LETTER TO THE EDITOR

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Ibrutinib-Associated Leukocytoclastic Vasculitis in a Patient with Chronic Lymphocytic Leukemia

Kronik Lenfositik Lösemi Tanılı Hastada Gelişen İbrutinib ile İlişkili Lökositoklastik Vaskülit

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To the Editor,

Ibrutinib is a Bruton's tyrosine kinase inhibitor approved for treatment of chronic lymphocytic leukemia (CLL). Leukocytoclastic vasculitis is one of the cutaneous adverse events seen with ibrutinib. Here we report a patient with CLL who developed multiple skin lesions 13 days after the initiation of ibrutinib.

A 63-year-old man, who was diagnosed with CLL in 2012 and treated with fludarabine, cyclophosphamide, and rituximab in 2014, presented with rapid doubling time of absolute lymphocyte count and fatigue after 8 years of observation. He was also diagnosed with prostatic adenocarcinoma and goserelin was administered 1 month ago. He was started on combination therapy with ibrutinib at 420 mg/day and allopurinol at 150 mg/day. On the 13th day after initiation of ibrutinib and allopurinol therapy, the patient developed a painless, non-pruritic, violaceous rash on his extremities and entire trunk. Physical examination revealed multiple violaceous lesions that did not fade with pressing. Treatment with allopurinol and ibrutinib was paused and a skin biopsy performed. An oral corticosteroid was started and then tapered off. The skin biopsy revealed fibrinoid necrosis of the vessel walls in the dermis and leukocytoclasis around those vessels, and the patient was diagnosed with leukocytoclastic vasculitis (Figure 1).

After his rash, which was thought to be due to the allopurinol, was completely resolved, ibrutinib re-challenge was attempted with a dose of 140 mg once daily. However, the rash developed again and resolved after ibrutinib administration was discontinued.

Leukocytoclastic vasculitis is a very rare side effect of ibrutinib treatment. We initially blamed allopurinol for the patient's rash. However, when treatment with ibrutinib alone was re-started, the rash appeared again. Thus, we concluded that the rash was not associated with allopurinol treatment and ibrutinib treatment was stopped.

The most common cutaneous adverse events with ibrutinib treatment are bruising (12%-51%), rash (12%-29%), petechiae (11%-16%), and skin infections (14%-16%). The possible mechanism of ibrutinib-associated skin toxicity is thought to be related to epidermal growth factor inhibition [1,2,3]. In a previous study, two types of skin reactions were described: palpable purpuric, pruritic rashes and non-palpable, petechial eruptions [2]. In our case, the skin rash was painless, non-pruritic, and purpuric with centripetal spread, which differs from the two aforementioned distinct types. Similarly to cases

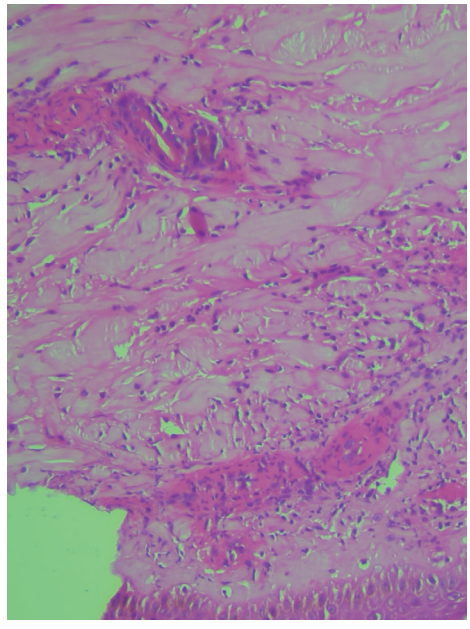

Figure 1. Skin biopsy revealed fibrinoid necrosis of the vessel walls in the dermis and leukocytoclasis around those vessels.

described in the literature, our patient was diagnosed with leukocytoclastic vasculitis by skin biopsy.

In a previous study, leukocytoclastic vasculitis was seen in three of 25 patients. One of those three cases was followed as CLL and the time of onset of the rash was 260 days [4]. In two other cases of patients with CLL treated with ibrutinib, leukocytoclastic vasculitis developed [4,5].

In conclusion, skin side effects are common with ibrutinib treatment, but leukocytoclastic vasculitis is a serious complication of treatment and may require ibrutinib discontinuation. In our case and some of the cases in the literature, ibrutinib treatment had to be discontinued. We wanted to draw attention to leukocytoclastic vasculitis, a serious complication of ibrutinib.

Keywords: Ibrutinib, Leukocytoclastic vasculitis, Chronic lymphocytic leukemia, Ibrutinib-associated vasculitis

Anahtar Sözcükler: İbrutinib, Lökositoklastik vaskülit, Kronik lenfositik lösemi, İbrutinib ilişkili vaskülit

Ethics

Informed Consent: Was received before submission.

Authorship Contributions

Surgical and Medical Practices: A.K., İ.A.; Concept: A.K., P.Ö.K.; Design: A.K., P.Ö.K.; Data Collection or Processing: A.K., U.Ç.; Analysis or Interpretation: A.K., İ.A., U.Ç.; Literature Search: A.K.; Writing: A.K., İ.A., P.Ö.K., U.Ç.

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