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AN UNCOMMON CAUSE OF HEPATITIS

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ABSTRACT

Syphilis virtually affects any organ. Hepatitis occurring as a complication of syphilis is rare. Here we present the case of a 50 years old patient with retroviral infection who presented with hepatitis for which no cause other than the positive syphilis serology could be found. He responded well to the treatment for syphilis.

KEYWORDS: Syphilis, syphilitic hepatitis, HIV.

INTRODUCTION

Syphilis is a sexually transmitted infection caused by the spirochete, *Treponema pallidum*. The natural course of the disease evolves from primary syphilis through secondary and tertiary stages if not treated. Primary syphilis is characterized by chancre, secondary syphilis by its distinctive rash and tertiary syphilis by gummata and cardiovascular manifestations. Neurosyphilis is another distinct manifestation of syphilis which can occur anytime during the course of illness.^[1] Syphilis is considered as the great imitator as multiple organs can be involved with diverse manifestations. Liver can also be affected by syphilis, however this is rare and has been reported rarely.^[2] Human immunodeficiency virus (HIV) infection and syphilis have similar modes of transmission and one infection can increase the risk of acquisition and transmission of the other. So prevalence of syphilis is higher in people with HIV infection. HIV infection can influence the clinical presentation of syphilis in the form of more severe organ involvement, florid rash or a rapid progression to neuro syphilis. Liver damage is common in HIV patients due to causes like opportunistic infections, drugs and malignancies. Hence a broad range of differential diagnoses should be considered including syphilitic hepatitis.^[3]

CASE REPORT

A 50-year-old male patient, known case of retroviral infection which was incidentally detected during evaluation for abdominal pain, was diagnosed with latent syphilis simultaneously. He was a diabetic well controlled on oral hypoglycemic agents and a smoker, but no history of alcohol intake for past 2 years. No history of intake of any indigenous medicines. No family history of liver disease or neuropsychiatric illness. At the time of detection, his CD4 count was 392 per μL , Venereal Disease Research Laboratory test (VDRL) was positive at 1:8 titer and *Treponema pallidum* hemagglutination (TPHA) was positive at 1:640 titer. He was treated with Doxycycline for 28 days and initiated on anti-retroviral therapy (ART), ALE regimen (Abacavir, Lamivudine and Efavirenz).

Eight months later, he presented with fatigue, anorexia and jaundice without fever. His BMI was 20. Examination revealed a firm, nontender hepatomegaly, and mild splenomegaly. Ophthalmic evaluation was normal. Other systems were unremarkable on examination. His initial investigations are shown in Table 1.

Table 1: Initial investigations.

Characteristics	
Imaging	
Chest X ray	Normal
Ultrasound Abdomen	Splenomegaly
ECG	Normal

Hemoglobin, g/dL	13.5
MCV, fL	99
Differential Count	
Neutrophil, %	53
Lymphocyte, %	32
Monocyte, %	14
White blood cells, per μ L	3900
Platelet count, per μ L	155000
ESR, mm/hr	9
INR	1.33
aPTT, sec	38
Random Plasma Glucose, mg/dL	121
Urea, mg/dL	27
Creatinine, mg/dL	1.1
Uric acid, mg/dL	4.3
Potassium, meq/L	4
Phosphorus, meq/L	1.23
Calcium, meq/L	8.9
Sodium, meq/L	137
TSH level, IU/mL	3.5
CD 4, per μ L	431
Urine Routine Examination	Normal
Iron, μ g/dL	116
Serum Ferritin, μ g/L	197.5
Total Iron Binding Capacity, μ g/dl	210
Transferrin Saturation, %	55.2
Ceruloplasmin, mg/dL	33.9
HBsAg and Anti HCV	Non-reactive
IgM HAV and HEV	Non-reactive
ANA	Positive
ANA profile	Negative
Anti SLA, LKM1 & SMA antibodies	Negative
IgG levels, mg/dL	126
CMV and HSV PCR	Negative

His repeat VDRL showed positivity at 1:16titer, TPHA at 1:320titer and CSF VDRL was negative. During the period of evaluation, he was given symptomatic management. He was observed for a month but symptoms failed to resolve. In view of the persistent VDRL positivity, treatment failure was considered as the cause. Since no other etiology could be obtained for

hepatitis, syphilis itself was considered as the cause and he was started on injection crystalline penicillin (CP) 4 million international units fourth hourly for 14 days. His symptoms as well as his liver function tests improved (Table 2). Liver biopsy was planned but deferred in view of striking symptomatic improvement and resolution of hepatitis with treatment.

Table 2: Blood parameters over the course of admission.

Investigations	Day 1	Day 7	Day 14
Total Bilirubin, mg/dL	13.6	1.7	0.8
Direct Bilirubin, mg/dL	5.7	0.6	0.3
Alanine aminotransferase, U/L	236	102	46
Aspartate aminotransferase, U/L	214	106	51
Alkaline phosphatase, U/L	147	109	103
Total protein, g/dL	6.4	7.4	7.6
Albumin, g/dL	3.2	4	3.9

DISCUSSION

Infectious causes of liver injury include hepatotropic as well as non-hepatotropic pathogens. *Treponema pallidum* is one non hepatotropic organism that can cause hepatitis.^[4] The diagnostic criteria of syphilitic hepatitis as described by Mullick includes.

1. Abnormal liver enzyme levels
2. Serological evidence for syphilis
3. Exclusion of other causes of liver diseases
4. Liver enzyme levels returning to normal after appropriate antimicrobial therapy

Our patient who was HIV positive on ART with past history of latent syphilis treated with Doxycycline for 28 days presented with clinical features of liver damage confirmed by abnormal LFT. He had no evidence of virological or immunological failure. Evaluation for hepatotropic viruses was negative. He has abstained from alcohol for the past two years and had no history of intake of any indigenous or hepatotoxic drugs. There was no evidence of metabolic syndrome. Although his antinuclear antibodies (ANA) test was positive, ANA profile and autoimmune hepatitis panel were negative. Wilsons disease and haemochromatosis were also ruled out. Since the syphilis serology (VDRL test) turned out to be positive at 1:16titre a provisional diagnosis of syphilitic hepatitis was kept and he was started on injectable crystalline penicillin. The liver enzymes started decreasing by the end of first week and were normalized by the end of second week of treatment. The LFT in syphilitic hepatitis shows markedly increased alkaline phosphatase and Gamma-Glutamyl Transferase and a mild increase in Alanine Aminotransferase and Aspartate Aminotransferase.^[5] Liver biopsy will show inflammatory infiltration of bile duct and hepatic granuloma.^[6] Spirochetes are only rarely identified in liver tissue on special staining.^[7] Liver biopsy was not done as our patient improved with treatment and was not further necessary for diagnosis. The patient tolerated the treatment well. He met all the criteria for syphilitic hepatitis.^[3] Penicillin is the first line treatment of syphilis and response to antimicrobial therapy is considered as a diagnostic criteria.^[8] The positive ANA in this patient is probably false positive caused by chronic infection of syphilis and HIV.^[9]

To conclude syphilitic hepatitis does not have any specific symptoms other than that of hepatitis. It needs a high degree of suspicion for diagnosis and should be considered as a diagnostic possibility of any hepatitis with an unidentified cause in HIV positive patients.

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