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Hepatitis: A Case of Infectious and Autoimmune Hepatitis Occurring with Neurosyphilis

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Abstract

The liver is an organ that withstands a lot of insults due to various things such as infection, toxins and even our own immune system. There are injuries to the liver that are relatively common in medicine such as viral hepatitis caused by different strains of Hepatitis A-E, autoimmune hepatitis, and injury by drugs such as acetaminophen. However, syphilis causing hepatitis is not seen often and there are certain features that distinguish syphilitic hepatitis that should be reported more to distinguish its characteristic features.

Keywords

Infectious Hepatitis, Autoimmune Hepatitis, Neurosyphilis, Syphilitic Hepatitis

Hepatitis is caused by a variety of etiologies including infectious, autoimmune, and drug-induced. The infectious causes can be broken down into five different types of viruses that include Hepatitis A-E. Hepatitis A and E are transmitted through the fecal-oral route while Hepatitis B, D and E are transmitted commonly through sexual contact and needle-stick injuries. There are different clinical features that present with the infection, but all have a commonality of causing inflammation of the liver. Some patients may present asymptomatically while others can progress to acute liver failure. Hepatitis B and C are more known to progress to chronic infection and lead to diseases such as cirrhosis or hepatocellular carcinoma. Our patient was a chronic carrier of Hepatitis C with ongoing inflammation of the liver which put him at risk for extensive liver damage.

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Autoimmune Hepatitis (AIH) is a form of chronic hepatitis that is commonly associated with other autoimmune conditions. This is typically diagnosed via the presence of a specific antibody known as anti-smooth muscle antibodies. Also, we can discover it based on histological findings on liver biopsy showing lymphoplasmacytic interface hepatitis along with bile duct changes. There will also be an elevation of biomarkers such as ALT, AST, ALP and GGT. The presentation can vary from patients being completely asymptomatic to showing signs of acute liver failure which may include jaundice, right upper quadrant pain, and fever.

Syphilis is caused by the bacterium, Treponema pallidum, which can spread to different organs including the liver. It can be broken down into different clinical stages of presentation. In the first stage, the disease is localized to the genital area in which there is a painless chancre described as a firm ulcer with indurated borders that has a smooth base. Secondary syphilis consists of dissemination of the spirochete which causes an immune reaction. The patient can present with constitutional symptoms, a disseminated rash, and condyloma lata which is a wart like papular erosion. The first two stages are more dermatological conditions, but the tertiary stage of syphilis which our patient presented with has a prominent effect on the cardiovascular and neurological systems. Tertiary syphilis consists of gummas which are granulomatous lesions, cardiovascular syphilis which presents as aneurysm formation due to large vessel vasculitis of the vasa vasorum, and neurosyphilis which is an inflammatory reaction of the meninges and the parenchyma of the cerebrum. Other features of neurosyphilis include Argyll Robertson pupils which are bilateral miosis of the pupils that accommodate but don't react to light. Also, there are tabes dorsalis which consists of demyelination of the dorsal columns and dorsal root ganglia which leads to impaired proprioception, loss of reflexes, and decreased sensation with sharp and shooting pains. We present a case of a male with a history of Hepatitis C, who presented with acute hepatitis A and B, autoimmune hepatitis (AIH) and syphilitic hepatitis.

2. Case Report

A 50-year-old male with history of Hepatitis C presented to the ED with abdominal pain lasting 2 weeks in duration. The pain was associated with increasing abdominal girth, and a rash on his hands and feet. The patient was homeless and had engaged in sexual activity with prostitutes for several years. Physical exam findings included jaundice, scleral icterus, abdominal distention, papular lesions on his palms and soles, and a painless chancre on his scrotum. Laboratory findings showed elevations in AST, ALT, Alkaline Phosphatase, total bilirubin and ammonia. CT scan of the abdomen revealed hepatosplenomegaly with varices and ascites (Figure 1). A hepatitis profile was positive for hepatitis A IgM, hepatitis B surface antigen (Ag), hepatitis B core antibody (Ab) total, hepatitis B core Ab IgM, hepatitis Be Ag, hepatitis C Ab, and Anti smooth muscle Ab (Figure 2).



Figure 1. CT abdomen and pelvis with contrast of the hepatic injury.

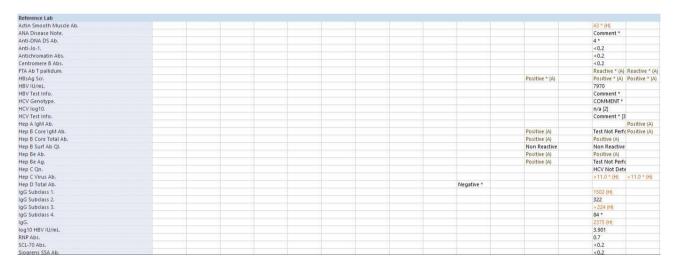


Figure 2. Laboratory findings table.

Serology							
RPR							Reactive
RPR Titer							1:64 (A)
Acetaminoph LvI							

Figure 3. Serology studies.

RPR was positive with a titer of 1:64. Fluorescent treponemal Ab absorption test was positive confirming the diagnosis of syphilis (**Figure 3**). The patient was admitted to the medical floors, received therapeutic paracentesis and was initiated on furosemide and spironolactone. CSF analysis revealed a positive VDRL test. CT-guided needle biopsy of the liver was performed which revealed dense lymphoplasmacytic infiltrate with scattered eosinophils in the portal areas, prominent cholestasis with bile ductular proliferation; immunostaining for *Treponema pallidum* was negative. The patient was given penicillin G 4,000,000 units every 4 hours IV for 10 days. The patient exhibited improvement of his

symptoms, however, left against medical advice prior to completion of his antibiotic therapy.

3. Discussion

Our patient presented with multiple etiologies of hepatitis occurring simultaneously including acute hepatitis A and B, and chronic hepatitis C infection. The biopsy exhibited anti-smooth muscle Ab and lymphoplasmacytic infiltrate of the portal system with eosinophils which are suggestive of Autoimmune Hepatitis. While the biopsy did not reveal *Treponema pallidum* organisms, infiltration of the portal system with inflammatory cells and cholestasis has been described in many case reports of syphilitic hepatitis. [1]

The patient also was a chronic carrier of hepatitis C infection and later acquired hepatitis A and B infection as well. These viruses are known to cause liver inflammation along with others such as EBV and CMV. However, the extent of the liver injury with all these different pathogens superimposed on each other hasn't been reported among patients. Viruses such as EBV and CMV have been known to involve the liver, and their presence is easier to distinguish as opposed to our patient who had syphilitic infection. Although liver involvement is common, hepatomegaly is seen only in 10% to 15% of cases, and spontaneously recovering elevated liver enzymes is seen in 80% to 90% of patients. LFT elevations are generally less than 5 times normal, and bilirubin levels rise less than 40 % of the basal value. [2] The extent of damage and diagnostic presentation isn't as much as infectious hepatitis, but still follows the same pattern of clinical features and diagnostic studies.

Autoimmune hepatitis was diagnosed for our patient as there were positive anti-smooth Abs from liver biopsy which also showed the portal system having lymphoplasmacytic infiltrate. The pathogenesis of autoimmune hepatitis isn't fully understood, but there are certain genetic and environmental factors that play a role in the disease process. Environmental factors associated with AIH include hepatitis A, B and C viruses, measles virus, varicella zoster virus, cytomegalovirus and Epstein-Barr virus. Viruses with hepatic tropism have the potential to cause AIH secondary to inflammation and subsequent cytotoxic immune response targeting the pathogen, leading to an abnormal T-cell response. [3] Our patient had infectious hepatitis that possibly led to the autoimmune hepatitis due to the cytotoxic immune response targeting the virus that is causing the ongoing inflammation.

The histological features of syphilitic hepatitis can include bile duct inflammatory infiltration, which may contribute to the elevated ALP and GGT levels in biochemistry tests. Hepatic granulomas are another characteristic of syphilitic hepatitis. [4] There are certain hepatic pathogens that specifically target the liver and cause direct damage. The pathogens include viruses like hepatitis A, hepatitis B, hepatitis E, Ebstein Barr Virus (EBV), Cytomegalovirus (CMV), and Herpes Simplex Virus. However, *Treponema pallidum* is not an organism that targets the

liver. It has different stages of presentation that affect multiple organ systems. The liver is not an organ that is affected; therefore, it is a rare presentation to have a patient with neurosyphilis present with liver damage that is characteristic of syphilitic hepatitis. Since the bacterium doesn't disseminate to the liver, there have to be commonalities and features from other reports of syphilitic hepatitis that distinguish it from other pathogenic organisms. Another case found a similar finding to our patient and reported that Syphilitic hepatitis can be defined as a cholestatic pattern of liver enzyme elevation with serological treponemal evidence in the absence of alternative causes of hepatic dysfunction. The most common stage that causes abnormal liver enzymes is secondary syphilis. [5] The only difference is that our patient has progressed to tertiary syphilis as they had clinical features consistent with neurosyphilis.

4. Conclusion

Many different pathogens causing damage to the liver simultaneously are quite rare. Especially with three different types of hepatitis viruses, *Treponema pallidum* infection in the tertiary stage of clinical presentation, and autoimmune hepatitis. There aren't many reported cases of syphilitic hepatitis and it is a rare presentation for a patient with neurosyphilis to have the bacterium disseminated to the liver. It typically involves the cardiovascular and neurological systems and not so much the hepatobiliary system. There are unique characteristics of syphilitic hepatitis that need to be reported as it is common for patients to have cholestasis and infiltration of the portal system with inflammatory cells. There need to be more reports distinguishing these characteristic features of syphilitic hepatitis to be able to recognize it quickly, provide adequate treatment, and avoid missing a diagnosis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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