Corresponde a menos de 1% dos LNH e 1.4% de todos os linfomas de células T. Predomina em adultos jovens e sexo masculino. A doença se dá pela proliferação clonal linfocitária nos sinusóides hepáticos e polpa vermelha do baço, pode ter acometimento medular. Pode haver dificuldade no diagnóstico, o qual muitas vezes só pode ser fechado através da combinação entre biópsia hepática e/ou esplênica, biópsia de medula óssea e avaliação sangue periférico com imunofenotipagem e achados citogenéticos/moleculares. As principais estratégias de tratamento são CHOP ou Hyper CVAD, tendo como opção CHOEP para pacientes FIT e consolidação com transplante autólogo ou alogênico de células tronco. Apresenta curso clínico rapidamente progressivo e baixa resposta às terapias atualmente disponíveis, com uma taxa de sobrevivência de 5 anos de 7% e a recidiva ocorre na maioria dos casos. O caso descrito reflete sobre a dificuldade diagnóstica da doença, o que leva ao atraso no tratamento - a qual ainda não é bem estabelecida, resultando em prognóstico reservado. **Conclusão:** Tendo em vista os obstáculos enfrentados nesta patologia, seja no diagnóstico ou na escolha da terapia adequada, é de extrema importância que o médico hematologista lembre dessa patologia como diagnóstico diferencial. Um maior acervo sobre a evolução clínica, tratamento e prognóstico de pacientes com LHCT associado a novos estudos com a finalidade de compreender melhor a patologia é de significativa relevância médica na área de hematologia.

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GRANULOMATOSE LINFOMATOIDE GRAU 3 EM PACIENTE COM MIELOMA MÚLTIPLO

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Objetivo: Apresentar aspectos clínicos, diagnósticos e terapêuticos de um caso incomum de Granulomatose Linfomatoide (GL). **Relato de caso:** Paciente do sexo feminino, 60 anos, ex-tabagista e pneumopata, foi diagnosticada com Mieloma Múltiplo em 2017 e tratada com terapia de indução seguida de transplante autólogo tandem associado a lenalidomida de manutenção por 40 meses, sendo a terapia suspensa por toxicidade hematológica em fevereiro/2022. Manteve remissão estrita, porém iniciou quadro de neuropatia periférica progressiva, extensamente investigado pela neurologia e inicialmente tratado com imunoglobulina endovenosa por suspeita de síndrome de Guillain Barré. Por piora neurológica, com dor neuropática e paraparesia, foi realizado estudo medular, que não evidenciou plasmocitose, mas malacoplaquia – alteração normalmente relacionada a infecção granulomatosa. Nas semanas seguintes a paciente evoluiu com febre diária, hepatoesplenomegalia, micronódulos pulmonares e hepáticos, sendo internada para elucidação diagnóstica. Diante da hipótese de etiologia infecciosa, recebeu amplo tratamento antimicrobiano empírico, incluindo esquemas antifúngicos e para micobacterioses. Sem melhora clínica, realizou PET-CT que demonstrou hipercaptação em lesões pulmonares e hepáticas, adenomegalias torácicas e retroperitoneais, além de lesões musculares. Submetida a biópsia de lesão nodular em coxa direita com anatomopatológico consistente com Granulomatose Linfomatoide Grau 3 e PCR para EBV sérico de 5755 UI/mL. Diante do diagnóstico, foi iniciado tratamento com R-DA-EPOCH sendo necessária sua interrupção após 2 ciclos devido intercorrências graves relacionadas ao esquema (toxicidade hematológica, colite neutropênica, insuficiência respiratória e choque séptico). Atualmente, paciente em proposta de rituximabe semanal, com último PCR para EBV indetectável e PET-CT em resposta completa. **Discussão:** A GL é uma linfoproliferação associada ao EBV que ocorre em pacientes imunossuprimidos. É uma desordem rara, com prevalência atualmente incerta. Tipicamente acomete pacientes na 4ª a 6ª décadas de vida, com apresentação predominantemente extranodal e envolvimento pulmonar >90% dos casos. Outros sistemas comumente acometidos são: neurológico, dermatológico, renal e hepático. Do ponto de vista laboratorial, a avaliação sorológica evidencia exposição prévia ao EBV, normalmente sem achados de infecção aguda. A doença é caracterizada por 3 graus histológicos, sendo o baixo grau (G1/2) relacionado a disfunção imune, o que permite abordagens terapêuticas como suspensão de imunossupressores, uso de anticorpos monoclonais anti-CD20, corticoterapia, interferon-alfa ou apenas observação. Já a apresentação de alto grau histológico (G3), uma linfoproliferação independente do efeito imune relacionado ao EBV, é tratada com esquemas quimioterápicos para linfomas B agressivos. A literatura é baseada em relatos de caso e estudos não controlados. O único estudo prospectivo, conduzido ao longo de 27 anos, encontrou sobrevida livre de progressão e sobrevida global de 28% e 66%, respectivamente, após tratamento com DA-EPOCH em 18 pacientes com doença de alto grau. Em casos refratários ou recidivados o transplante de células tronco hematopoiéticas pode ser uma opção.

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UP-FRONT ASCT OVERCOMES THE SURVIVAL BENEFIT PROVIDED BY HDAC-BASED INDUCTION REGIMENS IN MANTLE CELL LYMPHOMA: DATA FROM A REAL-LIFE AND LONG-TERM COHORT

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Introduction: Mantle cell lymphoma (MCL) is a rare malignancy with heterogeneous behavior. Despite the therapeutic advances recently achieved, MCL remains incurable. Currently, the standard of care for young and fit patients involves induction immunochemotherapy followed by up-front ASCT. However, the role of more intensive induction regimens, such

as those based on high-doses of cytarabine (HDAC) remains controversial in the management of ASCT-eligible patients. Based on this premise, the current study aims to describe clinical and laboratory characteristics, assess outcomes, determine survival predictors, and compare responses between different primary therapeutic strategies, with focus on assessing the impact of HDAC-based regimens on outcomes in ASCT-eligible patients. **Methods:** This retrospective, observational, and single-center study involved 165 MCL patients, diagnosed and treated at the University of São Paulo, Brazil, from 2010 to 2022. Endpoints included overall OS, EFS, and POD-24 from up-front treatment. Survival curves were constructed using the Kaplan-Meier method and the Log-Rank test was used to assess the relationship between variables and outcomes. Univariate analysis was performed using the semi-parametric Cox test and multivariate analysis by Cox regression method or proportional ratios model. The results were presented in HR and 95% CI, and a p-value ≤ 0.05 was considered statistically significant. **Results:** The median age at diagnosis was 65 years and 73.9% were male. More than 90% of cases had a classic nodal variant (cnMCL), 76.4% had bone marrow infiltration, and 56.4% presented splenomegaly. Bulky ≥ 7 cm, B-symptoms, ECOG ≥ 2, and advanced-stage III/IV were observed in 32.7%, 64.8%, 32.1%, and 95.8%, respectively. Sixty-four percent of patients were categorized as high-risk according to MIPI score. With a median follow-up of 71.1 months (95% CI: 61.8-80.4) the estimated 2-year OS and EFS were 64.1% (95% CI: 56.2-71.9%) and 31.8% (95% CI: 23.0-40.6%), respectively. The ORR for the whole cohort was 64.7% (95% CI: 57.1-71.7%), with CR achieved in 41.5% (95% CI: 34.1-49.1%). POD-24 was observed in 46.7% (95% CI: 39.1-54.3%), and the overall mortality rate during all follow-up was 58.2% (95% CI: 50.6-65.5%), with disease progression being the main cause of death. Patients treated with R-HDAC-based regimens (43.4%-66/152) had higher ORR (85.9% vs 65.7%, p = 0.007) compared to those receiving R-CHOP (46.0%-70/152), as well as lower POD-24 rates (61.9% vs 80.4%, p = 0.043) and lower mortality (43.9% vs 68.6%, p = 0.004). However, intensified induction regimens using R-HDAC were not associated with a real OS benefit in MCL patients undergoing up-front consolidation with ASCT (2-year OS: 88.7% for R-HDAC plus ASCT vs 78.8% for R-CHOP plus ASCT, p = 0.289). Furthermore, up-front ASCT was independently associated with increased OS (p < 0.001), EFS (p = 0.005), and lower POD-24 rates (p < 0.001) in MCL. Additionally, CNS involvement (HR: 3.12, p = 0.004), tumor lysis syndrome (HR: 2.79, p = 0.026), albumin < 3.5 g/dL (HR: 2.69, p < 0.001), and failure to achieve remission after induction therapy (HR: 3.71, p < 0.001) were predictors of poor OS. **Conclusion:** In the largest Latin American cohort of MCL reported to date, we confirmed the OS benefit promoted by up-front consolidation with ASCT in young anf fit patients, regardless of the intensity of the immunochemotherapy regimen used in the pre-ASCT induction. Although HDAC-based regimens were not associated with an unequivocal increase in OS, it was associated with higher ORR and lower rates of early-relapses.

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OUTCOMES, PROGNOSTIC FACTORS, PREDICTORS FOR TRANSFORMATION TO HIGH-GRADE B-CELL LYMPHOMA, AND THERAPEUTIC MANAGEMENT IN FOLLICULAR LYMPHOMA: REAL-WORLD EVIDENCE FROM A LARGE AND LONG-TERM LATIN-AMERICAN COHORT

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Introduction: FL is the most common low-grade B-cell NHL. Although indolent, it has heterogeneous biological behavior and variable clinical outcomes. Histologic transformation (HT) to high-grade B-cell NHL is associated with dismal survival. The therapeutic management of FL and its prognosis are highly dependent on its staging and tumor burden. Here we aimed to describe clinical characteristics, assess outcomes, determine predictors of survival and HT, and compare responses between different therapies applied in a large cohort of FL patients. **Methods:** This retrospective study involved 223 patients with FL G1-3A, diagnosed at USP, Brazil, from 2006 to 2022. FL patients were categorized into early-stage (I/II) (ES), advanced-stage (AS) (III/IV) with low tumor burden (LTV), and AS with high tumor burden (HTV) according to the GELF criteria. Endpoints were OS, PFS, early-relapse (< 24 months) and HT rates. Survival curves were constructed using the KM method and the Log-Rank test was used to assess the relationship between variables and outcomes. Univariate and multivariate analysis were performed. The results were presented in HR and 95% CI and p ≤ 0.05 was considered significant. **Results:** The median age at diagnosis was 60 years and 54.8% were female. 15% of cases had ES, 18.4% had AS-LTV, and 66.8% had AS-HTV. BM involvement, leukemic presentation, splenomegaly, and serous effusions occurred in 48.9%, 11.7%, 12.6%, and 21.1%, respectively. Bulky ≥ 7 cm, B-symptoms, ECOG ≥ 2, and involvement of ≥ 4 nodal areas were observed in 44.4%, 51.6%, 15.2%, and 56%, respectively. 49% of patients were categorized as high-risk according to the FLIPI score. With a median follow-up of 79.5 months (95% CI 67.0-92.0) the OS medians were 18 years (95% CI 14.9-21.1), 11 years (95% CI 9.2-12.9), and 10.5 years (95% CI 9.3-11.8) for ES, AS-LTV, and AS-HTV, respectively, p = 0.138. Similarly, the PFS medians were 6.7 years (95% CI 3.6-9.8), 8.4 years (95% CI 2.0-14.8), and 3.5 years (95 CI 1.8-5.3) for ES, AS-LTV, and AS-HTV, respectively, p = 0.171. Early-relapses occurred in 36.3% of cases, being 18.2%, 31.7%, and 41.0% for ES, AS-LTV, and AS-HTV, respectively, p = 0.032. The overall mortality rate was 29.1% for the whole cohort. HT was documented in 16.7% of cases, being 3.0%, 14.6% and 20.1% for ES, AS-LTV, and AS-HTV, respectively, p = 0.053. Among patients with AS-HTV, the R-CHOP regimen did not promote increased OS compared to the R-CVP regimen (p = 0.415), however it was associated with a substantial increase in PFS (p = 0.005). Age ≥ 60 years (HR 1.06, p < 0.001), ≥ 2 comorbidities (HR 3.85, p = 0.014), B-symptoms (HR 2.35, p = 0.015), HT (HR 2.77, p = 0.002) and thrombocytopenia (HR 2.96, p = 0.028) were predictors of poor