Letter to the editor: "Autoimmune hepatitis after COVID-19 vaccination"

To the editor,

We would like to correspond on the issue of autoimmune hepatitis (AIH) following COVID-19 vaccination.[1] Palla et al. discuss the possible association between AIH and COVID-19 vaccination.[1] Adverse effects of the vaccine are possible, and liver problems following vaccination present an interesting clinical problem. Some researchers propose that an abnormal immune response is the definitive cause of AIH.[2] However, it is usually hard to definitively state that AIH is induced by a vaccine. Almost all reported cases lack prevaccination laboratory data, and it is not possible to exclude the existence of prevaccination autoimmunity. Also, there is usually no complete investigation for other causes of hepatitis. Additionally, the AIH might be a coincidence. Coincidence of a medical problem after COVID-19 vaccination and differential diagnosis is hard. For example, dengue can co-occur in a vaccine recipient and cause platelet and liver problems.[3] After vaccination, there is also the possibility of excessive blood viscosity,[4] which might also be a trigger factor for liver problems.[5]

CONFLICT OF INTEREST

Nothing to report.

Rujittika Mungmunpuntipantip[1]
Viroj Wiwanitkit[2]

[1]*Private Academic Consultant, Bangkok, Thailand*
[2]*Honorary Professor, Dr DY Patil University, Pune, India*

Correspondence
Rujittika Mungmunpuntipantip, Private Academic Consultant, Bangkok 101800, Thailand.
Email: rujittika@gmail.com

ORCID

Rujittika Mungmunpuntipantip https://orcid.org/0000-0003-0078-7897

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Reply

We are pleased to respond to Drs. Mungmunpuntipantip and Wiwanitkit's observations on our recent paper.[1,2]

We completely agree that it is usually difficult to associate autoimmune hepatitis (AIH)-like syndrome with a drug or vaccine administration. However, more and more cases of post–anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination are being recorded.[3–5] Among them, Tun et al. reported a patient with liver injury after the first vaccine, with improvement until the second dose was administered; after that, the patient had a worsening of liver biochemistry.[5]

In our case, the patient underwent excessive laboratory testing, excluding other causes of transaminasemia, including viral hepatitis, Epstein-Barr virus, and cytomegalovirus. Moreover, the patient was followed up for 5 months before liver biopsy (LB) was decided so that other viral causes could be safely excluded. Our patient's LB was consistent with AIH-like syndrome, and she improved with corticosteroid treatment.

Overall, we think that even though pinpointing the cause of AIH-like syndrome is a difficult task, we now have cumulating evidence in the literature proving that this syndrome is a rare, but existent, side effect of mRNA-based anti-SARS-CoV-2 vaccines.

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We would like to thank Dr. Mungmunpuntipantip for his letter, allowing us to further discuss a very interesting matter.

CONFLICT OF INTEREST

Nothing to report.

Panagiota Palla[1]
Chrysovalantis Vergadis[2]
Stratigoula Sakellariou[3]
Theodoros Androutsakos[1]

[1]*Department of Pathophysiology, National and Kapodistrian University of Athens, Medical School, Athens, Greece*
[2]*Radiology Department, "Laikon" General Hospital, Athens, Greece*
[3]*First Department of Pathology, National and Kapodistrian University of Athens, Medical School, Athens, Greece*

Correspondence
Theodoros Androutsakos, Department of Pathophysiology, Medical School, National and Kapodistrian University of Athens, Mikras Asias 75, Athens, 115 27, Greece.
Email: t_androutsakos@yahoo.gr

ORCID
Theodoros Androutsakos https://orcid.org/0000-0003-2556-6230

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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