Received: 7 September 2021 | Revised: 8 September 2021 | Accepted: 9 September 2021

DOI: 10.1002/hep.32156

CORRESPONDENCE

Letter to the editor: Autoimmune hepatitis after COVID-19 vaccination: A rare adverse effect?

To the editor,

The vaccines against the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) were granted a fast-track authorization due to the catastrophic consequences of the coronavirus disease 2019 pandemic. Although these vaccines have proven their efficacy, safety has been a concern. Up till now, two cases of autoimmune hepatitis (AIH) after anti-SARS-CoV-2 vaccination have been reported.[1,2]

We report a case of AIH-like syndrome in a 40-year-old Caucasian woman after Pfizer-BioNTech-mRNA vaccination. The patient had a medical history of sarcoidosis for which she had never received treatment. On routine blood testing 1 month after completing her vaccination, abnormal liver function tests were found, with serum transaminases being 4× upper limit of normal (ULN). The patient was referred to our hepatology department for evaluation.

On arrival, the patient's physical examination and upper abdominal ultrasound were normal. Testing for hepatitis B, C, and E; Epstein-Barr virus; cytomegalovirus; and HIV infections was negative. Antinuclear-antibodies testing was positive with a titer of 1/640; testing for antimitochondrial, antismooth muscle and liver-kidney-microsome type-1 antibodies was also negative. Total IgG serum levels were markedly raised at 2.4 g/dl (normal values 0.7–1.2 g/dl).

Due to the possibility of vaccine-induced transaminasemia, monthly follow-up was decided. During the next 5 months, serum transaminases fluctuated around 3–4 × ULN, so a liver biopsy (LB) was performed.

LB revealed active hepatitis with significant interface necroinflammation and severe lobular inflammatory infiltration composed predominantly of lymphocytes with an admixture of plasma cells. Portal/periportal fibrosis was evident as well as fibrous septa with occasional bridging. Granulomas were not encountered (Figure 1A,B)

Based on elevated levels of serum transaminases and IgG and LB findings, the patient was started on 40 mg prednisolone. One-week after treatment initiation, serum transaminases declined to normal levels.

Because anti-SARs-Cov-2 vaccination might rarely cause transaminasemia,[3,4] drug-induced liver injury was a possible diagnosis in our patient, so LB was performed 6 months after vaccination due to persisting transaminasemia. This 6-month period coupled with the high serum IgG levels and the absence of recent use of hepatotoxic drugs and granulomas in LB make vaccine-induced AIH a probable diagnosis. However, because serum transaminases improved within a week post-treatment, AIH-like syndrome due to molecular mimicry to the vaccine is more likely. What makes our patient unique is the fact that she was neither postpartum nor was under any medical treatment as previously reported patients.[1,2]

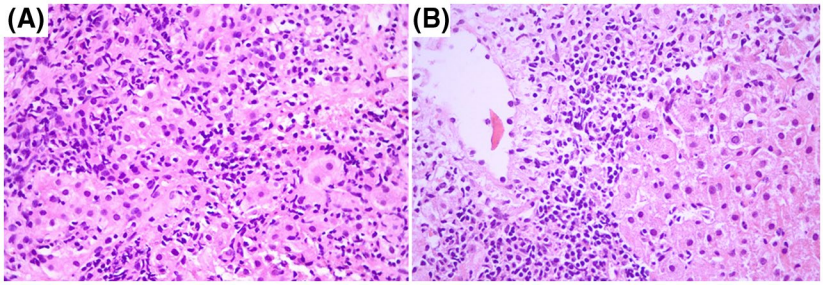

FIGURE 1 Active hepatitis. (A) Interface activity. (B) Centrilobular lymphoplasmacytic inflammation. (A, B) ×400

Overall, we believe that AIH-like syndrome may be a rare complication of SARS-CoV-2 vaccination and should be considered in cases of postvaccination persistent transaminasemia. However, under no circumstances should this rare side effect restrain patients from anti-SARS-CoV-2 vaccination because coronavirus disease poses a major threat to patients with liver diseases.[5]

CONFLICT OF INTEREST

Nothing to report.

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Letter to the editor: Serum bioavailable 25-hydroxyvitamin D levels correlate with hepatocellular carcinoma survival

To the editor,

It was with great interest that we read the article by Fang et al.[1] In this study, the researchers investigated the relationship between total, free, and bioavailable serum 25-hydroxyvitamin D (25-OHD) levels and survival in a large, prospective cohort of patients with HCC. The results showed that higher serum 25-OHD levels were significantly and independently associated with increased survival in the HCC cohort, but neither total nor free serum 25-OHD was associated with survival. This is an intriguing study with important clinical value, and we appreciate the efforts of the researchers. However, several concerns deserve to be discussed.

First, ultraviolet (UV) light from sunlight is known to convert 7-dehydrocholesterol in the skin into vitamin D3 (cholecalciferol), which is the main way to obtain endogenous vitamin D in humans.[2,3] In addition to the production of vitamin D in the body from UV radiation, vitamin D in food is also an important source, and the amount of vitamin D in different types of food varies.[4] When the level of vitamin D in the body increases, the level of 25-OHD, which is converted in the liver through hydroxylation, increases accordingly.[5] Therefore, the duration of sunlight exposure and dietary structure (type and amount of food) should be considered as important confounding factors affecting the prognosis of HCC. Second, although the researchers showed that elevated serum bioavailable 25-OHD was independently associated with a good prognosis in HCC patients, its predictive performance for HCC prognosis was not investigated. Therefore, we suggest that the researchers obtain the AUC by receiver operator characteristic curve analysis or calculate Harrell's concordance index (C-index) to assess the predictive power of bioavailable 25-OHD for HCC prognosis. Finally, we also suggest that the researchers use decision curve analysis to obtain the net benefit of prognostic indicators to assess the clinical utility of bioavailability 25-OHD.

CONFLICT OF INTEREST

None to report.

AUTHOR CONTRIBUTIONS

Lu-Lu Zhai, Shi-Hui Zhen, and Zhi-Gang Tang designed the study and wrote and reviewed the manuscript.