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LETTER TO THE EDITOR

# Autoimmune hepatitis triggered by COVID-19: A report of two cases

Recently, in the Liver International, Marabotto et al,[1] reported a patient who developed autoimmune hepatitis (AIH) during coronavirus disease 2019 (COVID-19). Here, we present two patients who developed high aminotransferases during COVID-19 and were ultimately diagnosed with AIH.

The general characteristics and outcome of these patients are summarized in Table 1. COVID-19 was diagnosed by PCR-based test. Serologies for acute and chronic viral hepatitis (anti-HAV IgM, HBsAg, anti-HBc IgM, anti-HCV, anti-EBV IgM and anti-CMV IgM) were all negative. AIH was diagnosed by the presence of positive autoimmune serology and high serum IgG levels. Immunosuppressive therapy was given during active COVID-19 to one patient but was delayed until the COVID-PCR test became negative in the other patient. Both patients showed good response to immunosuppressive therapy at the time of writing this paper.

New-onset or flare of immune-mediated disorders such as Guillain-Barre syndrome, autoimmune haemolytic anaemia and immune thrombocytopenic purpura has been described during or following COVID-19.[2] These reports suggest that COVID-19 can break immunological tolerance and lead to the onset of immune-mediated conditions. Serum levels of TNF-α, IFN-γ, IL-1β, IL-6 and IL-10 are increased in patients with COVID-19.[2] These cytokines have also critical roles in the inflammatory process of AIH. Therefore, it is reasonable to think that COVID-19 can cause new-onset or flare of silent AIH.

Drug-induced liver injury (DILI) may present with laboratory and serological features of AIH. Patient 1 was treated with hydroxychloroquine and favipravir for COVID-19. With the suspicion of DILI, immunosuppressive therapy was discontinued after three months of biochemical remission. He, however shortly displayed signs of biochemical relapse (elevated aminotransferases and IgG levels). After reinstitution of immunosuppression he again entered remission. This outcome strongly suggests that the diagnosis was indeed AIH rather than DILI. Patient 2 developed high aminotransferases levels during COVID-19 without any suspicion of DILI.

There is no evidence-based diagnostic algorithm or treatment recommendation for AIH in active COVID-19 patients.[3,4] Some experts suggest that an AIH diagnosis can be made without liver biopsy during COVID-19 if patients have typical laboratory and serological findings.[5] Our two patients had laboratory features strongly suggestive of AIH and we, therefore did not perform liver biopsies.

In patients with concomitant AIH and COVID-19, immunosuppressive therapy should be given after weighing potential risks and benefits. Patient 1 had mild features of AIH at presentation and therapy was delayed until COVID-19 PCR test became negative. Patient 2 had a clinically more severe form of AIH and was given immunosuppressive therapy which may be considered life-saving in severe AIH.

New-onset liver injury is a commonly observed clinical manifestation of COVID-19. Our two cases along with the report of Marabotto et al highlight that AIH should be considered among different possible diagnoses in subjects who develop elevated aminotransferases during or soon after COVID-19.

**KEYWORDS**

azathioprine, immunosuppression, liver transplantation, SARS-CoV-2, steroid

## CONFLICT OF INTEREST

None.

## AUTHORS' CONTRIBUTIONS

CE, GK and SW interpreted data and prepared manuscript for the final submission.

## DATA AVAILABILITY STATEMENT

All relevant data are presented in the manuscript.

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**TABLE 1** Clinical characteristics of patients diagnosed with AIH during COVID-19

| Patient demographics | Patient-1 | Patient-2 |
|---|---|---|
| Age/Sex | 49/Male | 72/Female |
| COVID-19 symptoms | Fever, cough, fatigue, | Fever, cough, dyspnoea |
| Hospitalization | 4 days | 12 days |
| Medications for COVID-19 | Hydroxychloroquine Favipravir | Hydroxychloroquine Favipravir |
| Oxygen therapy | No | 10 days |
| ALT at COVID-19 | 56 (7-40 IU/L) | 451 |
| Peak ALT | 264 (7-40 IU/L) | 640 |
| Peak total bilirubin | 1.6 (0.3-1.2 mg/dL) | 11.2 |
| IgG | 2260 (610-1560 mg/dL) | 4250 |
| Autoimmune serology | ANA+, 1/80 | SMA+, 1/640 |
| Time from COVID-19 to AIH therapy | 20 days | 2 days |
| Therapy for AIH | Prednisolone, 30 mg/day<br>+Azathioprine, 50 mg/day | Prednisolone, 40 mg/day<br>+Tacrolimus, 4 mg/day |
| ALT after therapy | 104 IU, day 14<br>30 IU, day 32<br>22 IU, day 122 | 356 IU, day 15<br>216 IU, day 30<br>93 IU, day 62 |
| Current therapy | Prednisolone, 10 mg/day<br>+Azathioprine, 50 mg/day | Prednisolone, 10 mg/day<br>+Tacrolimus, 4 mg/day |

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