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A Case of Syphilitic Hepatitis in an Adolescent

*Natalie V. Hoffmann, MD, †Jonathan A. Berken, MD, PHD, ‡Anna M. Banc-Husu, MD, *Sarah A. Taylor, MD, and *Alyssa Kriegermeier, MD

Abstract: The incidence of syphilis is rising among adolescents necessitating improved provider awareness and screening practices. We present a case of an adolescent with acute hepatitis ultimately diagnosed with secondary syphilitic hepatitis. Clinical presentation, laboratory abnormalities, and histologic features of syphilitic hepatitis are nonspecific, with diagnosis relying on clinical suspicion and targeted testing. This case highlights the importance of screening for syphilis in sexually active adolescents with acute hepatitis. The rising incidence of syphilis among adolescents, and the variety of clinical manifestations including those commonly seen by pediatric gastroenterologists, makes elevated clinical suspicion essential to prompt diagnosis and treatment. With improved provider awareness across general pediatric and subspecialty providers, the transmission of syphilis among adolescent patients can be reduced.

Key Words: acute hepatitis, syphilis, syphilitic hepatitis

INTRODUCTION

Syphilitic hepatitis is a rare but established cause of acute hepatitis (1–3). Over the past 2 decades, the incidence of syphilis has risen, especially among adolescent patients (4,5). Increased awareness of syphilitic hepatitis among pediatric gastroenterologists is critical for prompt diagnosis and treatment of syphilitic hepatitis in pediatric patients.

Syphilis is a sexually and vertically transmitted infection caused by the spirochete *Treponema pallidum* (4,6). It is notorious for its variable and often subtle clinical manifestations resulting from the local inflammatory response to spirochetes within tissues (4). The natural history of syphilis includes primary and secondary stages of infection, followed by a prolonged latent stage that can progress over more than 10 years (4,6). If untreated, individuals will develop tertiary syphilis, which can cause profound morbidity from cardiac, neurologic, ocular, dermatologic, or musculoskeletal complications (4,6). Despite reliable and inexpensive methods for diagnosis and treatment, syphilis remains a public health challenge globally (4). Control efforts have been hindered by poor health care access and provider unfamiliarity with the diverse clinical presentations (6). Adolescent populations remain especially at risk for transmission, highlighting the importance of provider awareness and widespread testing within pediatric clinics and hospitals. We present a case of an adolescent patient with acute syphilitic hepatitis. This case serves as a critical reminder to pediatric gastroenterologists of the importance of screening for syphilis in sexually active adolescents.

CASE REPORT

A 19-year-old patient with a history of anxiety and disordered eating presented to care with 1.5 weeks of generalized abdominal pain, weight loss, and jaundice. Pertinent history included sporadic use of over-the-counter weight loss supplements, binge drinking 3–4 times per week, and unprotected sexual activity with men. Examination findings included icteric sclera, nontender and nondistended abdomen, mild hepatomegaly to 2 cm below right costal margin, and no splenomegaly. Initial laboratory workup revealed elevated alanine aminotransferase (ALT) 2004 international units/L and aspartate aminotransferase (AST) 1594 international units/L, increased direct bilirubin of 6.1 mg/dL, and international normalized ratio 1.3. Abdominal ultrasound with Doppler demonstrated normal sonographic appearance of the liver and patent hepatic vasculature. He was admitted to the Hepatology service for workup and management of acute hepatitis. Hepatitis A, B, and C serologies were negative. Epstein-Barr virus (EBV) serologies of EBV immunoglobulin G (IgG) 6.5 international standardized ratio and EBV immunoglobulin M 0.12 international standardized ratio were consistent with prior infection (reference range: ≤0.90 negative, 0.91–1.09 equivocal, and ≥1.10 positive). Cytomegalovirus serologies were positive for IgG and immunoglobulin M; however, cytomegalovirus quantitative polymerase chain reaction had an undetectable viral load, thus unlikely to be the cause of the patient's hepatitis. Anti-nuclear antibody, anti-smooth muscle antibody, and anti-liver/kidney microsome type 1 antibody testing was normal, although total serum IgG was elevated to 2190 mg/dL (reference range: 613–1295 mg/dL). Additional studies demonstrated normal creatine kinase, ceruloplasmin, thyroid-stimulating hormone, celiac studies, and alpha-1 antitrypsin phenotype. Review of medications, herbal supplements, and illicit drug use did not clearly identify a source of likely drug-induced liver injury.

Further questioning revealed recent history of diffuse, nonpruritic, erythematous papular rash over the patient's chest, abdomen, and back that self-resolved over 2 days, and an ulcerated penile lesion that antedated the rash, caused mild discomfort, and resolved without treatment. Screening evaluation for syphilis with rapid plasma reagin was positive with titer of 1:128, and the patient received treatment with intramuscular benzathine penicillin. A *T. pallidum* particle agglutination assay was positive, confirming the diagnosis of syphilis. Screening tests for other sexually transmitted infections were negative, including tests for human immunodeficiency virus. Given the high index of suspicion for syphilitic hepatitis, a liver biopsy was deferred, and he was discharged with outpatient follow-up to complete 3-week course of weekly intramuscular benzathine penicillin. Although the suspicion for secondary

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From the *Department of Pediatrics, Division of Gastroenterology, Hepatology, and Nutrition, Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL; †Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL; and ‡Departmart of Pediatrics, Section of Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Texas Children's Hospital, Houston, TX.
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Correspondence: Natalie V. Hoffmann, MD, Division of Gastroenterology, Hepatology and Nutrition, Ann & Robert H. Lurie Children's Hospital, 225 E. Chicago Ave., Box 65 Chicago, IL 60611-2991. Email: nhoffmann@luriechildrens.org

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TABLE 1. Laboratory trend of selected hepatobiliary parameters at the time of presentation and following treatment with intramuscular penicillin

Laboratory values	Day 0 (PCN)	Day 1	Week 1	Month 1	Month 4
ALT (2–30 IU/L)	2023	1792	1773	220	18
AST (18–57 IU/L)	1649	1149	1226	97	28
Alk Phos (53–223 IU/L)	294	252	193	118	68
GGT (5–55 IU/L)	364	320		94	
T. bili (0.2–1.2 mg/dL)	8.8	8.8	6.6	2.0	1.4
D. bili (<0.3 mg/dL)	6.3	6.7	4.2	0.7	0.2
Albumin (3.6–4.7 g/dL)	4.2	4.1	4.4	4.5	5.2
INR	1.30	1.20		1.10	1.10

Alk Phos = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; D. bili = direct bilirubin; GGT = gamma-glutamyl transferase; INR = international normalized ratio; IU = international units; PCN = penicillin; T. bili = total bilirubin.

syphilitic hepatitis was high after rapid plasma reagin returned positive, the decision was made to treat conservatively with 3 doses of penicillin for presumed latent syphilis while comprehensive acute hepatitis work up was pending. Latent syphilis is defined by the Centers for Disease Control and Prevention as seroreactivity without evidence of primary, secondary, or tertiary syphilis, with late latent syphilis presumed if the timing of infection is unknown. Importantly, the patient's ALT and AST were uncharacteristically high and alkaline phosphatase uncharacteristically low compared to prior reports of syphilitic hepatitis, supporting further evaluation prior to diagnosis. After additional workup returned unrevealing and laboratory abnormalities improved, the patient was ultimately diagnosed with secondary syphilitic hepatitis. Laboratory trend showed improvement in transaminases by 20-fold and direct bilirubin by approximately 10-fold at 1-month follow-up and normalization of laboratory parameters at 4-month follow-up (Table 1, Fig. 1). Serum IgG also normalized after treatment, which suggests the initial elevation may have been secondary to activated immune response during infection. The patient was referred to Adolescent Medicine for counseling about safe sexual practices. To reduce ongoing transmission, he informed his sexual partner and encouraged testing.

DISCUSSION

Syphilitic hepatitis is rare, with a reported incidence of 0.25%–38% (5). There are 3 described cases of syphilitic hepatitis in adolescents patients younger than 18 years of age (7–9). Hepatic involvement of syphilis can occur at any stage of the disease, although most commonly in early syphilis with nonspecific symptoms, necessitating high index of suspicion for diagnosis (1,2).

The clinical manifestations of syphilis are attributed to the local inflammatory response elicited in by spirochetes in affected organs, including the liver. The precise mechanism by which *T. pallidum* causes liver damage and why certain patients are more susceptible remains unknown (1). The diagnosis of syphilitic hepatitis relies on the presence of abnormal liver enzymes, positive syphilis serologies, exclusion of other etiologies of liver disease, and clinical and biochemical response to antibiotic treatment (10). Liver biopsy is not required for diagnosis, as histologic features are nonspecific and spirochetes are rarely identified on biopsy specimens (1–3). Antibiotic treatment with penicillin shows rapid improvement in most cases of syphilitic hepatitis, as was observed in this case (1). Very rarely, syphilitic hepatitis can result in fulminant liver failure (1).

Syphilis is an ideal disease for public eradication. Although syphilis has high infectivity and morbidity if untreated, *T. pallidum* has no known animal reservoir, diagnosis relies on simple inexpensive tests, and treatment is curable (4). Public health efforts to control syphilis are feasible and include primary prevention, widespread testing, and the education and engagement of the providers that care for patients who engage in high risk sexual activities (6).

Although syphilis is a rare cause of hepatitis, the rising incidence of syphilis among adolescents calls for pediatric gastroenterologists to remain cognizant of the various disease manifestations. In the United States, syphilis incidence reached a historic low in 2000

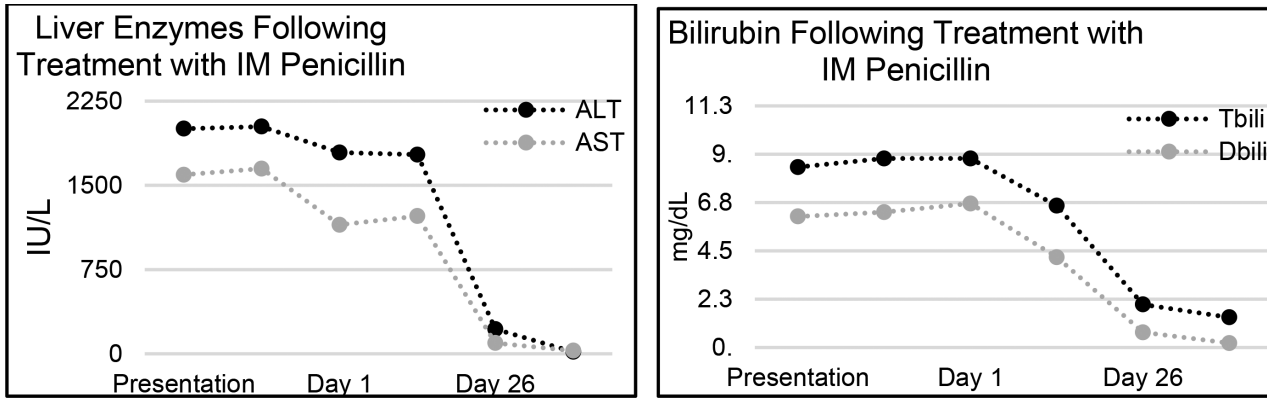

FIGURE 1. Liver enzymes and bilirubin following treatment with IM penicillin. ALT = alanine aminotransferase; AST = aspartate aminotransferase; D. bili = direct bilirubin; IM = intramuscular; T. bili = total bilirubin; IU = international units.

and 2001 but has since increased annually, rising 11.2% in 2018–2019 (5). Infections disproportionately affect adolescents and individuals in racial, ethnic, or sexual minorities, reflecting disparities in health care access as well as differences among sexual networks (5,6). In 2019, 55% of reported sexually transmitted infections were among adolescents ages 15–24 years (5). Men comprised 83% of primary and secondary syphilis cases, and women 17% (5). Men who have sex with men accounted for 57% of all male primary and secondary syphilis cases in 2019 (5). Although rates are lower in women, there was a 179% increase during 2015–2019, suggesting rapid increase in heterosexual transmission as well (5).

Prompt recognition and management of syphilis is essential to prevent progression and transmission, with the goal of eradicating this disease and its causal agent. We present a case of an adolescent male with acute hepatitis with significantly elevated ALT/AST and only minimally elevated alkaline phosphatase who was diagnosed with secondary syphilis, treated, and referred to appropriate resources for education about safe sexual practices. Given thorough history and diagnostic evaluation, we determined that the patient's presentation was consistent with syphilitic hepatitis. Liver biopsy was deemed unnecessary and was deferred to initiate prompt treatment that resulted in the rapid resolution of the patient's clinical and biochemical abnormalities. In high-risk populations, the differential diagnosis of acute hepatitis and liver failure should include syphilitic hepatitis.

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