Avaliação neurológica: afasia mista grave, disartria leve, hemianopsia homônima e hemiparesia direita (força grau IV), hemiparesia esquerda (força grau III), tônus e reflexos miotáticos profundos preservados. Exames: Hb 11.0 g/dL, leucócitos 3.410/uL, plaquetas 57.000/uL, LDH 355 U/L, eletroforese de proteínas sérica e imunofixação banda monoclonal IgM Kappa de 0.55 g/dL, IgA < 5 mg/dL, IgG < 108 mg/dL, IgM 1.050 mg/dL, relação Kappa/Lambda 1.24. Demais exames sem alterações significativas. RM de encéfalo com múltiplas lesões expansivas e infiltrativas intra-axiais comprometendo substâncias branca e cinzenta, com hipersinal em T2/FLAIR e pequenas áreas líquidas internas, com restrição à difusão e realce ao gadolíneo, edema vasogênico perilesional. RM coluna torácica e lombar com lesão nodular intra-axial em T8, lesão hipointensa comprometendo L3, além de diversas lesões esparsas com hipersinal em STIR e hipossinal em T1 comprometendo a coluna vertebral e ossos da pelve, maioria delas com realce ao gadolínio. O LCR revelou proteinorraquia e linfocitose. Citometria de fluxo, citopatológico, pesquisa infecciosa e demais exames sem alterações. As imagens e a investigação permitiram estabelecer provável síndrome de Bing–Neel (SBN) forma tumoral. O paciente recebeu corticóide e fenitoína, com melhora parcial dos sintomas e ante a performance foi optado pela paliação. **Discussão:** Dentro das manifestações neurológicas da MW, encontram-se neuropatia periférica, mielopatia, hiperviscosidade e SBN o qual acomete aproximadamente 1% dos pacientes, sendo uma complicação rara. Pode ocorrer em qualquer momento da doença: manifestação inicial, durante tratamento ou isoladamente a despeito de remissão com proteína monoclonal mantendo-se estável ou indetectável. Mediana do diagnóstico é de 3 anos. Padrão ouro para o diagnóstico é demonstração histológica no LCR ou através de biópsia cerebral. Outros exames complementares são a eletroforese de proteínas/imunofixação e pesquisa molecular: MYD88, CXCR4. Classifica-se como tipo A (75%): confirmação histológica no cérebro, medula espinhal, meninges ou LCR e tipo B onde os pacientes com análise normal do LCR, sugerindo que os sintomas são causados pelos depósitos de IgM mais do que por infiltração. Achados do LCR incluem pressão de abertura elevada, linfocitose, proteinorraquia e glicose normal ou diminuída. Na RNM o comprometimento pode ser dividido como difuso e tumoral. A forma difusa corresponde à infiltração de células linfóides na leptomeninge e espaços perivasculares, melhor avaliada em T1WI após gadolínio. A forma tumoral pode ser unifocal ou multifocal, geralmente localizada nas regiões hemisféricas subcorticais profundas, bem demonstradas em T1WI e FLAIR. A sobrevida geral aos 3 anos tem sido descrita em 59%. Dentro das opções de tratamento incluim-se quimioterapia sistêmica podendo combinar-se com tratamento intratecal, corticoide, radioterapia, terapia alvo e TCTH. **Conclusão:** SBN é uma manifestação rara da MW e seu diagnóstico deve contemplar-se ainda quando a doença estiver sem sinais de progressão.

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RHOA MUTATION IS A POTENTIAL BIOMARKER ASSOCIATED WITH ADVERSE PROGNOSIS AND HIGH- TUMOR BURDEN IN PATIENTS WITH NODAL PERIPHERAL LYMPHOMAS WITH T-HELPER FOLLICULAR PHENOTYPE (NPTCL-THF): DATA FROM A BRAZILIAN RETROSPECTIVE COHORT OF NPTCL

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Introduction: Nodal-PTCL constitute a rare group of aggressive malignancies with heterogeneous clinical-biological presentation and outcomes. Recently its pathophysiological knowledge has been highly improved, with descriptions of gene mutations associated with epigenetic phenomena and of the *RHOA* G17V mutation playing a fundamental role in the lymphomagenesis. However, the prognostic impact of these alterations is still controversial, and particularly, in the case of the *RHOA* mutation, it has never been previously accessed in the literature. The aim of this study was to evaluate the frequency and prognostic impact of mutations in the *IDH2*, *TET2*, *DNMT3* and *RHOA* genes in Brazilian patients with nPTCL. **Methods:** In this observational, retrospective and unicentric study, we analyzed the clinical-epidemiological characteristics, outcomes and mutational profile of 59 Brazilian patients with nPTCL treated at the HC-FMUSP, from January 2000 to December 2017. All cases were submitted to centralized histopathological review and were classified according to the criteria proposed by WHO-2016. FFPE tumor samples from patients with PTCL/NOS, AITL, ALK+/ALCL and ALK-/ALCL were deparaffinized and submitted to DNA extraction using *QIAmp DNA FFPE* kit. For amplification of specific products of target-genes primers flanking the hot spots regions were designed. After this step, the PCR products were submitted to first generation sequencing. Absolute and relative frequencies of mutations were accessed for the total cohort and its pathological subtypes. OS and PFS curves were constructed using the Kaplan-Meier method. Log-rank test was used to estimate the prognostic impact of mutations in the studied population. **Results:** With a median follow-up of 3.70 years, the estimated 2-years OS and PFS were 59.1% and 47.2%, respectively. ORR was 55.9%, with early relapse rate (< 12 months) of 14.3% and global death rate of 52.5%. In the total cohort, we found a mutation frequency of 3.4% (2/59) for the *IDH2* gene, 62.7% (37/59) for *DNMT3A*, 23.7% (14/59) for *RHOA* and 50.8% (30/59) for *TET2*. There was no statistically significant difference in the frequency distribution of *IDH2*, *DNMT3A* and *TET2* mutations between the different histological subtypes of nPTCL. However, there was a statistical trend towards a higher occurrence of the *RHOA* mutation in the AITL and nPTCL-Thf

subtypes (3/9–33.3% and 7/16-43.7%, respectively; p = 0.07). So, the mutation *RHOA* was predominantly found in THf cell-derived neoplasms in our cohort. The mutational status of *DNMT3A*, *RHOA* and *TET2* genes had no prognostic impact on OS, with p = 0.85, p = 0.13 and p = 0.95, respectively. The same was observed in relation to PFS for the *DNMT3A* (p = 0.70) and *TET2* (p = 0.52) mutations. However, the presence of the *RHOA* mutation was associated with the unfavorable PFS in our cohort (HR:1.98, p = 0.05). We observed 2-year PFS of 28.6% (95% CI: 8.8-52.4%) for mutated-*RHOA* cases versus 52.9% (95% CI: 37.3-66.3%) for wild-type-*RHOA* patients (p = 0.05). We also demonstrated that the presence of the *RHOA* mutation was a predictor of lower ORR to first-line therapy (p = 0.01) and was associated with high tumor burden (p = 0.03). **Conclusion:** For the first time we demonstrated the unfavorable prognostic impact of the *RHOA* mutation in patients with nPTCL with THf-phenotype, making it a potential molecular biomarker predictor of poor-PFS, associated with resistance to primary therapy and with high tumor burden.

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RITUXIMAB BIOSIMILAR RTXM83 POST-MARKETING SURVEILLANCE IN BRAZIL: EVALUATION OF THE ADVERSE EVENTS SPONTANEOUSLY REPORTED TO PHARMACOVIGILANCE

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Background: Biosimilars are highly similar to their reference products, but unlike generic drugs, they are not identical. Differences between a biosimilar and its reference product may arise because of the complexity of biologics, differences in the cell lines and processes used during manufacturing. Biosimilars are approved in Europe, United States and Brazil through a regulatory pathway based on comparative analytical, clinical studies and demonstration of no clinically meaningful differences from their reference products. Post marketing pharmacovigilance is a useful tool to confirm the safety profile of biosimilar medication in the general population, outside of controlled environment of clinical studies. In 2019, rituximab biosimilar RTXM83 was approved in Brazil. **Objective:** The purpose of this communication is to present rituximab biosimilar RTXM83 information collected from adverse events (AEs) spontaneous reports during post-marketing pharmacovigilance activities in Brazil. **Method:** Descriptive retrospective study. Treatment related data and AEs from all spontaneous reports with biosimilar rituximab RTXM83 were reviewed. AEs were classified according to medical terminology (MedDRA) and seriousness assessed by the CTCAE (Common Toxicity Criteria) version 5.0 scale. Descriptive analysis of demographic data and AEs reported was performed. **Results:** A total of 32 reports containing 59 adverse events (AEs) were received from spontaneous reports between September 2019 and July 2021. From 32 reports, 19 were female, 12 were male and 1 not informed. The patients mean age was 48,8 (13 to 81years). The treatment indication was hematology oncology diseases in 23 (72%) patients, autoimmune disease in 7 patients (22%) and not informed in 2 (6%) patients. Regarding AEs seriousness and expectedness, 26 (44%) were non-serious AEs (24 expected / 2 unexpected) and 33 (56%) were serious AEs (22 expected / 11 unexpected). The five most frequently reported AEs according to SOC (System Organ Classification) were immune system disorders 19 (32%), blood and lymphatic system disorders 14 (24%), nervous system disorders 4 (7%), investigations 3 (5%), respiratory, thoracic and mediastinal disorders 3 (5%). The five most commonly reported adverse events (MedDRA PT - Preferred term) were infusion related reaction 18 (31%), neutropenia 6 (10%), anaemia 3 (5%), leukopenia 2 (3%), thrombocytopenia 2 (3%). **Conclusion:** AEs spontaneously reported in patients treated with biosimilar rituximab RTXM83 were consistent with the reference safety information based on literature data and the Summary of Product Characteristics (SmPC) of the reference product. No new safety signals were detected.

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SARCOMATOID DIFFUSE LARGE B-CELL LYMPHOMA: A RARE MORPHOLOGICAL VARIANT WITH MULTI-VISCERAL INVOLVEMENT

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Introduction: Diffuse Large B-Cell Lymphoma (DLBCL) is the most frequent subtype of non-Hodgkin's lymphoma (NHL), accounting for 50% of all NHL cases seen at HC-FMUSP. Up to 40-50% of DLBCL cases have extranodal involvement. However, female genital tract involvement is very rare, accounting for less than 0.5% of cases. Spindle/sarcomatoid cell neoplasms usually have mesenchymal histogenesis, however rare cases of aggressive NHL with a spindle-shaped morphological aspect have been recently described, although this variant is still not fully recognized as a specific pathological entity. **Objectives:** To describe a rare case of DLBCL with primary uterine cervix involvement, and sarcomatoid morphological pattern, as well as multi-visceral involvement. We intend to highlight the importance of recognizing this entity in the differential diagnosis of spindle-shaped malignant neoplasms. **Case report:** A 51-year-old woman, with no previous comorbidities, sought medical service at the HC-FMUSP due to a vulvovaginal tumor with progressive growth over the last 12 months. Gynecological examination showed an ulcerated tumor in the cervix, extending to the vaginal cavity and exteriorizing through the vulvar introitus. Computed tomography showed a 7 cm tumor mass in the cervix and pathological bone fracture of the L3 vertebra. A biopsy of the uterine cervix showed atypical fusiform cell proliferation, inferring a diagnosis of uterine leiomyosarcoma. However, bone biopsy showed proliferation of large atypical lymphoid cells,