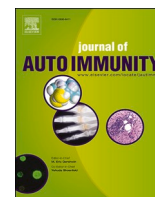




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## Acute autoimmune-like hepatitis with atypical anti-mitochondrial antibody after mRNA COVID-19 vaccination: A novel clinical entity?

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### ABSTRACT

Autoimmune phenomena and clinically apparent autoimmune diseases, including autoimmune hepatitis, are increasingly being reported not only after natural infection with the SARS-CoV-2 virus, but also after vaccination against it. We report the case of a 63-year old man without a history of autoimmunity or SARS-CoV-2 natural infection who experienced acute severe autoimmune-like hepatitis seven days after the first dose of the mRNA-1273 SARS-CoV-2 vaccine. Liver histology showed inflammatory portal infiltrate with interface hepatitis, lobular and centrilobular inflammation with centrilobular necrosis, in absence of fibrosis and steatosis. Serum immunoglobulin G was slightly elevated. Autoimmune liver serology showed an indirect immunofluorescence pattern on triple rodent tissue compatible with anti-mitochondrial antibody (AMA), but, unexpectedly, this pattern was not mirrored by positivity for primary biliary cholangitis (PBC)-specific molecular tests, indicating that this antibody is different from classical AMA. Anti-nuclear antibody (ANA) was also positive with a rim-like indirect immunofluorescence pattern on liver and HEP2 cell substrates, similar to PBC-specific ANA; however, anti-gp210 and a large panel of molecular-based assays for nuclear antigens were negative, suggesting a unique ANA in our patient. He carries the HLA DRB1\*11:01 allele, which is protective against PBC. Response to prednisone treatment was satisfactory. The clinical significance of these novel specificities needs to be further evaluated in this emerging condition.

### 1. Introduction

The ongoing pandemic caused by Severe Acute Respiratory Coronavirus 2 (SARS-CoV-2), a highly transmissible and pathogenic virus leading to coronavirus disease 2019 (COVID-19), is having a devastating global impact, leading to an unprecedented fast development of anti-COVID-19 vaccines. Two mRNA vaccines, BNTb262 and mRNA-1273, have recently been approved in Switzerland, and a massive vaccination campaign has started at the end of 2020. These vaccines trigger the interferon pathway as part of their mechanism of action, raising concerns about potential safety issues in patients predisposed to autoimmune conditions associated with interferon activation, including

autoimmune hepatitis (AIH) [1,2]. A diverse range of autoimmune diseases following COVID-19 and anti-SARS-CoV-2 vaccination are increasingly being reported [3–6]. Recently, autoimmune-like hepatitis following mRNA Covid-19 has been reported in four women, only one of whom having pre-existing extrahepatic autoimmune conditions [7–10]. We describe a well characterized case of autoimmune-like hepatitis in a 63-year old man arising one week after the first dose of the mRNA-1273 vaccine.

### 2. Case description

A 63-year old male Caucasian patient presented to his general

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