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Letter to the editor: Exacerbation of autoimmune hepatitis after COVID-19 vaccination

To the editor,

We read with interest the autoimmune hepatitis (AIH) case following COVID-19 vaccination[1] and the comment by Drs. Mungmunpuntipantip and Wiwanitkit.[2] COVID-19 vaccine could also act as a trigger in the disease course of AIH. We report a case of AIH exacerbation following inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac).

The patient is a 57-year-old Asian female without medical history. She developed choluria and acholic stools 2 weeks after the first dose of CoronaVac but did not seek medical advice and received the second dose CoronaVac after 3 weeks. Two days later, she developed generalized pruritus and deep scleral and sublingual icterus with markedly elevated total bilirubin (283.8 μmol/L), alanine aminotransferase (974 U/L), aspartate aminotransferase (819 U/L), alkaline phosphatase (212 U/L), and gamma-glutamyltransferase (238 U/L). She reported no consumption of alcohol or traditional medicine.

Viral serologic tests showed negative hepatitis A/B/C/D/E virus, HIV, cytomegalovirus, Epstein-Barr virus, and herpes simplex virus. Total IgG was slightly elevated (17.44 g/L; normal range, 8.6–17.4 g/L) with positive antinuclear antibodies (1:640, homogeneous pattern), anti–Sjögren syndrome antigen A, anti–major centromere autoantigen B, and weakly positive anti–Sjögren syndrome antigen B. The antimitochondrial, antimitochondrial-M2, anti–smooth muscle, anti–liver-kidney microsomal, anti–liver cytosolic, anti–soluble liver antigen, anti-glycoprotein-210, and anti-SP100 antibodies were all negative.

Contrasted CT and MRI showed no malignancy and biliary lithiasis or dilation. Liver biopsy revealed established fibrosis (Stage 2) and active hepatitis (Grade 2) with moderate to severe interface necroinflammation, severe lobular lymphocytic/lymphoplasmocytic infiltration, hepatic rosette formation, and a dense lymphoid infiltrate (Figure 1A–F). Both her revised original (20 points) and the simplified (7 points) score for AIH suggested a definite diagnosis of AIH. She had excellent responses to treatment (ursodeoxycholic acid and a tapering course of methylprednisolone overlapped with azathioprine) and no relapse during 5-month follow-up (Figure 1G).

Several cases of AIH following COVID-19 vaccine have been reported,[3] but unlike these cases, the presence of Stage-2 fibrosis in our case is against the hypothesis of vaccine-induced AIH onset but suggests vaccine-induced AIH exacerbation. The vaccination unmasks the undiagnosed AIH and triggers the disease

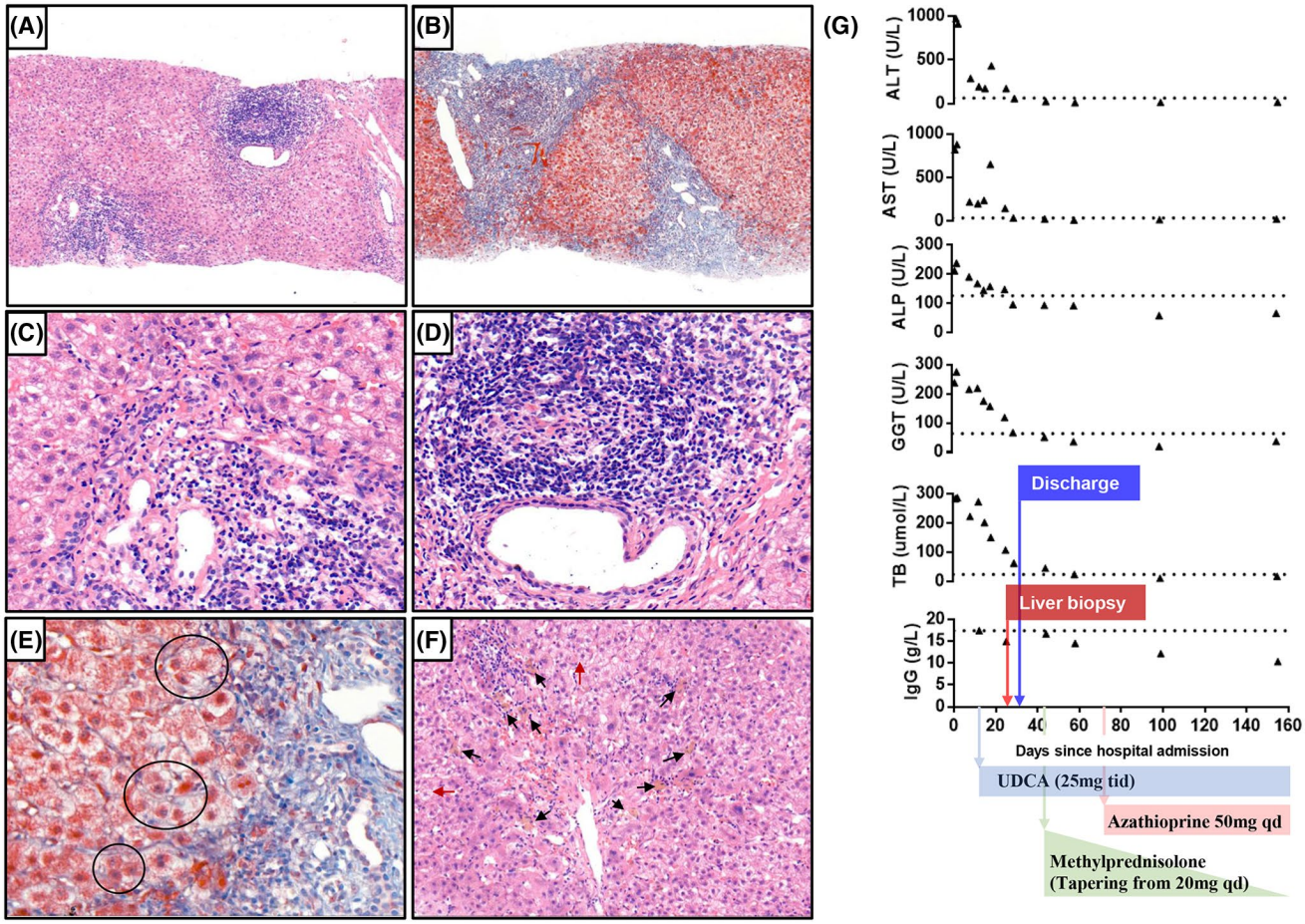

FIGURE 1 Histological findings and evolution of laboratory tests. At low-magnification (×100), hematoxylin and eosin staining shows moderate to severe interface hepatitis with a dense lymphoid infiltrate (A), and Masson staining shows the formation of fibrous septa (B). At high magnification (×400) with hematoxylin and eosin stain, the interface necroinflammation consists primarily of lymphocytes with plasma cells (C); the dense periductal lymphocyte infiltrate (D) and the hepatic rosette formation (black circle) were well observed with Masson stain (E). Feathery degeneration of hepatocyte (red arrow) and hepatic cholestasis (black arrow) were also observed (F) (×200 hematoxylin and eosin stain). (G) Trends of liver function tests, total bilirubin, and total IgG levels over time. Dashed lines are the respective lower limit of the normal range of each test. ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; TB, total bilirubin; UDCA, ursodeoxycholic acid

flare. Although CoronaVac vaccination in patients with autoimmune rheumatic diseases is generally safe,[4] our case suggests the need for data in patients with AIH.

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CONFLICT OF INTEREST

Nothing to report.

AUTHOR CONTRIBUTIONS

Zhujun Cao wrote the draft of the manuscript. Qing Xie and Honglian Gui revised the manuscript. Honglian Gui was involved in the clinical care of the patient. Zhujun Cao, Zike Sheng, Honglian Gui, Haiguang Xin, and Qing Xie were involved in the clinical care of the patient during hospitalization. All authors contributed to and approved the final manuscript.

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Letter to the editor: Autoimmune hepatitis after COVID-19 vaccination: Need for population-based epidemiological study

To the editor,

We have read with interest the study published by Palla et al.[1] regarding a possible link between COVID-19 vaccination and the development of autoimmune hepatitis (AIH).[2,3] We propose the need for population-based studies to gather data on the incidence, severity, and clinical features of COVID-19 vaccination-induced AIH by describing three cases of COVID-19 vaccination-induced AIH from our institution between January and October 2021.

Case 1 involves an 80-year-old woman diagnosed with a liver injury (aspartate aminotransferase 995 U/L, alanine aminotransferase 974 U/L, total bilirubin 3.5 mg/dl), based on her laboratory results 10 days after receiving the second dose of the BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine. The antinuclear antibody test was positive at a titer of 1:40. The serum immunoglobulin G level was 1936 mg/dl. A full serological screen excluded other causes of acute liver disease. Liver biopsy revealed lymphoplasmacytic infiltration in the portal area with moderate interface hepatitis,

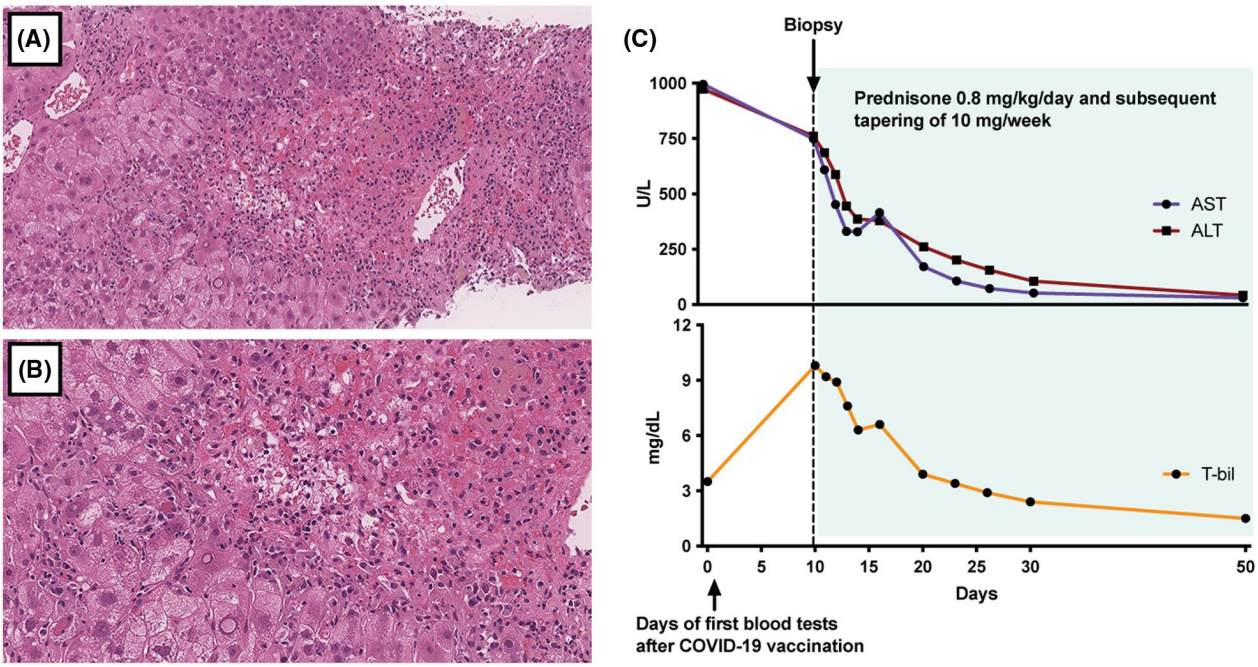

FIGURE 1 (A) Hematoxylin and eosin staining of liver biopsy specimen shows inflammatory infiltrate in the portal area (original magnification ×20). (B) The portal area shows a lymphoplasmacytic infiltration with severe interface hepatitis and acidophil bodies (original magnification ×40). (C) Longitudinal change in liver chemistries. ALT, alanine aminotransferase; AST, aspartate aminotransferase; T-bil, total bilirubin