

INTRODUCTION

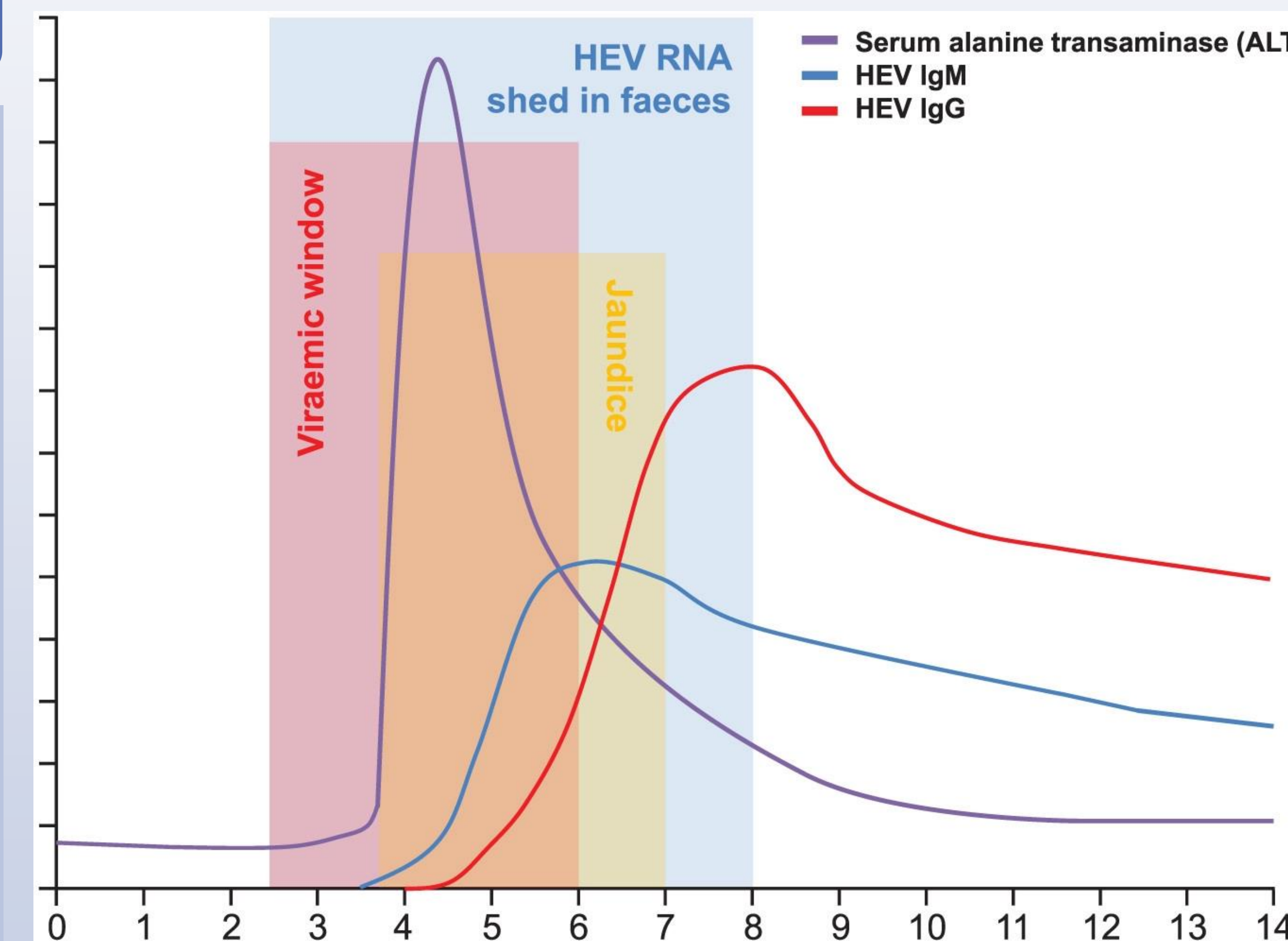
- Hepatitis E virus (HEV) can cause acute or chronic viral hepatitis and is an important public health concern, especially as it becomes endemic as a zoonotic infection in developed countries.
- We present a case of acute HEV infection in a male with false-positive cross-reactivity to Epstein-Barr Virus (EBV), and conclude that the diagnosis of viral hepatitis should be based on characteristic symptoms, elevated liver enzymes, serology, and confirmatory PCR testing.

CASE DESCRIPTION

- A 28-year-old Pakistani male with no past medical history presented with four days of right upper quadrant abdominal pain that was associated with subjective fevers and general malaise.
- His physical exam revealed vitals that were within normal limits and a benign abdominal exam. Laboratory studies were significant for hyperbilirubinemia of 6.6 with a direct bilirubin of 4.8, elevated alkaline phosphatase of 217, elevated aspartate aminotransferase (AST) of 1486, elevated alanine aminotransferase (ALT) of 2,600, and coagulation studies that revealed an international normalized ratio (INR) of 1.2.
- Computed tomography (CT) of the abdomen and pelvis with intravenous contrast revealed fatty infiltration of the liver and otherwise no acute abdominal or hepatobiliary pathology.
- Gastroenterology was consulted for further recommendations regarding the elevated liver enzymes and the patient was started on N-acetylcysteine infusion and admitted to for work-up and management of probable viral hepatitis. His abnormal liver tests were unremarkable except for detection of Hepatitis E antibody, Hepatitis E IgM antibody, and EBV IgM antibody with subsequent PCR analysis revealing no detection of Epstein-Barr Virus DNA.
- The patient was diagnosed with acute hepatitis E with a false-positive EBV infection due to serological cross-reactivity. Supportive care was continued, liver function tests trended down, and the patient clinically improved and was discharged with close outpatient follow-up.

DISCUSSION

- HEV is a single-stranded RNA virus that can cause acute or chronic viral hepatitis and is one of the most common causes of acute viral hepatitis worldwide.
- The incubation time for HEV infection can last up to six weeks and HEV RNA, anti-HEV IgM, and anti-HEV IgG antibodies can be detected at the time of diagnosis. Despite being an important serological marker for acute infection, Anti-HEV IgM antibodies have a relatively short window



- Serological and biochemical response to acute HEV infection over time.
- Courtesy of Webb GW, Dalton HR. Hepatitis E: an underestimated emerging threat. *Therapeutic Advances in Infectious Disease*. 2019;6.

of positivity at three to four months, whereas HEV RNA can be detected in the blood within three weeks with viral shedding lasting up to six weeks in the stool.

- The enzyme immunoassay is the most widely used serological method for the identification of anti-HEV IgG and IgM antibodies, but the identification of anti-HEV IgM and rising titers of anti-HEV IgG antibodies are inadequate for diagnosis due to the lack of specificity for these antibodies.
- Detection of HEV RNA in the blood or stool can also be used as a diagnostic means for confirming HEV infection, of which persistent detection for more than 3 months is used as a diagnostic criterion for determining chronicity of infection.
- Confounding the diagnosis of HEV is the increasingly acknowledged incidence of HEV, hepatitis HAV, CMV, and EBV cross reactivity, which is posited to be due to polyclonal B-cell stimulation. Due to the fact that the diagnosis of HEV infection in the clinical setting relies mainly on the performance of assays of anti-HEV IgM, the identification and awareness of factors influencing diagnostic accuracy is crucial regarding potential treatment options.

CONCLUSION

- In acute HEV infection, confirmatory testing with PCR analysis should be conducted to evaluate for false-positive serological cross-reactivity.
- The diagnosis of viral hepatitis should be based on characteristic symptoms, elevated liver enzymes, serology, and confirmatory PCR testing.