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Cytogenetic abnormalities occurs in almost half of myelodysplastic syndrome (MDS) patients and are considered to be the most important prognostic factor for survival, so they have been included in the International Prognostic Scoring System (IPSS) since 2007. Complex karyotype (CK) is defined as more than or equal to 3 independent chromosomal abnormalities at the same metaphase and is an independent poor prognostic factor, usually associated with a shorter median overall survival and propensity toward malignant transformation. From January 2008 through June 2022, 1744 patients with suspected or diagnosed hematological neoplasms (including MDS/AML) who had a bone marrow evaluation and concurrent conventional karyotype were identified. Karyotyping was successfully performed on 1167 (67%) of 1744 patients. In total, 914 (54%) with an adequate karyotypic analysis carried out a diagnosis of myelodysplastic syndrome. Among the cases, 9,7% were classified as complex karyotype. Del(5q)/-5 was identified in 52% of patients with complex karyotype, followed by chromosome 11 and chromosome 7 as well as chromosome 17 abnormalities, accounting for 38%, 23% and 23%, respectively. Besides, complex karyotype patients with translocations and derivation involvements, accounted for 28% and 14%, respectively. It is likely that pathogenetic mechanisms in del(5q) may involve hemizygous mutations or haploinsufficiency and be modified by additional somatic lesions affecting genes on other chromosomes. This report shows that the presence of deletion 5q may be the first step to the development of complex karyotype and is a determinant key of the genetic and genomic complexity and clonal hierarchy in MDS with 5q abnormalities.

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HOW IMPORTANT IS THROMBOCYTOSIS FOR PROGNOSIS OF MDS WITH 3Q21Q26 SYNDROME?

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The structural changes involving the long arm of chromosome 3 at bands 3q21 and 3q26.2 in the form of inversion are named paracentric inversion inv(3)(q21q26.2) and in myeloid neoplasms have long been recognized, but are rare. The 3q21q26 syndrome usually occurs in a high-risk myelodysplastic syndrome (MDS) or the setting of acute myeloid leukemia (AML) and is most commonly reported as inv(3)(q21q26.2). Myeloid neoplasms with inv(3) are rare disorders with an incidence of 1% in MDS and AML. Thus, this report aims to show a patient with MDS and high platelets count who presented inv(3)(q21q26.2). A 72-year-old woman looked for medical attention due to fatigue and weakness. The patient reported a history of smoking for 41 years and denied any exposure to toxic agents. At physical examination, only pale was detected. A complete blood count revealed hemoglobin 7g/dL, MCV = 94 fL, leukocytes 5,600/mm3, neutrophils 2,242/mm3 and thrombocytosis with a platelet count of 514,000/mm3. Bone marrow aspirate showed dyserythropoiesis in 30% of cells and 6,5% blasts. The bone marrow cytogenetic analysis showed 46,XX,inv(3)(q21q26.2)[16]/46,XX[4]. The diagnosis of MDS with excess blasts - 1 was established according to the 2016 World Health Organization classification and International Prognostic Scoring System was very high. While waiting for beginning treatment, the patient died of respiratory failure due to COVID-19. Myelodysplastic syndrome with inv(3)(q21q26.2) is a rare aggressive disorder that occurs in less than 1% of all MDS cases and has been associated with a poor outcome: chemoresistance, high risk of leukemic transformation and short survival. Our case showed thrombocytosis with a platelet count of 514,000/mm3. The incidence of thrombocytosis in MDS has been reported in 8% of cases with platelets $> 400 \times 109$/L. The major report which evaluated thrombocytosis in MDS studied 2,042 cases, detecting high platelets count in 5% of cases (102/2,042). It appears that thrombocytosis does not adequately capture the aggressive nature of inv(3)(q21q26.2) in MDS but still plays an important role in the pathogenesis of this heterogeneous and dynamic disease. Our patient reported herein showed dyserythropoiesis in 30% of cells and 6,5% blasts, but nothing was detected regarding megakaryocytic lineage. Our patient died very soon after diagnosis due to viral infection. Thrombocytosis is an unusual clinical feature in MDS associated with inv(3)(q21q26.2) and the unfavorable prognosis of inv(3) is independent of thrombocytosis.

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CASO CLÍNICO DE SMD RELACIONADA A QUIMIOTERAPIA PRÉVIA COM INDEPENDÊNCIA TRANSFUSIONAL APÓS TERAPIA DE SUPORTE ASSOCIADA A ELTROMBOPAGUE OLAMINA

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Objetivo: Relatar um caso de SMD após tratamento quimioterápico, conforme previsto na atual classificação OMS, com alterações no cariótipo e remissão dos clones linfoides, surgimento de citopenias, tratamento e recuperação com independência transfusional. **ECLS**, 69, F, natural de SP, admitida em nosso serviço em Janeiro de 2019, com perda ponderal maio que 10Kg, febre e sudorese noturna, apresentou o perfil imuno histoquímico associado aos achados morfológicos compatível com o diagnóstico de DLGCB: CD20+;CD3 -; KI67+, BCL-2+,CD5+,PAX5+,CD15-;CD3-, CD10-,MUM1+, perfil de células ativadas (CD5+) EC IV B (Infiltração medular) e múltiplas linfonodomegalias supra e infra-abdominais, cariótipo 46,XX[20]. Iniciou-se o 1° tratamento RCHOP por 6 ciclos em 22/05/19 e o 6°ciclo em 16/09/19. Após término do tratamento, foi feito PETSCAN (31/01/20) que demonstrou manutenção de doença em atividade e nova biopsia ganglionar, revelou-se a presença de Linfoma Linfocítico de Pequenas Células B neste momento realizou-se também o estudo citogenético o qual revelou 46,XX[20]. Como paciente não possuía comorbidades dignas de nota e protocolo disponível era baseado em quimioimunoterapia, a paciente recebeu 5 ciclos do protocolo de quimioterapia FCR, o 1°ciclo de FCR foi realizado em 18/02/20 e 5°ciclo de FCR em 06/07/20. A paciente não pôde receber o 6°ciclo deste protocolo por ter evoluído com neutropenia e plaquetopenia Grau IV. Após fim do tratamento, paciente mantinha-se em resposta completa e assintomática em relação ao Linfoma Linfocítico de Pequenas Células B, porém, a pancitopenia se tornou prolongada. Paciente seguiu acompanhada em ambulatório, foram realizadas investigações medulares, cariótipo normal, exames laboratoriais, transfusões de plaquetas e hemácias e início ao tratamento de suporte com alfaepoetina e filgrastima, semanalmente, resultando na melhora dos índices de anemia e da neutropenia. Realizou-se PETSCAN (20/10/21): alterações osteodegenerativas na coluna vertebral, mas não observadas áreas de aumento anormal do metabolismo que possam sugerir doença linfoproliferativa em atividade. Como paciente mantinha citopenias, principalmente neutropenia, foi iniciada terapia com eltrombopague olamina) na dose de 50mg como melhora das citopenias e foi possível atingir a independência transfusional. Maio de 2022 realizou-se novo carío-tipo que revelou alteração clonal em 25% das metáfases analisadas: 46,XX,der(5)del(5)(q31)t(5;7)(q31;q22)[5]/46,XX[15]. **Conclusão:** A SMD após agentes alquilantes e análogos da purina é uma situação muito conhecida em amplamente descrita na literatura médica. Nesta descrição de caso clínico foi possível verificar essa complicação após constarmos a presença de dois clones de neoplasia linfoproliferatia, apesar de terem tido excelente quimiossensibilidade, foram capazes de ocasiona danos ao DNA e alterações citogenéticas típicas para SMD. Agonistas da trombopoietina constituem uma classe de fármacos já com sabida resposta satisfatótia a condições autoimunes, tais como a púrpura trombocitopênica idiopática e a para anemia aplásica em pacientes não elegíveis ao TMO alogênico. Neste caso específico, a paciente chegou a apresentar neutropenia grave e plaquetopenia severa e, hoje, já está independente do ponto de vista transfusional apesar de não ter tido resposta hematológica completa. Em relação ao cariótipo sugere-se repetir o exame oportunamente para acompanhar remissão do clone ou surgimento de novos clones e melhor direcionamento da abordagem terapêutica.

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"REAL-WORLD" RESULTS OF HYPOMETHYLANT THERAPY IN MYELODYSPLASTIC SYNDROME, CHRONIC MYELOMONOCYTIC LEUKEMIA AND OLIGOBLASTIC ACUTE MYELOID LEUKEMIA

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Objectives: Myelodysplastic Syndrome (MDS) represents a heterogeneous group of myeloid neoplasms, resulting in progressive bone marrow failure and cytopenias. Although the allogeneic hematopoietic stem cell transplantation (HSCT) is the only potential curative treatment, only few patients are candidates. In this regard, hypomethylating agents (HMA)-Azacitidine (AZA) and decitabine (DEC) - appears as a standard treatment for higher-risk MDS, in addition to being considered in oligoblastic acute myeloid leukemia (AML) and chronic myelomonocytic leukemia (CMML). Although AZA improved the overall survival (OS) in clinical trials, results in real-world are discordant. This study aims to evaluate the clinical characteristics and outcomes of MDS patients treated with HMA in an academic hospital. **Material and methods:** Retrospective cohort, over 18 years of age, diagnosed with MDS, oligoblastic AML and CMML, *de novo* or secondary, treated with HMA and followed up at the cytopenias outpatient clinic at HCFMUSP from 2010 to June 2021. Data were collected from medical records and stored in REDcap. IWG 2006 criteria were used for response assessment. Kaplan-Meier curves were used for survival graphs, and Cox model regression for uni and multivariate analysis. **Results:** 70 patients, 60 (85%) treated with AZA and 10 (15%) with DEC. Median age at diagnosis was 60.9 years (IQR 48.7 – 68.3), 61.4% male. In relation to diagnoses, 28 had *de novo* MDS (32.9% with excess of blasts; 4.3% with multilineage dysplasia; 2.9% with ring sideroblasts); 7 had AML (10%); 24 secondary myeloid neoplasm (21.4% therapy related; 7.1% with germline/ Fanconi predisposition; 5.7% after acquired aplastic anemia). The median score of IPSS and IPSS-R was respectively 1.5 and 6.0 (high risk). Before treatment 35.4% of patients had poor or very-poor karyotype. Response evaluation was assessed in 51 patients (72.8%) at the end of fourth cycle. The overall response rate (ORR) was 66.6%, including complete, partial and marrow responses, besides hematological improvement. Twelve patients (17%) undergone HSTC. The median OS, since starting HMA, was 11.5 months (IQR 8.1 – 13.8 95% CI), with median follow-up of 15.9. In univariate analysis, variables associated with worse OS were late initiation of HMA (HR 2.39 95% CI 1.18 – 4.84, p =0.015), age (HR 1.03 95% CI 1.01 – 1.05, p