An Adolescent With Hepatitis

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Case Presentation
A 17-year-old girl presented with vomiting, diarrhea, generalized pruritis, scleral icterus, and a rash on her extremities. The patient’s rash had developed approximately 3 weeks prior to admission. Two weeks prior to admission, she began vomiting, had diarrhea, and noticed yellowing of her eyes. Due to persistence of symptoms, she presented for medical care. Her aminotransferase levels, bilirubin level, and international normalized ratio (INR) were noted to be markedly increased, at which point she was admitted to the hospital for further evaluation.

She had a past medical history remarkable only for Chlamydia trachomatis urethritis, which was treated appropriately 6 months prior to presentation. She took no medications and had no allergies. The patient reported no travel outside of the northeastern United States.

Figure 1. Patient’s hand with hyperpigmented macular rash, which was present on all extremities, chest, and abdomen.

Figure 2. Wrist with hyperpigmented macular rash. The rash was nonpruritic and nontender.
States and no animal exposures. She was sexually active with 4 lifetime partners; her last sexual activity was 1 month prior to presentation. There was no family history of liver disease or autoimmune disease.

On physical examination, the patient was an obese female who appeared to be well. Her temperature was 36.8°C, her pulse rate was 53/min, her respirations were 12/min, and her blood pressure was 126/69 mm Hg. The patient had a nontender abdomen with no palpable organomegaly. She had diffuse jaundice and scleral icterus. She had hyperpigmented macules on her abdomen, chest, palms, and soles (Figures 1–3). Her mental status was intact, and the remainder of the examination yielded normal results.

Laboratory evaluations revealed a total bilirubin level of 21.9 mg/dL (reference range, 0.6-1.4 mg/dL), conjugated bilirubin level of 13.3 mg/dL, alanine aminotransferase level of 3826 U/L (reference range, 5-35 U/L), aspartate aminotransferase level of 3448 U/L (reference range, 5-30 U/L), alkaline phosphatase level of 159 U/L (reference range, 50-130 U/L), and γ-glutamyltransferase level of 84 U/L (reference range, 9-23 U/L). The complete blood count was normal. The INR was 1.66 and the albumin level was 3.2 g/dL, indicating liver dysfunction.

Diagnoses strongly considered at this point included viral hepatitis and autoimmune hepatitis. Viral serologic and molecular testing, including for hepatitis A, B, and C, cytomegalovirus, and Epstein-Barr virus. Tuberculosis, toxoplasmosis, and other opportunistic infections associated with HIV can cause hepatitis. Noninfectious hepatitis may be caused by Wilson disease or autoimmune conditions such as systemic lupus erythematosus. This patient had a recent history of a sexually transmitted infection and a classic rash, which helped lead to the final diagnosis. Viral etiologies of hepatitis were excluded by serologic and molecular testing, antibody testing was not suggestive of an autoimmune process, and pathologic staining did not indicate heavy metal accumulation.

A rapid plasma reagin was reactive with a titer of 1:64 and a confirmatory fluorescent treponemal antibody absorption test was reactive, verifying a diagnosis of syphilitic hepatitis.

The patient received a diagnosis of C. trachomatis urethritis 6 months prior to developing hepatitis. Although there was no history given that suggested a chancre, this was likely the point at which she acquired syphilis.

She received 2.4 million units of benzathine penicillin G intramuscularly. Her acute symptoms resolved shortly after the first dose, and she was discharged from the hospital 4 days after admission. Her hepatic enzyme levels and INR decreased to normal levels within 8 weeks of treatment.

As of 2007, 100 000 new cases of syphilis are diagnosed each year in North America [1]. The frequency of hepatitis in secondary syphilis is unknown, but a 1943 review of more than 33 000 patients estimated a frequency of 0.24%. As expected, this number is higher in immunocompromised patients, and hepatitis has been reported in up to 38% of patients with HIV infection and early syphilis [2].

Clinically, syphilitic hepatitis is indistinguishable from many other etiologies of acute hepatitis. Patients may present with vomiting, diarrhea, tender hepatomegaly, jaundice, fatigue, and anorexia. Although
syphilitic hepatitis would not be expected to improve without intervention, viral hepatitis should be a self-limited illness [3]. The classic rashes of early syphilis aid in diagnosis: a chancre in primary syphilis, and a diffuse maculopapular rash involving the palms and soles in secondary syphilis as, seen in this patient.

Secondary syphilis is a stage of disseminated disease with a high burden of spirochetemia, and it has widespread clinical manifestations. Hepatic infection with Treponema pallidum is rare but well described and varies depending on the stage of disease [3, 4]. Early syphilitic hepatitis encompasses the spectrum of disease in patients with primary or secondary syphilis, with most hepatitis occurring during the secondary stage, which occurs 2-12 weeks following initial infection. Hepatic gummata occur in tertiary syphilis [2, 5].

The laboratory profile of syphilitic hepatitis classically involves a significantly increased alkaline phosphatase level with moderately increased amino-transferase levels and a normal to moderately increased bilirubin level. This patient had a less typical profile, including significant increases of aminotransferases and bilirubin levels, with a mild increase of alkaline phosphatase level. Similar laboratory findings have been described in other immunocompetent patients [5].

Warthin described finding spirochetes in liver tissue in 1918, although this finding is inconsistent in reports of syphilitic hepatitis [5]. Histopathology is nonspecific, although the hepatic architecture is usually preserved and a mixed inflammatory infiltrate is often seen around portal tracts [3, 4, 5]. The patient described here had evidence of inflammation at the interface of lobules and portal tracts, expanded portal tracts with extensive fibrosis, and multinucleated and necrotic hepatocytes. All of these findings have been described in other patients with syphilitic hepatitis [1, 2, 4]. Of note, Warthin-Starry stain to identify spirochetes in the liver was negative.

The diagnosis of syphilitic hepatitis is made when a patient meets the following criteria, which this patient did: (1) screening and confirmatory testing for syphilis are positive; (2) the patient has acute increase of liver enzyme levels; (3) there is no alternate diagnosis for hepatitis; and (4) hepatitis is resolved following treatment for syphilis [2].

Treatment of syphilitic hepatitis reported in the literature encompasses a range of options [2, 5]. This patient was treated according to the Centers for Disease Control Sexually Transmitted Diseases Guidelines, which state that the treatment for secondary syphilis regardless of organ involvement is 1 dose of intramuscular benzathine penicillin.

This patient differs from others described due to her young age, slightly atypical laboratory profile, and probable extended duration from primary infection to hepatitis. Many features of her disease are classic for early syphilitic hepatitis, and ultimately the resolution of symptoms and normalization of laboratory abnormalities after treatment proved a diagnosis of syphilitic hepatitis.

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