Introdução: A leucemia mieloide aguda (LMA) é uma neoplasia hematológica agressiva, caracterizada pelo acúmulo de células mieloides imaturas na medula óssea (MO) e no sangue periférico (SP). Alterações no microambiente da MO, contribuem para a progressão da doença e evasão tumoral. Além disso, mudanças genéticas, como a superexpressão do gene MN1, também estão ligadas a um fenótipo mais agressivo e resistência ao tratamento. Dentre os achados na MO leucêmica, destaca-se o aumento de macrófagos associados à LMA (AAMs), com perfil semelhante ao de macrófagos M2, de caráter anti-inflamatório e imunosupressor. Nesse cenário, estratégias terapêuticas que visam reprogramar esses AAMs para um fenótipo inflamatório e antitumoral, como o M1, vêm sendo exploradas. **Objetivos:** O objetivo deste estudo foi avaliar os efeitos imunomoduladores da plinabulina, um inibidor da polimerização da tubulina, sobre AAMs em modelos de LMA com superexpressão de MN1. **Material e métodos:** Monócitos do SP de indivíduos saudáveis foram polarizados em macrófagos M2 e tratados com plinabulina (0,125−0,5 μM) por 48 horas. A imunofenotipagem (CD80, CD86, CD206, CD163) foi feita por citometria de fluxo, e os níveis de citocinas (TNF-α, IL-1β, IL-10, TGF-β) foram quantificados nos sobrenadantes. Macrófagos derivados da MO de camundongos foram polarizados para o fenótipo M2 e tratados com plinabulina e a expressão gênica (Cd80, Tnf-α, Nos2, Cd206, Arg1, Cd163) foi feita por qRT-PCR. A expressão gênica também foi analisada em macrófagos cocultivados com células de LMA superexpressando o gene MN1. Ensaios funcionais incluíram testes de fagocitose e de proliferação leucêmica com macrófagos tratados. O sequenciamento de RNA foi usado para identificar alterações na expressão gênica e vias moduladas. A citotoxicidade ex vivo foi avaliada em amostras primárias de LMA (n = 25) tratadas por 72 horas com plinabulina, com análise de viabilidade de blastos e macrófagos por citometria de fluxo (Anexina V/DAPI e TMRE). A eficácia in vivo foi testada em camundongos com LMA MN1-GFP$^+$, tratados com plinabulina (7,5 mg/kg, i.p., diariamente), e a carga leucêmica foi avaliada por citometria de fluxo na MO, SP e baço. **Resultados:** Os resultados demonstraram que o plinabulina modulou a expressão de marcadores imunofenotípicos, aumentando a expressão de CD86 e reduzindo CD163 em amostras humanas, além de estimular a secreção de citocinas pró-inflamatórias (IL-1β, TNF-α) e reduzir TGF-β. Em amostras murinas, houve aumento da expressão de genes associados ao fenótipo M1 (Cd80, Tnf-α, Nos2) e redução da expressão de Arg1. Na cocultura com células de LMA, os macrófagos tratados apresentaram aumento da atividade fagocítica e inibiram a proliferação de células leucêmica. O cultivo dos macrófagos em meio condicionado de células de LMA induziu um perfil tolerogênico nos macrófagos, parcialmente revertido pelo tratamento. A análise transcriptômica mostrou que o plinabulina induziu a expressão de 4.829 genes, incluindo marcadores de resposta a lesões e remodelamento tecidual e resposta pró-inflamatória. O tratamento também suprimiu a via IL-6/JAK/STAT3, associada ao fenótipo M2. Plinabulina também demonstrou citotoxicidade sobre células CD34$^+$ leucêmicas de pacientes e, em modelo murino transplantado com células MN1$^+$, reduziu a frequência das células leucêmica na MO, SP e baço. **Discussão e conclusão:** Os achados reforçam o potencial da reprogramação de macrófagos como estratégia complementar no tratamento da LMA, como em casos de alto risco molecular com superexpressão de MN1.

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POOR OUTCOMES OF NPM1 MUTATED AML IN BRAZIL REGARDLESS OF TRADITIONAL RISK FACTORS AND RECENT INCORPORATION OF MOLECULAR MONITORING

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Introduction: NPM1 is the most frequent mutation in acute myeloid leukemia (AML), occurring in approximately 30% of cases and generally associated with a favorable prognosis when not accompanied by FLT3-ITD or adverse cytogenetics. This prognostic advantage, however, may be offset by additional adverse factors such as older age, elevated leukocyte count, secondary AML, DNMT3A co-mutation, and non-ABD NPM1 variants. Measurable residual disease (MRD) monitoring by NPM1 RT-qPCR after induction has emerged as a key prognostic tool, providing guidance for decisions regarding allogeneic stem cell transplantation (allo-HSCT) in first remission. In Latin America, AML outcomes remain poorer than in high-income countries, largely due to higher treatment-related toxicity, delayed transplant access, and socioeconomic constraints in public health systems. Within this context, no prior studies have specifically addressed NPM1-mutated AML or evaluated how these limitations affect outcomes in low-income countries (LMICs). Our study addresses this gap, representing the first report to include the initial implementation of molecular MRD monitoring in this setting. **Objectives:** To describe clinical characteristics and outcomes of patients with NPM1-mutated AML treated at a public cancer center in Brazil and to identify prognostic factors in a real-world setting. **Material and methods:** Retrospective observational cohort of 109 adults diagnosed with NPM1-mutated AML between 2018 and 2024 at the Instituto do Câncer (HCFMUSP). Outcomes included overall survival (OS), event-free survival (EFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM). Prognostic factors were evaluated using univariate and multivariate Cox models. MRD by NPM1 RT-qPCR was performed only in type A cases and implemented from 2022 onward. **Results:** Median age was 60 years; 56.9% were female. FLT3 mutations were present in 51.4% of tested patients; 38.5% were FLT3-ITD positive. A total of 88 received chemotherapy; 15 underwent allo-HSCT, all in second remission. Among 32 patients evaluated post-induction, 56.3% were MRD negative; after consolidation, 76.5% were MRD negative. Early mortality occurred in 14.8% overall and 19.3% of those receiving chemotherapy. Five-year OS was 19.9% overall and 24.7% among treated patients. FLT3-ITD was strongly associated with poor survival (5-year OS <5%).

OS was ~50% in patients <50 years and 25% in those ≥50 years. In chemotherapy treated patients, 5-year EFS was 18.9%; CIR was 46.7% and NRM 34.4%. Univariate analysis linked older age, thrombocytopenia, high blast count, elevated C-reactive protein (CRP), hypoalbuminemia, and FLT3 mutation to worse OS. Persistent MRD after induction I also predicted poor outcomes. In multivariate models, FLT3-ITD (HR = 2.51), older age (HR = 1.03), and hypoalbuminemia (HR = 0.58) were independently associated with worse OS. FLT3-ITD and elevated CRP remained significant for EFS. **Discussion and conclusion:** This study reveals notably poor outcomes in a cohort of NPM1-mutated AML patients treated in the Brazilian public system, particularly among those with FLT3-ITD and older age. High early mortality, limited access to FLT3 inhibitors, and delayed implementation of MRD-guided post-remission strategies likely contributed. These findings reinforce the need to improve access to molecular diagnostics, targeted therapies, and allogeneic transplantation across all treatment phases.

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PRIMARY UTERINE CERVICAL MYELOID SARCOMA AS THE INITIAL PRESENTATION OF ACUTE MYELOID LEUKEMIA WITH MONOCYTIC DIFFERENTIATION: A RARE CASE REPORT

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Introduction: Myeloid sarcoma (also known as granulocytic sarcoma or chloroma) is a rare extramedullary manifestation of acute myeloid leukemia (AML). Presentation as a gynecologic mass is exceptionally uncommon and often leads to diagnostic delay and suboptimal initial management. We report a case of AML with monocytic differentiation initially presenting as a cervical tumor, misinterpreted as undifferentiated carcinoma, later confirmed as myeloid sarcoma. **Case report:** A 37-year-old woman, G2P2, previously healthy, had a two-year history of abnormal uterine bleeding and dyspareunia under routine gynecologic follow-up. In February 2023, she developed abdominal pain, dizziness and vaginal bleeding. A cervical mass was detected, and biopsy suggested undifferentiated carcinoma. She was referred for oncologic assessment in March. Staging revealed multiple lytic bone lesions, in the spine and pelvis, and lymphadenopathy in pelvic, inguinal and abdominal chains, raising suspicion of metastatic disease. A cervical biopsy was performed. Initial immunohistochemistry of the cervical lesion showed diffuse positivity for LCA and negativity for cytokeratin and p40, raising suspicion for a hematolymphoid neoplasm. Concurrently, the presence of circulating atypical cells in peripheral blood during early hospitalization prompted hematologic evaluation. Bone marrow aspirate revealed 68% pleomorphic blasts and flow cytometry identified a population of myeloid blasts with monocytic differentiation (CD64++, CD4+, HLA-DR+, CD33++, CD36+, CD14−, CD11b+). Molecular testing for BCR-ABL, FLT3-ITD/TKD, NPM1, and RUNX1-RUNX1T1 mutations was negative. Induction chemotherapy with 7+3 (cytarabine and daunorubicin) was initiated in April. The clinical course was complicated by febrile neutropenia, mucositis and probable invasive fungal pneumonia, managed with liposomal amphotericin B, resulting in initial improvement. In mid-May, the patient developed persistent bone pain and headache. Imaging demonstrated new osteolytic lesions and findings suggestive of central nervous system involvement. Cerebrospinal fluid analysis confirmed leukemic infiltration, with 1.2% of atypical cells exhibiting the same immunophenotypic profile as the diagnostic marrow blasts. Given refractoriness to initial therapy, reinduction was undertaken with the MITO-FLAG protocol (mitoxantrone, fludarabine, high-dose cytarabine). The subsequent course was marked by prolonged aplasia, septic shock of undetermined origin and multiorgan failure, culminating in death on day +19 post-reinduction. **Conclusion:** The absence of recurrent mutations and the rapid clinical deterioration highlight the aggressive nature of AML with monocytic differentiation, particularly when associated with extramedullary involvement. In this case, disease progression occurred despite induction chemotherapy, with leukemic infiltration of the bone marrow, central nervous system and skeleton, further complicated by severe infectious events. Given its capacity to mimic solid tumors, myeloid sarcoma should be included in the differential diagnosis of neoplastic lesions with atypical features, even in the absence of circulating blasts. This is especially relevant in uncommon anatomical sites such as the uterine cervix. Early recognition may significantly impact therapeutic decisions. Ultimately, this case reinforces the importance of maintaining high clinical suspicion and ensuring early hematologic evaluation in patients with unusual tumor presentations.

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PROGRESSÃO DE SÍNDROME MIELODISPLÁSICA PARA NEOPLASIA DE CÉLULAS DENDRÍTICAS PLASMOCITOIDES BLÁSTICAS COM MANIFESTAÇÕES IMUNOLÓGICAS GRAVES

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