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CASE REPORT

Herpetic gingivostomatitis with severe hepatitis in a previously healthy child

Chun-Kuei Chen ^a, Shih-Hao Wu ^a, Yhu-Chering Huang ^{b,c,*}

^a Department of Emergency Medicine, Chang Gung Memorial Hospital, Taoyuan, Taiwan

^b Department of Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan

^c College of Medicine, Chang Gung University, Kweishan, Taoyuan, Taiwan

Received 25 May 2011; received in revised form 6 July 2011; accepted 10 August 2011

KEYWORDS

Acyclovir;
Gingivostomatitis;
Hepatitis;
Herpes simplex
virus-1

A previously healthy boy aged 9 years and 11 months was admitted due to herpetic gingivostomatitis with poor intake. He also had fever, neutropenia, and elevated serum aminotransferase level (> 1000 IU/mL). Prolonged prothrombin time, mild gastrointestinal hemorrhage and transient decreased conscious level were noted during hospital days 2 and 3. Intravenous acyclovir therapy commenced on hospital day 2 and his serum aminotransferase level peaked (> 4000 IU/mL) on hospital day 3 and then improved gradually. A throat swab was positive for human herpes simplex virus (HSV)-1, serological test was positive for acute primary HSV-1 infection, and a blood specimen was also strongly positive for HSV-1 by polymerase chain reaction. He received a 14-day course of intravenous acyclovir and recovered uneventfully. Herpetic gingivostomatitis, although mostly benign and self-limited, may be complicated with severe hepatitis, even in immunocompetent hosts.

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Introduction

Primary human herpes simplex virus (HSV)-1 infection usually occurs in childhood and mostly presents as herpetic gingivostomatitis. Herpetic gingivostomatitis is usually benign and self-limited.¹ However, HSV-1-induced hepatitis, although rare, has been reported and frequently results in unfavorable

outcomes, even fatality.¹ Previously reported pediatric cases of HSV hepatitis have mostly involved neonates as well as immunocompromised children.^{1–11} Here, we report a case of an immunocompetent school child who had primary HSV-1 infection with severe hepatitis that was successfully treated with intravenous acyclovir.

Case report

A previously healthy boy aged 9 years and 11 months presented to Chang Gung Memorial Hospital with a 5-day history

* Corresponding author. Department of Pediatrics, Chang Gung Memorial Hospital, No. 5, Fu-Shin Street, Kweishan, Taoyuan County 333, Taiwan.

E-mail address: ychuang@adm.cgmh.org.tw (Y.-C. Huang).

of fever, chills, generalized malaise and oral pain, with resultant poor intake and dehydration. On admission, he was febrile (temperature of 40°C) and had multiple oral ulcers, fetor oris, and reddened and swollen gums. Complete blood cell count showed leukopenia (white blood cell count 1800/ μ L with 61% neutrophils, 23% lymphocytes and 10% monocytes), 12.8 g/dL hemoglobin, and platelet count 125,000/ μ L. Serum biochemistry showed C-reactive protein level of 43 mg/L (normal, < 5 mg/L), aspartate aminotransferase 2046 U/L (normal, < 40 U/L), and alanine aminotransferase 1339 U/L (normal, < 40 U/L). Serum electrolytes, bilirubin level, cholesterol, triglycerides, blood urea nitrogen, creatinine, amylase and lipase levels were all within normal limits.

Initially, herpetic gingivostomatitis was suspected. However, from the clinical picture of fever, leukopenia and elevated aminotransferase level, we commenced antiviral therapy with intravenous acyclovir (5 mg/kg every 8 hours) on hospital day 2, under suspicion of HSV-induced severe hepatitis. On the same day, an abdominal ultrasound examination was performed and revealed moderate hepatomegaly. Later, he had an episode of vomiting with blood-tinged content, and mildly prolonged prothrombin time was noted (14 seconds/normal, 10.8 seconds). Under suspicion of possible hepatic coagulopathy with ongoing gastrointestinal bleeding, he was transferred to the pediatric intensive care unit for close observation and meticulous management. Fresh frozen plasma was administered on hospital days 2 and 3. On hospital day 3, his serum aspartate aminotransferase and alanine aminotransferase levels were still elevated and peaked at 4226 U/L and 2489 U/L, respectively. Serum ammonia level was 126 mg/L, and a decreased conscious level was noted. He continued intravenous acyclovir therapy and fortunately, his serum aminotransferase levels came down gradually and consciousness returned thereafter. He was transferred to an ordinary ward on hospital day 5. Leukopenia resolved on hospital day 6 and serum aminotransferase levels reduced to < 1000 U/L on hospital day 7. He completed a 14-day course of acyclovir therapy and recovered uneventfully during at least 6 months follow-up.

Throat swabs were obtained for virus isolation and identification on hospital days 2 and 3 and both specimens were positive for HSV-1. The serological test for HSV-1-specific IgM was positive and seroconversion of HSV-1-specific IgG was also found by paired sera, indicating acute primary HSV-1 infection. All the serological tests for hepatitis A virus, hepatitis B virus, hepatitis C virus, Epstein-Barr virus and cytomegalovirus were negative for acute infection. A blood sample sent for the detection of HSV-1 by polymerase chain reaction also showed a strongly positive result, indicating the presence of HSV-1 viremia.

Discussion

Hepatitis is a rare complication of HSV infection. Neonates, patients with malignancy, taking steroids, with myelodysplastic syndromes, or receiving solid organ transplantation, and pregnant women are at risk for HSV hepatitis.¹⁻⁸ Hepatitis caused by HSV is rarely seen in immunocompetent patients.⁹ No case of HSV hepatitis has been reported in immunocompetent adolescents. The present case had initial presentation of herpetic gingivostomatitis and

subsequently developed fever, leukopenia, and elevated serum aminotransferase levels, which is suggestive of HSV hepatitis.⁹ Although no tissue specimen provided direct evidence of the HSV implicated in the severe hepatitis of this patient, the virological and serological evidence of acute primary HSV-1 infection, no evidence of other hepatic viral infection, and the presence of HSV-1 viremia all suggested the association of HSV with severe hepatitis.

Harel et al¹⁰ previously have reported that viremia was detected by polymerase chain reaction in 34% of the 32 patients with primary herpetic gingivostomatitis, and the presence of viremia may have a potential role in viral dissemination. Severe HSV hepatitis in this case was probably disseminated from primary herpetic gingivostomatitis. HSV fulminant hepatitis has a high mortality rate. Overall, 74% of 134 cases progressed to death or required liver transplantation, with 51% of acyclovir-treated patients and 88% of untreated individuals.¹¹ Our patient received intravenous acyclovir therapy since hospital day 2 and fully recovered from severe hepatitis.

From this case, we can learn that hepatitis associated with acute primary HSV-1 infection, although rare and mostly implicated in neonates and immunosuppressed patients, may occur in previously healthy individuals. Early recognition of this association and prompt administration of intravenous acyclovir therapy may be life saving for this rare but severe disease.

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