

## Unusual presentation of markedly elevated transaminase levels in a triple viral infection: A case report

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### ABSTRACT

We report a rare and unusual case of a 21-year-old male presenting with extremely elevated transaminase levels secondary to co-infection with cytomegalovirus, Epstein–Barr virus, and herpes simplex virus. Despite being immunocompetent, the patient displayed an extraordinary liver enzyme profile, with aspartate transaminase levels of 17,598 U/L and alanine transaminase of 13,666 U/L, significantly higher than what is typically observed in viral hepatitis. This case highlights the rare phenomenon of triple viral hepatitis leading to such profound liver injury and emphasizes the importance of considering multiple viral infections in patients with unexplained hepatic injury and severely deranged liver function tests.

**Key words:** Cytomegalovirus, Epstein–Barr virus, Hepatitis in immunocompetent, Herpes simplex virus, Transaminase levels, Triple viral hepatitis

Markedly elevated transaminase levels are generally seen in conditions such as acute viral hepatitis, drug-induced liver injury, or autoimmune hepatitis. However, the degree of liver enzyme elevation observed in this case is highly unusual, especially in an immunocompetent individual without chronic liver disease or toxic drug exposure. Viral hepatitis, caused by infections such as cytomegalovirus (CMV), Epstein–Barr virus (EBV), and herpes simplex virus (HSV), can result in liver injury, but severe elevations to the extent seen in this patient are uncommon.

This report aims to discuss the pathophysiology behind the exceptionally high transaminase levels in a case of co-infection with CMV, EBV, and HSV and to explore the clinical challenges in diagnosing such cases. The rationale for reporting this case lies in its uniqueness, given the combination of multiple viral infections causing extreme hepatic insult and the learning points it offers for clinicians.


### CASE REPORT

A 21-year-old male presented on September 26, 2024, with a mild fever for 4 days and a rash for 2 days. The rash was generalized and non-itchy.

On general examination, the patient appeared alert and oriented, with no signs of acute distress. Vitals were as follows: Temperature 38.1°C, heart rate 112 bpm, blood pressure 100/80 mmHg, respiratory rate 22 breaths/min, and oxygen saturation 98% on room air. No significant findings were noted on systemic examination.

Laboratory investigations of the patient are given in Table 1. Further diagnostics, such as an ultrasound of the abdomen, showed calculus cholecystitis and minimal ascites. Contrast-enhanced computed tomography of the abdomen showed hepatosplenomegaly, gallbladder wall edema, and mild ascites. These findings were suggestive of viral hepatitis. The viral serology of the patient was as follows: CMV immunoglobulin M (IgM) 28.80 U/L, CMV immunoglobulin G (IgG) 89.4 U/L (positive), EBV IgM >160 U/L, EBV IgG >97.3 U/L (positive), and HSV-1 IgM positive.

Renal function and electrolyte levels were unremarkable, but a complete blood count showed thrombocytopenia, leading to the transfusion of 4 units of fresh frozen plasma. The patient was managed conservatively with supportive care and antibiotics. The patient was given L-ornithine L-aspartate infusion, rifaximin 550 mg BD, and ursodeoxycholic acid 300 mg TDS. By October 02, 2024, aspartate transaminase (AST) and alanine transaminase (ALT) levels had significantly decreased, indicating the resolution of the acute hepatic insult. The patient is clinically better, is improving, and has now started going to his job.

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**Table 1: Laboratory investigations of the patient**

| Investigation              | Day 1 values | Day 7 values |
|----------------------------|--------------|--------------|
| Aspartate transaminase     | 17,598 U/L   | 173 U/L      |
| Alanine transaminase       | 13,666 U/L   | 1,115 U/L    |
| Total bilirubin            | 4.9 mg/dL    | 7.0 mg/dL    |
| Direct bilirubin           | 2.4 mg/dL    | 1.2 mg/dL    |
| Alkaline phosphatase       | 237 U/L      | 124 U/L      |
| Gamma-glutamyl transferase | 303 U/L      | 105 U/L      |

## DISCUSSION

The hallmark of this case is the unusually high transaminase levels, which are not typically observed in viral hepatitis, even with multiple viral infections.

### CMV infection

A systematic review of immunocompetent patients with CMV infection reported that the colon and rectum were the most common primary sites [1]. Liver involvement is rare and can vary from tender hepatomegaly to fulminant hepatic failure [2,3]. Acute CMV hepatitis, though unusual, has been reported in immunocompetent adults [2-6]. In immunocompetent individuals, CMV hepatitis usually causes mild-to-moderate transaminase elevation (100–500 U/L), but severe cases with higher levels have been reported, though rarely as high as in this case.

### EBV hepatitis

EBV-related hepatitis can cause elevations in transaminases, but AST and ALT levels exceeding 1,000 U/L are uncommon. Serum transaminases are elevated but are less than fivefold the normal levels in most cases and rarely exceed 10 times the normal levels in primary EBV infections [7]. Severe cases of EBV-induced hepatitis are generally seen in immunocompromised patients, making this patient's enzyme levels strikingly unusual.

### HSV hepatitis

HSV-related hepatitis, while rare in immunocompetent individuals, can present with fulminant hepatitis and very high transaminase levels. HSV hepatitis is an uncommon cause of acute liver failure, accounting for 0.8% of all cases and only 2% of all viral hepatitis [8,9]. It is mostly seen in immunocompromised individuals and pregnant women in their third trimester following an orogenital HSV-1 or HSV-2 infection, though previous reports have shown up to 25% of cases in immunocompetent individuals [8]. Due to a lack of specific clinical findings, the diagnosis is frequently missed on presentation and can lead to rapid progression to fulminant liver failure and multiorgan collapse if untreated [10]. HSV-induced hepatitis is known to cause hepatocellular necrosis, which could account for the massive transaminase elevation in this patient.

The combined hepatic insult from CMV, EBV, and HSV likely led to a more severe inflammatory response than typically seen with a single viral infection. Each virus can induce liver damage through distinct mechanisms: CMV induces cytopathic effects and a robust immune response leading to hepatocyte damage, EBV causes hepatic inflammation primarily through T-cell-mediated immune responses targeting infected hepatocytes, and HSV causes direct cytopathic effects on hepatocytes, leading to hepatocellular necrosis.

The simultaneous presence of these viruses may have caused compound liver damage, explaining the marked transaminase elevations. Literature suggests that viral co-infections can act synergistically, exacerbating the inflammatory and cytopathic effects on the liver.

In cases of CMV-related hepatitis, transaminase levels are typically less extreme, ranging from 200 to 500 U/L, with rare reports of elevations exceeding 1,000 U/L. A case series reported by Fishman [11] noted that CMV infection alone is unlikely to cause transaminase levels above 2,000 U/L in immunocompetent individuals. EBV-induced hepatitis, described by Suh [12], rarely results in AST/ALT levels beyond 1,000 U/L, except in severe cases with multiorgan involvement. HSV-related hepatitis, though rare in immunocompetent hosts, has been reported to cause fulminant hepatic failure with transaminase levels reaching up to 10,000 U/L in some cases [13].

The simultaneous occurrence of these three viral infections represents a rare and severe hepatic insult that likely accounts for the remarkable elevation in transaminase levels in this patient.

## CONCLUSION

This case represents an extremely rare presentation of markedly elevated transaminase levels in an immunocompetent individual with triple viral hepatitis caused by CMV, EBV, and HSV. Such extreme elevations in transaminase levels are unusual and underscore the importance of considering multiple viral infections in cases of unexplained hepatic injury. Early diagnosis and supportive care are crucial for favorable outcomes in patients with such severe hepatic involvement.

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