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Introduction: Chronic myeloid leukemia (CML) is a myeloproliferative disorder effectively managed with tyrosine kinase inhibitors (TKIs) like imatinib. However, drug resistance and suboptimal responses remain challenges. Polymorphisms in drug transporter genes, such as ABCB1 and ABCG2, can influence imatinib plasma concentrations and treatment outcomes. **Objectives:** The primary research question was: "Is there an association between polymorphisms in the ABCB1 and ABCG2 genes and imatinib plasma concentration in patients with chronic myeloid leukemia?" **Material and methods:** We searched in Medline, Embase, and Web of Science databases for studies that evaluated the association between ABCB1 and ABCG2 polymorphisms and imatinib plasma concentrations in CML patients. Treatment effects were quantified using the mean difference (MD) with associated 95% confidence intervals (CIs). **Results:** Six studies were included with 654 heterozygous patients, 416 variants, and 470 wild-type. The follow-up ranged from 24 to 83 months. A significant increase in imatinib trough concentration (Ctrough) was observed in patients with the ABCB1 c.3435C>T TT genotype compared to the CC genotype (MD 207.54, 95% CI 101.46-313.62, $p = 0.051$). Additionally, patients with the ABCB1 c.2677G>T GG genotype exhibited significantly higher Ctrough levels compared to both GT (MD 432.52, 95% CI 241.24-623.79, $p = 0.006$) and TT genotypes (MD 396.96, 95% CI 190.12-603.79, $p < 0.001$). For the ABCB1c.1236C>T polymorphism, patients with the TT genotype had significantly lower Ctrough levels compared to TC genotypes (MD -350.50, 95% CI -559.51, -141.50, $p = 0.059$). No significant association was found between the ABCG2 c.412C>A polymorphism and imatinib Ctrough. **Discussion and conclusion:** Genetic polymorphisms of ABCB1 drug transporter proteins play an important role in the serum concentration of imatinib, since some mutations such as variant c.3435C, wild type c.2677G and variant c.1236C showed significant increase Ctrough level when compared to other variants. Mutations of the ABCG2 transporter did not show statistically significant differences. Further studies could be performed to evaluate the impact of implementation of genetic testing on clinical practice.

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IMPORTÂNCIA DO DIAGNÓSTICO INTEGRADO NA DETECÇÃO DE CRISE BLÁSTICA LINFOIDE AO DIAGNÓSTICO DE LEUCEMIA MIELOIDE CRÔNICA

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Introdução: Demonstrar a importância do diagnóstico integrado no diagnóstico de leucemia mieloide crônica no diagnóstico de crise blástica linfoide. **Descrição do caso:** Paciente do sexo feminino, 37 anos, previamente hígida, com relato de astenia, iniciado há um mês, com piora progressiva. Associado ao quadro apresentou síncope sem causa definida. Evoluiu com dor em arco costal direito, o que fez procurar atendimento de saúde. Negava sintomas constitucionais. Apresentava baço palpável a 4 cm do RCE. Durante a avaliação, foi evidenciada leucocitose (leucócitos totais:181.970/mm^3) 50% neutrófilos, 2% monócitos, 1% eosinófilos, 1% de basófilos, 4% promielócitos, 10% mielócitos, 10% metamielócitos, 1% de blasto e 10% linfócitos. Hb 11,2 g/dL, plaquetas 180.000. O mielograma foi sugestivo de LMC em fase crônica, com 3% de blastos; RT-PCR qualitativo para BCR::ABL1 positivo para o transcrito b2a2 (p210), cariótipo 46 XX, t(9;22)(q34;q11). A biópsia de medula óssea, foi hipercelular (>95%), com presença de megacariócitos hipolobulados e áreas com predomínio da série granulocítica com retardo maturativo (padrão fase crônica em 70% da amostra) e outras com proliferação difusa de células imaturas, em 30% da amostra, sugestiva de linhagem linfoide no HE. Padrão de fibrose reticulínica grau 2. A imunohistoquímica foi positiva para CD20, CD79A, PAX-5, CD3, CD5, CD10, CD34 (em cerca de 10% dos precursores imaturos). A citometria de fluxo mostrou a presença de 1,18% de blastos linfoides (CD34+ / CD19+ / nTdT+ / CD66c parcial (42%) / CD10+ / CD22 parcial (54%) / CD9 +) e 0,12% de blastos mieloides, confirmando o diagnóstico de crise blástica linfoide B. Nas tomografias computadorizadas de tórax e abdome foram visualizados esplenomegalia de 15 cm, lesões líticas em corpos vertebrais, sacro e bacia, evidenciados também no PET-CT. A paciente foi submetida a tratamento com Imatinibe associado ao protocolo GRAAPh, com retorno para fase crônica e resposta hematológica completa, sem atingir resposta molecular maior e posteriormente transplante de células-tronco hematopoéticas (TCTH) alogênico. A paciente evoluiu a óbito por choque séptico durante o TCTH. Discussão: o diagnóstico da LMC fase blástica ocorre em menos de 5% dos casos, com maior prevalência da crise blástica mieloide. A WHO 2022 atualmente classifica como crise blástica linfoide os casos com presença de focos de blastos extramedulares ou a presença de linfoblastos, (sem nenhum valor de corte) no sangue periférico ou na medula óssea. O estudo imunohistoquímico na crise blástica linfoide geralmente mostra positividade dos marcadores TdT e CD34 em precursores linfoide, além de marcadores Pan-B como PAX-5 e CD79a nos casos de crise blástica linfoide. Muitas vezes o diagnóstico diferencial entre crise blástica linfoide e LLA Ph+ é difícil, e exige a combinação entre dados clínicos, imunofenotípicos e moleculares, sendo o transcrito p190 mais comum na LLA Ph+. **Conclusão:** Ressaltamos a importância do

diagnóstico integrado, neste caso onde o hemograma e mielograma foram sugestivos de fase crônica e a biópsia de medula óssea e a citometria de fluxo detectaram a presença de linfoblastos, possibilitando diagnóstico de crise blástica linfoide.

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INFLAMMATORY INDICES AS INDICATORS OF IMMUNE ACTIVATION AND THROMBOTIC RISK IN PHILADELPHIA-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS

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Introduction: Philadelphia-negative myeloproliferative neoplasms (MPNs) are hematopoietic disorders characterized by clonal proliferation of myeloid cells, chronic inflammation, and an increased risk of thrombotic and hemorrhagic events. Hemogram-derived indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) have been investigated as accessible, non-invasive tools to assess the inflammatory status and thrombotic risk stratification in various diseases, including MPNs. However, clinical data supporting their application in this context remain limited. **Objectives:** To evaluate the inflammatory indices NLR, PLR, and SII in patients with MPNs compared to healthy controls, and to discuss their relevance as potential biomarkers of systemic inflammation and immune activation in these patients. **Material and methods:** Retrospective data from 16 patients with MPNs and 16 healthy individuals were analyzed. Inflammatory indices were calculated using absolute counts of neutrophils, lymphocytes, and platelets. NLR, PLR, and SII values were compared between groups, with emphasis on patients presenting the most significant alterations. This study was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES), Finance Code 001. **Results:** MPN patients showed significantly higher inflammatory indices compared to healthy controls. NLR values above 2.0 ($p = 0.0088$) and PLR values above 200 ($p = 0.0136$) indicate marked immune activation, a characteristic feature in these patients. Although the SII—which integrates platelet and neutrophil counts relative to lymphocyte count—was also elevated, it showed greater inter-individual variability ($p = 0.0014$). The integrated interpretation of these indices reinforces the presence of systemic inflammation and a potential increased thrombotic risk in MPN patients. **Discussion and conclusion:** NLR, PLR, and SII have emerged as predictors of adverse outcomes in malignancies and cardiovascular diseases. In the context of Philadelphia-negative myeloproliferative neoplasms (MPNs), chronic inflammation plays a central role in disease pathogenesis and contributes to endothelial activation, neutrophil extracellular trap (NET) release, and other hematologic alterations that promote thrombosis. Evaluating these indices, which are easily derived from routine complete blood counts, offers a practical, low-cost approach with promising clinical utility. Despite being still underutilized, these markers may assist in the early identification of patients at increased thromboinflammatory risk, enabling the timely implementation of antithrombotic prophylaxis. Taken together, the significant elevation of NLR, PLR, and SII in MPN patients supports their potential use as complementary biomarkers for assessing systemic inflammation and stratifying thrombotic risk in this chronically inflamed population. However, further large-scale studies are warranted to validate their applicability and support their incorporation into clinical decision-making processes.

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