(AHAI), mastectomized, returned to a follow-up declaring fatigue and indisposition. The hematologic perfil showed: direct coombs positive, reticulocytes 8.0%, hemoglobin 7.7 g/dL, leukocytes 1280, platelets 318,000, homogeneous nuclear ANA 1/640, hypergammaglobulinemia, anti-SSA 240.0 and Schirmer positive. She was submitted to multiple treatments with antihistamines and immunosuppressants, but had infectious complications and hospital admissions. In 2023, it was indicated a splenectomy due to refractory disease and she started to be followed up by a hematologist, who suggested treatment with rituximab (500 mg in two sections with intervals of 14 days) as an alternative to active AHAI secondary to SSL. The treatment showed a good clinical result with the hemoglobin increased to 10,6 g/dL. However, at the end of 2023, the patient was unable to undergo a new pulse therapy of mabthera due to changes in the follow-up examinations of previously treated breast adenocarcinoma. A new biopsy showed multiple adenopathy attributed to the SSL itself. In 2024, a new bone marrow aspirate was taken which showed dyserythropoiesis, dysgranulopoiesis, 2% blasts and, in the cytogenetics test, 47,XX,+14[4]/46,XX[16]. In this context, the patient was diagnosed with MDS with a low percentage of blasts (MDS-LB). **Discussion:** The immunological dysregulation and hyperactivation of T and B lymphocytes will destroy self-antigens present in the epithelium of the exocrine glands, characterizing SSL, and in the erythrocytes, as in AHAI, leading to the release of hemoglobin into the plasma and dysfunction in gas transport. Studies show that autoimmune manifestations can lead to secondary diseases in bone marrow and MDS is one of them. Recently, studies linked UBA1 somatic mutations as the recurrent cause of clinically complex diagnoses with overlapping hematologic features. This new disease entity is known as VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome. VEXAS syndrome is frequently associated with hematological disorders, around 30-50% of these patients have concurrent MDS. Interestingly, the 14 trisomy finding has been associated with hematologic neoplasias and MDS overlap syndromes. In addition, it is crucial to confirm UBA1 mutation to VEXAS-associated diagnoses in this context of inflammatory clinical presentation. The correct diagnosis of MDS overlap syndromes is essential because their prognosis differs from isolated disorders and may require specific treatments due to unique molecular vulnerabilities.

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THE DYNAMIC OF MDS DIAGNOSIS: FROM MULTI-LINEAGE DYSPLASIA AND HIGH BLASTS TO LMMC - A CASE REPORT

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Introduction: Myelodysplastic neoplasms (MDS) is a heterogeneous group of hematologic diseases characterized by cytopenias in one or more hematologic lineages and multiple dysplasias. Myeloproliferative neoplasms (MPN) are characterized by an increase in production of differentiated hematopoietic cells. MDS/MPN overlap syndromes diagnoses have different clinical manifestations and the most common of them is chronic myelomonocytic leukemia (CMML) which is defined by an abnormal production of monocytic cells and an increase of risk to secondary acute myeloid leukemia (AML) progression. According to the 2016 World Health Organization (WHO) classification, CMML, listed amongst the MDS/MPN overlap disorders, is divided into CMML-0 (cases with 2% blasts in the blood and 5% blasts in the bone marrow), CMML-1 (2 to 4% blasts in the blood and/or 5 to 9% blasts in the bone marrow), and CMML-2 (5 to 19% blasts in the blood and 10 to 19% blasts in the bone marrow). This report aims to exhibit the importance of follow-up patients to detect progression from MDS with a high percentage of blasts to CMML. **Case report:** A 73-year-old woman with asymptomatic pancytopenia was submitted to our care in 2018. The bone marrow aspiration and immunohistochemical exam showed multilineage dysplasia, 4% of blasts and the bone biopsy presented 85% cellularity. Also, the monocytic count was 1115/mm^3. The karyotype was normal in 20 metaphases. In 2019, the patient appeared with ecchymosis and new exams showed bicytopenia, 6% of blasts with 85% cellularity and the monocytic count was less than 1800/mm^3. In 2020, she was diagnosed with MDS with an IPSS-R score of 3.5, bicytopenia and the monocytic count was less than 1400. But, in 2021, the monocytic count rose to 6100/mm^3. It was then that her clinical condition evolved to a CMML-1. She was 76 years old when it was decided that she be treated with hydroxyurea. The first response wasn't as expected, so the medication was replaced to azacitidine in the middle of 2022. The second response to treatment was very well documented, however, the treatment with azacitidine suffered several interruptions due to lack of medicine which led the monocyte count to rise. **Discussion:** Patients with MDS who showed relative monocytosis (≥10% in peripheral blood) and an increase of absolute count of monocytes (≥ 1×10^9/L) are related to a high risk of progression to CMML with a positive predictive value (PPV) of 71,4%. The follow-up and the correct diagnosis is essential in MDS/MPN overlap syndromes since their prognosis and clinical implications differ from these isolated disorders. The patient in question started to be followed up in 2018 where multiple exams were made to discard other diseases, but the monocyte count was always carefully observed due to the risk of progression to CMML, which was detected in 2021. Then, the treatment was required. The use of hypomethylating agents can be considered for CMML patients if excess blasts or poor prognosis factors are present. The azacitidine was used and was able to revert to a normal monocyte profile with improved hemoglobin count, although the interruption of

treatment because of lack of medicine in Unified Health System (SUS) demonstrates a treatment failure. **Conclusion:** Monitoring the progress of MDS in the patient was able to detect CMML at the beginning and already start the treatment.

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NFKB, TRAF6, AND MYDDOSOME GENE EXPRESSION IN MYELODYSPLASTIC NEOPLASM (SMD) AND ACUTE MYELOID LEUKEMIA MYELODYSPLASIA RELATED (AML-MR)

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Myelodysplastic neoplasms (MDS) are myeloid neoplasms, with bone marrow dysplasia, cytopenias, and increased risk of Acute Myeloid Leukemia (AML). Genotoxic agents and chronic inflammation can promote mutations, with clonal hematopoiesis and genetic instability. Chronic autoimmune and inflammatory disorders increase the risk of MDS. Several molecular and genetic mechanisms are involved in chronic inflammatory signaling of MDS, especially the activation of Toll-Like Receptors (TLRs), whose main intracellular adapter protein, MYD88, combines with IRAK kinases family (IRAK1, IRAK2, and IRAK4) in a complex called Myddosome, promoting TRAF6 phosphorylation and activation of NFKB and MAPK pathways and cytokine secretion. This study evaluated TRAF6, NFKB, and myddosome genes (MYD88, IRAK1, IRAK2, and IRAK4) expression in patients with MDS and AML Myelodysplasia Related (AML-MR), and its association with clinical variables and karyotype. Eighty-two patients, (76 with MDS and 6 with AML-MR) and 10 healthy controls were included. The cytogenetic study was carried out using G-Band and real-time PCR (RT-qPCR) methodology to analyze gene expression. IRAK4 and NFKB expression were higher in MDS with increased blasts (MDS-IB) compared to MDS with low blasts and ring sideroblasts ($p < 0.001$ and $p = 0.026$, respectively). MYD88 expression was lower in AML-MR patients compared to controls ($p = 0.041$), lower in patients with hemoglobin levels below 8 g/dL compared with hemoglobin levels above 10 g/dL ($p = 0.036$), lower in patients with bone marrow blast percentage > 10% compared to ≤ 10% ($p = 0.027$) and lower in patients with complex karyotype compared to normal karyotype ($p = 0.005$). IRAK1 expression was lower in patients with bone marrow blast percentage > 10% compared to ≤ 10% ($p < 0.001$) and lower in patients with abnormal karyotype compared to normal karyotype ($p = 0.031$). IRAK2 expression was lower in patients with bone marrow blast percentage > 10% compared to IPSS blasts categories (≤ 2%, > 2-< 5%, 5-10%) ($p = 0.007$, $p = 0.043$, and $p = 0.012$, respectively). Lower expression of MYD88, IRAK1, and IRAK2 was found in patients with adverse prognostic clinical features. Studies describe hyperactivity of TLRs pathways and their downstream molecules mainly in the initial phases of disease or low-risk MDS, while in high-risk diseases and advanced phases, reduced immune responses contribute to clonal evolution and progression to AML. Higher expression of IRAK4 and NFKB were found in patients with adverse prognostic clinical features, despite the downregulation of myddosome pathway, suggesting involvement of alternative pathways. In thiscohort, anomalous expression of NFKB and innate immune genes were observed in MDS and AML-MR patients, suggesting downregulation of myddosome pathway in the presence of adverse prognostic features, as well as hyperexpression of NFKB and IRAK4, both critical in MDS pathogenesis.

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DIAGNÓSTICO PRESUNTIVO DE NEOPLASIA MIELODISPLÁSICA ASSOCIADA A SÍNDROME VEXAS EM UM HOSPITAL PÚBLICO

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Introdução: Neoplasias Mielodisplásicas (SMD) correspondem a uma entidade hematológica responsável por alterações morfológicas em células medulares, resultando em citopenias, além de possuir risco de evolução para Leucemia Mieloide Aguda. Exposição quimioterápica prévia, exposição a substâncias mielotóxicas e doenças autoimunes são fatores de risco estabelecidos. Dentre as causas autoimunes, a Síndrome VEXAS (vacuolização, enzima ativadora de ubiquitina E1, ligação ao X, autoinflamação, síndrome somática) deve ser considerada. **Relato de caso:** Paciente masculino, 73 anos, previamente hipertenso. Admitido em nosso serviço devido a quadro de edema articular, inicialmente sem artralgia associada, perda ponderal de 10 quilos e pancitopenia com 5 meses de evolução. Nos exames de imagem, observado esplenomegalia e opacidades pulmonares em vidro fosco, podendo corresponder a pneumopatia de pequenas vias aéreas. Realizado aspirado de medula óssea, com mielograma hipercelular, exibindo displasia nas três linhagens, incluindo a presença de vacuolização de citoplasma nas células precursoras. A imunofenotipagem comprovou as alterações sugestivas de mielodisplasia. Exames laboratoriais com fator reumatóide e anti-Ro positivo em altos títulos. Aproximadamente 30 dias