Objectives: This study aimed to investigate how FLT3-ITD burden and clonal dominance influence immune status and treatment response. **Material and methods:** NK and T cells were assessed by flow cytometry in a Flt3-ITD knock-in mouse model. Bone marrow from 148 de novo AML patients (normal karyotype, known FLT3/NPM1 status) was evaluated for leukemia arrest stage and NK subsets. Drug sensitivity was analyzed using the Beat AML 2.0 dataset. **Results:** In the murine model, the Flt3 mutation was associated with reduction in NK cell (CD45hiCD19-CD3-NK1.1+) content characterized by predominance of immature phenotypes (CD27+CD11b-) and a reduction in cytotoxic subpopulations (CD27-CD11b+). These results were corroborated by an extended phenotypic analysis using CD122, NK1.1, CD49b, and NKp46 expression to identify four NK cell maturation stages. Among these, a reduction in the frequency of more mature subsets (NKII to NKIV) was observed in Flt3-mutated homozygous mice, whose NK cells exhibited an increased expression of DNAM-1 and TIM-3. In the T cell compartment, an increase in short-lived effector cells (CD127-KLRG1+) was observed among $CD4^+$ T cells specifically in homozygous animals. In the $CD8^+$ T cell population, homozygous animals showed an increased frequency of central memory (CD62L+CD44+) and memory precursor effector cells (CD127+KLRG1-), accompanied by elevated expression of activation and inhibitory receptors, including NKG2D, TIM-3, and CTLA-4. Furthermore, $\gamma\delta$ T cells were expanded in homozygous mutant animals compared to wild-type mice. The influence of Flt3 mutation content on the immune profile prompted us to investigate NK cells in AML samples across different stages of leukemia arrest, which revealed that FLT3mut/NPM1wt patients (n = 36) were predominantly associated with CMP-L (CD34+/-CD117+CD13+CD33+/-HLA-DR+MPO+) and GMP-L (CD34+/-CD117+/-CD13+/- CD33+HLA-DR+MPO+) leukemias, whereas FLT3wt/NPM1mut patients (n = 80) predominantly presented GP-L (CD34-CD117+/-CD13+CD33+HLA-DR-MPO+) leukemias. Double-mutant patients (FLT3mut/NPM1mut, n = 32) exhibited a similar profile to FLT3wt/NPM1mut patients, with a predominance of MP-L and GP-L stages. As compared to other maturation stages of leukemia arrest, GMP-L leukemias were associated with disease persistence after the first induction therapy and a trend toward earlier relapse, although impact on overall or relapse-free survival was not observed. In agreement, in silico analysis using the Beat AML 2.0 dataset indicated higher resistance to cytarabine, midostaurin, and azacitidine in patients with GMP-L FLT3mut/NPM1wt cells. No differences were observed in the frequencies of CD56+ NK cells, CD56bright, or CD56dim subsets among the FLT3/NPM1 profile. However, in FLT3-mutated patients, high AR showed a trend toward fewer CD56dim and more CD56bright NK cells compared to low AR. Regarding leukemic maturation, a trend toward increased CD56bright and decreased CD56dim populations was observed in differentiated leukemias (GMP-L, MP-L, and GP-L). **Discussion and conclusion:** Collectively, our findings indicate that FLT3-ITD promotes immune evasion by disrupting the maturation and activation of cytotoxic immune cells. Immature leukemic subsets may contribute to this disruption, potentially leading to resistance and poor outcomes.

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GANGRENA DE FOURNIER EM PACIENTE JOVEM PORTADOR DE LEUCEMIA MIELOIDE AGUDA: RELATO DE CASO

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Introdução: A Síndrome de Fournier é uma doença infecciosa grave, cujos principais locais de acometimento são região genital, perianal e perineal. Quanto mais extensa e profunda, mais grave tende a ser o prognóstico do paciente. Ainda, costuma ter um início insidioso, mas uma evolução fulminante. Há predomínio pelo sexo masculino, maiores de 50 anos e tem como fatores de risco a diabetes mellitus, trauma local, tromboses associadas e pacientes imunossuprimidos. **Descrição do caso:** Homem, 37a, iniciou quadro de perda de peso, bicitopenia (Hb 5,4 g/dL; plaquetas 92.000), leucocitose (27.300 com 89% de blastos em sangue periférico), além de astenia progressivas, sendo encaminhado para investigação. À admissão, o paciente não apresentava lesões de pele ou mucosa. Em mielograma e imunofenotipagem admissional, foram visualizados: 91% de blastos mielóides com positividade para: CD13, CD33, CD34, CD56, CD71, CD117, CD123, MPO. A biologia molecular foi negativa para FLT3, BCR-ABL P210, AML1-ETO, NPM1 e CBFB-MYH11. O cariótipo é 46, XY. Por elegibilidade a tratamento intensivo, foi optado pelo protocolo 3+7. Apresentou neutropenia febril e necessidades transfusionais. Após término do esquema de indução, o paciente evoluiu com abscesso em região anal, com crescimento progressivo e sem resposta a antibioticoterapia ampla (Meropenem, Vancomicina, Amicacina), prescrita na ocasião. Evoluiu com febre diária e supuração do abscesso, além de área necrótica em bordo anal direito, medindo cerca de 12 cm, em íntimo contato e extensão à região perianal. Foi realizado desbridamento e biópsia da lesão, que demonstraram a presença da bactéria Klebsiella pneumoniae multirresistente, sensível apenas a Tigeciclina e Cloranfenicol - sem outros microrganismos associados. Foi realizada cobertura com Tigeciclina e Meropenem em dose dobrada em consonância com a infectologia do serviço, além de curativos diários. O paciente evoluiu em melhora da lesão, com fechamento por segunda intenção e sem necessidade de novos desbridamentos ou esquemas medicamentosos. **Conclusão:** A maioria das gangrenas de Fournier é uma doença rara, com mortalidade entre 22 e 55%, apresentando mais comumente cultura polimicrobiana e está mais associada a doenças vasculares periféricas e/ou pacientes diabéticos. Neste relato, a lesão ocorreu em paciente jovem, portador de leucemia mieloide aguda e sem história de comorbidades prévias, tornando esse diagnóstico ainda mais raro quando comparado aos demais relatos na literatura. Essas lesões podem acompanhar ou suceder o tratamento de LMA, principalmente em decorrência da intensa neutropenia causada pelos protocolos, e servem de alerta para necessidade de diagnóstico e intervenções precoces.

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GENOMIC INSTABILITY IN AML: ASSOCIATION BETWEEN FLT3-ITD AND CHROMOSOMAL TRANSLOCATION

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Introduction: Myelodysplastic Neoplasms (MDS) and Acute Myeloid Leukemia (AML) represent spectra of a common clonal hematologic process, whose progression is often associated with genomic instability and the acquisition of somatic mutations in genes that regulate hematopoiesis. Among these alterations, the FLT3-ITD mutation stands out as a significant molecular marker of poor prognosis, whose early detection may aid in risk stratification and monitoring of clonal evolution. **Objectives:** This study aimed to investigate the presence of the FLT3-ITD mutation in patients with MDS and AML, with emphasis on karyotype analysis and mutation confirmation via Sanger sequencing. **Material and methods:** A total of 45 bone marrow samples were analyzed from patients diagnosed with MDS (subtypes EB1 and EB2) and AML (de novo and secondary), collected in EDTA tubes. Genomic DNA was extracted using the PureLink® kit (Invitrogen) and subjected to amplification of the ITD region of the FLT3 gene by end-point PCR using primers described in the literature. PCR products were visualized by 2% agarose gel electrophoresis, with preliminary detection of the mutation based on band patterns suggestive of insertions. Samples with a suspected ITD pattern were purified and subjected to Sanger sequencing, with results analyzed via electropherograms and alignment to the reference sequence from NCBI using BLAST. In parallel, conventional cytogenetic analysis was performed on bone marrow using G-banding, with at least 20 metaphases evaluated per sample. **Results:** Among the 45 patients analyzed, a 33-year-old female patient with de novo AML presented with an abnormal karyotype, showing a chromosomal translocation between chromosomes 2 and 11 [t(2;11)], a non-recurrent alteration associated with genomic instability. The FLT3-ITD mutation was initially suggested by gel electrophoresis, with a band pattern indicative of a mutated fragment. Sanger sequencing confirmed the mutation, revealing a 27-base pair insertion in the region between exons 14 and 15 of the FLT3 gene, within the juxtamembrane domain, with 94% identity to the BLAST reference sequence. **Discussion and conclusion:** The simultaneous presence of a structural chromosomal abnormality and an activating FLT3 mutation reinforces the role of genomic instability in the progression of myeloid neoplasms. Moreover, the study demonstrated the effectiveness of Sanger sequencing as the gold standard method for confirming ITD mutations, particularly in scenarios where the size and exact location of the duplication directly impact clinical interpretation. The association between altered karyotype and point mutations highlights the importance of integrating classical cytogenetics and molecular analysis in the diagnosis and prognosis of hematologic malignancies.

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GEOSPATIAL ANALYSIS OF GENE FUSIONS IN PEDIATRIC ALL AND THEIR POSSIBLE ASSOCIATION WITH ENVIRONMENTAL FACTORS IN THE AMAZON REGION (PARÁ, 2023–2025)

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Introduction: Acute Lymphoblastic Leukemia (ALL) is the most common childhood cancer, accounting for 25% to 30% of pediatric neoplasms. The disease is characterized by chromosomal translocations and aneuploidies, genetic alterations that determine prognosis and treatment response. In the state of Pará, an estimated 360 new cases of leukemia are diagnosed annually, an incidence that may be influenced by regional genetic and environmental factors. **Objectives:** To investigate the potential influence of regional environmental factors on the distribution of gene fusions in patients diagnosed with ALL in the state of Pará between 2023 and 2025, considering the geographic origin of each case. **Material and methods:** This study (Ethics Committee approval No. 4.040.805) analyzed patients with ALL diagnosed at the Octávio Lobo Children's Cancer Hospital (HOIOL) between 2023 and 2025. From blood samples, RNA was extracted, converted to cDNA, and used to detect five specific gene fusions (*BCR::ABL*, *TCF3::PBX1*, *KMT2A::AFF1*, *ETV6::RUNX1*, and *SIL::*