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GLIOMA DE ALTO GRAU EM PACIENTE COM HISTÓRIA PRÉVIA DE LEUCEMIA LINFOBLÁSTICA AGUDA T

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Introdução: A leucemia linfoblástica aguda (LLA) é a neoplasia maligna mais frequente na infância, e o subtipo T (LLA-T) corresponde a cerca de 15% a 20% dos casos em crianças e adolescentes. O advento de protocolos de tratamento combinando poliquimioterapia intensiva, profilaxia do SNC — inicialmente com radioterapia craniana e atualmente substituída em grande parte por quimioterapia intratecal — e manutenção prolongada permitiu elevação expressiva das taxas de sobrevida. Em centros especializados, a sobrevida global em 5 anos para LLA-T em pacientes pediátricos e adolescentes pode superar 75%, e para LLA-B chega a 85-90%. O aumento da sobrevida tornou mais evidente a ocorrência de efeitos tardios do tratamento, que incluem toxicidades endócrinas, metabólicas, cardiovasculares, neurocognitivas e, em menor proporção, o desenvolvimento de segundas neoplasias malignas (SNM). Estas podem resultar de mutações induzidas por quimioterapia, radioterapia ou pela interação dessas terapias com predisposição genética subjacente. Os tumores sólidos do SNC como SNM, especialmente gliomas de alto grau, têm sido descritos principalmente em pacientes previamente expostos à radioterapia craniana. O presente relato descreve um caso de glioma de alto grau sem outras especificações (NOS) em paciente jovem previamente curado de LLA-T, discutindo a fisiopatologia, a evidência epidemiológica, os desafios diagnósticos e as opções terapêuticas disponíveis. **Descrição do caso:** Paciente masculino, 27 anos, história de LLA-T diagnosticada em 2016, SNC negativo, risco intermediário, foi submetido ao protocolo BFM 2009, com profilaxia de SNC que incluiu radioterapia craniana (12 Gy, 8 sessões, janeiro/2017). Após sete anos em remissão completa, apresentou episódio convulsivo tônico-clônico generalizado, sem déficit neurológico focal subsequente. A avaliação demonstrou glioma de alto grau (NOS) frontal direito, confirmado por estudo histopatológico e imuno- histoquímico, excluindo recaída leucêmica no sistema nervoso central (SNC). Realizada ressecção cirúrgica parcial, radioterapia adjuvante, e plano terapêutico com temozolomida. Discute-se a relação entre tratamento oncológico prévio e risco de SNM, com ênfase nos tumores primários do SNC, e a importância do seguimento prolongado de sobreviventes de câncer infantil e juvenil. **Conclusão:** O desenvolvimento de SNM após LLA é um evento raro, mas com implicações prognósticas severas. A incidência de SNM em sobreviventes desta condição varia entre 1% e 3% aos 10 anos. Os principais fatores de risco são: exposição à radioterapia, especialmente craniana, uso de agentes alquilantes e epipodofilotoxinas, idade jovem ao tratamento e predisposição genética (ex.: mutações TP53, síndrome de Li-Fraumeni) A radiação ionizante causa danos diretos ao DNA (quebras de dupla fita) e indiretos por geração de radicais livres, promovendo mutações irreversíveis e instabilidade genômica. Células do SNC, apesar de serem em grande parte pós-mitóticas, apresentam nichos progenitores sensíveis, especialmente na infância. A interação com quimioterapia citotóxica potencializa o risco, sinergizando o dano ao DNA e reduzindo a capacidade de reparo. Mesmo com protocolos modernos e doses reduzidas de radioterapia craniana, há risco concreto de desenvolvimento de SNM, inclusive no SNC. O acompanhamento de longo prazo deve integrar protocolos de vigilância para detecção precoce, buscando equilíbrio entre eficácia terapêutica e toxicidade tardia.

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HEMATOLOGICAL AND EPIDEMIOLOGICAL PROFILE OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA WITH THE T (1;19) TCF3::PBX1 TRANSLOCATION

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Introduction: Acute Lymphoblastic Leukemia (ALL) is the most common pediatric neoplasm and the leading cause of cancer-related death in children worldwide. In ALL, gene fusions are genetic variants that contribute to tumorigenesis, and the detection of the specific molecular biomarker is a key element in disease diagnosis. Among these gene fusions is TCF3::PBX1 t(1;19), which accounts for approximately 3–5% of pediatric ALL cases and is associated with poor prognosis and increased risk of central nervous system (CNS) infiltration. The TCF3 gene encodes transcription factors regulating B-cell development, whereas PBX1 controls genes related to the hematopoietic system. **Objective:** This study aimed to evaluate the hematological profile of pediatric patients diagnosed with ALL carrying the TCF3::PBX1 biomarker. **Materials and methods:** The study was approved by the Research Ethics Committee under protocol number 4.040.805 and included a total of 44 patients diagnosed with ALL and the t(1;19) translocation at the Hospital Oncológico Infantil Octávio Lobo between 2017 and 2025. Clinical data (white blood cell count, platelet count, and hemoglobin levels) and epidemiological data (sex and age) were retrieved from the hospital database. For biomarker analysis, cDNA was obtained for detection by conventional PCR using specific primers. Agarose gel electrophoresis was performed for visualization of PCR products, and Sanger sequencing was subsequently conducted to

confirm PCR results. Descriptive statistics were used for qualitative variables, determining absolute and relative frequencies. For quantitative variables, median values and standard deviations were calculated. ANOVA was applied to assess associations between age groups, according to NCI risk criteria, and clinical data, adopting a p-value ≤ 0.05 as statistically significant. Statistical analyses were performed using RStudio 12.1. **Results:** Regarding sex distribution, 65% of patients were male and 35% female. The median age was 7 years. Median white blood cell count was 19,350/mm^3, median platelet count was 31,000/mm^3, and median hemoglobin level was 8 g/dL. ANOVA revealed no statistically significant differences between NCI age- based risk groups (1–6 years, 6–10 years, and >10 years) and the evaluated hematological parameters. **Discussion:** Studies conducted in Nordic countries, Egypt, China, and Mexico have reported a higher prevalence of females with t(1;19), differing from our findings, which revealed male predominance (ratio 1.86:1). In terms of age, previous reports indicate a median of 5–8 years for patients with the TCF3::PBX1 biomarker, consistent with our observations. Regarding leukocyte count, literature shows a median of approximately 22,000/mm^3 in such patients, aligning with the present study and reinforcing the association of this gene fusion with an unfavorable prognosis during ALL treatment. Conclusion: The TCF3::PBX1 gene fusion activates genes encoding proteins with malignant potential and may also lead to CNS involvement. Further investigation into the leukemogenic mechanisms of this biomarker is warranted. In this cohort, 7% of patients were classified as high-risk according to NCI guidelines due to age >10 years combined with a white blood cell count >50,000/mm^3.

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IMMUNE EVASION IN AML: NK CELL LIGAND ALTERATIONS LINKED TO LEUKEMIC STEM CELL PERSISTENCE

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Introduction: Natural Killer (NK) Cell-Mediated Immune Evasion Plays a Key Role in Clonal Persistence, Refractoriness, and Relapse in Acute Myeloid Leukemia (AML). Growing evidence indicates that alterations in the expression of innate immune recognition ligands by leukemic blasts contribute to the inhibition of NK cell effector responses, thereby favoring disease maintenance. However, the immunophenotypic mechanisms underlying this process remain poorly understood. **Objectives:** In this study, we investigated the expression profile of NK cell ligands on leukemic blasts and their association with clinical outcomes and measurable residual disease (MRD). **Material and methods:** A total of 127 bone marrow samples collected at diagnosis from adult AML patients were analyzed. Samples were processed within 24 hours, lysed using ammonium chloride solution, and stained with monoclonal antibodies targeting CD45, CD34, CD38, CD123, CD112, CD155, and HLA-E. Flow cytometry analysis was performed using a FACSCanto II cytometer (BD Biosciences), applying validated panels for both diagnosis and MRD assessment. At least 500,000 viable events were acquired per sample, and analysis was standardized using internal controls and healthy donor bone marrow samples. Patients were treated according to standard AML therapeutic protocols, including induction with cytarabine and anthracyclines (7+3 regimen), followed by high-dose cytarabine (HiDAC) consolidation, according to clinical and biological eligibility. Leukemic stem cell (LSC)-enriched subpopulations were defined as CD45dim/CD34$^+$/CD38$^-$/CD123$^+$, along with CD34$^-$ blasts. Activating (CD112, CD155) and inhibitory (HLA-E) NK ligands were assessed by both the frequency of positive cells and median fluorescence intensity (MFI). MRD was measured in post-induction samples with a minimum sensitivity of 10^{-4}, and clinical outcomes (remission, relapse, refractoriness, early death) were obtained from electronic medical records, with a minimum follow-up of 12 months. **Results:** Patients with unfavorable clinical outcomes showed, at diagnosis, a significant reduction in CD112 ($p = 0.004$) and CD155 ($p = 0.013$) expression, along with increased HLA-E levels ($p = 0.009$), when compared to patients in remission and healthy controls. MRD positivity after induction was associated with higher HLA-E expression ($p = 0.027$) and a trend toward decreased CD112 ($p = 0.078$) and CD155 ($p = 0.065$), particularly within the CD34$^+$ subpopulation. Among CD34$^+$ blasts, higher HLA-E expression ($p = 0.006$) and lower CD155 levels ($p = 0.021$) were observed compared to CD34$^-$ cells, suggesting enhanced immune evasion capacity in the LSC-enriched fraction. **Discussion and conclusion:** These findings support the hypothesis that phenotypic alterations in NK cell recognition ligands contribute to immune escape and MRD persistence. The consolidation of the inhibitory HLA-E/NKG2A axis as a key mechanism of immune suppression in AML highlights its potential as a therapeutic target. Altogether, our results support the development of immunomodulatory strategies aimed at restoring innate immune surveillance and preventing LSC persistence, with the potential to reduce relapse rates and improve clinical control of AML.

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IMPACTO DE MUTAÇÕES FLT3-ITD E FLT3-TKD NO PROGNÓSTICO E NAS DECISÕES SOBRE USO DE INIBIDORES ALVO

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