



HAL
open science

Acute icteric hepatitis as the first isolated symptom of COVID-19

Pierre-Clément Thiebaud, Christelle Hermand, Jennifer Sobotka,
Pierre-Alexis Raynal

► **To cite this version:**

Pierre-Clément Thiebaud, Christelle Hermand, Jennifer Sobotka, Pierre-Alexis Raynal. Acute icteric hepatitis as the first isolated symptom of COVID-19. *BMJ Case Reports*, 2021, 14 (6), pp.e242853. 10.1136/bcr-2021-242853 . hal-03253492

HAL Id: hal-03253492

<https://hal.sorbonne-universite.fr/hal-03253492v1>

Submitted on 8 Jun 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

TITLE OF CASE

Acute icteric hepatitis as the first isolated symptom of COVID-19

SUMMARY

COVID-19 patients may be asymptomatic or present with extra-respiratory symptoms, such as liver injury. It has been reported that 22.5-46.2% of patients have moderate elevation of liver enzymes. To our knowledge, acute hepatitis has never been described as an isolated symptom of COVID-19 in a previously healthy patient. We report the case of a 53-year-old patient with COVID-19 whose first clinical presentation was acute icteric hepatitis, several days before the development of others symptoms. During the pandemic, we suggest that patients with acute hepatitis be considered COVID-19 suspects, tested and isolated.

BACKGROUND

Since December 2019, more than 110 million people have been infected by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) worldwide and more than 2.5 million patients have died. Controlling the pandemic is difficult because exhaustive identification of cases is complex, as COVID-19 patients might be asymptomatic or present with extra-respiratory symptoms, such as liver injury. It has been reported that 22.5-46.2% of patients have moderate elevation of liver enzymes.[1-4] To our knowledge, acute hepatitis has never been described as an isolated symptom of COVID-19 in a previously healthy patient. We hereby report the case of a patient with COVID-19 whose first clinical presentation was acute icteric hepatitis, several days before the development of others symptoms.

CASE PRESENTATION

A previously healthy 53-year-old man presented to the emergency department (ED) with a three days fatigue and jaundice history, including scleral icterus and dark urine. He reported no other

symptoms, particularly no fever, cough, shortness of breath, sore throat, rhinorrhea, myalgia, headache, chest pain, anosmia, dysgeusia or digestive trouble. He did not take any medication or use any drugs. He had not recently traveled or declared any contact with sick people. On presentation, he was afebrile (36.3°C) and his vital signs were normal. His respiratory rate was 16 breaths per min, his oxygen saturation was 99% on room air and his lung fields were clear on auscultation. Apart from jaundice, the physical examination was unremarkable.

INVESTIGATIONS AND DIFFERENTIAL DIAGNOSIS

Complete blood count was normal including absolute lymphocyte count (1650 cells/mm³), and inflammatory markers (c-reactive protein, procalcitonin) were negative. Liver function tests read as follows: aspartate aminotransferase 1366 IU/L (normal <35), alanine aminotransferase 2495 IU/L (normal <55), alkaline phosphatase 258 IU/L (normal <115), gamma-glutamyl transferase 311 IU/L (normal <45), total bilirubin 2.7 mg/dL (normal <1), direct bilirubin 1.7 mg/dL (normal <0.35) and prothrombin time >100%. Abdominal ultrasound with doppler showed normal liver and gallbladder with a patent portal and hepatic circulation. As the patient spent the night in the ED observation unit, a nasopharyngeal swab was done and RT-PCR was negative for COVID-19. The following serological tests were performed and all came back negative (no antibodies or immunity): hepatitis A, B, C, D, E, EBV, CMV, HIV, HSV1, HSV2, HHV6, HHV8, Parvovirus B19, leptospirosis, listeria. Blood cultures and screening for autoimmune hepatitis markers (antinuclear, anti-soluble liver antigen, anti-smooth muscle, anti-mitochondrial, anti-liver cytosol, anti-liver kidney microsomal and anti-gastric parietal cell antibodies) were also negative.

OUTCOME AND FOLLOW-UP

The patient was discharged home without any specific treatment with an outpatient follow-up. Two days later, he developed a fever up to 40°C. Then four days later, he presented with sudden anosmia. He immediately performed a SARS-Cov-2 antigen test which confirmed COVID-19. After an uncomfortable week (fever, fatigue, myalgia, headache), the patient totally recovered. Liver function tests gradually improved until they completely returned to normal at two months.

DISCUSSION

As other causes of acute hepatitis were ruled out, it seemed highly probable that acute hepatitis was directly caused by COVID-19. However, even if screening for usual viral hepatitis have been repeated and were negative, a later seroconversion cannot be formally excluded. The risk of a false positive result on the COVID-19 antigen test is low because to be implemented, such tests must comply with the clinical performance criteria defined by the French National Authority for Health (*Haute Autorité de Santé*). These must report a sensitivity greater than or equal to 80% and specificity greater than 99% in symptomatic subjects. In addition, the patient presented with anosmia, a typical symptom of COVID-19.[5] As the patient spent one night in the ED, the hypothesis of nosocomial COVID-19 was also mentioned. This is very unlikely because there are strict hygiene measures in the department, the patient stayed in a single room and no other patient in the observation unit tested positive for COVID-19 on that day.

To our knowledge, this is the first report of an acute icteric hepatitis as the first and isolated sign of COVID-19 in a previously healthy patient. However, two similar cases have previously been described: the first, an acute non-icteric hepatitis in a patient treated for HIV who developed fever and respiratory symptoms on day 2;[6] the second, a fulminant hepatic failure in patient treated for a systemic lupus erythematosus who presented lymphopenia and elevated C-reactive protein at admission.[7] Other reports described acute hepatitis associated with other typical symptoms of COVID-19 [8] or co-infection with acute hepatitis B.[9]

The mechanism of liver injury due to COVID-19 remains unclear. It could be a direct infection of the liver cells with SARS-CoV-2 replication in hepatic cells, an indirect effect by sepsis-induced physiological changes (inflammation, hypoxemia, hypotension), drug hepatotoxicity or exacerbation/reactivation of an underlying liver disease.[10,11] This liver damage is usually moderate and temporary, although patients with COVID-19 and liver dysfunction appear to present with more severe disease and to have a higher mortality.

LEARNING POINTS/TAKE HOME MESSAGES

- Acute hepatitis is a rare presentation of COVID-19.
- The mechanism of liver injury by SARS-CoV-2 remains unclear.
- Patients with acute hepatitis should be considered COVID-19 suspects, tested, isolated and monitored.

REFERENCES

- [1] Ding ZY, Li GX, Chen L, et al. Association of liver abnormalities with in-hospital mortality in patients with COVID-19. *J Hepatol* 2020;S0168-8278(20)33885-X. doi:10.1016/j.jhep.2020.12.012
- [2] Hao SR, Zhang SY, Lian JS, et al. Liver enzyme elevation in coronavirus disease 2019: a multicenter, retrospective, cross-sectional study. *Am J Gastroenterol* 2020;115(7):1075-1083. doi:10.14309/ajg.0000000000000717
- [3] Phipps MM, Barraza LH, LaSota ED, et al. Acute Liver Injury in COVID-19: Prevalence and Association with Clinical Outcomes in a Large U.S. Cohort. *Hepatology* 2020;72(3):807-817. doi:10.1002/hep.31404
- [4] Yip TC, Lui GC, Wong VW, et al. Liver injury is independently associated with adverse clinical outcomes in patients with COVID-19. *Gut* 2020;gutjnl-2020-321726. doi:10.1136/gutjnl-2020-321726
- [5] Villerabel C, Makinson A, Jaussent A, et al. Diagnostic Value of Patient-Reported and Clinically Tested Olfactory Dysfunction in a Population Screened for COVID-19. *JAMA Otolaryngol Head Neck Surg*. 2021;147(3):271-279. doi:10.1001/jamaoto.2020.5074
- [6] Wander P, Epstein M, Bernstein D. COVID-19 Presenting as Acute Hepatitis. *Am J Gastroenterol* 2020;115(6):941-942. doi:10.14309/ajg.0000000000000660
- [7] Melquist S, Estepp K, Aleksandrovich Y, et al. COVID-19 presenting as fulminant hepatic failure: A case report. *Medicine (Baltimore)* 2020;99(43):e22818. doi:10.1097/MD.00000000000022818

[8] Bongiovanni M, Zago T. Acute hepatitis caused by asymptomatic COVID-19 infection. *J Infect* 2021;82(1):e25-e26. doi:10.1016/j.jinf.2020.09.001

[9] Colaneri M, Valsecchi P, Perotti L, et al. Running out of bullets: The challenging management of acute hepatitis and SARS-COV-2 from the SMatteo COvid19 Registry (SMACORE). *Liver Int* 2020;40(11):2655-2659. doi:10.1111/liv.14609

[10] Nardo AD, Schneeweiss-Gleixner M, Bakail M, et al. Pathophysiological mechanisms of liver injury in COVID-19. *Liver Int* 2021;41(1):20-32. doi:10.1111/liv.14730

[11] Anirvan P, Bharali P, Gogoi M, et al. Liver injury in COVID-19: The hepatic aspect of the respiratory syndrome - what we know so far. *World J Hepatol* 2020;12(12):1182-1197. doi:10.4254/wjh.v12.i12.1182

INTELLECTUAL PROPERTY RIGHTS ASSIGNMENT OR LICENCE STATEMENT

I, **Pierre-Clément THIEBAUD**, the Author has the right to grant and does grant on behalf of all authors, an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the relevant stated licence terms for US Federal Government Employees acting in the course of their employment, on a worldwide basis to the BMJ Publishing Group Ltd (“BMJ”) and its licensees, to permit this Work (as defined in the below licence), if accepted, to be published in BMJ Case Reports and any other BMJ products and to exploit all rights, as set out in our licence [author licence](#).

Date: March 1st, 2021