Considerando que a síntese de imunoglobulina é realizada pelos plasmócitos que, por sua vez, são originados pelos linfócitos B, é justificável que os distúrbios linfoproliferativos possam estar associados a picos monoclonais de imunoglobulinas. No contexto apresentado, o excesso de IgM pode levar a complicações relacionadas à hiperviscosidade sanguínea, semelhante ao quadro que pode ocorrer na macroglobulinemia de Waldenstrom. Ainda que com patogêneses distintas, devido a ausência de um protocolo bem estabelecido para a conduta referente a associação do caso, foi optado pela realização da plasmaférese, com objetivo de reduzir a concentração de IgM, em conjunto com a imunoquimioterapia, terapêutica já bem estabelecida e com bons resultados clínicos para LDGCB. **Conclusão:** Dessa forma, devido a raridade do caso, destaca-se a importância da investigação complementar durante o diagnóstico dos linfomas B, incluindo a Eletroforese de Proteínas e dosagem de imunoglobulinas. O presente relato acrescenta a ocorrência à literatura e mostra um manejo com bom resultado.

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LINFOMA PLASMABLÁSTICO ASSOCIADO A LESÃO EM SISTEMA NERVOSO CENTRAL: PROPOSTA DE TRATAMENTO A UM RARO CASO NA LITERATURA

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Introdução: O linfoma plasmablástico (LPB) é um linfoma raro e agressivo, CD20-negativo, de mau prognóstico com as opções de tratamento disponíveis. É uma patologia normalmente associada à infecção pelo vírus da imunodeficiência humana e com poucos casos relatados com acometimento de sistema nervoso central (SNC). **Objetivo:** Relatar o caso de um paciente com diagnóstico de LPB com lesão em SNC, assim como seu diagnóstico e tratamento . **Relato do Caso:** Paciente masculino, 51 anos, portador do vírus da imunodeficiência humana (HIV) que já realizou tratamentos prévios de neurocriptococose, neurotoxoplasmose e tuberculose pulmonar, iniciou em março de 2024 com ptose palpebral e rinorreia à esquerda. Ressonância de crânio apresentava lesão expansiva em seio cavernoso direito de 1,7 × 1,2 cm. Os exames laboratoriais na chegada não mostravam alterações. Considerando a dificuldade de abordagem diagnóstica, foi iniciado tratamento empírico para neurotoxoplasmose e neurocriptococose, sem melhora sintomática. Durante o mês de abril, paciente evoluiu com lesão ulcerada na axila direita. Realizada biópsia da lesão axilar, a qual teve estudo imunohistoquímico compatível com linfoma plasmablástico com EBER (ISH) positivo e Ki67 100%. Foi iniciada quimioterapia com protocolo EPOCH (Etoposide, Prednisona, Vincristina, Ciclofosfamida e Doxorrubicina) com plano de 6 ciclos. Até o momento foram realizados 2 ciclos, apresentando regressão completa da lesão axilar e melhora dos sintomas oculares, com a ressonância de encéfalo demonstrando redução das dimensões da lesão expansiva localizada no seio cavernoso direito, que mede atualmente cerca de 1,0 × 0,8 cm nos maiores eixos axiais. **Discussão:** Estima-se que o LPB represente 2% de todos os linfomas relacionados com o HIV. Afeta indivíduos de todas as idades e sexos, embora a maioria dos pacientes sejam adultos, com predominância masculina. Os locais extranodais mais comumente afetados incluem a cavidade oral, o trato gastrointestinal, os gânglios linfáticos, os seios paranasais e a pele. Os locais menos comumente afetados incluem osso esquelético, trato geniturinário, sistema nervoso central, fígado e pulmão. Um estudo retrospectivo multicêntrico de 50 pacientes com LPB e HIV positivos diagnosticados e tratados entre 2000 e 2010 revelou uma sobrevida mediana de 11 meses. A maioria dos dados sobre o tratamento são extrapolados do tratamento do Linfoma Não Hodgkin associado ao HIV, com poucos estudos direcionados especificamente para a neoplasia relatada. O caso do nosso paciente é ainda mais peculiar, visto a raridade do acometimento do SNC. Considerando o relatado, nota-se a importância de que sejam realizados estudos prospectivos para que a doença e o seu tratamento sejam melhor elucidados, garantindo uma melhor sobrevida dos pacientes acometidos por essa patologia.

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THE NUMBER OF EXTRANODAL SITES IN NODAL PTCL: A PROPOSAL FOR A FEASIBLE PROGNOSTIC MARKER FOR OUTCOMES IN LOW-INCOME COUNTRIES. A COLLABORATIVE STUDY GRUPO DE ESTUDIO LATINO-AMERICANO DE LINFOPROLIFERATIVO (GELL) & T-CELL BRAZIL PROJECT (TCBP)

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Introduction: PTCL accounts for 10-15% of all NHL. As previously demonstrated, Latin America has its own epidemiological distribution, with a high frequency of ATLL and ENKT, likely influenced by distinct genetic profiles and viral epidemiology. 3-year OS is about 40%. Treatment advances have also been limited, except for BV-CHP in some countries. The IPI, which includes extranodal (EN) site as a variable, has been validated for PTCL. However, the specific impact of EN involvement on nodal PTCL (such as PTCL-NOS, AIT, ALCL ALK+/ALK-) and its biological implications remain unclear. Simplification could improve the reproducibility and applicability of these models, especially in low-income countries. **Objective:** To evaluate number of EN sites in nodal PTCL lymphomas as a risk factors or surrogate for outcomes, as OS and PFS in Latin America cohort. **Methodology:** Patients (pts) aged ≥18 years with newly diagnosed nodal PTCL-NOS, AITL and ALCL ALK+/ALK-) from GELL (n = 339, 2000-2023, retrospective), TCBP (n = 427, 2015-2022, ambispective). Treatment outcome was determined by OS and PFS. REDcap Platform (by Vanderbilt) was used to collect and store data, whereas statistical analysis the IBM-SPSS v.24. This trial is registered at Clinical trials (NCT03207789). **Results:** 766 pts [427pts - TCBP and 339 - GELL] diagnosed with nodal PTCL were grouped according to the number of EN: no EN involvement (No EN - 383); one EN involvement (EN1 -168); and ^{3}2 (EN2 - 215). Considering all, 61% male; median age 56 y/o; 74% were staged III/IV; 69% IPI ^{3}2; 60% was PTCL-NOS, 19% ALCL ALK- and 12% AITL. 61% had B symptoms and 55% elevated LDH. CHOEP was used in 47% and 34% CHOP, and 47% achieved CR after first line; 16% used transplant as consolidation. No EN, EN1 and EN2 were similar regarding clinical characteristics, except, for stage III/IV (58% vs. 79% vs 96%; p < .0001); IPI ^{3}2 (58% vs. 59% vs. 99%; p < .0001); ECOG>1 (58% vs. 92% vs. 99%; p < .0001); BMO involvement (16% vs. 24% vs. 63%%; p <.0001), elevated LDH (54% vs. 47% vs. 61%; p =.03) and Hypoalbuminemia (33% vs. 38% vs. 58%; p <.0001). NHL-T subtypes showed better OS and ALCL ALK+ better PFS. Among No EN, EN1 and EN2 the response CR after 1st line had a statistically difference (54% vs 46% vs 37%, p = 0.002), 60-month OS (45% vs. 44% vs. 27%, p <.0001) and PFS (31% vs. 34% vs. 18%; p <.0001). **Conclusion:** EN2 presented more advanced disease, with possible distinct biology, hence, the number of EN involvements can

be useful as a practical and informative surrogates for outcomes, suggesting number of EN sites involvement assessed by CT and PET-CT as feasible clinical surrogate for outcomes in this population. New biomarkers are essential to better stratify patients with PTCL. Still, in practice, it is also necessary to have ways to stratify these patients using clinical data, mainly in regions with low-income resources. These indicators reflect distinct biological characteristics that merit further molecular investigation, potentially enhancing tailored therapies. Registries are essential given the rarity and poor prognosis associated with these diseases as well as generate hypotheses.

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NANATINOSTAT WITH OR WITHOUT VALGANCICLOVIR IN PATIENTS WITH RELAPSED/REFRACTORY EBV-POSITIVE PERIPHERAL T-CELL LYMPHOMA (NAVAL-1 STAGE 1)

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Introduction: Epstein-Barr virus-positive (EBV +) lymphomas are a heterogeneous group of malignancies that harbor latent EBV within the lymphoma cells and are associated with variable clinical features. Outcomes of EBV + Peripheral T-Cell Lymphoma (PTCL) patients are typically inferior to their EBV − counterpart, and thus represent an unmet medical need. Nanatinostat (Nstat) is a potent Class-I histone deacetylase inhibitor. With a novel mechanism of action, Nstat induces expression of the lytic BGLF4 protein kinase, which activates the nucleoside analog ganciclovir (GCV), derived from valganciclovir (VGCV) via phosphorylation. Incorporation of phosho-GCV into cellular DNA results in termination of DNA replication and apoptosis. **Materials and methods:** NAVAL-1 (NCR05011058) is an adaptive Phase 2, open-label, single-arm, two-stage, basket trial. In Stage 1 of the relapsed/refractory (R/R) EBV + PTCL cohort, 20 patients were randomized 1:1 to receive Nstat (20 mg orally once daily, 4 days/week) alone or in combination with VGCV (900 mg orally once daily, 7 days/week) and followed for efficacy and safety. Results: As of 28 June, 2024, the investigator-assessed overall response rate (ORR) by Cheson 2007 in the 10-patient Nstat+VGCV arm was 50% (with a duration of response that is maturing) with a complete response rate (CRR) of 20% in the intent-to-treat (ITT) population (ORR 71% and CRR 29% in the efficacy-evaluable population). One responding patient discontinued Nstat+VGCV to undergo allogeneic stem cell transplantation and remains lymphoma-free over 1 year. In the 10-patient Nstat monotherapy arm, the ORR and CRR were 10% and 0%, respectively, in the ITT population. Five patients without monotherapy response crossed over to combination therapy, including one who had a partial response and another with stable disease for 24+ weeks, both still ongoing. Most TRAEs have been hematological or gastrointestinal in nature and primarily Grade 1-2 in severity. Most Grade ≥3 TRAEs have been generally manageable or reversible except for one patient with Grade 5 TRAE of sepsis in the context of severe cytopenias. **Conclusion:** Combination Nstat+VGCV is a promising, generally well-tolerated treatment for patients with R/R EBV + PTCL that has shown improved efficacy over Nstat monotherapy in the challenging scenario of R/R PTCL.

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A GLOBAL PHASE 2 TRIAL OF NANATINOSTAT AND VALGANCICLOVIR IN PATIENTS WITH RELAPSED/REFRACTORY EBV-POSITIVE PERIPHERAL T-CELL LYMPHOMAS (NAVAL-1 STAGE 1-2)

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