LETTER TO THE EDITOR / EDİTÖRE MEKTUP

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Acute Viral Hepatitis-B in a COVID-19 Patient with Respiratory Failure

Solunum Yetmezliği Olan Bir COVID-19 Hastasında Akut Viral Hepatit-B

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Dear Editor,

Coronavirus Disease of 2019 (COVID-19) is caused by a novel coronavirus, named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 is typically characterized by the presentation of the symptoms of viral pneumonia such as fever, fatigue, dry cough, anosmia, and headache, which may progress to respiratory failure[1]. It causes systemic disease by inducing changes in circulating lymphocytes and the immune system[2]. In addition to the respiratory symptoms, gastrointestinal symptoms such as vomiting, diarrhea, abdominal pain, and elevated liver enzyme and/or bilirubin levels have been reported in association with COVID-19[3]. The frequency of elevated liver enzymes in hospitalized COVID-19 patients, primarily elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and slightly elevated bilirubin, ranges from 14% to 53%[2]. This elevation may be the result of any liver damage occurring during a disease and its treatment or it may occur due to primary liver diseases[4]. We have reported herein a case of COVID-19 with hepatitis-B (HB) virus (HBV) coinfection presenting as an acute symptom.

A 57 year-old woman with a history of diabetes mellitus, asthma, and coronary artery disease, was admitted applied the to emergency department with complaints of nausea, vomiting, dry cough, and fever for 3-4 days. The patient was febrile (38.2 °C), conscious, and displayed orientation cooperation. Her physical examination revealed the following: Glasgow Coma Scale 15, blood pressure 135/84 mm/Hg, heart rate 107/min, respiratory rate 23/min, and oxygen saturation 88% in room air. She also displayed bilateral rales on respiratory examination. Her thorax tomography revealed widespread infiltration.

The initial blood work showed remarkably elevated liver function. Pertinent laboratory findings are presented in Table 1.

In the emergency department, the nasopharyngeal swab was taken and her COVID-19 polymerase chain reaction test result was found positive. Then, she was hospitalized and subjected to symptomatic treatment for SARS-CoV-2. Detailed examinations of her liver function tests were planned in light of previously negative hepatitis serology and no familial hepatitis history. Apart from her recent dental treatment, she had no history of consuming alcohol, drug abuse, or unprotected sexual intercourse. Her serological tests were negative for human immunodeficiency virus, hepatitis A, and hepatitis C. Further liver examination revealed positive HB surface antigen, positive HB core antibody (Ab) immunoglobulin M, positive HBe Ag, and negative HBe antibody (Ab). Her HB-DNA viral load was 171,400,000 IU/mL, confirming the diagnosis of an acute HBV infection. The liver ultrasound did not show any anomalies but showed an echogenic liver without cirrhosis, common bile duct obstruction, or gallstones.

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In the initial days of hospitalization, a reduction in liver function was observed with symptomatic treatment while the bilirubin levels increased. The relation between liver function tests and bilirubin level is presented in Figure 1.

After the 5th day, the patient's respiratory complaints increased and her oxygen saturation started to decrease to 65% in the room air. At this stage, high doses of steroids and immunoplasma had to be supplemented in the treatment for COVID-19. Meanwhile, tenofovir disoproxil fumarate was started for viral HB. After 4 weeks of follow-up, her respiratory symptoms gradually began to improve and the patient's liver function tests also reached the normal level. As the patient's respiratory symptoms started to improve, the steroid dosage was gradually tapered and then discontinued and the patient was discharged from the hospital. After 15 days of discharge, in her polyclinic follow-up examination, her HB surface antigen became negative and her HB surface Ab value was (21.34 mIU/mL) positive. Four months later, this value reached over 1,000 mIU/mL. Her antiviral treatment was also discontinued after 1 year of the HB surface Ab positive result.

Table 1. Laboratory test results for the case patient

Laboratory examination	Result	Reference range
WBC	8.89 mcL	4-10 mcL
Creatine	1.22 mL/dL	0.51-0.95 mL/dL
AST	1,768 u/L	0-50 u/L
ALT	1,903.7 u/L	0-50 u/L
Total bilirubin	1.08 mg/dL	0.20–1.20 mg/dL
Direct bilirubin	0.46 mg/dL	0-2 mg/dL
C-reactive protein	90.89 mg/L	0-5 mg/L
HBsAg	5,802.79 S/CO	0-0.99 S/CO
Anti HBc IgM	42.64	0-0.99
Anti HBc IgG	3.42	0-0.99
Anti HBs	0 mIU/mL	0-10 mIU/mL
Anti HCV	0.05 S/CO	0-0.99 S/CO
HIV Ag/Ab	0.08 S/CO	0-0.99 S/CO
INR	1.61	0.8-1.20
D-dimer	1,550 ng/mL	0-500 ng/mL

HIV: Human immunodeficiency virus, WBC: White blood cell, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, HbsAg: Hepatitis B surface antigen, HBc IgM: Hepatitis B core immunoglobulin M antibody, HBc IgG: Hepatitis B core immunoglobulin G antibody, HBs: Hepatitis B, HCV: Hepatitis C virus, HIV Ag/Ab: HIV antigen/antibody, INR: International normalized ratio

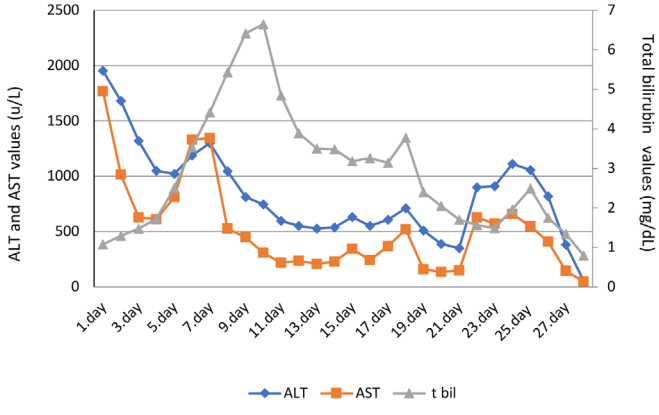

Figure 1. Change chart for the ALT, AST, and bilirubin values
AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

COVID-19 caused a pandemic that affected a wide area across the world. Symptomatic SARS-CoV-2 infections are mostly mild to moderate, and not severe. The most common serious manifestation is pneumonia. Chest radiographs are usually normal in the early stages of this disease. At 10–12 days after the onset of symptoms, lung infiltration may increase and the disease may worsen[5]. Our patient showed a tolerable oxygen saturation with oxygen support on room air when she was first admitted to the hospital. In the following days of follow-up, her respiratory complaints increased in line with the course of COVID-19 and her oxygen saturation level began to decrease, as such, high-dose corticosteroids and immune plasma treatment were initiated as supportive treatment.

Elevated liver enzymes are common in COVID-19, as seen in 18.2% of nonsevere cases and up to 39.4% in severe cases[6]. Liver damage in COVID-19 patients may be attributed to the viral infection as well as drug hepatotoxicity. In addition, immune-mediated inflammation and pneumonia-associated hypoxia may contribute to liver injury. Liver disease including chronic-acute viral hepatitis, non-alcohol fatty liver disease, and alcohol-related liver disease represents a major disease burden globally. Although liver enzyme elevation due to COVID-19 is common, its coincidence with acute viral HB is rare. Such rare cases have been reported earlier, and most of these cases were exacerbations of the underlying viral hepatitis disease. Previously, there have been reports of cases showing serological compatibility with acute viral hepatitis but with generally fulminant unknown hepatitis serology[7,8]. Our patient's HB profile showed no history of hepatitis, suggesting an early acute HB infection[9] (Table 1). Treatment for acute HBV is mainly supportive. HBV infection recover clinically and virologically without antiviral therapy in more than 95% of adults. Only patients with severe acute HB, characterized by coagulopathy, and protracted course or signs of acute liver failure should be treated with nucleoside analogs. Past data support the use of tenofovir disoproxil fumarate, entecavir, or lamivudine for such cases[10]. In the present case, as we opted for immunosuppressive treatment for respiratory failure and because the patient's bilirubin levels tended to increase during this period, we planned oral antiviral treatment to prevent liver failure. In the follow-up of our clinically recovered patient, anti HB seroconversion was detected after treatment.

In conclusion, serological tests should be conducted in each patient showing high liver enzymes and the coexistence of the two diseases simultaneously. Such cases should be managed by considering the progression of each disease and the appropriate treatment options.

Footnotes

Authorship Contributions

Design: S.S.Y., F.K.B., Data Collection or Processing: S.S.Y., F.K.B., Analysis or Interpretation: S.S.Y., F.K.B., Literature Search: S.S.Y., F.K.B., Writing: S.S.Y., F.K.B.

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