patient with high risk IPSS-R and trisomy 8, mutation of different prognosis. **Case report:** 60-year-old female, reporting no toxic exposure, no elitism or smoking, monitored on the hematology clinic was diagnosed with MDS-IB1 (MDS with increased blasts 1) at the age of 59. The patient has pre-existing conditions including systemic arterial hypertension (SAH) and type 2 diabetes mellitus (DM II) which are treated with losartan, metformin, ferrous sulfate and folic acid. Presents with pancytopenia, including macrocytic anemia (hemoglobin of 6,9 g/dL and VCM of 127 fL), low white cells count (Neutrophils of 1769/mm^3), and thrombocytopenia (96,7 x 10^3/mm^3). Bone marrow examination revealed mild hypocellularity as well as dyserythropoiesis, dysgranulopoiesis and 5% blasts. In March 2022, a karyotype examination showed, out of the 26 analyzed metaphases, trisomy 8 in 10 metaphases and trisomy 20 in 10 other metaphases. In February 2023, a follow-up karyotype scan revealed trisomy 8 in 11 out of the 21 metaphases analyzed. Based on risk stratification of IPSS-R and according to the results of hemogram (Low Hemoglobin: 1.5 points, low Absolute Neutrophil Count: 0.5 point, Low Platelets: 0 point) myelogram (percentage of blasts in bone marrow: 2 points), and karyotype (Cytogenetics with intermediate risk: 2 points), the patient obtained a score of 6, classifying her as high risk of evolution to Acute Myeloid Leukemia. Initially, the patient was treated with Erythropoietin (EPREX), but there was no significant improvement in her clinical condition. **Discussion and conclusion:** This study highlights the presence of high-risk MDS, characterized by the recurrent occurrence of trisomy 8, a mutation that presents a range of different prognosis. It emphasizes the importance of a comprehensive karyotype evaluation and appropriate risk stratification, enabling informed decision-making regarding the patient's treatment. The study of this mutation has shown an improved response to immunosuppressive therapies, indicating a strong presence of an immunological mechanism for bone marrow failure. However, further studies are necessary to determine the optimal therapeutic approach and ensure careful monitoring of this patient's condition.

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SCREENING OF ONCOGENIC VARIANTS IN DNA POLYMERASES WITH TRANSLESION SYNTHESIS ACTIVITY IN MYELODYSPLASTIC NEOPLASM

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Introduction: Myelodysplastic Neoplasm (MDS) is characterized by cytogenetic alterations in 40-60% of cases and 94% have at least one oncogenic mutation. Tolerance to non-repairable DNA damage is performed by translesion synthesis DNA polymerases (TLS), which bypass or correct the lesions in a relatively error-prone way, which can generate point mutations. TLS polymerases are likely key contributors to mutagenic signatures and their study is important in oncological diseases. **Aims:** This study aimed to perform a genetic screening to identify, characterize and classify genetic variants in DNA polymerases with TLS activity (*REV3L, POLQ, REV1, POLI, POLH, POLK, POLL,* and *POLN*) in MDS. **Materials and methods:** Bone marrow samples from 30 patients (17 MDS with excess blasts - MDS-EB1 and 2, and 13 MDS with ring sideroblasts - MDS-RS-SLD/MDS-RS-MLD, according to the 2016 WHO Classification) were sequenced by NGS-Targeted Sequencing-Illumina. Variants pathogenicity analysis was performed by five *in silico* pathogenicity prediction tools (Ensembl VEP, Mutation Taster, Sift, Mutpred, and Provean). For the oncogenicity analysis of these variants, standards for the classification of oncogenicity of somatic variants (SOP), recommended by the Clinical Genome Resource (ClinGen), Cancer Genomics Consortium (CGC), and Variant Interpretation for Cancer Consortium (VICC) was performed. This study selected loss-of-function (LoF-frameshift, inframe, stop gained, stop loss, splice donor, and splice acceptor) variants for oncogenicity classification. **Results:** Targeted sequencing of the *POLQ* gene detected 194 variants (85 missenses, 38 synonymous, and 17 LoF), 10 were classified as VUS and 1 as Probably Benign, according to SOP. For the *REV3L*, 284 variants were identified (85 missenses, 38 synonymous, and 17 LoF), 18 were classified as Potentially Oncogenic, 7 as VUS, and 3 as Benign, according to SOP. For the *POLI*, 58 variants were identified (22 missenses, 7 synonymous, and LoF), 3 were classified as Potentially Oncogenic, 1 as VUS, and 2 as Benign or Probably Benign, according to SOP. For the *REV1*, 108 variants were identified (39 missenses, 12 synonymous, and 8 LoF); 2 were classified as Potentially Oncogenic and 4 as VUS, according to SOP. For the *POLH*, 22 variants were identified (18 missenses and 4 synonymous). **Discussion and conclusion:** Altered levels or polymorphism and mutations in TLS polymerases are associated with cancer progression. We identify that patients classified as MDS-EB had a higher incidence of LoF variants in the *POLQ* and *REV3L* genes, compared to patients of the MDS-RS subtype, representing a loss of the translesion synthesis mechanism in high-risk patients. Patients of the MDS-RS subtype with normal karyotype had less frequency of LoF variants and higher frequency of missense variants in *REV1* and *POLI* genes, as well as high rates of non-LoF variants, which may represent a biomarker of genomic instability in MDS. A patient with a complex karyotype presented an accumulation of LoF mutations in *POLQ* and *REV3L* genes, which suggests that the higher genetic instability observed in patients with multiple chromosomal alterations may be present due to the absence of the TLS mechanism. The increased loss of function and oncogenic variants in *REV3L* and *POLQ* genes could contribute to genome instability during MDS progression to acute leukemia and reinforce the impact of genetic mutations on the pathophysiological process of MDS, mainly affecting genes not included in current prognostic risk scores.

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