A case report of disseminated herpes simplex hepatitis masquerading as spinal headache

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ABSTRACT
Hepatitis is a rare complication of herpes simplex virus (HSV) which can lead to acute liver failure, liver transplant, or death. This complication is more commonly seen in neonates, immunocompromised, or pregnant patients. Early recognition of disease facilitates prompt treatment with antiretrovirals and prevent its progression. To our knowledge, only 30 cases have been reported. Our patient presented with headaches and elevation of transaminases followed by vesicular rash. Culture tested positive for HSV1 and HSV2 and the patient was successfully treated with Acyclovir.

1. Introduction
Hepatitis is a rare and potentially lethal complication of herpes simplex virus (HSV), most commonly affecting immunosuppressed patients. It is typically diagnosed via autopsy due to its nonspecific clinical presentation. Although this disease has been associated with high morbidity and mortality, if recognized and treated early, the prognosis can be favorable. We describe a case of an immunocompetent 31-year-old female who presented with an acute headache, fever, and elevated aminotransferases. Disseminated HSV hepatitis was diagnosed after the development of vesicular lesions tested positive for HSV.

2. Case
A 31-year-old female with a past medical history significant for hidradenitis suppurativa presented to the emergency department complaining of headache associated with fever. The headache was described as band-like, retro-orbital pressure, worsened with movement. Oral temperature was 102.0°F. The remaining vital signs were within normal limits. The physical exam was completely unremarkable including a normal-appearing fundoscopic examination, negative Brudzinski’s and Kernig’s sign. A chest x-ray, electrocardiogram, and computed tomography of the head were without any abnormalities. A lumbar puncture was completed. The cerebrospinal fluid (CSF) appeared clear. CSF laboratory analysis was grossly unremarkable except for 15 red blood cells/µL. The patient improved with one dose of acetaminophen/butalbital and was discharged home from the emergency department. The patient returned later the same day with retro-orbital pressure, worsened with movement. Oral temperature was 102.0°F. The remaining vital signs were within normal limits. The patient was admitted for further evaluation. Magnetic resonance imaging (MRI) of cervical, thoracic, and lumbar spine was obtained which demonstrated a CSF leak with moderate inflammation of the epidural space; concerning epidural abscess. She was treated empirically with vancomycin and cefepime. She remained afebrile on Naprosyn. A viral meningoencephalitis panel of the CSF returned negative, as well as bacterial culture. Further testing of liver pathology including antimitochondrial antibody, smooth muscle antibody, alpha-1 antitrypsin level, and antinuclear antibodies, all of which were negative. Cytomegalovirus and Epstein-Barr virus IgM and IgG antibody titers were negative as well. On the fourth day of hospitalization, the patient developed a papulovesicular rash involving the right thenar eminence, left forearm, left subclavian region, and back. Plasma HSV DNA level via PCR came back positive for HSV 2. She was also remarkable for HSV1 and HSV 2 immunoglobin M antibody titers of ≥1:320. Culture of the vesicles on her hand came back positive for Herpes Simplex isolate. Enzyme immunoassay for syphilis antibody returned negative. She was started on intravenous acyclovir 10 mg/kg every 8 hours for disseminated herpes infection. Human immunodeficiency virus-1 (HIV-1) RNA quantitative PCR returned negative. Following the initiation of Acyclovir, her LFTs continued to trend down. Prior to discharge, she had an ALP 155 U/L, AST 75 U/L, and ALT 175 U/L. After 3 days, the patient was transitioned to oral valacyclovir and discharged home. Unfortunately, Patient’s beta-hCG was negative. Liver function tests (LFT) were remarkable for alkaline phosphatase (ALP) 224 U/L, aspartate aminotransferase (AST) 356 U/L, alanine aminotransferase (ALT) 371 U/L, total bilirubin 0.6 mg/dL. Amylase and lipase were within normal limits. The patient was admitted for further evaluation. 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the patient did not follow up as an outpatient to undergo repeated LFT testing to confirm normalization.

3. Discussion

We performed a literature review using MEDLINE with search terms including ‘hepatitis’, ‘immunocompetent’ ‘herpes simplex virus’. Only 29 cases have been reported from 1986 to 2019 pertaining to HSV hepatitis in an immunocompetent host. The criteria for inclusion of cases were: patient age 18 years or older and an immunocompetent state. Immunocompromised or pregnant patients were excluded from our search. HSV hepatitis is a disease that more commonly affects immunocompromised patients [1]. While the mechanism of disseminated infection in immunocompetent patients remains unclear, it has been thought to be directly related to a high inoculation of HSV viremia during primary infection overcoming immunological defenses [1]. Skin manifestations are present in less than one-half of reported HSV hepatitis cases [2]. HSV is responsible for less than <2% of the viral causes of fulminant hepatitis and less than <1% of all causes of acute liver failure [3]. Clues to the possible diagnosis include the triad of fever, transaminitis, leukopenia, and low bilirubin levels [4]. Diagnosis can be confirmed by rapid HSV DNA levels via PCR in plasma or transjugular liver biopsy with virus identification on tissue sections [5]. Early recognition and treatment are imperative as it is highly responsive to acyclovir treatment, preventing the progression to fulminant liver failure. Review of the literature also suggests the initiation of empirical therapy in patients with progressive hepatic failure with no underlying cause [6]. We recommend keeping disseminated HSV hepatitis as a differential diagnosis in any patient who presents with elevated aminotransferases and fever of unknown etiology in the presence or absence of skin lesions.

4. Conclusion

Prompt diagnosis of HSV hepatitis prevents the progression of liver failure. Our patient was successfully treated with intravenous acyclovir followed by oral valacyclovir. Diagnosis of HSV hepatitis is often complicated by its rarity and nonspecific signs and symptoms. For this reason, clinicians should be aware of this condition and maintain it as a differential diagnosis in any patient who presents with aminotransferases of unknown etiology.

Disclosure statement

The authors report no conflict of interest.

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