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Case report

Acute hepatitis as a manifestation of primary HSV infection in a healthy child

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Abstract

Several herpesviruses can cause hepatic injury, but herpes simplex virus (HSV) is rarely involved in immune-competent patients, beyond the neonatal age. We report a rare case of acute hepatitis associated with primary HSV infection in a previously healthy child. Therefore, HSV infection should be actively investigated in healthy children developing acute hepatitis without acute liver failure, if the most common infectious agents have been excluded, despite the absence of the typical vesicular herpetic skin and/or mucosal manifestations.

Keywords

Hepatitis, herpes simplex virus, immune-competent children.

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Introduction

In addition to the common hepatitis viruses (from HAV through HEV), other viral agents could cause liver injury. Among those, herpesviruses may be involved: the occurrence of abnormalities in liver enzymes (associated to acute hepatitis and/or acalculous acute cholecystitis) is not unusual during

infections caused by EBV, CMV, adenovirus and VZV in the immune-competent patients. In children, more severe hepatic involvement (leading to acute hepatitis and, less frequently, to acute liver failure and fulminant hepatitis) has been described in immune-compromised patients and in neonates. As regards herpes simplex virus (HSV), in addition to the mucosal disease, a visceral involvement has been described occasionally and it was generally limited to neonatal infections, pregnancy and patients with immunodeficiency. Thus, HSV is a very uncommon cause of acute hepatitis in immune-competent patients [1-3].

Case report

Here, we report the clinical case of a 9-year-old girl who came to the attention of the Pediatric Emergency Department because of fever and diffuse scarlet fever-like skin rash persisting for a couple of days. The physical exam was normal, except for a moderate and not exudative pharyngitis; in particular, no liver and/or spleen enlargement was noticed. Importantly, no significant problem emerged from her past medical history.

However, the blood tests (day 1) revealed the significant increase of liver enzymes (AST = 218 IU/l, n.v. < 35 IU/l; ALT = 374 IU/l, n.v. < 35 IU/l; GGT = 324 IU/l, n.v. < 40 IU/l) and moderate elevation of total and direct bilirubin (2.52 mg/dl and 2.15 mg/dl, respectively). The coagulation panel was normal, as regards PT, aPTT and fibrinogen level. Those findings induced to admit the patient to the pediatric ward, in order to monitor the liver disease. As for other tests, total plasmatic proteins and coagulation parameters remained in the normal range. Blood cell count was balanced and a mild elevation of C-reactive protein was detected (10 mg/dl, n.v. < 5 mg/dl).

During the hospitalization, the child always remained in good clinical conditions and the biochemistry was repeated after 48 hours (day 3), showing a decreasing trend of liver enzymes in plasma (AST = 175 IU/l; ALT = 218 IU/l; GGT = 276 IU/l). In the meantime, in addition to the pharyngeal swab and ASO titer, all the usual serological tests for acute hepatitis (including HAV, HBV, HCV, EBV, CMV, *Toxoplasma gondii*, coxsackieviruses) were performed, but all resulted negative.

Actually, the following control (day 5) showed an unexpected and notable increase of liver enzymes (AST = 363 IU/l; ALT = 365 IU/l; GGT

= 582 IU/l); however, total and direct bilirubin decreased (1.68 mg/dl and 1.21 mg/dl, respectively) and serum amylase was normal (50 IU/l, n.v. < 100 IU/l). Moreover, the abdominal ultrasonography showed no liver enlargement with a conserved structure devoid of any focal lesion and the spleen had a normal size. Anyway, a second level work-up for hepatitis was performed, because of the unusual clinical course, which excluded Wilson disease, alpha1-antitrypsin deficiency, celiac disease and autoimmune hepatitis; anyway, the past medical history provided no relevant clues supporting the presence of any chronic underlying disease. Interestingly, we were able to detect a borderline elevation of anti-HSV-1 IgM, without the concomitant presence of specific IgG.

In accordance with the benign clinical course, the control at day 7 showed a consistent reduction of plasmatic liver enzymes (AST = 53 IU/l; ALT = 169 IU/l; GGT = 283 IU/l) along with complete normalization of bilirubin in the blood. Such a positive trend was eventually confirmed at day 11 (AST = 40 IU/l; ALT = 83 IU/l), when HSV-1 serology was re-evaluated and showed a 4-fold increase of specific IgG, supporting a diagnosis of primary HSV infection.

Discussion

We reported a rare case of acute hepatitis associated with a primary infection with HSV in an immune-competent child. Indeed, pediatric liver diseases caused by HSV have been mostly reported in newborns infected during the delivery, in immune-compromised children (e.g., organ or bone marrow transplantation, chemotherapy, primary immunodeficiency). In neonates, HSV hepatitis can occur with multi-organ involvement leading to a high mortality rate; in immune-compromised children, severe hepatitis with acute liver failure may occur, but acceptable rates of recovery have been reported, provided that the antiviral therapy is timely established [1, 4].

Although mild asymptomatic elevations of aminotransferases levels can be detected in less than 15% of healthy adults with acute HSV genital infection, comparable data are not available for the pediatric population [1]. Moreover, descriptions of HSV-related hepatitis in immune-competent children are very limited. Very recently, Chen et al. reported a case of HSV severe hepatitis in a healthy boy during stomatitis; here, the liver injury was associated with high elevation of

aminotransferases (> 1,000 IU/l) and to a general deterioration of the clinical condition: thus, acyclovir treatment was established and the child recovered completely [5].

Conversely, our clinical case showed no mucosal disease suggesting HSV infection and she maintained good clinical conditions during all disease course. Thus, the diagnosis of primary HSV infection was achieved through the exclusion of more common causes of acute hepatitis. Interestingly, our patient recovered spontaneously, as no antiviral therapy was necessary. Indeed, she showed only a scarlet fever-like skin rash (but not typical HSV vesicular lesions anywhere), that initially suggested a mononucleosis syndrome, but EBV and CMV serology always resulted to be negative after repeated controls during the clinical course. However, Norvell et al. reported the occurrence of unspecific skin rashes in more than 40% of the cases of HSV hepatitis they analyzed in their review of the medical literature [6].

In conclusion, HSV infection should be actively searched in healthy children developing acute hepatitis without acute liver failure, which is associated with common hepatotropic viruses. However, if those are not involved, before looking for non-infectious causes of liver disease through expensive diagnostic investigations, HSV should be considered and can be ruled out easily. Interestingly, the liver involvement during a primary HSV infection may not be accompanied by the typical vesicular mucosal manifestations of such a herpetic infection, although unspecific exanthems can manifest.

Informed consent

Informed consent was obtained from the guardian of the individual described in the study.

Compliance with Ethical Standards

This study received no funds.

Declaration of interest

The Authors declare that they have no conflict of interest.

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