

# Recurrent Herpes Infection in Two Cases with Chronic Myeloid Leukemia Using Dasatinib

## Dasatinib Kullanan Kronik Myeloid Lösemi Tanılı İki Olguda Tekrarlayan Herpes Enfeksiyonu

Süreyya YİĞİT KAYA

Manisa City Hospital Hematology Department, Manisa

### Öz

Viral enfeksiyonlar, özellikle herpes virüs ve varicella zoster virüs hematolojik malignitesi olan hastalarda en önemli komplikasyonlardır. Dasatinib kullanımı süresince ve sonrasında gelişecek enfeksiyöz komplikasyonların çeşitliliği bilinmemektedir. Burada dasatinib ile tedavi edilen iki kronik myeloid lösemi olgusunda tekrarlayan herpes labialis ve herpes zoster enfeksiyonu sunulmuştur.

**Anahtar Kelimeler:** Dasatinib, Herpes Labialis, Herpes Zoster, Kronik Myeloid Lösemi

### Abstract

Viral infections especially herpes virus and varicella zoster virus are common complications in patients with hematologic malignancies. The spectrum of infectious complications during and after dasatinib therapy are not known. I report here recurrent herpes labialis and herpes zoster infections in two chronic myeloid leukemia cases treated with dasatinib.

**Keywords:** Dasatinib, Herpes Labialis, Herpes Zoster, Chronic Myeloid Leukemia

### Introduction

Chronic myeloid leukemia (CML) is a neoplastic disorder of hematopoietic stem cells caused by a BCR-ABL1 fusion protein that results from t(9;22)(q43;q11). CML therapeutic landscape has changed dramatically with the development of small molecule tyrosine kinase inhibitors (TKIs) (1).

Dasatinib is a potent tyrosine kinase inhibitor used in chronic myeloid leukemia patients resistant or intolerant to prior TKI therapy and in patients with blastic phase CML (2). Unlike imatinib, dasatinib is a potent inhibitor of multiple tyrosine kinases including BCR-ABL kinase, SRC family kinases, c-KIT, platelet-derived growth factor receptor and ephrin A receptor kinase (3). CD8 + and CD4 + T cell proliferation and activation are also inhibited and this is an important risk factor for potentially infectious complications (4). I present here recurrent herpes labialis and herpes zoster infections in two CML cases treated with dasatinib. Informed consent was obtained from the patients on 18-10-2021.

### Case

*Case 1:* A 62-year old female patient was diagnosed with Philadelphia chromosome (Ph) positive-CML in December 2009 and treated with imatinib 400 mg po daily. In May 2016 treatment was switched to

dasatinib due to imatinib induced side effects. She had achieved complete cytogenetic response with dasatinib 100 mg po daily and no side effects were observed except pleural effusion. The patient referred to the outpatient clinic in February 2018 with fever and vesicular lesions on the nose and lip. Valacyclovir 1000 mg three times daily were given for herpes labialis infection. On the 3rd day of follow-up parenterally acyclovir was started due to spreading of vesicular lesions to the buccal area. Lesions were completely resolved at the 7th day of treatment. After 3 months of follow-up the patient admitted to the outpatient clinic again with fever and vesicular lesions on the nose and lip. Valacyclovir orally was given and lesions were completely resolved and the patient is still being followed with prophylactic acyclovir at a dose of 500 mg once daily.

*Case 2:* A 35-year old male patient was diagnosed with Ph positive CML in October 2014 and treated with imatinib 400 mg po daily. The patient lost molecular response after three years of imatinib treatment and treatment was switched to the second line dasatinib 100 mg po daily. He had achieved molecular response with dasatinib and no side effects were observed. In May 2018, he presented to the outpatient clinic with complaints of painful skin rash and blisters on the right shoulder. Valacyclovir orally was given for 7 days with the diagnosis of herpes zoster. The lesions regressed during the follow-up. At the second month of follow-up the patient referred to the outpatient clinic again with the same lesion on the left shoulder. Valacyclovir orally was given, however there was no regression on the 5th day control. Parenterally acyclovir was started after the dermatology and infectious diseases consultations. On the 10<sup>th</sup> day of treatment rash and

Süreyya YİĞİT KAYA ORCID No  
0000-0001-6732-8068

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Adres / Correspondence : Süreyya YİĞİT KAYA  
Manisa City Hospital Hematology Department, Manisa

e-posta / e-mail : sureyyayigitkaya@hotmail.com

pain regressed and the treatment was switched to nilotinib because of dasatinib side effect.

## Discussion

CML is a hematologic disorder associated with a mutual chromosomal translocation between chromosomes 9 and 22 resulting in the formation of the Philadelphia chromosome. This gene fusion codifies a chimeric protein BCR-ABL which is associated with uncontrolled tyrosine kinase ABL activity. The available TKIs for the frontline treatment of CML include imatinib, dasatinib and nilotinib. The most common adverse events observed during dasatinib treatment are cytopenias, fluid retention, pleural effusion, dyspnea, gastrointestinal disorders, skin rash, headache and fatigue (5).

Dasatinib suppresses the function of natural killer cells and T cells by inhibiting SRC-family kinases. Thus, dasatinib may decrease immune tolerance reducing the number of immunoregulatory cells and inhibiting signal transduction pathways.

In the literature review there were a few cases associated with recurrent herpes infection in CML patients using dasatinib. Sunami Y. et al. reported dasatinib related cytomegalovirus colitis in a CML patient (6). García-Muñoz R. et al. reported a CML case with recurrent viral infections such as acute parvovirus B19 infection, reactivation of cytomegalovirus and herpesvirus 6 under dasatinib treatment (7). Also, Rodriguez GH. et al. reported a retrospective analysis of records among 69 patients treated with dasatinib. 35 patients (%51) developed 57 episodes of infection. Compared with the patients who did not developed infection, the patients with infection were significantly more likely to have acute lymphocytic leukemia and received another antineoplastic agent (8).

My patients have been using dasatinib for a long time. Molecular response was obtained in one of the

patients and cytogenetic response was obtained in the other patient. There were no other risk factors for recurrent viral infection. In one of the patients the treatment was switched to nilotinib because of dasatinib side effect.

Physicians should keep in mind the potential immunological mechanisms that may increase the risk of herpes infections and other opportunistic infections in patients using dasatinib. Monitoring the risk of infection is required during the treatment of hematologic malignancies.

**Written consent:** Written consents of the patients were obtained on 18.10.2021.

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