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.

https://doi.org/10.1016/j.htct.2024.09.754

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

JVC Goes [a,b], LR Sampaio [a,b], RTG Oliveira [a,b], DP Borges [a,b], RDB Dias [a,b], CLA Araujo [a,b], PRC Passos [a,b], HLR Junior [a,b], SMM Magalhães [a,b], RF Pinheiro [a,b]

[a] *Cancer Citogenomic Laboratory (LCC), Universidade Federal do Ceará (UFC), Fortaleza, Brazil*
[b] *Center of Research and Drugs Development (NPDM), Universidade Federal do Ceará (UFC), Fortaleza, Brazil*

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.

https://doi.org/10.1016/j.htct.2024.09.755

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

SCC Carneiro [a,b], ACG Lavor [a,b], JVG Gama [a,b], PRC Passos [a,b], MML Melo [a,b], JVC Goes [a,b], LR Sampaio [a,b], LO Laurindo [a,b], SMM Magalhães [a,b], RF Pinheiro [a,b]

[a] *Cancer Cytogenomic Laboratory (LCC), Universidade Federal do Ceará (UFC), Fortaleza, Brazil*
[b] *Center for Research and Drug Development (NPDM), Universidade Federal do Ceará (UFC), Fortaleza, Brazil*

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