apresentou uma variante em região doadora na SMD-EB. Já o gene REV1 apresentou duas variantes na região aceptora também na SMD-EB. Por outro lado, tanto o gene POLL quanto POLM apresentaram variantes na SMD-SA, sendo duas variantes na região aceptora de POLL e uma variante na região doadora de POLM. **Discussão e conclusão:** Este é o primeiro trabalho a estudar variantes nas regiões canônicas de splicing dos genes TLS na SMD. Apesar do número limitado de casos, os achados sugerem que alterações em POLI, POLQ, POLN e REV1 podem associar-se a fenótipos de maior gravidade, pois as variantes nestes genes foram associadas à maior dependência transfusional e à pacientes de alto risco. Nos casos de SMD-SA, subtipo que possui menor agressividade clínica e forte associação a mutações em genes de splicing, a presença de variantes nos genes POLL e POLM sugere alterações no mecanismo de splicing na célula. Dessa forma, a presença de variantes patogênicas nas regiões de splicing de DNA polimerases com atividade TLS sugere que estes genes podem ser alvo de variações nos mecanismos de splicing da SMD, e uma vez afetados pela presença de variantes patogênicas, podem levar a alterações no splicing alternativo, gerar transcritos disfuncionais e impedir o mecanismo de síntese translesão responsável pela estabilidade genômica. Nossos achados demonstram a necessidade de estudos mais amplos para elucidar o papel prognóstico de DNA polimerases TLS na SMD.

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ANALYSIS OF MYELOID NEOPLASMS OF GERMLINE ORIGIN IN A REFERENCE HOSPITAL IN BRAZIL

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Introduction: Latin American data on myeloid neoplasms of germline origin are scarce. Currently, WHO lists over 50 associated genes, with up to 15% of myelodysplastic syndromes (MDS) in adults potentially having a germline origin. **Objectives:** To describe the clinical and genetic data of individuals with myeloid neoplasms of germline origin. **Material and methods:** Patients with MDS and AML under follow-up at a public hospital in São Paulo between 2021 and 2024 were included. The study was approved by the local Research Ethics Committee (CAAE: 7965622.7.0000.0068). Suspected germline origin was assessed based on established criteria (NCCN, ELN). Whole-genome sequencing was funded by the Brazilian Rare Genomes Project and performed on peripheral blood using the Illumina® platform (22 cases). Oncomine™ Myeloid Research Assay panel was used to screen for somatic variants in 79 genes (10 cases). In three cases, PCR for specific genes were performed. Cytogenetic testing (karyotype and FISH) was also conducted. In five selected cases, variant analysis was performed on fibroblast culture-derived DNA to confirm germline origin. **Results:** Twenty-five patients (5 AML, 20 MDS; median age 34 years [24–53]; 48% male) met the criteria for germline origin screening. Of these, 20 cases had an identified target gene mutation (CEBPA = 2, TP53 = 2, ERCC6L2 = 2, MPL = 2, RUNX1 = 3, ANKRD26 = 4, TET2 = 1, SAMD9 = 1, GATA2 = 1, BLM = 2). Notably, five of these variants were classified as VUS (Variants of Uncertain Significance) in databases. Regarding features suggestive of germline origin, 75% had a positive family history, and 70% had MDS diagnosed before age 40. Among MDS patients, five progressed to AML, with only one alive and in remission post-allogeneic stem cell transplantation. Clonal evolution was studied in ten cases of MDS and identified in four patients (TP53, NPM1, SF3B1, and complex karyotype), two of whom progressed to AML. The ERCC6L2 cases involved siblings sharing the rs574312958 variant, previously unreported in databases and initially classified as VUS. We highlight that this gene is not a part of most commercial NGS panels. Notably, the proband who developed AML exhibited clonal evolution with the emergence of a pathogenic TP53 variant (rs121912651), a well-documented association in the literature. Another remarkable case involved siblings with a BLM variant (c.2207_2212delATCTGAinsTAGATTC), typically a founder mutation in Ashkenazi Jewish populations associated with Bloom syndrome, despite the patients lacking classic phenotypic features or Jewish ancestry. Interestingly, one sibling also carried an NF1 microdeletion (chr17:31328557-31398568x1), which is germline in up to half of cases and was associated with a neurofibromatosis phenotype (café-au-lait spots, freckling, and a scalp neurofibroma). A novel variant (ANKRD26: c.4952A>C) was identified in a 53-year-old female with pancytopenia and two brothers with isolated thrombocytopenia. **Discussion and conclusion:** This is one of the few studies on myeloid neoplasms of germline origin in Latin America, describing novel variants and assessing clonal evolution. This initiative aims to be expanded, with results contributing to the establishment of a dedicated follow-up and genetic counseling clinic for patients and their families.

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CARACTERIZAÇÃO CITOGENÉTICA E GENÔMICA EM PACIENTES COM DIAGNÓSTICO DE NEOPLASIA MIELODISPLÁSICA

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Introdução: As neoplasias mielodisplásicas (SMD) constituem um grupo heterogêneo de doenças hematológicas clonais da