



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

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## TITLE OF CASE

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

## SUMMARY

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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

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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

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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

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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

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Complete blood count was normal including absolute lymphocyte count (1650 cells/mm<sup>3</sup>), 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

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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

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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

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- 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.

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