Letters to the Editor

Turk J Hematol

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

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To the Editor,

Ibrutinib, an irreversible inhibitor of Bruton’s tyrosine kinase, was approved for treating chronic lymphocytic leukemia (CLL). Utilization of it 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 the treatment [2].

Lipsky et al. 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 [3]. 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 by decreasing the dose of ibrutinib.

An 85-year-old male showed lymphocytosis which were compatible with CLL in the 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, hemoglobin level was 10.4g/dL; leukocyte, lymphocyte and PLT count were 102.8x10^9/L, 87x10^9/L, and 72x10^9/L respectively. Lactate dehydrogenase, C reactive protein and hematinic parameters were found within normal reference ranges. Peripheral blood FISH examination revealed del 17p and trisomy 12 negative, del 11q 44%, and del13q 24% positive. On October 13, 2021, ibrutinib (140 mg/day) treatment was started. To manage side effects, it was planned to increase the dose to a daily dose of 420 mg in time.

On the 9th and 19th days of the treatment, the PLT count decreased to 48 and 16x10^9/L, respectively (confirmed by a peripheral blood smear). On 19th day, ibrutinib was not interrupted, and the dose was revised to 140 mg every other day. Supportive therapy was not given because of no symptoms. One week after the dose revision, the PLT counts increased to over 50x10^9/L and remained within 50-100x10^9/L for ten weeks. By January 2022, it surpassed 100x10^9/L, leading to an elevation of the ibrutinib dose to 140 mg/day. After four 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 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 280 mg/day ibrutinib.

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 hematologic 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].

Keywords: B cell neoplasms, chronic lymphocytic leukemia, ibrutinib, megakaryocytes, thrombocytopenia

Anahtar Sözcükler: B hücreli neoplaziler, ibrutinib, kronik lenfositik lösemi, megakaryositler, trombositopeni

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References

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