

ajuda a reconhecer padrões de mau prognóstico e antecipar decisões, como terapias de resgate ou transplante. **Conclusão:** A avaliação morfológica seriada evidenciou evolução desfavorável, com transição de blastos indiferenciados para fenótipo monocitoide e, por fim, necrose medular extensa. O caso reforça a importância de integrar análise citomorfológica e acompanhamento clínico para melhor compreensão da dinâmica da LMA e seu prognóstico. A apresentação contará com fotos sobre os momentos morfológicos.

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EXAMES DIAGNÓSTICOS E PROGNÓSTICOS EM PACIENTES COM LEUCEMIA MIELOIDE AGUDA (LMA) RECÉM-DIAGNOSTICADOS: RECOMENDAÇÕES DA EUROPEAN LEUKEMIANET VERSUS PRÁTICA CLÍNICA EM UM HOSPITAL PRIVADO EM SALVADOR/BA

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Introdução: A Leucemia Mieloide Aguda (LMA) é uma neoplasia hematológica agressiva, marcada por grande heterogeneidade genética e prognóstica. As diretrizes do ELN 2022 recomendam a realização rápida de testes citogenéticos e moleculares para adequada classificação, estratificação de risco e definição terapêutica. A citogenética deve estar disponível preferencialmente em 5–7 dias; mutações com impacto terapêutico, como FLT3, IDH1, IDH2 e NPM1, em 5–7 dias; rearranjos gênicos como PML::RARA e BCR::ABL1 em 3–5 dias; e mutações como CEBPA, DDX41, TP53, ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1 e ZRSR2 ao longo do primeiro ciclo de tratamento. Contudo, mesmo no sistema privado de saúde de uma capital brasileira, o acesso completo e dentro dos prazos preconizados é frequentemente inviável. **Objetivos:** Comparar o tempo de obtenção dos exames prognósticos realizados em pacientes adultos recém-diagnosticados com LMA em um hospital privado de Salvador/BA. **Material e métodos:** Estudo observacional retrospectivo, com revisão de prontuários de pacientes com LMA (exceto M3), idade >18 anos, diagnosticados entre janeiro/2023 e junho/2025 no Hospital da Bahia, Salvador/BA. O desfecho primário foi o tempo decorrido entre a coleta e a liberação dos exames. **Resultados:** Foram incluídos 16 pacientes, cujas características clínicas e laboratoriais foram analisadas. O cariótipo foi realizado em todos, exceto 1, sendo 5 amostras (31%) provenientes de sangue periférico devido a dificuldade técnica (obesidade mórbida, sangramento ativo ou recusa do paciente/família à punção medular). Em 6 casos (37,5%) não houve metáfases. O tempo médio para liberação foi de 19,6 ($\pm$ 9,4) dias, muito superior aos 5–7 dias recomendados. Onze pacientes (78,5%) foram testados para FLT3-ITD e TKD por

PCR, com resultado em média 5,3 ($\pm$ 2,5) dias. O painel mioelóide por NGS foi realizado em 11 pacientes (68,7%), com liberação média em 26,8 dias ($\pm$ 8,8), portanto ainda no curso do primeiro ciclo de tratamento. **Discussão e conclusão:** Pacientes sem NGS eram idosos frágeis (70–88 anos), não candidatos a quimioterapia intensiva com inibidor FLT3, recebendo AZA e venetoclax. A estratificação de risco ELN 2022 foi possível em 6 pacientes (37,5%), 4 risco intermediário e 2 adverso; nos demais, a ausência de metáfases ou do NGS inviabilizou a classificação. Identificaram-se discrepâncias entre as recomendações do ELN e a prática institucional, apenas nos dias de liberação do cariótipo e no acesso ao IDH1, IDH2 e NPM1, cuja análise obtivemos pelo NGS. Os principais fatores críticos foram: tempo na liberação do cariótipo, ausência de metáfases, indisponibilidade de PCR para genes com terapias-alvo não aprovadas no Brasil e falta de cobertura do NGS pela saúde suplementar, limitando seu uso. A incorporação de mutações associadas à LMA secundária na classificação ELN reforça a necessidade de acesso a análise citogenética e molecular para estratificação prognóstica adequada. Contudo, barreiras técnicas e de acesso ainda dificultam a aplicação plena dessas diretrizes e o uso apropriado de terapias direcionadas. O desenvolvimento de infraestrutura e/ou capacitação profissional locais pode contribuir para análises de citogenética, e a ampliação do acesso a exames moleculares mais rápidos são essenciais para aprimorar o cuidado em LMA. É igualmente necessário articular com operadoras e gestores para garantir a cobertura desses exames e viabilizar terapias custo-efetivas e direcionadas.

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EXPLORATION OF MUTATIONAL PATTERNS AND THEIR IMPACT ON THE IMMUNE EXPLORATION OF MUTATIONAL PATTERNS AND THEIR IMPACT ON THE IMMUNE MICROENVIRONMENT IN ACUTE MYELOID LEUKEMIA THROUGH IN SILICO ANALYSES

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Introduction: Acute myeloid leukemia (AML) is a hematological malignancy characterized by significant genetic and prognostic heterogeneity. Identifying recurrent mutations in genes such as FLT3, NPM1, DNMT3A, RUNX1, ASXL1, IDH1/IDH2, and TP53 is crucial for risk stratification and therapeutic personalization. However, understanding the interactions between these mutations and their impact on the AML immune microenvironment remains limited. **Objectives:** This study aims to integrate the analysis of mutations present in AML patients to identify genetic patterns that influence disease prognosis and treatment response. **Material and methods:** Using public data from 671 patients from the Beat

AML2.0 database, we investigated the frequency and co-occurrence of mutations in genes relevant to AML pathogenesis and their association with the hematopoietic microenvironment and cellular subtypes. Statistical analysis was performed using the Kruskal-Wallis test, $p < 0.05$ considered significant, followed by Dunn's post-hoc test adjusted by the Bonferroni method. **Results:** Our analysis identified the presence or absence of mutations in FLT3 (23.55%), NPM1 (25.93%), DNMT3A (14.60%), IDH2 (8.49%), TP53 (8.94%), and RUNX1 (12.82%) were detected in significant proportions, highlighting their role in AML biology. Less frequent mutations were found in GATA1 (0.74%) and KRAS (3.72%), which, though limited in their role, may contribute to AML pathogenesis in specific cases. FLT3 and NPM1 mutations predominated in de novo AML patients, indicating their relevance in this clinical context, which aligns with the prevalence observed in our cohort. Conversely, TP53 mutations were more common in secondary AML, often associated with poorer prognosis. Recurrent mutations in AML are believed to distinctively influence the hematopoietic microenvironment, promoting uncontrolled proliferation or aberrant differentiation, which could determine immune outcomes. We also analyzed common AML mutations in specific cellular subpopulations. FLT3-ITD, DNMT3A, NPM1, and NRAS mutations frequently occurred in effector memory CD8 T cells, suggesting an association with increased presence or activation of this cell type. Similarly, RUNX1, NRAS, KMT2A, DNMT3A, CEBPA, and ASXL1 mutations exhibited higher scores in hematopoietic stem cells, indicating a potential impact on early hematopoiesis. KRAS and TET2 mutations showed notable distribution in mesenchymal stem cells. GATA1 mutations were frequent in NK cells, while other mutations had low scores in this immune cell type. Notably, the KMT2A mutation was linked to a multifaceted influence, affecting both early hematopoiesis and immune subtypes. Although mutations in the FLT3/NPM1 groups did not show significant differences in cellular distribution, phenotypic variations seem more reflective of the broader molecular context of the disease than of specific alterations in cellular subtypes. Investigating the impact of these mutations on the cellular microenvironment revealed that FLT3-ITD, DNMT3A, and NPM1 were associated with effector memory CD8 T cell activation, while RUNX1, KMT2A, DNMT3A, and ASXL1 mutations showed increased expression in hematopoietic stem cells, suggesting a role in hematopoiesis regulation. **Discussion and conclusion:** These findings reinforce the hypothesis that mutations in AML not only drive neoplastic proliferation but also influence the immune and hematopoietic microenvironment, potentially affecting treatment response.

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EXPRESSION AND EPIGENETIC REGULATION
OF PDCD1 AND HAVCR2 GENES IN PATIENTS
WITH ACUTE MYELOID LEUKEMIA:
PROGNOSTIC IMPLICATIONS

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Introduction: Acute myeloid leukemia (AML) is an aggressive hematologic malignancy characterized by the uncontrolled proliferation of immature myeloid cells in the bone marrow, impairing normal hematopoiesis. Although conventional chemotherapy remains the standard treatment, particularly in patients under 60 years of age, overall survival remains limited, mainly due to high relapse rates. One of the mechanisms implicated in disease progression is immune evasion, driven by the overexpression of inhibitory receptors, such as PD-1 and TIM-3, on T cells, leading to an exhausted phenotype characterized by impaired proliferation, cytokine production, and cytotoxic activity. Additionally, the tumor microenvironment contributes to this scenario by expressing high levels of ligands such as PD-L1, thereby promoting disease progression. **Objectives:** This study aimed to: (i) evaluate the expression of the PDCD1 (PD-1) and HAVCR2 (TIM-3) genes in AML patients; (ii) correlate gene expression levels with overall survival; and (iii) analyze the promoter methylation profiles of these genes across different age groups. **Material and methods:** Public data from the TCGA were analyzed using the GEPIA2 and UALCAN platforms. PDCD1 and HAVCR2 expression was compared between 173 AML patients and 70 control individuals. Overall survival was assessed using Kaplan-Meier curves, stratifying patients into high- and low-expression groups ($n = 53$ per group), with the log-rank test applied ($p < 0.05$; 95% CI). **Results:** Promoter methylation was evaluated in 193 AML samples, stratified by age. Expression levels of PDCD1 and HAVCR2 were significantly higher in AML patients compared to controls ($p < 0.001$). Overexpression of these genes was associated with reduced overall survival ($p = 0.0017$) and a 2.4-fold increased hazard ratio ($p = 0.0022$). Patients aged 21–40 years showed promoter hypermethylation of PDCD1 ($\beta = 0.72$) compared to the 61–80 ($p = 0.00290$) and 81–100 age groups ($p = 0.00292$). For HAVCR2, hypomethylation was observed in individuals aged 41–60 years ($\beta = 0.34$) compared to the 61–80 group ($p = 0.0062$). **Discussion and conclusion:** These findings underscore the central role of immune exhaustion in AML pathophysiology, highlighting the overexpression of PDCD1 and HAVCR2 as contributors to a tumor-permissive microenvironment and worse prognosis. The epigenetic analysis suggests age-related regulation of these genes, with PDCD1 hypermethylation in younger patients—possibly indicating active transcriptional repression—and loss of this regulation in older individuals. The HAVCR2 hypomethylation observed in middle-aged patients may explain its increased expression and the intensification of the T cell exhaustion phenotype in this group. The overexpression of PDCD1 and HAVCR2 is associated with immune exhaustion, reduced survival, and probable epigenetic dysregulation in AML patients. These findings reinforce their potential as prognostic biomarkers and highlight the relevance of exploring epigenetically modulated immunotherapeutic targets in AML.

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