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**Single Case**

# Cholestatic Liver Injury in a Patient with Tertiary Syphilis

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**Abstract**
Syphilis is a common infection that has variable presentations. We report a rare case of a 64-year-old male with 3 weeks of abdominal pain, back pain, and neurologic deficits including memory impairment who was found to have neurosyphilis causing a cholestatic liver injury. Workup included a positive rapid plasma reagin (RPR) and enzyme immunoassay (EIA), a positive cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL), and a liver biopsy, which was compatible with a diagnosis of syphilitic hepatitis. Completion of a 14-day course of penicillin and 1 month of physical therapy resulted in near full-functional and biochemical recovery.



## Introduction

Tertiary syphilis is a constellation of meningovascular events of the uncontrolled spirochetal infection. It is rare in the developed world thanks to the ability to detect and adequately treat it in earlier stages. This form of syphilis is classically defined by symptoms of general paresis or tabes dorsalis [1].

One of the less common effects of syphilis is cholestatic hepatitis, first described in 1943. The criteria for diagnosis were described most recently in 2004 by Mullick et al. [2], which require abnormal liver enzyme levels, serologic evidence of syphilis, exclusion of other causes

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of liver disease/enzyme elevation, and liver enzyme levels returning to baseline following appropriate antimicrobial treatment [3]. While cases of syphilitic hepatitis have been described, they are rare and are mainly diagnosed when the patient has primary or secondary syphilis. Here, we describe a case of a 64-year-old male with jaundice, abdominal pain, and significant neurologic symptoms, found to have a cholestatic pattern of transaminitis and transverse myelitis due to tertiary syphilis, also known as neurosyphilis.

## Case Report

A 64-year-old man with a history of frequent travel to Guatemala and multiple sexual partners presented to the hospital with 3 weeks of nonspecific abdominal pain, lumbago, jaundice, and several neurologic deficits including numbness from the mid-chest to feet, weakness of the lower extremities, right-sided facial droop, and short-term memory impairment. Physical exam on admission was remarkable for scleral icterus, mild abdominal distention with tenderness to palpation of the flanks bilaterally, along with the following neurologic findings: right facial droop; left eye ptosis; patchy decreased sensation of right lower face; 4/5 strength on hip flexion bilaterally; decreased sensation to pinprick at chest, abdomen, and anterior thighs with patchy loss of pinprick sensation on bilateral arms and legs; 1 + brachioradialis and biceps reflexes bilaterally; absent patellar and ankle jerk bilaterally; and wide-based unsteady gait.

Initial laboratory workup was relevant for white blood cell (WBC) count 14,800, total bilirubin 7.0, direct bilirubin 5.8, alkaline phosphatase (ALP) 1,140, gamma-glutamyl transpeptidase (GGT) 586, aspartate aminotransferase (AST) 164, alanine aminotransferase (ALT) 249, and international normalized ratio (INR) 1.20. Rapid plasma reagin (RPR) and syphilis-specific antibody EIA titers returned positive at 1:128. Lumbar puncture revealed cerebrospinal fluid (CSF) with 5 red blood cells, 9 WBCs, protein 119, glucose 82, venereal disease research laboratory (VDRL) reactive at 1:2 titers, and Borrelia Burgdorferi antibody positive by enzyme-linked immunoassay (ELISA). The remaining workup for elevated transaminases was unremarkable. Ultrasound of the abdomen showed no biliary ductal dilation. MRI abdomen with contrast MRCP revealed mild peripheral heterogeneous hepatic parenchymal enhancement and periportal edema, consistent with hepatitis, along with minimal wall enhancement of the common bile duct, suggestive of cholangitis (shown in Fig. 1). MRI of the spine revealed transverse myelitis at spinal level C6, and the patient was treated with 3 days of methylprednisolone. The patient subsequently underwent liver biopsy which showed portal mixed inflammation with cholangitis and mild hepatocellular cholestasis, compatible with a diagnosis of syphilitic hepatitis (shown in Fig. 2). Interestingly, a treponema stain of the specimen returned negative. Interdisciplinary discussion with neurology, infectious disease, pathology, and gastroenterology

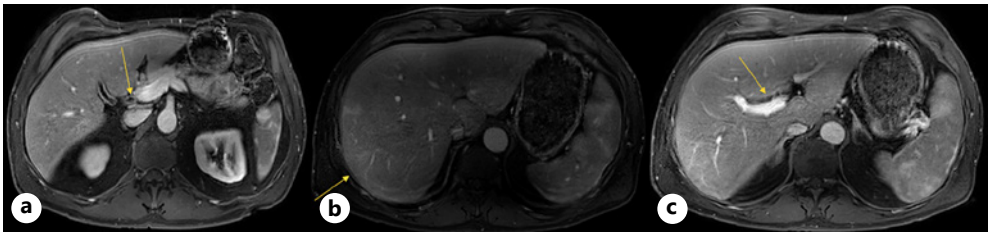


**Fig. 1.** T1-weighted, contrast-enhanced images from the patient's MRI abdomen with contrast MRCP. **a** Wall enhancement of the common bile duct, suggestive of cholangitis. **b** Mild peripheral heterogenous hepatic parenchymal enhancement, consistent with hepatitis. **c** Periportal edema, consistent with hepatitis.

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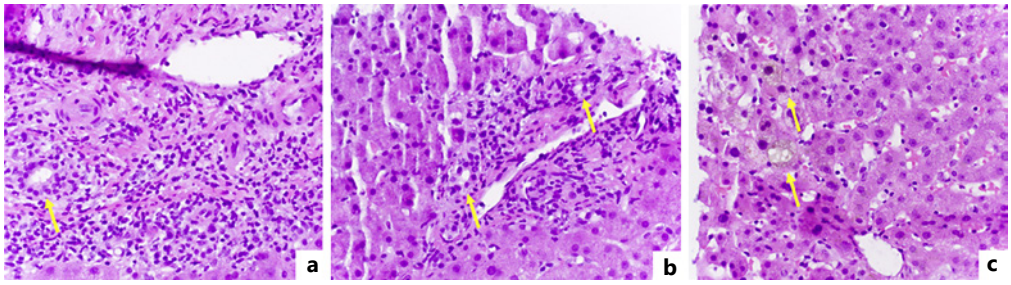


**Fig. 2.** Histology of liver biopsy. **a**, **b** Portal mixed inflammation, with lymphocytic cholangitis. **c** Hepatocellular cholestasis. All images are at ×400 magnification.

agreed upon tertiary syphilis as the most likely diagnosis. The patient was discharged to finish a 14-day course of intravenous penicillin. At follow-up 1-month post-discharge, the patient reported near full recovery of his symptoms with significant improvements in laboratory work (total bilirubin 0.9, ALP 302, AST 50, ALT 95, INR 1.0).

## Discussion

Cholestatic patterns of liver injury are defined by biliary ductal damage causing elevations in liver function tests (LFTs) with a predominant elevation of ALP and bilirubin compared to AST and ALT. It is then further subdivided into intra- and extrahepatic biliary diseases. Common etiologies of cholestatic liver injury include choledocholithiasis, malignant obstruction of the bile ducts, biliary strictures, drug-induced liver injury, primary biliary cholangitis, primary sclerosing cholangitis, alcohol-associated hepatitis, infiltrative diseases, and infection. Infection and sepsis can lead to cholestasis due to decreased basolateral and canalicular transport of bile acids [4].

One such cause of cholestasis is syphilis, as described in our case report. Although rare, there have been previously published case reports detailing transaminitis as a manifestation of syphilitic infection; however, these articles almost exclusively describe cases of secondary syphilis [5, 6]. In these cases, liver injury caused by syphilis is associated with a dermatologic rash [7] and patients frequently have an immunosuppressive condition, such as HIV [8].

This case, however, was unique as it highlights the importance of keeping tertiary syphilis on the differential diagnosis of a patient presenting with cholestatic hepatitis, even without dermatologic findings on exam or comorbid immunosuppressive conditions. The diagnosis was supported by LFTs, syphilis screening and confirmatory testing on serum and CSF studies, and pathology findings from liver biopsy. It was important to note that despite having a more advanced stage of syphilis, this patient with tertiary syphilis achieved a complete recovery after treatment with intravenous penicillin, as evidenced by significant improvement in his LFTs and resolution of his neurologic symptoms.

While this case provides some guidance on the clinical course of patients presenting with cholestatic liver injury in tertiary syphilis, it is important to note some limitations. Although the final diagnosis was tertiary syphilis, the patient was initially given doxycycline to treat possible Lyme disease while the final diagnosis was still in question. The patient's CSF Lyme antibody was positive; however, this was likely a false positive, which occurs in cases of neurosyphilis when CSF VDRL is positive and serum studies are negative [9, 10]. While the treponemal stain of the liver biopsy was negative, the patient had already been initiated on penicillin by the time of biopsy, potentially obscuring this result. Treponemal stains also have low sensitivity, only identifying spirochetes 50% of the time [6, 11]. Despite this possibility,

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interdisciplinary discussion deemed it more likely given his history, symptoms, and laboratory and pathologic findings that the patient had tertiary syphilis as the cause of his presentation.

This case report stresses the importance of recognizing tertiary syphilis as a rare but treatable cause of cholestatic liver injury. With early detection and initiation of appropriate antibiotics, patients can be expected to make a full recovery.

## Statement of Ethics

Ethical approval is not required for this case report in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

## Conflict of Interest Statement

The authors of this case report have no conflicts of interest to declare with regard to the publication of this case report.

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## Author Contributions

Sahaj Mujumdar was instrumental in the construction of this case report, including caring for this patient during his stay, obtaining informed consent, writing initial and final drafts of this case report, and reviewing and editing portions of the case report. Jason Goldenberg, Alice S. Pang, and Robert Coben were instrumental in the construction of this case report, including caring for this patient during his stay, writing initial and final drafts of this case report, and reviewing and editing portions of the case report. Steven Bieser was instrumental in the construction of this case report, including caring for this patient during his stay, obtaining informed consent, and writing initial and final drafts of this case report.

## Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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