LETTER TO THE EDITOR

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Successful Management of Ibrutinib-Induced Thrombocytopenia in a Patient with Chronic Lymphocytic Leukemia: No Interruption, Only Reduction

Kronik Lenfositik Lösemili Bir Hastada İbrutinibe Bağlı Trombositopeninin Başarılı Yönetimi: İlacı Kesme, Doz Azalt

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To The Editor,

Ibrutinib, an irreversible inhibitor of Bruton's tyrosine kinase, was approved for treating chronic lymphocytic leukemia (CLL). Its utilization is associated with an increased risk of transient thrombocytopenia [1]. Studies have reported that grade 3 to 4 thrombocytopenia induced by ibrutinib occurs in 2% to 17% of patients undergoing treatment [2].

Lipsky et al. [3] found that a significant number of patients exhibited a slight decline in platelet (PLT) counts by day 2 and notable elevation in PLT counts several days later with ibrutinib. In real-world clinical settings, the administration of ibrutinib has demonstrated an improvement in PLT counts among CLL patients with pre-existing thrombocytopenia [2,4].

Herein we present a patient with CLL who experienced grade 4 thrombocytopenia with ibrutinib treatment and our management of the case by decreasing the dose of ibrutinib.

An 85-year-old man showed lymphocytosis compatible with CLL in flow cytometric analysis ($CD5^+$, $CD19^+$, $CD20^+$, $CD23^+$) in 2015. He was reassessed in October 2021 when B symptoms appeared while being followed without treatment. There was diffuse lymphadenomegaly; however, the liver and spleen sizes were normal. In laboratory tests, the hemoglobin level was 10.4 g/dL; leukocyte, lymphocyte, and PLT counts were $102.8x10^9$/L, $87x10^9$/L, and $72x10^9$/L, respectively. Lactate dehydrogenase, C-reactive protein, and hematinic parameters were found to be within normal reference ranges. Peripheral blood fluorescence in situ hybridization examination was negative for del 17p and trisomy 12, 44% positive for del 11q, and 24% positive for del13q. On October 13, 2021, ibrutinib (140 mg/day) treatment was started. To manage the side effects, it was planned to increase the dose to a daily dose of 420 mg over time.

On the 9^{th} and 19^{th} days of treatment, the PLT count had decreased to $48x10^9$/L and $16x10^9$/L, respectively, as confirmed by peripheral blood smear. On the 19^{th} day, ibrutinib was not interrupted and the dose was revised to 140 mg every other day. Supportive therapy was not given because of the lack of symptoms. One week after the dose revision, the PLT count increased to over $50x10^9$/L and remained within the range of $50\text{-}100x10^9$/L for 10 weeks. By January 2022, it surpassed $100x10^9$/L, leading to an elevation of the ibrutinib dose to 140 mg/day. After 4 months, with the PLT count exceeding $150x10^9$/L, the dose was further escalated to 280 mg/day.

Figure 1 illustrates how the patient's lymphocyte and PLT counts changed throughout the course of treatment. At the time of writing, in August 2023, the PLT count was $146x10^9$/L and the lymphocyte count was $3.9x10^9$/L under ibrutinib administration of 280 mg/day.

Typically, ibrutinib-related hematotoxicity manifests within the initial months of therapy, but its impact tends to diminish over time [4,5]. Although dose reduction has been implemented in response to hematological toxicities, there is currently no conclusive evidence regarding the effectiveness of this strategy [6].

The reason behind the temporary decrease in PLT counts observed in patients undergoing ibrutinib treatment is still not fully understood. It appears to primarily result from the inhibition of early-stage megakaryopoiesis. Further research is required to investigate the factors contributing to the PLT recovery observed in response to ibrutinib [7].

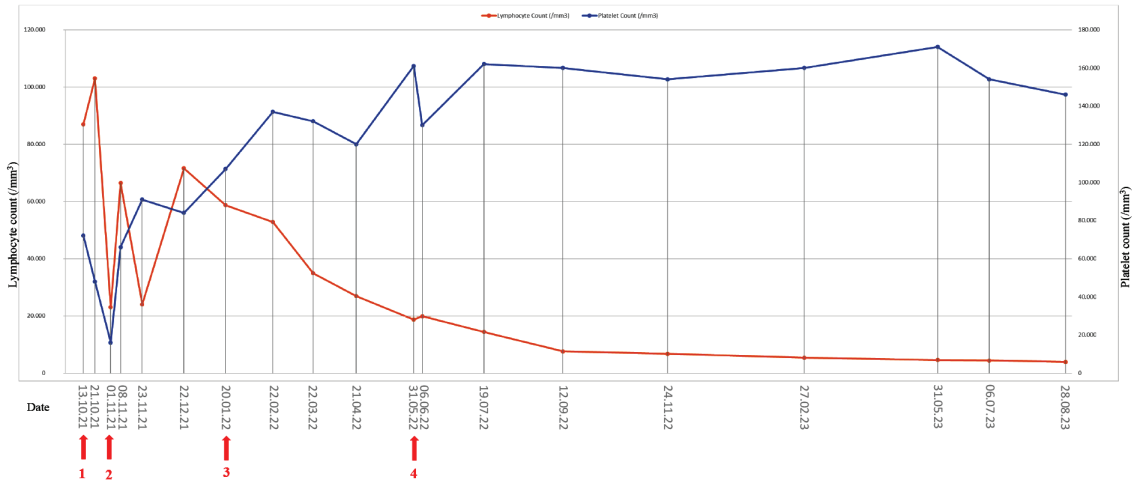

Figure 1. Changes in platelet and lymphocyte counts with ibrutinib therapy. Point 1: Ibrutinib therapy was initiated at 140 mg/day. Point 2: The dose was reduced to 140 mg every other day. Point 3: The dose was increased again to 140 mg/day. Point 4: The dose was increased to 280 mg/day.

Keywords: B-cell neoplasms, Chronic lymphocytic leukemia, Ibrutinib, Megakaryocytes, Thrombocytopenia

Anahtar Sözcükler: B-hücreli neoplaziler, Kronik lenfositik lösemi, İbrutinib, Megakaryositler, Trombositopeni

Ethics

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Surgical and Medical Practices: M.N.; Concept: M.N.; Design: M.N.; Data Collection or Processing: S.E.; Analysis or Interpretation: S.E.; Literature Search: S.E.; Writing: S.E.

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