para a população pediátrica e a manifestação distinta da doença nesse grupo tornam o diagnóstico desafiador. Mishra (2020) relata uma série de casos em que a maioria dos pacientes pediátricos com MF apresentou-se com anemia, hepatoesplenomegalia, ausência de causas secundárias para a doença, ausência de leucoeritroblastose e com resultado negativo para JAK2. Esses achados são semelhantes aos observados no presente relato e fortalecem o diagnóstico de MF primária, assim como ajudam a ressaltar as diferenças em relação à apresentação típica da doença em adultos. **Conclusão:** Dada a raridade, complexidade e diferenças na apresentação quando comparada a pacientes adultos, é de suma importância o consenso em relação aos critérios diagnósticos da MF em pediatria, objetivando o aprimoramento da condução desse quadro.

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THE ATAXIA-TELANGIECTASIA MUTATED (ATM) GENE PLAYS A PIVOTAL ROLE IN THE REPAIR OF DNA IN CASES OF MYELODYSPLASTIC NEOPLASM

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Myelodysplastic Neoplasm (MDS) is an age-associated neoplasia characterized by frequent epigenetic abnormalities being hypermethylation the most common, frequently associated with transformation to acute myeloid leukemia (AML). DNA repair genes have been constantly downregulated in MDS during progression to AML, but these genes have not been evaluated regarding methylation status or mutational profile. Using three different cohorts of MDS (Cohort A- 56 patients; Cohort B- 100 patients; Cohort C- 76 patients) in three sequential steps we evaluated with complementary methods (pyrosequencing, real-time PCR, immunohistochemistry, cytogenetics and search of mutations) the DNA repair genes for the following analyses: methylation of single-strand (*XPA, XPC, XPG-ERCC5, CSA-ERCC8*, and *CSB-ERCC6*) and double-strand (*ATM, BRCA1, BRCA2, LIG4*, and *RAD51*) DNA repair genes by pyrosequencing; gene expression by RT-qPCR of the *ATM* gene; and protein expression by immunohistochemistry of ATM, 5-methylcytosine (5mC), and 5-hydroxymethylcytosine (5-hmC). Additionally, we used cBioPortal to search for mutations in single-strand and double-strand DNA repair genes. Regarding methylation of single strand repair genes, we detected *XPA* with higher methylation for low risk MDS than high risk MDS ($p < 0.0001$) while for double-strand repair pathway, only *ATM* showed higher methylation for patients who transformed to AML compared to cases who did not transform into AML ($p = 0.016$). In a second step, we evaluated the gene expression of ATM, showing downregulation in MDS compared to controls ($p = 0.042$). In a third step, when we divided patients according to WHO classification of 2022, we detected a progressive reduction of *ATM* expression from subtypes considered as low risk disease (Hypoplastic MDS, MDS with Ring Sideroblasts, MDS with deletion (5q)) compared to high risk MDS (increased of blasts 1 and 2) and AML. We also detected patients who transformed into AML showed a higher ratio of 5mc/5hmC than cases who did not transform ($p = 0.045$). In addition, we observed a higher tissue methylation score (M-score of 5mC%) in patients classified as poor cytogenetic risk by the IPSS-R than patients classified as good cytogenetic risk ($p = 0.035$). Finally, using the most recent platform CBioportal (including the cases of Molecular IPSS with more than 7000 patients), we detected *ATM* as the most mutated, among the DNA repair genes, with the greater variety of mutations such as frameshift, missense and splice compared to others and only *ATM* mutations were classified as oncogenic according to the standards for the classification of pathogenicity of somatic variations in cancer (SOP 2022). We believe all the results presented herein suggest that *ATM* is silenced or down regulated in MDS by methylation or mutations, ultimately increasing the chance of AML transformation.

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SJÖGREN-LARSSON SYNDROME ASSOCIATED WITH MYELODYSPLASTIC SYNDROME: A CASE REPORT

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Introduction: The Sjögren-Larsson Syndrome (SSL) is a rare autoimmune disease that causes glandular inflammation, normally in salivary and lacrimal glands. It can be classified as primary, when it is isolated, or secondary, when it is concomitant with other syndromes. Several studies correlate immune diseases with bone-marrow neoplasias, between them, the Myelodysplastic neoplasms (MDS). MDS is a heterogeneous group of hematologic diseases characterized by cytopenias in one or more hematologic lineages. Also, immunological disorders and chronic immunological stimulation are shown to be a trigger to ineffective hematopoiesis in patients with genetic predisposition. This report aims to describe MDS diagnosis in a patient with a rare immune disease and to demonstrate the complications associated with this condition. Case report: A 76-year-old woman, diagnosed with secondary SSL and autoimmune hemolytic anemia

(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