

Letter to the Editor

Rapid Progression after Ibrutinib Discontinuation in a Mantle Cell Lymphoma Patient with Severe COVID-19 Infection

Fehmi Hindilerden¹, İpek Yönel Hindilerden², Reyhan Diz Küçükkaya³

¹Clinic of Hematology, University of Health Sciences, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey

²Department of Internal Medicine, İstanbul University İstanbul School of Medicine, İstanbul, Turkey

³Department of Molecular Biology and Genetics, İstanbul University İstanbul School of Science, İstanbul, Turkey

Address of Correspondence: İpek Yönel-Hindilerden, Department of Internal Medicine, İstanbul University İstanbul School of Medicine, İstanbul, Turkey

ipekyonal@hotmail.com

+90 535 687 59 92

Received: 20 September 2020

Accepted: 12 October 2020

DOI: [10.4274/balkanmedj.galenos.2020.2020.9.106](https://doi.org/10.4274/balkanmedj.galenos.2020.2020.9.106)

Cite this article as: Hindilerden F, Yönel Hindilerden İ, Diz Küçükkaya R. Rapid Progression after Ibrutinib Discontinuation in a Mantle Cell Lymphoma Patient with Severe COVID-19 Infection. *Balkan Med J*

To the Editor,

Lymphoma patients with Coronavirus 2019 (Covid-19) require special consideration because of their deficient immune status and exposure to anti-tumor treatment.

In November 2014, a 78 year-old male was diagnosed with mantle cell lymphoma (MCL) by palatine tonsil biopsy. His previous treatment history included R-CHOP (rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone), BORID (bortezomib, rituximab, and dexamethasone) and R-BAC (rituximab, bendamustine, cytarabine). In September 2017, he presented with stridor due to bilateral tonsillar mass and MCL relapse was diagnosed. Ibrutinib 560 mg/day was started and CR was achieved. In May 2020, he presented with diarrhea and dyspnea. His vital signs were as follows: temperature 38°C, pulse 112/minute and respiratory rate of 22 breaths/minute. His SpO₂ on ambient air was 91%. RT-PCR assay detected presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in the nasopharyngeal swab. Chest computed tomography (CT) showed patchy peripheral ground glass opacities in both lungs, findings consistent with severe Covid-19 pneumonia. Complete blood count (CBC) showed the following: Hgb 11 g/dL, total leukocyte count 1580/mm³, neutrophil 800/mm³, lymphocyte 428/mm³ and platelet 212000/mm³. The following laboratory tests were abnormal: C-reactive protein 5.67 mg/dL (0–0.5), ferritin 660 ug/L (23–336), D-dimer 1.24 mg/L (0–0.5). Hydroxychloroquine, levofloxacin and prophylactic low-molecular-weight heparin were initiated (1). Because of grade 3 neutropenia and fever, ibrutinib was stopped. Six days after discontinuation of ibrutinib, he presented with left orbital swelling and a mass lesion over the left hard palate (Figure 1). His CBC showed hematological recovery. Thus, dexamethasone 8 mg/day for four days and ibrutinib 560 mg/day were restarted. One week later, orbital swelling and the mass lesion over the hard palate mass regressed. Two weeks later, symptoms associated with Covid-19 pneumonia completely regressed. Currently under treatment of ibrutinib, MCL is still in remission and the patient is free of Covid-19 infection.

Interruption of ibrutinib during the course of MCL treatment has not been extensively evaluated. Studies require continuous dosing even after remission has been achieved. Taking into consideration the potential toxicities of continuous therapy, more research is warranted to evaluate shorter durations of therapy, depth of response and planned dose interruptions in responding patients (2). In this patient who had ongoing long-lasting remission with ibrutinib, we had to interrupt ibrutinib because of hematological toxicity at the time of diagnosis of Covid-19 pneumonia. Yet shortly after cessation, disease recurred with mass lesions over the orbita and hard palate. Recently, a study suggested that targeting excessive host inflammation with a bruton kinase inhibitor is a therapeutic strategy in severe Covid-19 (3). Ibrutinib is associated with increased incidence of bleeding and proarrhythmia, which may worsen the outcome in severe Covid-19 (4). Our data support that ibrutinib can be used with careful monitoring in Covid-19.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: No financial disclosure was declared by the authors.

References

1. Klok FA, Kruip MJHA, van der Meer NJM. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020;191:145-7.
2. Stephens DM, Spurgeon SE. Ibrutinib in mantle cell lymphoma patients: glass half full? Evidence and opinion. *Ther Adv Hematol* 2015;6:242-52.
3. Roschewski M, Lionakis MS, Sharman JP, Roswarski J, Goy A, Monticelli MA, et al. Inhibition of Bruton tyrosine kinase in patients with severe COVID-19. *Sci Immunol* 2020;5:eabd0110.doi: 10.1126/sciimmunol.abd0110.
4. Owen C, Berinstein NL, Christofides A, Sehn LH. Review of Bruton tyrosine kinase inhibitors for the treatment of relapsed or refractory mantle cell lymphoma. *Curr Oncol* 2019;26:e233-40.



FIG. 1. The appearance of the lesions after interruption of ibrutinib treatment. Mass lesion over the left orbita (a) and left hard palate (b).