, involving 185 patients with DLBCL, NOS aged ≥ 70 years, diagnosed and treated at the Department of Hematology, University of São Paulo, Brazil, from January 2009 to December 2020. **Results:** The median age at diagnosis was 75 years (70-97) and 58.9% (109/185) were female. Comorbidities were prevalent, including 19.5% (36/185) of immobility, 28.1% (52/185) of desnutrition, and 25% (46/185) of polypharmacy. Advanced clinical stage (III/IV) was observed in 73.6% (134/185), 48.6% (90/185) had bulky disease ≥ 7 cm, 63.2% (117/185) had B-symptoms, 76.2% (141/185) had ≥ 1 extranodal site involved by lymphoma, 67% (124/185) had intermediate-high/high-risk IPI, and 52.3% (57/109) had GCB-like phenotype detected by IHC. Ninety-eight percent of patients (182/185) received at least one line of therapy, 65.9% (120/182) underwent cytoreduction, 50.5% (92/182) received intrathecal CNS chemoprophylaxis, and 41.8% (76/185) experienced radiotherapy. The R-miniCHOP elderly regimen had a lower overall response rate (ORR) (p = 0.040), however patients in this group had unfavorable clinical and laboratory characteristics, including higher rates of hypoalbuminemia (p = 0.001), IPI ≥ 3 (p = 0.013) and NCCN-IPI ≥ 3 (p = 0.002). For the entire cohort, ORR was 68.1% (95% CI: 60.8-74.8), 13.2% (95% CI: 8.6-18.9) were chemorefractory, early-mortality rate (< 100 days) was 18.7% (95% CI: 13.3-25.1), and overall mortality rate was 52.4% (97/185). With a median follow-up of 6.3 years (95% CI: 5.5-6.7), the estimated 5-year OS and PFS were 50.2% (95% CI: 42.4-57.5) and 44.6% (95% CI: 37.0-51.9), respectively. In multivariate analysis, age ≥ 75 years [HR 2.22, p = 0.001], advanced-stage III/IV [HR 2.36, p = 0.003], neutrophilia ≥ 7.0 × 109/L [HR 2.25, p = 0.001] and lymphocyte/monocyte ratio > 4 [HR 1.98, p = 0.01] were associated with decreased overall survival. Similarly, age ≥ 75 years [HR 2.33, p < 0.001], stage III/IV [HR 2.38, p = 0.002], B-symptoms [HR 1.62, p = 0.032], LDH ≥ 1.5 x UVN [HR 1.09, p = 0.047], neutrophilia [HR 2.25, p = 0.001] and high lymphocyte/monocyte ratio [HR 2.08, p = 0.005] predicted poor PFS. **Conclusion:** In the largest real-life Latin American cohort including patients with DLBCL, NOS older than 70 years, age ≥ 75 years, advanced clinical stage III/IV, neutrophilia and high lymphocyte/monocyte ratio were independent predictors associated with decreased overall survival.

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HIGH TUMOR MUTATION BURDEN IN EPIGENETIC REGULATORY GENES PREDICTS DECREASED OVERALL SURVIVAL IN NODAL PERIPHERAL T-CELL LYMPHOMAS

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Introduction: Nodal peripheral T-cell lymphomas (nPTCL) constitute a heterogeneous group of rare malignancies with aggressive biological behavior and poor prognosis. Epigenetic phenomena involving genes that control DNA-methylation and histone deacetylation, such as *IDH2*, *DNMT3A*, *TET2* and *RhoA*, play a central role in their pathogenesis. Tumor mutation burden (TMB) has emerged as a prognostic biomarker in numerous solid neoplasms. Furthermore, TMB reflects the process of clonal evolution, with progressive acquisition of additional molecular-genetic abnormalities. Recent studies were capable to establish a relationship between TMB and response to anti-cancer treatments. In 2021 Fachi et cols. established a correlation between high TMB in epigenetic regulatory genes and higher response rates to 5-azacytidine and romidepsin in nPTCL. However, the potential prognostic impact of epigenetic TMB remains unknown in nPTCL. Based on this premise, here we aimed, in a pioneering way, to search for a correlation between epigenetic high TMB and adverse prognosis in nPTCL. **Methods:** This is a retrospective, observational and single-center study, involving 59 patients with nPTCL diagnosed and treated at the Department of Hematology, University of São Paulo, Brazil, from January 2000 to December 2019. FFPE diagnostic tumor samples were submitted to Sanger sequencing with a target-panel, involving *IDH2*, *DNMT3A*, *TET2* and *RhoA* genes to search for recurrent mutations. **Results:** The median age was 50 years (IqR 38-61), and 57.6% (34/59) were male. Thirty-nine percent (23/59) had bulky disease ≥ 7 cm, 83% (49/59) had B-symptoms, 94.9% (56/59) had advanced stage III/IV, 27.1% (16/59) had ECOG ≥ 2, 27.1% (16/59) had ≥ 2 extranodal sites involved by lymphoma, and 55.9% (33/59) had intermediate-high/high-risk IPI. Seventy-six percent (45/59) received up-front therapy with CHOP-like regimens (CHOP or CHOEP), 23.7% (14/59) experienced radiotherapy, and 33.3% (20/59) were consolidated with ASCT. With a median follow-up of 3.7 years (95% CI: 0.9-12.4), the estimated 2-year OS and PFS were 57.1% (95% CI: 45.5-70.4) and 49.2% (95% CI: 34.0-59.2), respectively. *Missense*, *non-sense* or *frameshift* mutations in the *IDH2* gene were observed in 3.3% (2/59) of cases, *DNMT3A* in 3.3% (2/59), *RhoA* in 23.7% (14/59) and *TET2* in 37.2% (22/59). Among the 59 patients included, 23/59 (38.9%) had no mutations in the target-genes, 25/59 (42.4%) had 1 mutation, and 11/59 (18.6%) had two or more mutations. Therefore, the cases were categorized into low TMB (< 2 mutations) [n = 48/59 – 81.3%] or high TMB (≥ 2 mutations) [n = 11/59 – 18.7%]. The median overall survival was 51.4 months (95% CI: 0-124.1) for low TMB and only 3.1 months (95% CI: 3.1-15.2) for high TMB, p = 0.08. The estimated 2-year OS was 64.3% (95% CI: 50.6-78.0) for low TMB and 36.4% (95% CI: 8.0-65.0) for high TMB. Similarly, median