

## Acute colitis presenting with hematochezia in a patient with chronic myeloid leukemia during dasatinib therapy

To the Editor,

Dasatinib (DAS) is a second generation tyrosine kinase inhibitor (TKI) that is used in the treatment of chronic myeloid leukemia (CML). DAS is effective against BCR-ABL and Src kinases, and may cause acute colitis and rectal bleeding. Here we present a CML patient who presented with hematochezia under DAS, which resolved shortly after DAS was interrupted.

An 18-year-old male patient was diagnosed with a high Sokal risk chronic-phase CML in January 2000. He first received hydroxyurea (HU) for six years, and then he was admitted to our hematology department and imatinib mesylate (IM) 400 mg/daily was initiated in September 2006. He never achieved major molecular and complete cytogenetic responses with IM, and he did not have a donor for allogeneic hematopoietic stem cell transplantation. DAS 100 mg/day was started in September 2007, six weeks after the initiation of DAS, the patient presented with rectal bleeding and diarrhea. He never had such complaints prior to DAS. A colonoscopic examination was performed in November 2007, which revealed exudation, erosions and multiple ulcers with nodular hyperemic lesions in the entire colon. Histopathological examination showed non-specific colitis. First glucocorticosteroid then oral 5-aminosalicylic acid (5-ASA) was started, and his complaints were diminished but never totally resolved. A BCR-ABL kinase domain mutation analysis was performed which lead to the identification of T315I, and dasatinib was stopped in June 2008. After the interruption of DAS, his rectal bleeding and diarrhea were completely resolved. HU was restarted, but during the follow-up, he was deceased due to myeloid blast crisis in September 2010.

Acute colitis is characterized by the infiltration of lamina propria by inflammatory cells. DAS may cause acute colitis both by decreasing immune tolerance against intestinal microflora by reducing immunoregulatory

cells and inhibiting signal transduction pathways (1). It has been shown that DAS inhibits the proliferation and function of T regulatory lymphocytes (2). The therapeutic activity against Src kinases is responsible for the several "off-target effects" (i.e. pleural effusion) of DAS (3). Gastrointestinal bleeding may occur during DAS, it usually occurs during the advanced phases of CML, and it is aggravated by thrombocytopenia (4). Our case as well as the patient presented by Erkut et al. (1) were in the chronic phase. They both did not experience any bleeding diathesis that can play a role in this clinical picture.

In conclusion, hematochezia and acute colitis may develop during dasatinib, and they usually recover after cessation of the drug. Switching to another TKI is a reasonable strategy in the case of hematochezia due to DAS.

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**Ahmet Emre Eskazan<sup>1</sup>, İbrahim Hatemi<sup>2</sup>, Seniz Öngören Aydın<sup>1</sup>, Muhlis Cem Ar<sup>1</sup>, Teoman Soysal<sup>1</sup>**

<sup>1</sup>Division of Hematology, Department of Internal Medicine, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

<sup>2</sup>Division of Gastroenterology, Department of Internal Medicine, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

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**Address for Correspondence:** Ahmet Emre Eskazan, Department of Hematology, Diyarbakir Training and Research Hospital, Diyarbakir, Turkey  
E-mail: emreeskazan@hotmail.com

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