COVID-19 Vaccine Induced Liver Injury: A Case Series

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Introduction

The COVID-19 pandemic has caused > 248 million cases and > 5 million deaths worldwide.

Although vaccines have excellent safety profiles, there is a risk of adverse effects such as fever, fatigue, arthralgias, injection site pain, and, less commonly, anaphylactic reaction.

Drug-induced hepatotoxicity (DIH) is a rare side effect of vaccines that has rarely been reported.

We report a cohort of four patients who presented with DIH following COVID-19 vaccination.

Cases Description

Our cohort includes four patients, aged 39-70, who presented between 12 to 82 days after their second dose of Pfizer COVID-19 vaccine.

- All patients had normal ALT and AST within one year before presentation.
- All patients demonstrated a hepatocellular pattern of liver injury (peak ALT range of 57 to 904 U/L and AST range of 51 to 828 U/L).
- Tests for acute viral hepatitis were negative.
- No evidence of fibrosis on fibroscan
- 2 of 3 liver biopsies obtained suggested evidence of toxic/drug induced liver injury while the other demonstrated nonspecific inflammation.

Patients' characteristics									Peak lab values					Relevant work up (labs, imaging, pathology)				
Case	Age, Sex	Race	BMI	Alcohol use (per week)	Co-morbid conditions	Liver disease co-morbidities	Presenting symptoms	Presentation (days) after 2nd vaccine *	ALT (U/L)	AST (U/L)	ALP (U/L)	Total Bilirubin (mg/dL)	Ferritin (ng/mL)	Antibody Panel	Transient Elastography	Liver Biopsy	Liver Imaging	Return of ALT & AST to baseline
1	58, M	White	25.4	<1 drink	HLD	Hepatic Steatosis	Fatigue, arthralgias	12	101	51	77	0.8	478.12	ANA: - **AMA: +** ASMA: - IgM: 78 IgG: 882	CAP 231 kPa 5.1	Mild porto-sinusoidal vascular disease. Mild ferritin and hemosiderin deposition. No evidence of autoimmune hepatitis or steatohepatitis.	Not performed	Yes
2	46, F	White	27.4	2-4 drinks	Migraines, OSA	None	Fever, fatigue, arthralgias	42	57	58	147	0.4	662	ANA: - AMA: - ASMA: -	Not performed	Not performed	Not performed	Yes
3	70, F	Black	28.9	7 drinks	HTN, HLD, Grave's disease	None	Incidental elevation of liver function tests	82	904	828	85	0.8	604	ANA: + AMA: - ASMA: + IgM: 66 IgG: 2127	CAP 152 kPa 3.5	Mixed lymphoplasmacellular infiltrates with mild to moderate interface hepatitis, focal bridging necrosis and focal multicinar necrosis. Consistent with AIH superimposed by DILI or DILI-initiated AIH.	US: Normal	Yes
4	39, F	White	19.6	<1 drink	HSV2	None	Fever, chills, myalgias, LAD	81	596	454	213	1.7	358	ANA: - AMA: - ASMA: - IgM: - IgG: - **cANCA: +**	CAP 155 kPa 3.4	Focal portal fibrosis. Perivenular necroinflammation with hepatocyte dropout, mild lymphocytic inflammation and ceroid-containing macrophages. Mild predominantly centrilobular small-droplet steatosis. Consistent with acute drug /toxin induced liver injury.	US: mildly echogenic liver MRCP: Normal	Yes

* All patients received Pfizer vaccination.

BMI: Body Mass Index, HTN: Hypertension, HLD: Hyperlipedemia, OSA: obstructive sleep apnea, HSV2: herpes simplex virus, LAD: Lymphadenopathy, ALT: alanine transaminase, AST: aspartate aminotransferase, ALP: Alkaline phosphatase, ANA: antinuclear antibodies, ASMA: anti-smooth muscle antibody, AMA: Antimitochondrial antibodies, IgM: Immunoglobulin M, IgG: Immunoglobulin G, cANCA: Antineutrophil Cytoplasmic Autoantibody, CAP: controlled attenuation parameter, kPa: kilopascal, AIH: autoimmune hepatitis, DILI: Drug Induced Liver Injury, US: ultrasound, MRCP: Magnetic resonance cholangiopancreatography.

Figure 1: Patient demographics and characteristics.

Discussion

DIH leads to 10% of all cases of acute hepatitis and up to 50% of all cases of liver failure, making it one of the common reasons for withdrawal of medications from the market.

Our patients developed hepatic injury after Pfizer COVID-19 vaccination.

Vaccine-induced immune-mediated hepatitis is a known phenomenon thought to be secondary to the COVID-19 spike protein triggering an autoimmune-like hepatic condition.

This could explain the findings seen in our patients, raising the question of inflammatory response in patients with underlying autoimmune conditions.

It is important that these patients receive pre and post vaccination laboratory monitoring, especially given the emergence of booster vaccinations.

There is a need to follow these patients in the long-term to monitor for changes in clinical and laboratory studies in order to assess the risk of complications and outcomes.