ACUTE MYELOID LEUKEMIA WITH CUTANEOUS INFILTRATION AND RESPONSE TO TREATMENT WITH AZACITIDINE PROTOCOL ASSOCIATED WITH HIGH DOSES OF VITAMIN

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Objective: To report a case of acute myeloid leukemia (AML) with cutaneous infiltration and response to the AZAVIT-ABCDEF protocol (Plataforma Brasil CAAE: 53015421.0.0000.5463). Methods: to describe the single clinical case carried out through data collection from medical records and literature review. **Results:** Female, 79 years old, admitted due to chills and night sweats for 30 days, associated with an ulcerated lesion with erythematous edges, about 8 cm in the dorsal region of the right foot. Complete blood count with 6,8 g/dL hemoglobin, 105.140 leukocytes/mm^3 with 70% blasts and 12.000 platelets/mm^3; DHL= 1.493 U/L. Hydroxyurea 1 g/day was started for cytoreduction, transfusion support and antibiotic therapy due to suspected infection in the skin lesion. Myelogram with 83% of blasts. Positive immunophenotyping for CD13, CD15, CD33, CD34, CD38, CD71, CD117, CD123, HLA-DR. FISH for the 5p15 regions. 31 / 5q31.2, 7q31.2 / 7q22.1-q22.2, 21q22.12 / 8q21.3, 11q23.3, 16p13.11 / 16q22.1, 20q13.12 / 20q12 with trisomy 5 (20) %), 7 (10%), 8 (10%), 11 (20%), 16 (10%), 20 (10%) and tetrasomy of chromosomes 5 (40%), 8 (40%), 11 (40%), 16 (30%) and 20 (40%). Karyotype 46 XX. A diagnosis of AML was made, and the protocol started with cycles of 28 days. Evolved with control of leucocyte, maintaining levels within 10.000/mm^3. The skin lesion remained with inflammatory signs even after the end of antibiotic therapy, and it was decided to start prednisone 20 mg/day for 10 days, however, without resolution. Biopsy of the lesion diagnosed infiltrative blastic lesion in the dermis with a perivascular pattern. Immunohistochemistry was positive for myeloperoxidase, lysozyme, CD34 and negative for CD117. August/23: patient in the 5th cycle with a significant reduction in the need for transfusion. Blood count: 2 / 6 Hb = 10,8 g/dL, Leukocytes = 7810 (64.2/0.8/0.4/30.4/4.2) and platelets = 178 mil/mm^3. There was complete resolution of the skin lesion and absence of blasts in the periphery. Discussion: cutaneous infiltration by neoplastic leukocytes occurs sporadically in AML, being more frequent in monocytic leukocytes. The lesions can range from infiltrative nodular erythematous to ulcerated lesions, sometimes there is a report of pruritus. Extramedullary involvement may precede the diagnosis of acute leukemia and is also called chloroma. The genetic event and the molecular mechanism for the occurrence of this infiltration are not well established. Prognosis is poor with short survival. Eckardt et al in 2022 carried out a survey with 1583 patients with AML, in these, 14% had chloroma and cutaneous infiltration was the most frequent. There was no difference between genders or age. They had high white blood cell count and high LDH. The most common molecular alterations were PTPN11, NPM1 and FLT3-ITD. Complete remission was rarely found with intensive schemes and deaths in the first 30 days of diagnosis were higher. In multivariate models, the presence of chloroma in the "ELN2017 risk groups and age" remains an independent factor of poor prognosis. **Conclusion:** The present case reiterates an unusual presentation of AML with cutaneous infiltration by neoplastic leukocytes. It also demonstrates resolution of the skin lesion with the AZAVIT-ABCDEF protocol and improvement of cytopenias with transfusion independence.

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ESTUDO DO PAPEL DE DNMT3A E TDT NA PROMOÇÃO DE MUTAÇÕES EM FLT3 E NPM1 NA LEUCEMIA MIELOIDE AGUDA

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Introdução e objetivos: A leucemia mieloide aguda (LMA) é uma neoplasia maligna do tecido hematopoiético, na qual células precursoras da linhagem mieloide adquirem uma série de mutações que bloqueiam seus programas de diferenciação e maturação. A etiologia da doença está associada a uma paisagem genômica altamente heterogênea, na qual alterações nos genes FLT3 e NPM1 destacam-se por seu impacto no prognóstico clínico. Mutações nestes genessão identificadas em 25% e 33% dos pacientes com LMA e parecem atuar sinergicamente na manutenção do estado leucêmico. Em 2019, um grupo de pesquisadores propôs que a enzima desoxinucleotidil-transferase terminal (TdT) fosse responsável pela formação de pequenas inserções ou duplicações nos genes FLT3 (FLT3-ITD) e NPM1 (NPM1c). Essas alterações estão associadas a outras mutações pré-existentes nas células, em especial as que afetam o gene DNMT3A. Como essa DNA metiltransferase pode regular a expressão gênica na célula, nós buscamos investigar se mutações em DNMT3A podem contribuir para a desregulação da expressão de TdT e, com isso, facilitar a ocorrência de mutações em FLT3 e NPM1 na patogênese molecular da LMA. **Material e métodos:** Este trabalho foi desenvolvido primeiramente em uma coorte exploratória obtida a partir de dados do TCGA (The Cancer Genome Atlas) e uma segunda etapa foi conduzida em uma coorte de validação, a partir de amostras de medula óssea e ou sangue periférico para obter DNA e RNA de pacientes diagnosticados com LMA. Os DNA 's extraídos