

PREVALENCE OF RENAL DYSFUNCTION IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA USING FIRST AND SECOND-GENERATION TYROSINE KINASE INHIBITORS

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The use of tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of chronic myeloid leukemia (CML), making it possible for patients to have a life expectancy similar to that of the healthy population. To improve treatment adherence and effectiveness, it is necessary to understand the side effects that the medications may cause. On the other hand, the importance of TKI discontinuation studies are strengthened by recognition of long term adverse events. The primary objective of this study is to assess the prevalence of renal insufficiency in a cohort of CML patients who use first and second-generation tyrosine kinase inhibitors and compare this prevalence between the two generations of the medication. The secondary objective is to identify risk factors for the development of renal alterations secondary to the use of TKIs. Methods: this is an observational, cross-sectional, and analytical clinical study, with a sample consisting of 160 CML patients at the outpatient clinic of a reference hospital in Brazil between October 2000 and January 2023. Clinical and laboratory data available since the start of hospital follow-up were analyzed from the medical records of these patients. Categorical variables were expressed as counts and percentages, and compared using chi-square tests. The Mann-Whitney test was applied for continuous variables. Logistic regression was used for identifying risk factors for renal dysfunction. P-values less than 0.05 were considered statistically significant. Data were collected and tabulated in Microsoft Excel® spreadsheets and analyzed using the Statistical Package for the Social Sciences - SPSS® software (IBM® SPSS® Statistics v. 25.0, SPSS Inc, Chicago, USA). **Results:** The univariate analyses showed a significant relationship between the presence of renal dysfunction and the use of Imatinib ($p = 0.0026$), advanced age ($p = 0.00001$), and presence of comorbidities ($p = 0.001$), particularly systemic arterial hypertension (SAH) ($p = 0.0001$). With the multivariate analysis, independent variables for renal dysfunction found were, advanced age ($p = 0.0023$; OR: 2.08; CI: 1.30-3.32), having SAH ($p = 0.0142$; OR: 1.91; CI: 1.14 – 3.20), and the use of Imatinib ($p = 0.0131$; OR: 1.89; CI: 1.14 – 3.14). **Conclusion:** The study findings suggest that the use of Imatinib therapy in patients with chronic myeloid leukemia may be associated with a reduction in glomerular filtration rate and an increase in the occurrence of chronic kidney disease in this population in the long term, especially when combined with other risk factors such as advanced age and the presence of comorbidities, particularly SAH.

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CASE REPORT: CML PROGRESSION TO AML-MR WITH CLONAL CHROMOSOMAL ABNORMALITIES

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Introduction: The advancement of chronic myeloid leukemia (CML) treatment through tyrosine kinase inhibitors (TKIs) has brought about a revolutionary transformation in patient outcomes, clinical responses, and survival rates. Nevertheless, specific patient subsets exhibit inferior responses to therapy and poor prognosis. Moreover, a small fraction of patients might develop clonal chromosomal anomalies in Philadelphia-negative (Ph-) cells, referred to as CCA/Ph-, which the European Leukemia Net (ELN) designates as having an adverse prognosis. In this study, we present a unique case of a CML patient who underwent CCA/Ph- evolution. **Case report:** GSB, a 78-year-old male, received a CML diagnosis in 2019 at 74 years old, with an intermediate Sokal risk classification. At diagnosis, 100% of cells were Ph+ (Philadelphia chromosome positive), and p210 BCR-ABL was detected. Due to severe grade 3 skin lesions caused by Imatinib, the patient was switched to Dasatinib in August 2019, exhibiting good tolerance. In December 2021, pleural effusion occurred, accompanied by clinical and radiological deterioration, leading to furosemide treatment in May 2022. Dasatinib was temporarily suspended in November 2022, resulting in progressive clinical improvement. By December, the dose was adjusted to 80 mg/day, maintaining a major molecular response (BCR-ABL1: 0.00375, International Scale). In June 2023, the patient presented with acute malaise, nausea, and diarrhea. Notably, a complete blood count revealed substantial bicytopenia (anemia and thrombocytopenia), prompting the suspension of Dasatinib. A bone marrow evaluation in August 2023 unveiled myeloid blast transformation, with BCR-ABL1 p210 remaining nearly undetectable (0.002%). Immunophenotyping disclosed that 10.2% of myeloblasts were positive for CD4, CD13, CD33, CD34, CD38, CD45, CD117, HLA-DR, and cMPO, while being negative for cCD3, CD7, CD10, CD11b, CD14, CD16, CD19, CD56, CD64, cCD79a, and CD123. Moreover, 59.1% of viable cells were categorized as monocytes/monoblasts and positive for CD4, CD11b, CD13, CD14 (partial, 88.7%), CD33, CD34, CD38, CD45, CD56 (partial, 38.0%), CD64, HLA-DR, cMPO and negative for cCD3, CD7, CD10, CD16, CD19, cCD79a, CD117, CD123. Cytogenetic analysis exhibited a monosomy of chromosome 7 (45, XY, -7[20]) in all metaphases. **Discussion and conclusions:** In this context, we portray a case of a 74-year-old patient who developed AML, myelodysplasia-related (AML-MR) after four years of a major molecular response to second line TKI treatment. The earliest documented instance of a patient developing monosomy 7, following 12 months of imatinib therapy, with hypoplastic bone marrow and dysplastic features, dates to 2002. Among CML patients treated with TKIs, around 25% with CCA/Ph- exhibit chromosome 7 abnormalities (-7/del(7q)) and derive the greatest benefits from second line TKIs. Drawing from prior descriptions, as well as