Reminder of important clinical lesson

Unusual manifestations of Epstein-Barr virus infection in an 8-month-old male infant

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Summary

Severe acute hepatitis is a rare complication of Epstein-Barr virus (EBV) infection. The authors report a case of an 8-month-old male infant who presented with subacute fever and jaundice. The physical examination showed hepatosplenomegaly and ecchymoses on his abdomen, chest wall and extremities. He received vitamin K therapy and prednisolone, and he recovered well without further complications or sequelae. Although severe acute hepatitis is a rare complication of EBV infection, clinicians should recognise this condition in order to provide a prompt treatment.

BACKGROUND

Hepatic involvement is a common presentation of EBV infection. Moderately elevated serum transaminase are found in more than 80% of cases but jaundice occurs in less than 5%, and severe acute hepatitis is rare.^{1–3} EBV-related acute hepatitis should be considered as a possible causative agent, if there is no other reason for acute hepatitis with jaundice in infants.¹ There are different degrees of severity of EBV hepatitis ranging from asymptomatic to liver failure.⁴ Adequate supportive treatment and close follow-up is necessary to help patients recover from their clinical symptoms.¹ We present an opportunity for healthcare providers to identify and be aware of EBV-related acute hepatitis in infants.

CASE PRESENTATION

An 8-month-old infant had high-grade fever and generalised ecchymosis on his abdomen, chest wall and both legs 8 days before admission to the Chiang Mai University Hospital (CMUH). He did not have epistaxis, neither haematemesis nor haematochezia. 5 days before admission to the CMUH he developed jaundice and was admitted to a provincial hospital. Physical examination showed that his temperature was 38°C, that he looked pale and that he

had generalised ecchymosis. He received pack red cell transfusion (10 ml/kg) and intravenous antibiotics (ampicillin and gentamycin) for 2 days before admission to CMUH. The mother reported no history of antenatal care, vaccine and underlying diseases. He was born at home and his birth weight was unknown. He did not have a family history of malignancy or liver diseases. At the CMUH, the physical examination revealed a temperature of 38.2°C, alertness, failure to thrive (his body weight of 6 kg and height of 64 cm were both below the third percentile), moderate pallor, marked jaundice and hepatosplenomegaly (his palpable liver was 4 cm below the right costal margin and his spleen 3 cm below the left costal margin; figure 1). Multiple ecchymoses were seen on his abdomen, chest wall and extremities (figure 2).

INVESTIGATIONS

Laboratory values showed a haemoglobin level of 6.1 g/dl, haematocrit of 19.5%, and a total white blood cell count of 10.6×10^9 cells/l with 67% lymphocytes and 9% atypical lymphocytes. The platelet count was 378×10^9 /l. A peripheral smear showed few schistocytes and few polychromasia. Malaria was not found from a thick and thin film. A liver function test revealed albumin of 2.8 g/dl,

Figure 1 Jaundice and hepatosplenomegaly.

Figure 2 Multiple ecchymoses on abdomen, chest wall and extremities.

total bilirubin of 13.4 mg/dl, direct bilirubin of 7.8 mg/dl, aspartate aminotransferase (AST) of 323 U/l, alanine transaminase (ALT) of 266 U/l, γ -glutamyl transpeptidase (GGT) of 55 U/l, a prothrombin time (PT) of 226.9 s, a partial thromboplastin time (PTT) of 96.9 s and an international normalised ratio (INR) of 19.3. Factors V and VII analyses were not performed because the patient had ecchymoses without clinical symptoms of active bleeding and responded well to vitamin K treatment. After administration of 1 dose of vitamin K, his PT decreased to 28.3 s, his PTT to 44.4 s and his INR to 2.57. Ultrasound abdomen revealed hepatosplenomegaly without focal lesion. There was no ascites or lymphadenopathy, no dilatation of bile ducts and the gall bladder was normal. Hepatitis B serologies and cytomegalovirus (CMV) antibody tests were negative. The EBV capsid antigen IgM and IgG were analysed before the patient received a blood transfusion and the result was positive. The analyses for Epstein-Barr nuclear antigen (EBNA), early antigen (EA) and viral load were not done because they were not available in our hospital. The HIV antibody test was non-reactive and the haemoculture was negative.

DIFFERENTIAL DIAGNOSIS

- Severe acute hepatitis induced by EBV infection
- Severe malnutrition and vitamin K deficiency

TREATMENT

The patient received 3 mg of vitamin K intravenously once a day for 3 days, and prednisolone (1.5 mg/kg/day) for 14 days along with supportive fluid therapy.

OUTCOME AND FOLLOW-UP

PT and PTT became normal within 2 days after initiation of vitamin K therapy. The patient's symptoms and laboratory abnormalities improved within 2 weeks after treatment.

DISCUSSION

Most EBV infections in children are asymptomatic. Primary infection in adolescents and adults results in acute infectious mononucleosis syndrome. In young adults, the complications of severe acute hepatitis from EBV infection are uncommon.¹ Most EBV-infected cases have a mild elevation of liver enzymes during infection but the clinical symptoms of severe hepatitis with jaundice are rare.² Most cases present with asymptomatic or mild illness accompanied by a mild elevation of hepatic enzymes.^{1–3} Generally, the levels of liver enzymes are not higher than three times the normal level.⁵ Liver enzymes most likely elevate during the second week of illness and return to normal within 2–6 weeks. Less than 10% of patients

develop jaundice, mainly among the older population.^{2–4} Physicians should base their diagnosis of EBV infection on clinical manifestations, virological and serological evidence and the exclusion of conditions that are related to extrahepatic biliary obstruction.² We diagnosed this patient to have EBV induced acute hepatitis based on the evidence of (1) a positive result for EBV capsid antigen IgM which normally rises in the first few weeks of acute infection,⁶ (2) AST and ALT and levels which were markedly higher than the GGT level, (3) the exclusion of other common viral infections such as HIV and CMV infections and (4) the exclusion of conditions related to biliary tract obstruction such as biliary atresia. In this case, we suspected that the patient had a vitamin K deficiency because he had never received it since birth as other new-borns that are delivered in a hospital. The lack of vitamin K may partially account for his severe hepatitis after being infected with EBV. Treatment of EBV is mainly supportive and symptomatic, and most hepatic conditions resolve spontaneously. In this case, we therefore provided vitamin K therapy for 3 days intravenously accompanied by fluid therapy. In severe cases, steroids and antiviral medications such as acyclovir and ganciclovir may be used; however the efficacy of these medications has not been proven through randomised trials.^{3–4} Indications for the use of corticosteroids include marked tonsillar inflammation with impending airway obstruction, massive splenomegaly, myocarditis, haemolytic anaemia or haemophagocytic lymphohistiocytosis.⁶ Steroid therapies may cause complications or delay the recovery period in some cases and physicians should be aware of this and provide the treatment under close monitoring.⁷ In this case, we treated the patient with prednisolone for 2 weeks since he had massive splenomegaly and severe hepatitis, and his clinical symptoms improved satisfactorily.

Learning points

- Severe hepatitis related to Epstein-Barr virus (EBV) infection is a rare condition in infants.
- Physicians should base their diagnosis of EBV infection on clinical manifestations, virological and serological evidence, and the exclusion of conditions that are related to extrahepatic biliary obstruction.
- Indications for the use of corticosteroids in EBV infections include marked tonsillar inflammation with impending airway obstruction, massive splenomegaly, myocarditis, haemolytic anaemia or haemophagocytic lymphohistiocytosis.⁶

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Uluğ M**, Celen MK, Ayaz C, *et al*. Acute hepatitis: a rare complication of Epstein-Barr virus (EBV) infection. *J Infect Dev Ctries* 2010;**4**:668–73.
2. **Doğan I**, Ergün M, Cindoruk M, *et al*. Acute hepatitis induced by Epstein-Barr virus infection: a case report. *Turk J Gastroenterol* 2007;**18**:119–21.
3. **Katz BZ**. Epstein-Barr virus infection. In: Long SS, Pickering LK, Prober CG, eds. *Principles and practice of pediatric infectious diseases*. 3rd edn. Philadelphia: Elsevier, 2008:1036–44.
4. **Crum NF**. Epstein Barr virus hepatitis: case series and review. *South Med J* 2006;**99**:544–7.
5. **Kofteridis DP**, Koulentaki M, Valachis A, *et al*. Epstein Barr virus hepatitis. *Eur J Intern Med* 2011;**22**:73–6.
6. **American Academy of Pediatrics**. Summaries of infectious diseases. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2012 Report of the Committee of Infectious Diseases*. Elk Grove Village, IL: American Academy of Pediatrics, 2012:318–21.
7. **Jenson HB**. Acute complications of Epstein-Barr virus infectious mononucleosis. *Curr Opin Pediatr* 2000;**12**:263–8.

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