and mortality. Although thrombocytosis is a common feature of MPN, platelet count alone does not fully explain or predict thrombotic burden in MPN. Several evidence suggest that altered surface markers expression and metabolic reprogramming may exert a more impactful role in MPN-associated thromboinflammation. Therefore, we hypothesized that immunophenotypic, transcriptomic, and metabolic alterations in platelets may contribute to a thromboinflammatory state in MPN. **Objectives:** To characterize platelet immunophenotype, gene signature, and bioactive lipids profile in patients with PV, ET, and MF. **Material and methods:** Peripheral blood was collected from PV (n = 25), ET (n = 15), MF (n = 20) patients, and controls (n = 25). Platelet-rich plasma (PRP) was isolated and supplemented with prostaglandin E1 to prevent autonomous activation. Platelet activation markers (CD41, CD62P, CD36, CD63, CD154) were analyzed by flow cytometry at baseline and after stimulation with 0.5 μM calcium ionophore (A23187) or 50 U/mL thrombin, and control platelets were incubated with 10% MPN plasma to assess inflammatory activation. Gene Set Enrichment Analysis (GSEA) was applied to a public dataset (GSE26049) to assess platelet transcriptome. For metabolomics, purified platelets were stimulated with A23187 for eicosanoids detection or left at baseline for sphingolipids quantification, then submitted to high-resolution liquid chromatography–mass spectrometry (HRLC-MS). **Results:** MPN platelets showed increased CD62P, CD36, CD63, CD154 and reduced CD41 expression at baseline, indicating a pre-activated state. Thrombin responses were reduced in MPN platelets, and exposure to MPN plasma increased platelet activation. GSEA revealed downregulation of genes involved in cytoskeletal regulation, integrin signaling, and vesicular trafficking (eg.: ZYX, FLNA, ACTN4, GNAI2, HGS, PFN1). The downregulated genes were more prominent in MF and less in PV. In eicosanoid analysis, PV platelets showed increased levels of prostaglandins and oxidized lipids (PGE_1, 15-HETE); ET presented moderate increase in 12-HHTrE and $PGF_2\alpha$; and MF presented dysregulation in TXB_2, long-chain fatty acids, polyamines, and amino acid–related metabolites. Sphingolipid analysis revealed reduced glucosylceramides (GlcCer C18:0, C24:1) and ceramide-1-phosphate (Cer1P) in PV; increased dihydroceramides (DHCer C18:0) and reduced long-chain sphingomyelins (SM C24:1, C22:1) in MF, and moderate alterations in long-chain sphingomyelins (SM C24:0) in ET. **Discussion and conclusion:** Platelets are intrinsically activated, transcriptionally altered, and metabolically dysregulated in MPN, fueling a sustained thromboinflammatory state in PV, ET, and MF. This profile persists despite the standard treatments and suggests that immunometabolic alterations in platelets directly contribute to the paradox of thrombosis and bleeding in MPN. Altogether, these observations reveal that platelets can offer new potential therapeutic targets to effectively treat MPN-associated thromboinflammatory complications. **Funding:** The study was financed by FAPESP (2022/13366-2) and CNPq.

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LEUCEMIAS AGUDAS

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NEOPLASIAS SINCRÔNICAS: PRIMEIRA DESCRIÇÃO DE LEUCEMIA LINFOBLÁSTICA AGUDA ASSOCIADA A ANGIOSSARCOMA HEPÁTICO

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Introdução: A leucemia linfoblástica aguda (LLA) é uma neoplasia hematológica caracterizada pela proliferação clonal de precursores linfóides imaturos na medula óssea, sangue periférico e, eventualmente, em sítios extramedulares. Apresenta incidência de 1 a 5 casos por 100.000 habitantes, com distribuição bimodal — pico na infância e em adultos acima dos 60 anos. Aproximadamente 70–80% dos casos têm imunofenótipo precursor B e 20–25% linfóide T. Alterações citogenéticas, como a t(9;22)/BCR-ABL1 e rearranjos de KMT2A, impactam no prognóstico e direcionam a terapêutica, em conjunto com a avaliação da doença residual mínima (DRM). O angiossarcoma hepático, responsável por apenas 2% dos tumores malignos do fígado, é uma neoplasia endotelial rara e agressiva, com sobrevida mediana de aproximadamente seis meses. A ressecção cirúrgica é a única opção com impacto comprovado em sobrevida, enquanto a quimioterapia tem papel paliativo e o transplante hepático é contraindicado pela alta taxa de recidiva. Tumores sincrônicos, definidos como duas neoplasias diagnosticadas em intervalo inferior a seis meses, são raros, especialmente quando envolvem simultaneamente tumores sólidos e neoplasias hematológicas. Neste relato descrevemos um caso de LLA B comum sincrônica ao angiossarcoma hepático, associação não descrita previamente na literatura. **Descrição do caso:** Paciente masculino, 20 anos, previamente hígido, diagnosticado em 2023 com angiossarcoma hepático e submetido à hepatectomia segmentar. Em maio de 2025 apresentou recidiva local, sendo iniciado tratamento com paclitaxel. Após três ciclos, evoluiu com fadiga, pancitopenia e presença de blastos em sangue periférico. O diagnóstico de LLA B comum foi confirmado por imunofenotipagem (CD19+, CD10+, TdT+, ausência de marcadores T e mieloides). Com função hepática preservada, foi iniciado protocolo GMALL, mantido até o momento, com suspensão temporária da quimioterapia para o angiossarcoma. **Conclusão:** A coexistência de LLA e angiossarcoma hepático não foi descrita previamente. Embora a associação de tumores sólidos e hematológicos seja relatada, as neoplasias mais comuns nesse contexto são leucemia linfocítica crônica, leucemia mieloide crônica e mieloma múltiplo. A presença de LLA como tumor sincrônico é rara e

confere desfecho adverso. Não há opções de tratamento padrão disponíveis para neoplasias hematológicas e tumores sólidos sincrônicos. O manejo desses casos deve ser individualizado, considerando agressividade de cada tumor, risco de progressão e condições clínicas do paciente. No caso relatado, a decisão de priorizar o tratamento da LLA deveu-se ao risco iminente de óbito, com interrupção temporária da terapia do angiossarcoma hepático. Este é o primeiro relato, até onde sabemos, de associação entre angiossarcoma hepático e LLA. O caso ressalta a importância do reconhecimento de tumores sincrônicos e evidencia os desafios terapêuticos impostos, podendo auxiliar na condução de casos futuros.

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ETV6::RUNX1 FUSION IN ACUTE LYMPHOBLASTIC LEUKEMIA: FREQUENCY AND REGIONAL DISTRIBUTION IN THE STATE OF PARÁ

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Introduction: Acute Lymphoblastic Leukemia (ALL) accounts for about 75% of leukemia cases. In Northern Brazil, the state of Pará ranks second in the number of ALL cases. Among the genetic alterations frequently associated with ALL, gene fusions such as ETV6::RUNX1, resulting from the translocation between chromosomes 12 and 21, t(12;21), stand out. This fusion is the most common and is associated with a favorable prognosis, making it crucial for guiding treatment. **Objectives:** This study aims to evaluate the incidence of the *ETV6::RUNX1* fusion in municipalities of Pará and its association with sex and age. **Material and methods:** Data were collected from patients diagnosed with ALL by immunophenotyping at the Octávio Lobo Children's Oncology Hospital, who signed informed consent between 2023 and June 2025. Epidemiological data, such as sex, age, and municipality, were retrieved from medical records. For gene fusion analysis, RNA was extracted from patients and converted into cDNA for the detection of molecular biomarkers by nPCR, using specific primers, with visualization of the products by agarose gel electrophoresis. Data from patients positive for *ETV6::RUNX1* were used in statistical analyses. The chi-square test was performed to assess the frequency of cases by municipality, and the ANOVA test was used to evaluate significant differences in patient age. Other descriptive statistics, such as mode and mean, were also applied, all using RStudio 12.1. **Results:** A total of 56 patients participated in the study, of which 33 children presented the *ETV6::RUNX1* fusion; 9 of these were excluded due to missing data. During the study period, there was no significant predominance between sexes, except in 2024, when approximately 63% were male. The mean age of patients ranged from 6 to 7 years (SD = 4.12). The ANOVA test showed no significant difference in age distribution ($p = 0.791$). In contrast, the chi-square test indicated a statistically significant difference in case distribution by municipality ($p = 0.04585$). Among the municipalities, Belém and Macapá stood out, concentrating 29.17% and 16.67% of cases, respectively. Furthermore, the Belém Metropolitan Region accounted for one-third of all positive cases. **Discussion and conclusion:** The mean age of patients is consistent with the literature, despite the standard deviation of 4.12 years, indicating considerable variation around the mean. The ANOVA test presented a value above the significance level (0.05), indicating no statistical difference. Conversely, the chi-square test showed a p-value below the significance level, indicating a significant difference in case distribution, highlighting the concentration in Belém and Macapá. This finding may reflect greater access to molecular diagnosis and the oncology reference network in these cities. It is concluded that this study highlights the relevance of the *ETV6::RUNX1* fusion as a biomarker in ALL due to its high incidence. The analysis revealed significant differences in the distribution of cases, and the representation of the Metropolitan Region of Belém suggests the influence of access to diagnosis and the oncology network, as well as the concentration of cases in Belém and Macapá. These results reinforce the need for molecular and epidemiological mapping to expand diagnosis in municipalities outside the metropolitan area, making it more accessible. For this purpose, multicenter studies with broader regional coverage are necessary to deepen the understanding of the fusion's distribution in the Northern region.

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ALTERAÇÕES GENÉTICAS, IMPACTO PROGNÓSTICO E ABORDAGENS TERAPÊUTICAS NA PROGRESSÃO DA LEUCEMIA MIELOIDE CRÔNICA PARA LEUCEMIA MIELOIDE AGUDA: REVISÃO NARRATIVA

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Introdução: A Leucemia Mieloide Aguda (LMA) representa uma das neoplasias hematológicas mais complexas e agressivas, caracterizada pela proliferação descontrolada de células progenitoras mieloides na medula óssea, podendo ser advinda de uma desregulação hematopoiética primária ou a partir da evolução de uma outra neoplasia hematológica, como a leucemia mieloide crônica (LMC). Esta doença possui uma patogênese molecular heterogênea, onde mutações genéticas desempenham papéis fundamentais no