(neoplasia). Casos de MDS são agora classificados como os que possuem anormalidades genéticas definidoras e os que são morfologicamente definidas. Acrescentou-se também a diferenciação entre MDS com baixa contagem de blastos (MO<5% e no SP < 2%) e MDS com aumento no número de blastos, esta por sua inclui MDS com fibrose (MDS-f). A LMA relacionada à MDS (AML-MR), foi definida como ≥20% de blastos expressando um fenótipo e abrigando alterações citogenéticas e moleculares específicas (mutação em um dos 8 genes - SF3B1, ZRSR2, ASXL1, EZH2, BCOR, U2AF1, SRSF2, STAG2). Conseguimos classificar o caso relatado como portador de MDS com fibrose (MDS-f) ao diagnóstico, e após evolução do quadro como LMA relacionada a MDS (AML-MR), com mutação no gene ZRSR-2. **Conclusão:** A classificação WHO 5ªedição (2022) agrega novas possibilidades de classificação para os neoplasmas mieloides.

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ATM DNA METHYLATION ASSOCIATED WITH POOR PROGNOSIS AND LEUKEMIA TRANSFORMATION IN MYELODYSPLASTIC SYNDROME PATIENTS

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Myelodysplastic syndrome (MDS) is a clonal disease of hematopoietic progenitors with a risk of progressing to acute myeloid leukemia. MDS etiology is mainly related to age, but one of the risk factors is exposure to pesticides that causes aberrant reprogramming of the genome by DNA methylation. The aim of this work was evaluating the methylation profile of genes acting in the single-strand DNA (ssDNA) repair (CSA, CSB, XPA, XPC and XPG) and double-strand DNA (dsDNA) repair (ATM, BRCA1, BRCA2, LIG4 and RAD51), and its relationship with gene expression. The analysis was performed using bone marrow samples from 56 MDS patients, 69 farmers exposed to pesticides and 10 controls without exposition or MDS. The methylation profile and gene expression were evaluated using pyro-sequencing technique and quantitative real-time PCR. Regarding ssDNA repair genes, in cases with MDS, patients under 60 years old showed a higher methylation for the XPA and CSB genes than patients over 60 years old ($p = 0.008$; $p = 0.017$). Furthermore, XPA showed increased methylation levels in initial forms of MDS ($p = 0.019$). The MDS group presented a higher percentage of XPA methylation than exposed farmers ($p = 0.000$) and the control group ($p = 0.011$). In the prognostic classification, lower risk presented higher methylation than high-risk ($p = 0.027$). Among the dsDNA repair genes methylation in MDS patients, only ATM gene showed significant results with increase of methylation levels in (1) males ($p = 0.037$); (2) patients aged up to 60 years ($p = 0.002$) and (3) those who progressed to AML ($p = 0.016$). Regarding the methylation between the groups of exposed farmers, MDS advanced forms and controls, we also detected significant differences with levels always increased in the control group: ATM (control group vs. farmers $p = 0.000$), BRCA1 exposed vs. control group, $p = 0.001$; MDS vs. control, $p = 0.001$;), BRCA2 (farmers vs. control, $p = 0.027$; MDS vs. control, $p = 0.004$), LIG4 (farmers vs. control, $p = 0.001$; MDS vs. control, $p = 0.012$) and RAD51 (farmers vs. controls, $p = 0.047$). The correlation analysis between methylation and expression showed a positive and strong correlation for LIG4 gene in the advanced forms MDS group ($r = 0.798$) and a positive and weak correlation for BRCA1 gene in the exposed farmers group ($r = 0.340$). Surprisingly, in the ssDNA repair genes, the expression and methylation of both farmers and MDS patients were not correlated, suggesting that the change in the expression of these genes is not motivated by the DNA methylation mechanism. Furthermore, the analysis of dsDNA repair genes in this study corroborates the phenomenon of relative hypermethylation in some DNA repair genes in MDS.

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VERY COMPLEX KARYOTYPE IN YOUNG MYELODYSPLASTIC SYNDROME PATIENT AFTER CHRONIC EXPOSURE TO CHLOROFORM

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Introduction: Myelodysplastic Syndrome (MDS) is marked by biological and clinical heterogeneity, characterized by dysplasia in the bone marrow and blood cells with the presence of cytopenias. MDS is recognized as a disease in elderly