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Case report

HSV-1 hepatitis in an immunocompetent patient – Act before you know

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ABSTRACT

Herpes simplex virus type 1 (HSV-1) hepatitis is an unusual complication of HSV infection, which frequently results in acute liver failure. Even though the most affected individuals are immunosuppressed patients, around 25 % patients who present with HSV hepatitis are immunocompetent. We report a case of an anicteric febrile hepatitis in a 46-year-old immunocompetent women in which the early suspicion of HSV hepatitis allowed empirical treatment and later diagnosis confirmation by liver biopsy.

Introduction

Herpes simplex virus (HSV) hepatitis is an unusual complication of HSV infection, which frequently results in acute liver failure (ALF) [1]. It accounts for less than 1% of all ALF cases and less than 2 % of all viral etiologies [1]. The most affected individuals are immunosuppressed patients, such as solid organ transplant recipients and pregnant women in their third trimester [1,2]. However, around 25 % patients who present with HSV hepatitis are immunocompetent, in which multiple mechanisms have been proposed to explain disseminated infection [1, 3]. The diagnosis of HSV hepatitis is frequently missed on presentation due to lack of specific clinical findings, especially in individuals without risk factors for disseminated infection, which can lead to rapid progression to ALF in the absence of early antiviral therapy [4].

Case

A 46-year-old Brazilian woman living in Portugal for the past 3 months was recently admitted to our gastroenterology ward due to a one-week course of intense nausea and vomiting. Past medical history included total thyroidectomy 14 years before due to thyroid papillary carcinoma and bariatric surgery 12 years before. On the first day of hospitalization, she developed persisting fever and on the following day obnubilation and psychomotor lentification was seen. Due to *E. coli* bacteriuria, amoxicillin with clavulanate was started. On day 5, laboratory results revealed *de novo* elevation of aspartate aminotransferase (AST) (1111 U/L; normal: < 32 U/L) and alanine aminotransferase (ALT) (507 U/L; normal < 33 U/L) with normal total bilirubin (0,25; normal: < 0,9) and raised LDH (1959 U/L; normal: 135–225 U/L) and RCP (10,1 g/dL; normal < 0,5 g/dL). Liver doppler ultrasound was normal, excluding acute or chronic pathology, including vascular liver disease. At this point, the patient was found to have severe hypothyroidism (T4 < 1,3 pmol/L; normal: 12–22 pmol/L and TSH 76,9 uUI/ml; normal: 0,27–4,20 uUI/ml) since she was not taking her usual medication for one week due to vomiting. She promptly begun thyroid function correction. Furthermore, due to suspicion of drug-induced liver injury, amoxicillin with clavulanate was stopped. On day 8, aminotransferases and LDH peaked at AST 4889 U/L, ALT 1373 U/L and LDH 3451 U/L with an INR of 2,1 and maintaining normal total bilirubin. Initial workup showed inconclusive IgM HSV1 and positive IgG HSV1 with the remaining investigation being negative, including ANA, ASMA, immunoglobulins, SLA-LP, LKM, LC1, ceruloplasmin, AgHBs, AcHBs, AcHCV, IgM and IgG HEV, IgM and IgG HAV, IgM and IgG EBV, IgM and IgG CMV, IgM and IgG adenovirus, DNA adenovirus, IgM and IgG HSV-2 and HIV. Given the acute liver insufficiency preceded by persisting fever and obnubilation, disseminated HSV infection presenting with hepatitis and encephalitis was considered and empiric acyclovir was initiated (10 mg/kg 8/8 h). Transjugular liver biopsy revealed extensive areas of intralobular necrosis with nuclear positivity for HSV-1 in several cells at the periphery of the necrosis zones, thus confirming the diagnosis of HSV-1 hepatitis. During the following days, the patient had complete resolution of fever and mental status, as well as normalization of transaminases and INR, having completed 21 days of acyclovir.

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Discussion

HSV hepatitis' clinical presentation is non-specific, being thus usually misdiagnosed and this case had additionally several pitfalls that made it even more challenging. First, AST/ALT ratio was atypical for viral etiology and, in combination with an elevated LDH, initially pointed out to ischemic etiology. However, clinical course was atypical for ischemia and doppler liver ultrasound excluded vascular etiology. Second, altered mental status could have been mistaken either for hepatic encephalopathy in the context of ALF, or for severe hypothyroidism, masking the hypothesis of a central nervous system infection. On the other hand, HSV encephalitis can also explain the higher rise of AST comparing to ALT. Third, even though only 30–50 % of patients present with characteristic mucocutaneous lesions, its absence hindered the diagnosis [3]. Since HSV serology was inconclusive, blood HSV PCR was not available at our hospital and lumbar puncture could not be performed due to rapid-onset coagulopathy, the only way to confirm the diagnosis was by liver biopsy, for which it was crucial to have already considered the diagnosis in order to be able to request HSV identification.

The key point is that, when facing an anicteric febrile hepatitis, HSV should always be considered even in immunocompetent individuals, since it constitutes a medical emergency and empirical therapy should be immediately instituted pending diagnostic confirmation.

CRediT authorship contribution statement

Ana Rita Franco: Writing – original draft, Conceptualization. **Rui Mendo:** Writing – review & editing. **Rita Barosa:** Conceptualization, Writing – review & editing, Supervision. **Pedro Figueiredo:** Conceptualization, Writing – review & editing, Supervision.

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Ethical approval

N/A.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of interest

The authors have nothing to declare.

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