

Case Report

Acute Liver Failure Due to Herpes Simplex Virus Hepatitis in an Immunocompetent Patient

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Abstract

Herpes Simplex Virus (HSV) is a rare etiology of Acute Liver Failure (ALF) especially in immunocompetent patients. Here, we describe the case of a 44-year-old immunocompetent male who was admitted for ALF due to HSV hepatitis. Intravenous acyclovir was initiated prior to PCR HSV confirmation due to a recent history of an unprotected sexual encounter. The patient's liver function recovered and liver transplant was avoided. In conclusion, a detailed medical history is critical in establishing an ALF diagnosis in immunocompetent patients and to initiate empiric treatment.

Keywords: Herpes simplex virus; Acute liver failure; Acyclovir

Introduction

The most common causes of Acute Liver Failure (ALF) in developed countries are drug-induced toxicity and viral infections. Among cases caused by viruses, disseminated Herpes Simplex Virus (HSV) is a rare but treatable etiology for ALF and often missed on initial presentation. Appropriate treatment will be delayed if ALF is not identified promptly, and the mortality rate for ALF can be >80% if it goes undiagnosed. HSV hepatitis represents <1% of ALF cases in immunocompetent patients [1]. Reports of disseminated HSV causing ALF have been reported in pregnant patients or patients with recent surgery [2,3]. Patients with disseminated HSV often present with nonspecific symptoms like fever, myalgias, and abdominal pain. The lack of typical mucocutaneous lesions with HSV makes it a difficult diagnosis in an otherwise healthy patient. A high index of suspicion and the initiation of Intravenous (IV) acyclovir in the proper clinical context is critical in improving survival outcomes.

Case Presentation

A 44-year-old immunocompetent male with a history of psoriatic arthritis presented to the hospital with a six-day history of abdominal pain, pharyngitis, and generalized weakness. The patient was not on chronic immunosuppressive agents for his psoriasis. He recently completed a two-week 40 mg prednisone course, an old prescription, one week prior to this hospitalization. He reported a three-day course of unprescribed ciprofloxacin and kratom for his pharyngitis. He was hemodynamically stable on arrival. His physical exam was significant

for herpetic whitlow of the left fourth finger, pharyngitis, and diffuse abdominal pain. His neurological status was intact and at baseline. His liver enzymes were elevated on admission and consistent with ALF, including an aspartate aminotransferase level of 11,261 U/L, alanine transaminase level of 10,320 U/L, total bilirubin level of 2.5 mg/dL, alkaline phosphatase level of 151 U/L, ferritin level of >10,000 ng/mL, and an INR of 2.7. He also had an Acute Kidney Injury (AKI) with oliguria on presentation with a creatinine level of 1.80 mg/dL. His acetaminophen level was <10 mcg/mL. An ultrasound of the abdomen with Doppler was negative for portal vein thrombosis (Figure 1). A computed tomography scan (without contrast) of the abdomen revealed hepatosplenomegaly (Figure 2).

During a detailed history, the patient related that his last unprotected sexual encounter with his long-term partner was nine months previous and his sexually transmitted disease test results at that time were negative. His history was negative for most common causes of ALF including Tylenol toxicity and drugs. Based on this information he was started on empiric IV acyclovir and N-acetylcysteine. On day two, a HSV PCR was positive with a viral load of 40,786,000 copies. He underwent a bone marrow biopsy for hemophagocytic lymphohistiocytosis and malignancy; it was negative. Testing was also negative for Wilson's disease and hereditary hemochromatosis. The patient also had concurrent ciprofloxacin-induced nephrotoxicity contributing to his oliguric AKI stage 3. He was treated with three days of molecular adsorbent recirculating system and continuous renal replacement therapy for an increasing total bilirubin level (peak: 33 mg/dl) and oliguric AKI with ciprofloxacin crystals, respectively. He received three doses of IV Immunoglobulin (IVIG) and the maximum renal-adjusted dose of acyclovir for his high HSV viral load. The patient was not a transplant candidate due to his uninsured status.

The patient improved on supportive treatment and IV acyclovir. His creatinine level improved with return of kidney function. The patient was sent home on 500 mg PO valacyclovir to be continued until his outpatient appointment with Infectious Disease. The patient was seen in an outpatient clinic four weeks after discharge with improved liver enzymes and return of kidney function to normal.

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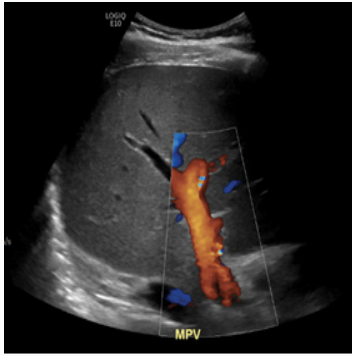


Figure 1: Ultrasound of the abdomen with Doppler image. Arrows indicate a patent main portal vein.



Figure 2: Computed tomography scan (without contrast) of the abdomen. Arrows indicate hepatosplenomegaly.

Discussion

HSV hepatitis is a rare form of ALF, comprising only 1% of ALF cases and 2% of viral-associated ALF cases [4]. It occurs more commonly in immunocompromised patients, including cases of steroid use, pregnancy, human immunodeficiency virus, and autoimmune diseases [1]. In a retrospective study of 137 patients with HSV hepatitis <50% had a rash; most (>58%) of the cases were diagnosed on autopsy [5]. ALF caused by HSV hepatitis can quickly progress to fulminant liver failure in immunocompetent patients if diagnosis and treatment are delayed. In the above-mentioned study, 74% of cases progressed to death or liver transplant; 51% of those patients were treated with acyclovir and 88% were untreated ($P=0.03$) [3]. Together, this indicates the importance of early diagnosis and treatment of HSV hepatitis with IV acyclovir. IV acyclovir is currently not a standard empiric treatment for ALF.

Very few cases of ALF due to HSV in immunocompetent patients have been described in the literature [6-9]. Poley et al. [6] described the case of a 41-year-old female with no significant history who presented with a nonspecific viral illness and systemic inflammatory response syndrome. The patient died within 70 hours of admission and postmortem biopsy indicated HSV hepatitis as the cause of her fulminant liver failure. Francis et al. [7] described the case of a 58-year-old female with a remote medical history of breast cancer and chemotherapy that was found to have HSV hepatitis. Due to her persistent fevers along with symptoms of right upper quadrant abdominal pain and elevated liver enzymes, she was tested for HSV and a diagnosis was later confirmed with liver biopsy. She was started on IV acyclovir with complete resolution of liver enzyme levels and recovery [7]. Down et al. [8] described a rare case of a 67-year-old

male with history of prostatectomy due to prostate cancer seven years prior who presented with flu-like illness and mild elevation in liver enzymes. This patient was found to have multiple bilobar hypoattenuating lesions within the liver on CT imaging. Liver biopsy and aspiration of the lesions revealed HSV hepatitis and the patient was started on IV acyclovir with complete resolution of his symptoms. In this case, the patient did not meet criteria for ALF and hence had time for further evaluation leading to a good outcome. Most recently in August 2022, Franco et al. [9] described the case of a 46-year-old immunocompetent female with history of total thyroidectomy due to papillary carcinoma 14 years prior who presented with one week of nausea and vomiting. After admission, the patient developed obtundation, psychomotor lentification, and ALF [9]. Due to her symptoms, she was started on empiric IV acyclovir for HSV hepatitis, which was later confirmed by liver biopsy. The patient recovered with normalization of liver function and completed 21 days of acyclovir [9]. In all the above cases, the early initiation of IV acyclovir in otherwise immunocompetent patients in ALF likely resulted in complete recovery.

In this case report, the patient's sexual encounter history, physical exam findings of pharyngitis, and herpetic whitlow in an otherwise immunocompetent patient, resulted in a differential diagnosis of HSV infection and rapid initiation of empiric IV acyclovir. Due to an extremely high viral load, he also received three doses of IVIG. The patient was recently on a two-week 40 mg prednisone steroid taper for his otherwise asymptomatic psoriasis, which likely predisposed him to HSV hepatitis. He was otherwise immunocompetent, and the early initiation of IV acyclovir likely improved the outcome in this patient.

Conclusion

A detailed history in patients with ALF, especially in an immunocompetent patient, is critical in establishing a diagnosis. There should be a low threshold to initiate empiric IV acyclovir; the acyclovir regimen can be reconsidered upon receipt of negative HSV test results.

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