Turk J Hematol 2020;37:207-219

COVID-19, Renin-Angiotensin System, and Hematopoiesis

COVID-19, Renin-Anjiotensin Sistemi ve Hematopoez

Rafiye Çiftçiler, İbrahim C. Haznedaroğlu

Hacettepe University Faculty of Medicine, Department of Hematology, Ankara, Turkey

To the Editor,

We had initially indicated that there is a local hematopoietic bone marrow (BM) renin-angiotensin system (RAS), active in the physiological and pathological hematopoiesis (reviewed by Haznedaroglu and Beyazit [1]). Turkish Journal of Hematology has already published two critical research papers on the impact of the local BM RAS on the pathobiological course of neoplastic hematological disorders [2,3].

Angiotensin-converting enzyme 2 (ACE2), an essential component of the RAS, is also the critical receptor of the SARS-CoV-2 virus, which is the responsible agent of the currently ongoing pandemic COVID-19. COVID-19 affects hematopoiesis [4] besides its well-known pulmonary involvement like other previous SARS viral infections [5]. The receptor binding domain for the spike protein of the SARS-CoV-2/ACE2 seems to be similar to that of the coronavirus strain involved in the 2002-2003 SARS outbreak [6].

Here we would like to point out that the hematopoietic effects of COVID-19/SARS viral infections including lymphopenia, leukoerythroblastosis, and macrophage activation syndrome may be linked to the viral effect on the local RAS [1] in the BM microenvironment. Leukoerythroblastic reactions associated with normocytic anemia, occasional nucleated red blood cells, mild anisocytosis, and rare dacrocytes were observed during the clinical course of COVID-19 infections [4]. Lymphopenia is a critical prognostic biomarker of the severity and hospitalization of the patients with COVID-19 [7]. The imbalance between the ACE/angiotensin II/AT1R pathway and ACE2/angiotensin (1-7)/Mas receptor pathway in the RAS leads to the multi-system inflammation [8]. Likewise, macrophage activation syndrome is an essential integral part of the COVID-19 pathophysiology [9]. Similarly, enhanced expression of ACE in the lymphoma-associated macrophages in the lymph nodes in Hodgkin's disease was previously demonstrated with regard to the local RAS [10].

The interrelationship between COVID-19, RAS, and hematopoiesis is not just an academic concern since the future modulation of the local RAS may be performed with directed RAS modulators, such as soluble ACE2, angiotensin (1-7), TXA127, and MAS receptor agonists. Topical soluble ACE2 has already been suggested as a 'drug-of-hope' for the pharmacobiological management of COVID-19 based on future controlled clinical trials [11].

Keywords: COVID-19, Renin-angiotensin system, Hematopoiesis, SARS-CoV-2

Anahtar Sözcükler: COVID-19, Renin-anjiotensin sistem, Hematopoez, SARS-CoV-2

Authorship Contributions

Data Collection or Processing: İ.C.H.; Analysis or Interpretation: İ.C.H.; Writing: R.Ç.

Conflict of interest statement: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Financial Disclosure: The authors declared that this study received no financial support.

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Address for Correspondence/Yazışma Adresi: Rafiye Çiftçiler, MD, Hacettepe University Faculty of Medicine, Department of Hematology, Ankara, Turkey
Phone : +90 312 305 30 50
E-mail : rafiyesarigul@gmail.com ORCID: orcid.org/0000-0001-5687-8531

Received/Geliş tarihi: April 15, 2020
Accepted/Kabul tarihi: May 11, 2020
DOI: 10.4274/tjh.galenos.2020.2020.0174

Hepatitis B Virus Reactivation under Ibrutinib Treatment in a Patient with Chronic Lymphocytic Leukemia

Kronik Lenfositik Lösemili Bir Hastada İbrutinib Tedavisi Altında Hepatit B Virüsü Reaktivasyonu

Gülşen İskender[1], Dicle İskender[2], Mustafa Ertek[1]

[1]Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Ankara, Turkey
[2]Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Clinic of Hematology and Blood and Marrow Transplantation, Ankara, Turkey

To the Editor,

Immunosuppression in patients with hepatitis B virus (HBV) infection may result in viral reactivation. This risk is higher in patients with present than past HBV infection (hepatitis B surface antigen (HBsAg)-positive vs. HBsAg-negative, anti-HBc positive) and in patients with hematological malignancies and related treatments [1,2]. Ibrutinib is a Bruton's tyrosine kinase inhibitor (TKI) indicated in the treatment of relapsed/refractory chronic lymphocytic leukemia (CLL) [3]. The American Gastroenterological Association Institute categorized patients with past HBV infection treated with TKIs as having a moderate risk for HBV reactivation (HBVr) (1%-10%). There is only a weak recommendation for routine viral prophylaxis for HBVr in that guideline [2], whereas in the ECIL-5 guideline, there is no suggestion about the management of these patients [4]. Here we describe a case of HBVr under ibrutinib monotherapy in a patient with past HBV infection and relapsed/refractory CLL. A 58-year-old man was diagnosed with CLL. His HBV serology was compatible with past infection (Figure 1). According to existing guidelines [1,2], follow-up of liver enzymes, HBV serology, and HBV-DNA every 3 months was planned without antiviral

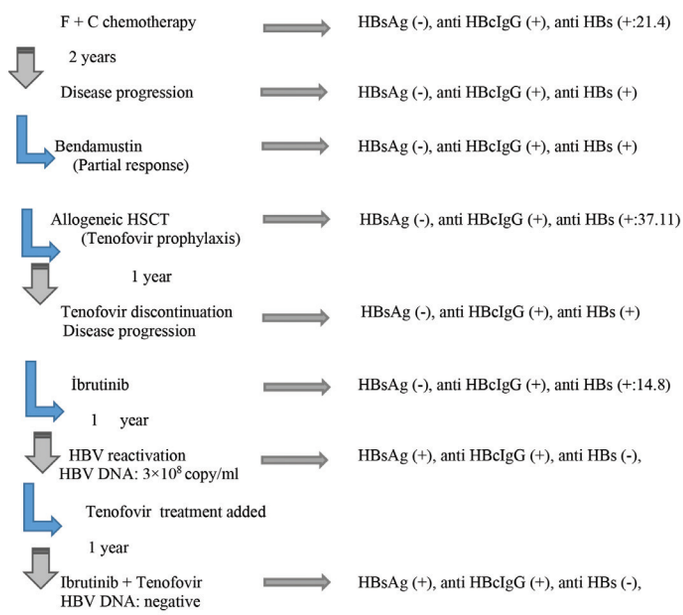

Figure 1. Summarized course of the disease.
HBsAg: Hepatitis B surface antigen.