ECRONICON OPEN ACCESS

EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Case Report

Herpetic Hepatitis Resolution in an Immunocompetent Patient After Early Treatment with Acyclovir

Fernanda Cruz-Nunes[1], Vivian Rotman[1,2], Klaus Steinbrück[1,3]*, Reinaldo Fernandes[1,4] and Rodrigo Luz[1,5]

[1]Hepatobiliary Surgery and Liver Transplantation Unit, Complexo Hospitalar de Niterói, Niterói, Brazil

[2]Hepatology Department, Clementino Fraga Filho University Hospital, Rio de Janeiro Federal University, Rio de Janeiro, Brazil

[3]Hepatobiliary Unit, Bonsucesso Federal Hospital, Health Ministry, Rio de Janeiro, Brazil

[4]Surgery Department, Antonio Pedro University Hospital, Fluminense Federal University, Niterói, Brazil

[5]Internal Medicine Department, Antonio Pedro University Hospital, Fluminense Federal University, Niterói, Brazil

***Corresponding Author:** Klaus Steinbrück, Hepatobiliary Surgery and Liver Transplantation Unit, Complexo Hospitalar de Niterói, Niterói and Hepatobiliary Unit, Bonsucesso Federal Hospital, Health Ministry, Rio de Janeiro, Brazil.

Received: October 28, 2022; **Published:** October 18, 2022

Abstract

Herpes Simplex virus (HSV) hepatitis accounts for only 1% of all acute liver failures and lethality rates can be extremely high (up to 75%). High levels of viral load during first infection and immunocompromised hosts are major risk factors for poor outcome. Delayed diagnosis without antiviral therapy also contributes to the unfavorable outcome. Due to its severity, is acceptable to start treatment empirically with acyclovir in cases of acute liver failure of unknown origin. PCR for HSV is an important non-invasive tool for diagnosis but not always available. Liver biopsy may be needed to confirm the diagnosis of HSV and should be consider carefully owing to elevated risk of bleeding in critical patients.

Herein we describe a case of an immunocompetent young patient with herpetic hepatitis resolution after early treatment with acyclovir.

Keywords: *Herpes Simplex; Hepatitis; Infection; Treatment; Acyclovir*

Introduction

Herpetic hepatitis is a rare complication of Herpes Simplex Virus (HSV) infection, with a wide clinical spectrum. Although pathogenesis is not completely elucidated, it is well known that its complications are associated with high mortality rate. Indeed, it can rapidly end in fulminant hepatic failure, that occurs more frequently in immunocompromised patients or during pregnancy, particularly in the third trimester. Early treatment is essential for a positive outcome [1-4].

Case Report

A 21-year-old woman, with no significant past medical history, presented with a five-day course of odynophagia and fever treated unsuccessfully with amoxicillin/clavulanic acid. She was admitted at the hospital with sialorrhea, abdominal pain and vomits. Physical examination revealed tonsillitis, ascites, hepatomegaly and painful liver. Jaundice, asterixis or other signs of liver failure were not present. Laboratory exams showed elevated inflammatory parameters, highly increased aminotransferases (roughly thirteen times the upper reference value), low prothrombin activity (64%), low albumin and fibrinogen levels (2.4 mg/dL and 163 mg/dL, respectively), elevated

gamma-glutamyltransferase (468 mg/dL), normal alkaline phosphatase, bilirubin and factor V. Bacterial cultures including blood and urine were negative.

Abdominal MRI revealed ascites, pleural effusion and splenohepatomegaly. Liver parenchyma had a diffuse heterogeneous signal, with reticular areas, without dominant nodules (Figure 1). Ceruloplasmin, autoimmune markers, total IgG levels, VDRL, serology for hepatitis A, B and C viruses, cytomegalovirus (CMV), parvovirus B19, adenovirus, HIV, Epstein-Barr-IgM, Chagas disease, toxoplasmosis, *Chlamydia psittaci* and HSV-6 were negative. HSV 1-2 IgM serology was positive and IgG negative, therefore parenteral acyclovir (10 mg/kg every eight hours) was initiated in the first 48h of hospitalization. Laparoscopy with liver biopsy was performed. Macroscopically, liver surface was smooth and with many whitish spots (Figure 2). Histopathological analysis was consistent with infection by HSV-1, and immunohistochemistry analysis had positivity for HSV-1 antibodies and immunonegativity for HSV-2 and CMV.

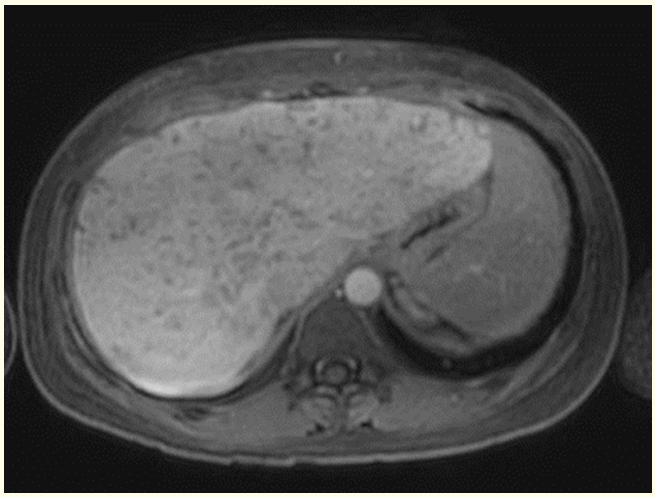

Figure 1: *MRI T1 weight image showing liver parenchyma with a diffuse heterogeneous signal and reticular areas.*

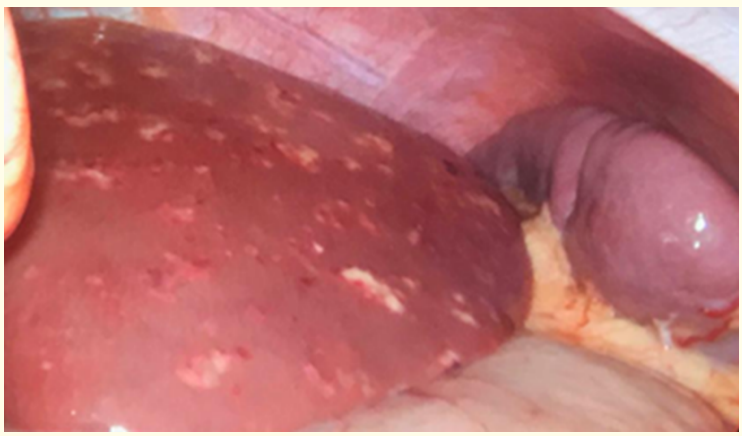

Figure 2: *Laparoscopic image of the liver showing a smooth surface with many whitish spots.*

After three days of intravenous acyclovir, liver function tests began to improve, and treatment was switched to oral valacyclovir (1g thrice daily) on the 5th day of treatment. Patient was discharged 13 days after hospitalization. Laboratory parameters were completely normal at the end of a four-week treatment course and no sequel or recurrence was observed after 24 months of follow-up.

Discussion

Herpes Simplex virus hepatitis causes less than 1% of all acute liver failures. Twenty-five percent of cases occurs in immunocompetent individuals. Advanced age, male gender, encephalopathy, coagulopathy, pregnancy, and immunosuppression are the main risk factors for poor outcomes [4]. Mechanisms favoring infection dissemination have been hypothesized, such as high levels of viral load during a first infection, high virulence promoted by a new infection caused by a different virus strain and an infection caused by hepatotropic strains. In immunocompromised status, disseminated infection could be also related to dysfunction of macrophages, cytotoxic T lymphocytes and impairment of delayed-type hypersensitivity reactions [3].

Clinical presentation could be indistinguishable from other acute hepatitis causes, although literature describes the anicteric pattern as a common finding [1-4]. The most observed symptom in herpetic hepatitis is fever (>80%) followed by increased serum aminotransferases, thrombocytopenia, leucopenia, hepatomegaly, abdominal pain, nausea/vomiting, encephalopathy and acute liver failure [3,4]. Half of the patients do not manifest classic mucocutaneous lesions, which could make diagnosis more difficult [1,3]. Serological tests are limited due to low positive and negative predictive values. Since HSV PCR is not always easily available, liver biopsy (considered the gold standard method), is an option for diagnostic elucidation [1,3]. In the case described, laparoscopic liver biopsy was done, due to unavailability of HSV PCR, combined with a high diagnostic suspicion and absence of contraindications to the biopsy.

Liver macroscopic examination reveals a mottled appearance, riddled with multiple red-yellowed lesions, as observed in this case. Histopathology analysis shows focal or confluent areas of acidophilic type necrosis, scarce inflammation and predominant centrilobular necrosis with minimal portal involvement [3].

MRI scan findings are non-specific, but may show hepatomegaly along with diffuse hypodense 1 - 4 mm lesions, related histologically to foci of acute hepatic necrosis. Other infections, such as candida/fungal hepatitis and systemic varicella zoster, could have similar appearance. Although these tiny lesions are not readily visualized on ultrasound, this method can help in the differentiation between focal fatty deposition and focal hepatic necrosis that may appear similarly on computed tomography. In pregnancy, ultrasound could play a role on excluding acute fatty liver disease that would typically appears as a diffusely increased hepatic parenchymal echogenicity [5].

Regarding treatment, based on the observed delay in HSV diagnosis, low frequency of severe side effects of Acyclovir and improved outcomes with early treatment, preemptive acyclovir administration is the main recommendation of reference centers, especially for patients with high probability of Herpes hepatitis presenting with acute liver failure [4].

Conclusion

Herpetic hepatitis is a rare cause of fulminant hepatitis. Prompt diagnosis with early anti-viral treatment allows quick resolution and better outcome.

Diagnosis is harder in the oligosymptomatic presentation, thus, it is important to consider HSV infection in hepatitis cases without an identified common etiology, especially in those with fever or in immunocompromised patients.

Bibliography

1. Riediger C., *et al*. "Herpes simplex virus sepsis and acute liver failure". *Clinical Transplantation* 23 (2009): 37-41.

2. Magawa S., *et al*. "A literature review of herpes simplex virus hepatitis in pregnancy". *Journal of Maternal-Fetal and Neonatal Medicine* 33 (2002): 1774-1779.

3. Kaufman B., *et al*. "Herpes simplex virus hepatitis: case report and review". *Clinical Infectious Diseases* 24 (1997): 334-338.

4. Norvell JP., *et al*. "Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases". *Liver Transplant* 13 (2007): 1428-1434.

5. Tripuraneni V., *et al*. "Fulminant herpes simplex viral hepatitis: ultrasound and CT imaging appearance and a review of the imaging literature". *Clinical Imaging* 38 (2014): 191-194.

Volume 9 Issue 11 November 2022
©All rights reserved by Klaus Steinbrück*., et al.*