**Syphilitic Hepatitis**

by Lauren M. Bleich, Howard L. Taubin

A 21 year-old homosexual male presented to his primary care physician with a five-day history of right upper quadrant abdominal pain exacerbated by meals. He also endorsed generalized pruritis, dark urine and fatigue. He denied fever, chills, nausea or vomiting. He had no significant past medical history, and denied taking medications or supplements. His social history was significant for a history of intravenous (IV) drug use in the past and several tattoos. On physical exam, he exhibited mild tenderness to palpating in the epigastrum but the exam was otherwise unremarkable. Blood work demonstrated abnormal liver enzymes including aspartate transaminase (AST) 314U/L, alanine transaminase (ALT) 627U/L, alkaline phosphatase 317U/L, total bilirubin 2.1mg/dL and GGT 654U/L. Synthetic hepatic function was preserved with an INR of 1.0. Abdominal ultrasound was significant for increased echogenicity suggestive of fatty infiltration. A complete hepatitis panel including Hepatitis B DNA and Hepatitis C RNA viral loads were normal.

The patient’s alkaline phosphatase continued to increase over the next few weeks and peaked at 590U/L, while the AST and ALT decreased but did not return to the normal range. Two weeks after the patient’s initial presentation, he returned with symptoms including night sweats, a maculopapular palmar rash, and a painless penile chancre. A skin biopsy was performed of the left palm, which demonstrated the presence of spirochetes, consistent with the diagnosis of secondary syphilis (Figure 1). Rapid plasma reagin (RPR) and fluorescent treponemal antibody-absorption (FTA-ABS) tests were both reactive. The patient was treated with a single dose of benzathine penicillin G 2.4 million units intramuscularly and his symptoms resolved. Repeat liver enzymes three months later were normal including an alkaline phosphatase of 47U/L.

Described by William Osler as the great imitator, syphilis is thought to originate from the area now known as Haiti. The New World theory proposes that Christopher Columbus acquired the disease and carried it to Europe in the 1400s. By 1495, syphilis was widespread throughout the continent. In 1905, Treponema pallidum was linked to the disease. Throughout history, many famous people are thought to have been infected with syphilis, including Napoleon Bonaparte, Vincent Van Gogh, Beethoven and Mussolini.

Early syphilis is a reportable infection in the United States. It is estimated that one fourth of syphilis cases in the United States were reported in HIV-infected patients. In the early 1990s, a mini epidemic of syphilis occurred, corresponding with increasing number of HIV cases. In 2010, the rates of infection are highest among the group of men age 20-24, and African American men are 15 times more likely to be infected than their Caucasian counterparts. Syphilis continues to remain a worldwide issue. In 2009, according to the World Health Organization, there were an estimated 1.2 million new cases of syphilis reported in the United States. This epidemic is the result of increasing rates of HIV infection among gay and bisexual men. Syphilis continues to remain a worldwide issue. In 2009, according to the World Health Organization, there were an estimated 1.2 million new cases of syphilis reported in the United States. This epidemic is the result of increasing rates of HIV infection among gay and bisexual men.
Health Organization, there were 3-4 million new cases of syphilis in each Southeast Asia, Sub-Saharan Africa and Latin America.4

Transmission of Treponema pallidum usually occurs through direct contact with an infectious lesion during sexual intercourse. The spirochete accesses the new host via disrupted epithelium at sites of minor trauma. Early lesions of primary syphilis, including chancres, mucous patches, and condyloma lata, are infectious and transmission occurs in one-third of patients exposed to these lesions. Syphilis can also be acquired by passage through the placenta. Median incubation time before the onset of clinical symptoms is approximately three weeks, but can range from 3 to 90 days.

The natural course of untreated syphilis is well documented in history. In the late 19th century, a Norwegian physician described the progression of infection in over 1,400 patients with primary and secondary syphilis. Between 1932 and 1972, data was collected on 431 African American men with untreated syphilis in Tuskegee, Alabama. Although separate stages, there is no clear demarcation between primary and secondary syphilis. As many as one-third of patients with secondary syphilis will still have a primary chancre present. It had been reported that up to 60% of patients with secondary syphilis do not recall having a skin lesion.5 This is particularly the case in the female population, where primary lesions tend to be internal.

Before 1980, only a few cases of syphilitic hepatitis were reported in the literature. Clinical manifestations are varied, but include jaundice, dark urine, malaise, anorexia and arthralgias, similar to our patient’s presentation. The most common finding is an abnormally disproportionate elevation of the alkaline phosphatase. Minor elevations of AST, ALT and bilirubin can be seen as well. Histologic preservation of the liver architecture is usually seen, with occasional granulomas and focal hepatocyte necrosis. Treponema pallidum organisms within the liver biopsy confirm the diagnosis, however more commonly the spirochete is demonstrated within other tissue samples. Non-treponema tests including RPR and VDRL are used for primary screening. Secondary treponemal testing (ie: FTA-ABS) are used to confirm the diagnosis.

Clinical symptoms of syphilitic hepatitis are likely due to dissemination of Treponema pallidum from the site of primary infection to the liver. The pathogenesis of liver injury is not well understood. Hypotheses include direct injury by the spirochete to the portal venous system and an immune complex-mediated autoimmune reaction.6

Treatment for primary, secondary and latent syphilis includes a single dose of benzathine penicillin G (2.4 million units IM). If the duration of latent syphilis is unknown, the patient should be treated with 3 doses of benzathine penicillin G at 1-week intervals. A patient’s symptoms should decline along with liver function abnormalities when appropriate treatment is given, thereby confirming the diagnosis. A Jarisch-Herxheimer reaction may occur within 24 hours of treatment. This acute febrile reaction, accompanied by headache and myalgia, is thought to be the result of pyrogens released from the dying spirochete into the body. All patients should have re-examination of clinical symptoms and serologies at six and twelve months following treatment. Syphilitic hepatitis should not lead to sequelae of chronic liver disease.

References