functional roles of DEGs in Myelodysplastic Syndrome (MDS) pathobiology. We categorized the DEGs of CD34+ HSC and PBMC into functional categories using GO analysis. In CD34+ HSC, the most enriched pathways were signal transduction, negative regulation of transcription, and immune response. In PBMC, the immune response, signal transduction, and innate immune response pathways were significantly activated. We also performed KEGG pathway analysis for upregulated and downregulated DEGs in both CD34+ HSC and PBMC samples. In CD34+ HSC, the top pathways were involved in hematopoietic cell lineage, cell receptor signaling, and primary immunodeficiency. These pathways were also identified in PBMC, along with cancer and cell cycle pathways. **Discussion and Conclusion:** To summarize, our study uncovered disparities in DEGs between CD34+ HSC and PBMC cell types in MDS. However, we also observed a certain degree of similarity in the activated pathways of both cell samples based on Gene Ontology and KEGG pathways enrichment analyses. Of particular importance in our study was the role of the immune system and the activation of hematopoietic cell lineage pathways as the most activated in MDS, regardless of the cell type evaluated. These findings provide novel insights into DEGs biomarkers associated with MDS pathogenesis, holding clinical significance.

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CASE REPORT: ADVANCED SYSTEMIC MASTOCYTOSIS ASSOCIATED WITH HEMATOLOGICAL NEOPLASIA

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Objective: Report a clinical case of Advanced Systemic Mastocytosis Associated with Hematological Neoplasia (MAS-ANH) under treatment with the AZAVIT-ABCDEF protocol, 7 days every 28 days (azacytidine associated with high doses of vitamins B1, C, and D, with erythropoietin and filgrastim). Brazil Platform CAAE: 53015421.0.0000.5463. After obtaining informed consent. **Methodology:** Assessment of patient's information from HSPE's computer-based patient records. **Clinical case:** A 71-year-old male with fatigue, diarrhea, pruritus, and extensive skin lesions in the groin, lymph node enlargement, and splenomegaly. Hb = 8.2 g/dL, platelets = 64,000/mm^3, and leukocytes = 11.38 thousand/mm^3 (1/5/54/0/0/37/3), Alkaline phosphatase = 239 U/L (30-120 U/L). Myelogram showed dysplastic changes, 4% blasts, and moderate mastocytosis. Bone marrow biopsy revealed 60% cellularity and mastocytosis. Immunohistochemistry: CD117 (+). Lymph node and skin biopsy showed infiltration by mast cells. Bone scintigraphy showed increased uptake in the skull, pelvis, spine, and femurs. Initially treated with alpha interferon, which resulted in increased cytopenias and worsening of constitutional symptoms. Decided to start zoledronic acid and AZAVIT-ABCDEF protocol, receiving 27 cycles every 28 days. Showed improvement in hemogram with sporadic blood component transfusions and reduction in splenomegaly. Pruritus and diarrhea improved significantly, and the patient gained weight. Triptase level still at 145 μg/mL (normal = 11 μg/mL) with slight improvement in skin lesions. Current blood count: Hb = 10.8 g/dL, platelets = 71,000/mm^3, and leukocytes = 9.280/mm^3 (1/5/59/1/0/14/20). **Discussion:** MAS-ANH is a rare entity associated with a mutation in the KIT D816V gene that encodes the receptor for stem cell factor (CD117). Additional mutations are commonly found, such as TET2 (29%), ASXL1 (17%), and CBL (11%). The main manifestations are hematological and gastrointestinal disturbances. Other symptoms include pruritus, urticaria, skin infiltration, bone pain, fatigue, fever, headache, and anaphylactic reactions. A prognostic index showed worse outcomes for cases with age > 60 years, thrombocytopenia, anemia, elevated alkaline phosphatase, and the presence of adverse mutations (ASXL1, RUNX1, and NRAS). Treatment options include KIT gene inhibitors (midostaurin, imatinib, and avapritinib), alpha interferon, and 2-CDA, with short-lived responses and the possibility of worsening cytopenias. Antihistamines and corticosteroids are used symptomatically. The good hematological response observed in this case probably occurred due to the presence of hematological clonal abnormalities resembling myelodysplastic neoplasia without mastocytosis. We believe that the protocol promotes differentiation by increasing the transcription of factors related to cell differentiation and improving aerobic metabolism. **Conclusion:** MAS-ANH is an aggressive pathology with a median survival of 20 months, even with the use of KIT gene loop inhibitors. At diagnosis, the patient presented with 4 out of 5 poor prognostic features and has already achieved a survival of 41 months. Further studies will be required to confirm the improvement in quality of life and survival with the AZAVIT-ABCDEF protocol.

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PLATELET DYSFUNCTION IN A PATIENT WITH CHRONIC MYELOMONOCYTIC LEUKEMIA (CMML) AND RECURRENT SUBDURAL HEMATOMA.

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Objectives: To report a case of a patient diagnosed with CMML with recurrent subdural hematomas and platelet dysfunction. **Materials and methods:** The case report was based on data recorded in the electronic medical record and literature review. **Results:** A 62-year-old female diagnosed with CMML in February 2022 during investigation of persistent monocytosis associated with anemia and thrombocytopenia. Hemoglobin: 8.9 g/dL; White blood cell count: 11,860/mm^3 (69/0/0/9/20); Platelets: 45,000/mm^3. BCR-ABL and JAK2 tests were negative. Bone marrow examination revealed erythroid and granulocytic hypercellularity with dysplastic changes.

Megakaryocytes were hypolobulated. The patient presented with a left subdural hematoma following a mild traumatic brain injury in October 2022, requiring neurosurgical intervention. At that time, coagulation profile and platelet levels were normal. In December 2022, she experienced headaches again, with a subdural hematoma on the right side without any history of local trauma. The hematoma was drained once more, and laboratory tests continued to show normal platelet levels and coagulation profile. After discharge, the patient presented with neurological symptoms in January 2023, and a new right-sided subdural hematoma required two additional surgical interventions. Structural abnormalities were not detected on imaging exams. Given the recurrent episodes of severe intracranial hemorrhage with a risk of herniation, the hypothesis of platelet dysfunction associated with CMML was considered, and platelet transfusion was performed. After this intervention, there were no further bleeding episodes, and subsequent platelet aggregation testing confirmed hypoaggregation with collagen, ristocetin at a concentration of 1.2 mg/mL, adrenaline, and arachidonic acid. In outpatient follow-up, the patient showed an increase in white blood cell count and anemia with thrombocytopenia, and she received the AZAVIT-ABCDEF protocol (azacitidine, erythropoietin, filgrastim associated with high doses of vitamin B1, C, and D3) after signing the informed consent. There was no recurrence of central nervous system bleeding, and the leukocytosis and monocytosis were controlled. **Discussion:** CMML is a condition characterized by persistent monocytosis associated with dysplastic morphology in the bone marrow and can exhibit features of either myelodysplastic neoplasms or chronic myeloproliferative diseases. It is associated with various mutations, including the TET2 gene mutation, which occurs in up to 60% of patients and appears to lead to mild platelet dysfunction. Platelet transfusions stopped the intracranial hemorrhage, and high doses of vitamin C possibly restored the function of the TET2 gene. **Conclusion:** Advanced in molecular studies may further elucidate the heterogeneity of these myeloid disorders with uncertain clinical behavior and assist in therapeutic decision-making. The patient in this case was diagnosed with CMML and presented with recurrent subdural hematomas in the context of platelet dysfunction, with bleeding cessation achieved through platelet transfusion.

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INVESTIGATING THE IMPACT OF EGCG ON INEFFECTIVE HEMATOPOIESIS IN A MDS MOUSE MODEL

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Background and aims: Green tea catechins, particularly, epigallocatechin-3-gallate (EGCG), exhibit a range of beneficial effects, like apoptosis and differentiation-promoting effect which can help to counteract the uncontrolled proliferation and impaired differentiation trait of leukemia and myelodysplastic syndrome. This study aims to evaluate the effect of EGCG in vivo in mice model of myelodysplastic syndrome (NHD13 mice). **Methods:** To assess the effects of EGCG on MDS, 10-week-old female NUP98-HOXD13 mice and their littermate WT mice were treated with EGCG (50 mg/kg/day 5x/week i.p. for 4 weeks) or vehicle. Animals were sacrificed and bone marrow and spleen were obtained to evaluate immune system by flow cytometry and histology analyses. In addition, automated hematological counts and clinical biochemistry parameter analysis were done. Moreover, a 71-year-old man diagnosed with high-risk myelodysplastic syndrome (MSD) with 9% blast presence in the bone marrow, underwent a daily treatment of 800 mg EGCG intake, administered orally. Throughout this period, the patient underwent weekly regular clinical assessments and laboratory studies for monitor any potential toxicities. Additionally, peripheral blood samples were evaluated before and after the treatment to observe any alterations in immune cell composition. **Results and discussion:** NDH13+ exhibited, before the treatment, a reduction in the number of leukocytes, platelets and hemoglobin levels, which was in line with literature. EGCG treatment ameliorates the hematological parameters, visualized by the increase in the number of leukocytes (monocytes and neutrophils) and platelets; with no signals of toxicity - not morphological features nor enzyme levels changes in the liver. The expansion of Foxp3+ regulatory T cells leads the suppression of host antitumor responses and is a characteristic of progression to aggressive subtypes of the disease. Interestingly EGCG did not alter the percentage/frequency Foxp3+ regulatory T cells (CD4+CD25+ and/or CD4+FOXP3+), as well as the percentage/frequency of immature cells (CD45*Int*CD34+), in bone marrow and spleen. Our preliminary results showed an increase in extramedullary hematopoiesis in the spleen. One patient treated by EGCG for a month, exhibit reduction of regulatory T cells CD4+CD25+ and CD4+FOXP3+), and increased CD8+ T cells (CD3+CD8+) and natural killer cells (CD16+CD56+) accompanied with an increase of mature leukocytes (monocytes and neutrophils), with no changes in hemoglobin levels and platelets number. **Conclusion:** Our initial findings indicate that EGCG treatment may reduce ineffective hematopoiesis leading to an improvement of hematological parameters. These results align with the data obtained from one patient with high-risk myelodysplastic syndrome HR-SMD who received EGCG treatment. In summary, EGCG might be a promising adjuvant compound in the treatment of MDS. Further research and clinical studies are warranted to validate and explore its therapeutic benefits fully.

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