Contents lists available at www.cmro.in
JOURNAL OF CURRENT MEDICAL AND RESEARCH OPINION
Journal homepage: http://cmro.in/index.php/jcmro

A Stubborn Case of Syphilitic Hepatitis

Marco Campitelli[1], Hassan Al Moussawi[1], Nabil Zeineddine[1], Stephen Maslak[1]

[1]Staten Island University Hospital - 475 Sea view avenue, Staten Island, NY, 10305

ARTICLE INFO

Corresponding Author:
Nabil Zeineddine
Staten Island University Hospital - 475 Seaview avenue, Staten Island, NY, 10305

Keywords: Syphilitic, Hepatitis, Intravenous, Antibodies.

ABSTRACT

Background

Syphilitic hepatitis is a rare occurrence, but delay in its diagnosis can expose patient to unnecessary testing. The treatment available for this condition can also vary from one intramuscular injection of Penicillin G to a 2-weeks course of intravenous penicillin.

Case presentation:

A 53 years old male, presented for fever and abdominal pain, was found on physical examination to have a macular rash on the palms and soles, with fever and abdominal tenderness.

Laboratory findings revealed AST 199 IU/L, ALT 132 IU/L, positive RPR, FTA-ABS and HIV antibodies test and a high HIV viral load.

He was diagnosed with secondary syphilis and HIV co-infection. His hepatitis did not improve after intramuscular injection of penicillin G, his symptoms continued to worsen. A liver biopsy was done and revealed acute hepatitis and canalicular cholestasis, without evidence of treponemes.

Patient was started on intravenous penicillin. He showed significant clinical improvement, and his LFT normalized.

Conclusion:

This case describes severe syphilitic hepatitis with unusual cytolytic disturbance of the liver function that failed to improve with one intramuscular penicillin injection. It demonstrates the need of intravenous penicillin therapy to achieve adequate clinical response, particularly in patients with severe laboratory evidence of liver inflammation.

INTRODUCTION

Syphilitic hepatitis is a previously reported manifestation of secondary syphilis that can increase healthcare expenditure especially when not recognized earlier. It is also a condition that can change the choice of therapy of patients affected with syphilis, particularly when it is severe. This report is a presentation of a severe syphilitic hepatitis in an undiagnosed HIV infected patient.

Case presentation:

Our patient is 53-year-old man who presented with fever, non-pruritic rash and pleuritic chest pain of 4 days' duration. Symptoms started while he was on a 1 week visit to the Dominican Republic. He returned to the United States 3 days prior to presentation. He reported unprotected vaginal intercourse with 2 different partners in the past 3 months. He denied alcohol abuse or use of illicit drugs and had no pets.

Physical exam showed macular rash on the palms and soles without lymphadenopathy (figure 1). Abdominal examination showed right upper quadrant tenderness. Laboratory findings included normal complete blood count and creatinine, ALT 199 IU/L, AST 132 IU/L, alkaline phosphatase 126 IU/L and total bilirubin 0.5mg/dl.
Chest radiograph, echocardiography and CT chest, abdomen, and pelvis were negative. Workup included a negative blood smear for parasites, negative serologies for Rickettsia, Ehrlichia, EBV and hepatitis A, B and C. HIV antibodies test was also sent.

On Day 2 of the hospitalization, fevers persisted and labs showed an increase in AST and ALT level. Workup showed negative ANA, AMA, anti-smooth muscle AB, HSV PCR, hepatitis B PCR with normal ceruloplasmin, and transferrin saturation level, a CMV PCR of 15638 IU/ML, and ferritin level of 2418 ng/ml. RPR was positive 1:64 with Treponemal antibodies >70.00. HIV AB test result was positive with an HIV PCR of 666,450 copies/ml, and a CD4 count of 476. Secondary syphilis was diagnosed and the patient was given a single dose of 2.4 million units Benzathine Penicillin intramuscularly.

Over the next several days his transaminases continued to increase and his right sided pleuritic chest pain persisted. On the 5th day of hospitalization, AST reached 949 IU/L, ALT 907 IU/L. His alkaline phosphatase was 215 IU/L and the total bilirubin was 1mg/dl. Two sets of blood cultures were negative. Liver biopsy was done and patient was started on IV Penicillin Potassium 4 million Units q 4 hours for 14 days. Two days after starting penicillin, liver enzymes started to decrease, and fever and chest pain resolved. At discharge his AST and ALT levels were 60 IU/L and 199 IU/L, respectively. Liver biopsy was negative for spirochetes, but showed evidence of portal inflammation with lymphocytic infiltrate and canalicular cholestasis consistent with acute hepatitis (figure 2 and figure 3). The patient was diagnosed with acute HIV with secondary syphilis complicated with syphilitic hepatitis that improved with penicillin therapy.

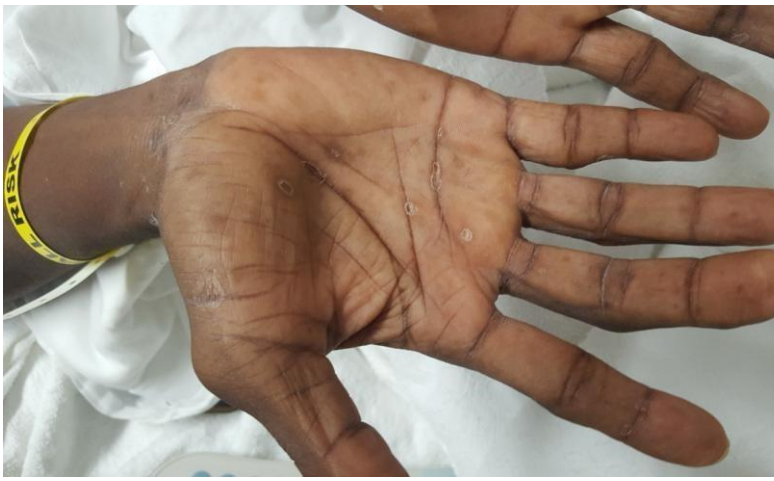

Figure 1 rash involving palms. Picture taken at day1 of presentation

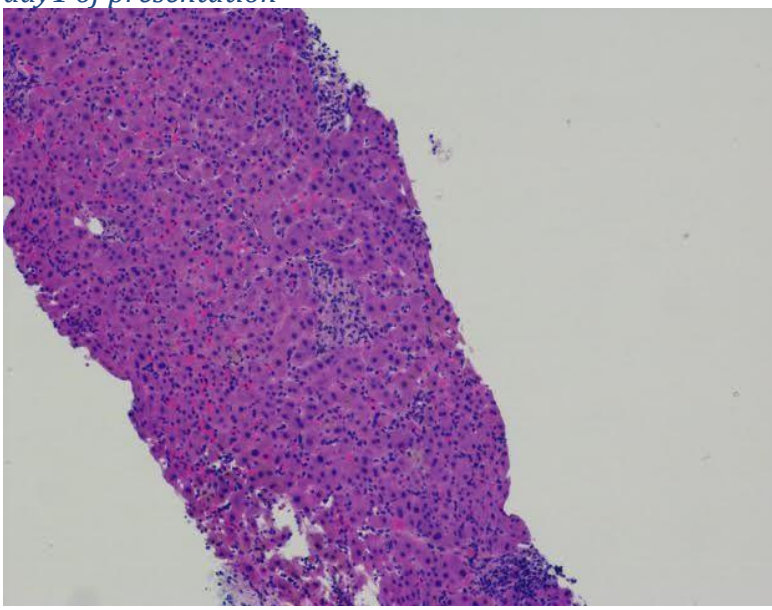

Figure 2 Liver biopsy (H&E stain) with finding of portal inflammation.

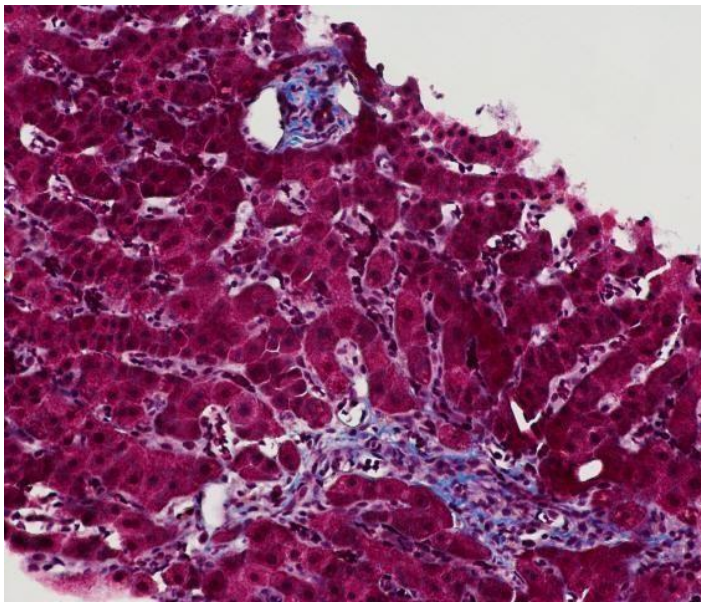

Figure 3 Liver biopsy (Trichrome stain). No evidence of fibrosis.

Case Discussion:

Syphilis impact on HIV is particularly challenging with an associated decrease in CD4 cells count and an increase in HIV viral load (1). The co-infection has a bidirectional synergistic effect that facilitates transmission and progression of both infections (2). Treponema pallidum is known to cause disease in virtually every organ in human body, and while hepatic dysfunction in HIV patients can be attributable to many causes including CMV, Mycobacterium avium complex, hepatotoxic medications, hepatitis viruses and cryptosporidium infection, syphilis has been reported as a rare cause of hepatitis in those patients (3).

Our patient presented for secondary syphilis and was found to have HIV infection with high viral load. The presence of hepatic involvement was suspected based on the presence of right upper quadrant tenderness, and the pleuritic chest pain, and was confirmed by the disturbed liver function tests. While many reviews on syphilitic hepatitis showed that hepatomegaly is a common clinical finding (4), this feature was absent in our patient. Consideration of the other diagnosis was suggested, but the absence of profound immunosuppression, with a CD4 count of 470, made etiologies like CMV hepatitis, MAC or parasitic infections less likely. The absence of history of alcohol abuse or over the counter medications including Tylenol or other herbal preparations use made these etiologies of liver dysfunction less convincing.

While available case reports describe a predominant cholestatic pattern of liver disease in syphilitic hepatitis (5, 6), our patient had a cytolytic pattern of hepatic dysfunction with minimal increase in alkaline phosphatase. This might be explained by less intense pericholangiar inflammation (7) and mild canalicular cholestasis seen in our patient. His higher CD4 cells count relatively to other HIV patients co-infected with syphillis might explain the clinically overt hepatitis as sequelae of a more robust inflammatory response in the liver.

A Jarisch-Herxheimer reaction had to be considered in our patient, but the presence of LFT disturbance prior to initiation of penicillin, and the absence of worsening of the rash and other constitutional symptoms after penicillin therapy as typically seen in this reaction (8) made the diagnosis less likely.

Suggested criteria to diagnose syphilitic hepatitis include abnormal liver enzymes, serological and clinical evidence of acute secondary syphilis, exclusion of alternative causes of hepatic damage, and improvement in the liver enzymes after initiation of antimicrobial therapy against Treponema pallidum (3). Our patient fulfilled all these criteria, and thus, the diagnosis of syphilitic hepatitis was confirmed.

Recommended treatment for secondary syphilis consists of one intramuscular injection of 2.4 million units of penicillin G. Even though our patient had secondary syphilis, we decided to treat with penicillin G intravenously for 2 weeks based on the severity of the disturbance of the transaminase enzymes and the presence of published reports describing similar treatment strategies for syphilitic hepatitis(3). Treatment failures have been described previously with penicillin given as single 2.4 million units intramuscular (9). This report suggests that more aggressive penicillin treatment may be needed in patients with severe hepatitis who do not respond to conventional single dose IM penicillin.

The recognition of this manifestation of syphilis by the clinician might decrease medical costs related to evaluation of etiology of high liver enzymes in HIV and syphilis infected hosts. Syphilitic hepatitis should be in the differential diagnosis of patients with abnormal liver tests in

the appropriate clinical context and appropriate antibiotic therapy should be given to reverse this treatable condition.

Conflict of interest:

The authors declare that there is no conflict of interest regarding the publication of this paper

Funding source:

none

References:

1. Palacios R, Jiménez-Oñate F, Aguilar M, et al. Impact of syphilis infection on HIV viral load and CD4 cell counts in HIV-infected patients. *J Acquir Immune Defic Syndr* 2007; **44**:356-9.

2. Roberts CP, Klausner JD. Global challenges in human immunodeficiency virus and syphilis coinfection among men who have sex with men. *Expert Rev Anti Infect Ther* 2016:1-10.

3. Mullick CJ, Liappis AP, Benator DA, Roberts AD, Parenti DM, Simon GL. Syphilitic hepatitis in HIV-infected patients: a report of 7 cases and review of the literature. *Clin Infect Dis* 2004; **39**:e100-5.

4. Fehér J, Somogyi T, Timmer M, Józsa L. Early syphilitic hepatitis. *Lancet* 1975; **2**:896-9.

5. Tiliakos N, Shamma'a JM, Nasrallah SM. Syphilitic hepatitis. *Am J Gastroenterol* 1980; **73**:60-1.

6. Schlossberg D. Syphilitic hepatitis: a case report and review of the literature. *Am J Gastroenterol* 1987; **82**:552-3.

7. Lee RV, Thornton GF, Conn HO. Liver disease associated with secondary syphilis. *N Engl J Med* 1971; **284**:1423-5.

8. Gelfand JA, Elin RJ, Berry FW, Frank MM. Endotoxemia associated with the Jarisch Herxheimer reaction. *N Engl J Med* 1976; **295**:211-3

9. Ghanem KG, Erbelding EJ, Cheng WW, Rompalo AM. Doxycycline compared with benzathine penicillin for the treatment of early syphilis. *Clin Infect Dis* 2006; **42**:e45-9.