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CASE REPORT | LIVER

Acute Hepatitis A and Hepatitis B Coinfection

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ABSTRACT

Hepatitis A (HAV) has emerged in outbreaks across the United States particularly in at-risk populations such as men who have sex with men, as well as patients with a history of drug use, homelessness, and incarceration. Immunization among these high-risk populations remains underused. In this study, we describe a case of acute HAV and hepatitis B (HBV) coinfection in an MSM patient occurring in the period of these outbreaks. Clinical resolution of acute HAV and HBV coinfection was attained by 5 months from the time of initial hospitalization without viral hepatitis treatment. This case highlights the need for increased awareness of at-risk populations for HAV and HBV infection in promoting guideline-based vaccination efforts.

INTRODUCTION

Outbreaks of acute infection with hepatitis A virus (HAV) have emerged across the United States (U.S.) since 2017 through person-to-person contact, particularly in at-risk populations such as injection/noninjection drug users, homeless, incarcerated, and men who have sex with men (MSM).[1] While hepatitis B (HBV) and hepatitis C (HCV) viruses share mode of transmission through blood and bodily fluids, HAV transmission is fecal/oral. Thus, although acute HBV/HCV coinfection and superimposed HAV on chronic HBV are well-reported,[2,3] to date, there have been few reported cases of acute HAV/HBV coinfection, and none thus far in the United States. We present a suspected case of acute symptomatic HAV/HBV coinfection in an MSM patient.

CASE REPORT

A 41-year-old previously healthy man from Japan presented to our hospital with 1 week of worsening jaundice, subjective fevers, chills, and malaise. He also reported pruritus and dark urine. One month before admission, the patient had visited Las Vegas and reported an acute episode of nausea and vomiting lasting 2 days. He was sexually active with an established male partner during the trip and reported multiple partners over the past 3 months with inconsistent use of barrier protection. He denied substance use, homelessness, incarceration, or history of viral hepatitis.

On presentation, his vitals were within normal limits. His physical examination was notable for jaundice and marked scleral icterus, but no abdominal tenderness or distention, hepatosplenomegaly, asterixis, or cutaneous stigmata of chronic liver disease. Initial laboratory evaluation was significant for an aspartate aminotransferase (AST) level elevated to 447 U/L, alanine aminotransferase (ALT) level elevated to 1101 U/L, and total bilirubin (TB) 9.3 mg/dL. His acute hepatitis panel resulted with reactive HAV IgM, although borderline assay signal-to-cutoff ratio (SCO) of 1.13 (cutoff $\geq$1.10), reactive HBV surface antigen, and reactive HBV core IgM with SCO of 46.4 (cutoff $\geq$1.0). He was HBV early antigen (HBeAg) positive with an HBV deoxyribonucleic acid (DNA) level of 23,500 IU/mL. Human immunodeficiency virus (HIV) and HCV antibody testing were negative.

Initial evaluation was also negative for anti–smooth muscle antibody, rheumatoid factor, *Cytomegalovirus* IgM, Epstein-Barr virus DNA polymerase chain reaction, HSV1/2 IgM, and HIV Ag/Ab/RNA. He denied any medications nor supplement ingestion to suggest drug-induced liver injury. Abdominal ultrasound was normal with no biliary dilation seen to suggest extrahepatic

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obstruction. The patient was given a presumptive diagnosis of acute HBV with possible acute HAV coinfection, although borderline HAV IgM reactivity was inconclusive. The patient was discharged 1 day later with downtrending liver enzymes (Figure 1).

One week later, the patient was readmitted with worsening jaundice. On readmission, laboratory test results showed AST 527 U/L, ALT 1035 U/L, and TB increased to 13.7 mg/dL. Repeat HAV IgM was again positive, now with a definitive SCO of 6.9. Repeat HBV DNA had decreased to 4440 IU/mL. No viral hepatitis treatment was given, and liver enzymes improved before discharge.

Four weeks later, AST was 110 U/L, ALT 247 U/L, and TB 2.0 mg/dL. Repeat HBV core IgM SCO was 6.5 (cutoff ≥1.0), and he had seroconverted to a negative HBeAg. At the following 3-month follow-up, AST, ALT, and TB had completely normalized. HBV DNA was no longer detectable, and he had seroconverted to a negative HBsAg. HAV IgM remained detectable at this follow-up, as well as on subsequent follow-ups, although with declining SCO values (Figure 1).

DISCUSSION

Thirty U.S. states, including Nevada, still report active ongoing HAV outbreaks, posing a significant public health threat.[1] Approximately 67% of reported cases required hospitalization and 2.7% resulted in death. MSM was identified as a risk factor in 21% of men presenting with HAV who reported sexual practices.[1] We present a notable case of suspected acute simultaneous coinfection with HAV and HBV in an MSM patient with postulated exposure to both viruses through oral-anal sexual contact in an area with known outbreaks.

Because no previous HBV serologies were available, the question arises as to whether our patient may have had reactivation of chronic HBV in the presence of acute HAV rather than acute coinfection with HBV. We would argue that high HBV core IgM SCO levels, rapid seroconversion from HBeAg positive to negative, and HBsAg loss at 6 months are more consistent with the latter. Furthermore, in 1 study, an HBV core IgM SCO ratio cutoff >8 had 96% sensitivity and 90% specificity in differentiating between acute and reactivated HBV (46.4 in our patient).[4]

Another possibility to consider is a false-positive HAV IgM. This is a well-described occurrence in the setting of acute

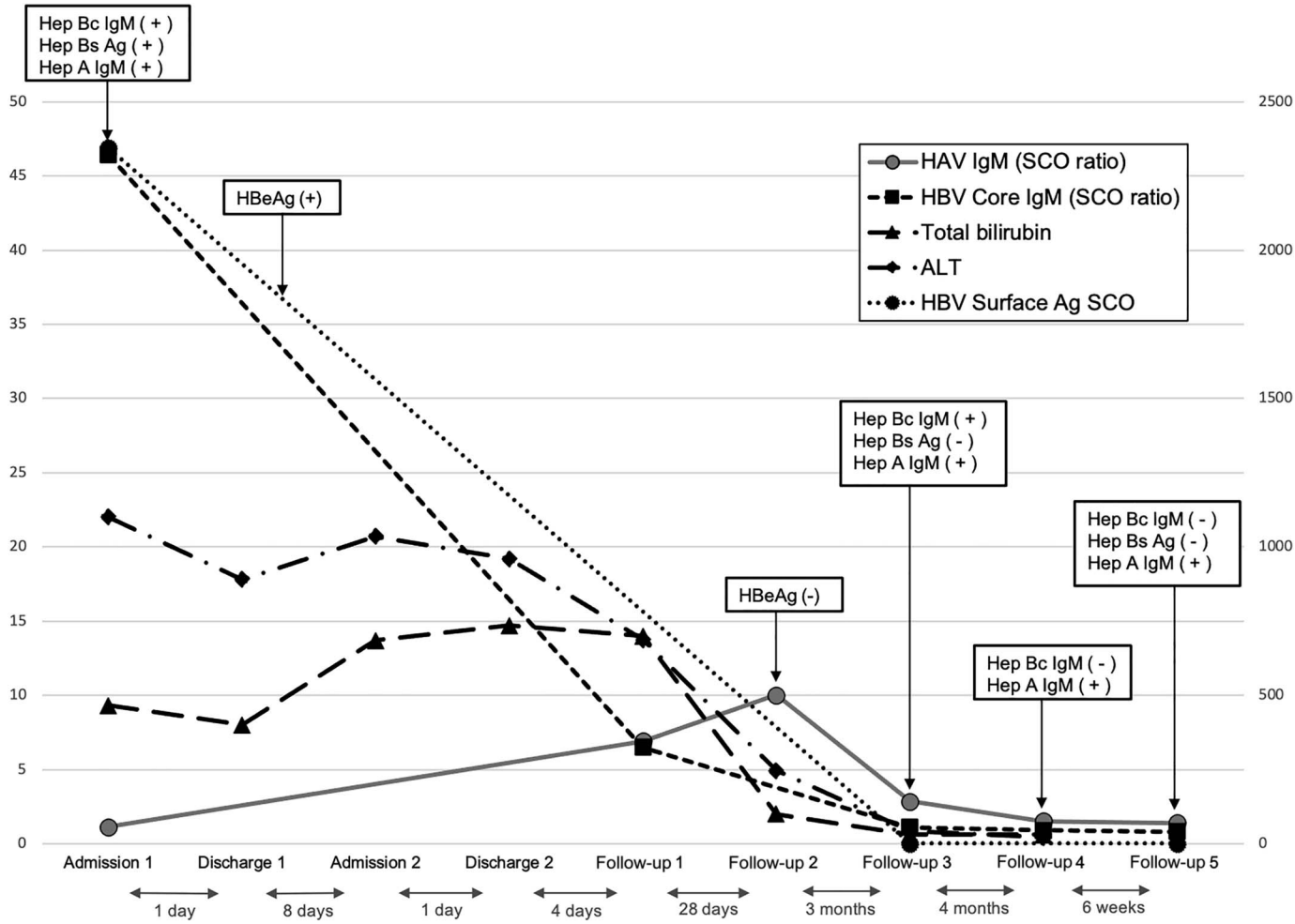

Figure 1. Laboratory values over key timepoints of evaluation. ALT, alanine aminotransferase; HAV, hepatitis A; HBV, hepatitis B; SCO, signal-to-cutoff ratio.

hepatitis from both viral and autoimmune etiologies, with polyclonal B-cell activation and molecular mimicry as likely mechanisms. However, multiple characteristics of this case argue for true acute HAV infection. First, HAV IgM persisted long after HBV had been cleared, and HBV core IgM was no longer detectable. Persistence of HAV IgM 10 months after the presentation is consistent with previous reports of prolonged antibody presence (up to 420 days) in subsets of patients with acute hepatitis A infection.[5] Second, common etiologies for cross-reactivity such as anti–smooth muscle antibody, rheumatoid factor, and IgM for other viral etiologies such as herpes simplex virus 1 and 2, HIV, Epstein-Barr virus, and *Cytomegalovirus* were notably absent. Finally, this case demonstrated a secondary peak in transaminases and bilirubin levels, a feature more often seen in the clinical course of HAV infection. A limitation of our case was that additional serologic testing for HAV including HAV IgG (not total), RNA polymerase chain reaction, and HAV Ag that may have helped differentiate between true- and false-positive testing was not available at our institution.

Based on limited data, HAV immunity among MSM in the United States ranges 18%–57%, under the critical threshold of 70% needed to prevent outbreaks.[6–8] Furthermore, lack of immunity to HBV in this population remains a problem (35%–50%), particularly in men born before universal HBV vaccination.[9,10] This case reinforces the need to increase awareness of at-risk populations for HAV and HBV infection and promote guideline-based vaccination of MSM to avert further morbidity and mortality.[11]

DISCLOSURES

Author contributions: B. Hiramoto and Y. Liu contributed equally to this study, wrote the manuscript, and revised the manuscript for intellectual content. L. Dara and K. Zhou revised the manuscript for intellectual content. K. Zhou is the article guarantor.

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Informed consent was obtained for this case report.

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