

81 anos, com dados clínicos não informados. A imunofenotipagem por citometria de fluxo e o mielograma foram prejudicados devido à provável hemodiluição e hipocelularidade da amostra. O cariótipo apresentou as seguintes alterações: 46,XX,? ider(20)(q10)del(20)(q11.2)[19]/46,XX,del(5)(q? 22),? t(12;14)(q13;q32)[1]. O terceiro paciente, sexo masculino, 79 anos, tinha como hipótese diagnóstica SMD. A imunofenotipagem por citometria de fluxo foi inconclusiva diante das características da amostra (hipocelularidade e baixa viabilidade celular). O mielograma mostrou discreta hiperplasia medular, apresentando alterações dismórficas em todas as séries. Foi encontrado o seguinte cariótipo: 46,XY,del(20)(q13.1)[9]/46,XY,-20,+mar[5]/46,XY[6]. Os resultados indicam que através da citogenética convencional é possível identificar a presença do ider(20q). Entretanto, a depender da resolução cromossômica e expertise do analista, este pode ser interpretado como um pequeno marcador cromossômico metacêntrico, aparentemente associado à monossomia do cromossomo 20, 45,XY,-20,+mar, como relatado no terceiro paciente, corroborando os achados na literatura. Sugere-se que a perda de genes contidos no braço curto deste cromossomo, del(20p), poderia explicar a agressividade de ider(20q) em comparação com del(20q). Entretanto, o prognóstico de pacientes com SMD com ider(20q) permanece controverso, devido ao pequeno número de casos relatados. Apesar da reduzida casuística no presente resumo, estes relatos ilustram a contribuição da análise do cariótipo para a investigação de alterações cromossômicas e esclarecimento diagnóstico da SMD.

<https://doi.org/10.1016/j.htct.2023.09.825>

BEYOND OF MORPHOLOGY DIAGNOSIS: A CASE REPORT OF PYODERMA GANGRENOSE AS THE FIRST MANIFESTATION OF MYELODYSPLASTIC NEOPLASIA

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Introduction: Pyoderma gangrenosum can be the first cutaneous manifestation of paraneoplastic syndromes. Among the associated diseases include hematological malignancies.

These disorders may have atypical clinical characteristics, with the association of Myelodysplastic Neoplasm (MDS) with the bullous form being the most described and its appearance associated with poor prognosis. **Objective:** To report a case of skin lesion as a first manifestation of MDS. **Case report:** A 68-year-old woman started with fatigue and pain in the legs, evolving with the appearance of plaques with haemorrhagic blisters in the left calf and the presence of cytopenia was identified in laboratory tests (Haemoglobin 6.7 g/dL, leukocytes 2.300/mm³, and neutrophils 552/mm³, and platelets 95.000/mm³). Patient sought medical assistance and started a clinical investigation. During follow-up serologies were performed with all negative results. Myelogram was performed and immunophenotyping showed the presence of 18.7% of myeloid lineage blasts with aberrant CD7 marking. The patient was diagnosed with MDS, the treatment with dapsone was started, but the patient died a few months after diagnosis. **Discussion:** The diagnosis of pyoderma gangrenosum is one of exclusion and other causes of ulcer disease should be investigated. Myelodysplastic Neoplasm should always be considered in patients with pyoderma gangrenosum accompanied by some mono, bi or pancytopenia and may appear at the same time with the hematological disease or, in its evolution, as a marker of malignant transformation. **Conclusion:** Myelodysplastic neoplasm should always be considered in patients with pyoderma gangrenosum accompanied by some cytopenia.

<https://doi.org/10.1016/j.htct.2023.09.826>

TRISOMY 8 IN HIGH RISK MDS PATIENT

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Introduction: Myelodysplastic neoplasms (MDS) are a diverse group of clonal diseases affecting hematopoietic stem cells (HSCs). They are characterized by ineffective hematopoiesis, cytopenias, dysplasias, and the potential to progress to acute myeloid leukemia. Diagnosis of MDS involves assessing clinical, morphological, and genetic factors. Cytogenetic analysis plays a crucial role in identifying clonality in suspected MDS patients. Approximately 50-60% of patients exhibit cytogenetic abnormalities, with the most common anomalies being del(5q), monosomy or deletion of 7q, trisomy 8, and del(20q). **Objective:** To show clinical manifestations of a MDS

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/mm³), and thrombocytopenia (96,7 x 10³/mm³). 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.

<https://doi.org/10.1016/j.htct.2023.09.827>

SCREENING OF ONCOGENIC VARIANTS IN DNA POLYMERASES WITH TRANSLATION 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 Proven). 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.

<https://doi.org/10.1016/j.htct.2023.09.828>