Paternal hepatitis B virus infection with different clinical courses between siblings

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Abstract

No countermeasures have been established against horizontal infection in non-vaccinated children. We reported about siblings with different clinical courses of HBV paternal infection. To eradicate HBV, we should encourage HBV vaccination of all children and HBV infection screening of fathers and other family members.

Introduction

The incidence of hepatitis B virus (HBV) infection is expected to reduce in the future with the implementation of HBV mother-to-child infection prevention projects and universal HBV vaccination. In addition, the development of antiviral drugs for HBV has contributed to the reduction of the infection rate. However, to date, no countermeasures have been established against horizontal infection such as paternal infection of HBV in non-vaccinated children. Here, we report a case of paternal HBV infection that resulted in different clinical courses of HBV infection between siblings.

Case History

Case 1

The first patient was a 1-year-4-month-old girl. Her birth and medical history were unremarkable. She presented with vomiting 3 days and diarrhea 2 days before being admitted to our hospital with a diagnosis of acute rotavirus gastroenteritis. Her laboratory findings on admission showed severe liver dysfunction, with an alanine aminotransferase (ALT) level of 583 U/L and aspartate aminotransferase (AST) level of 406 U/L. Simultaneously, the tests for hepatitis B surface antigen (HBsAg) and immunoglobulin M antibody to hepatitis B core antigen were positive. Therefore, she was diagnosed with acute hepatitis B. She had not been vaccinated against HBV. With conservative treatment such as rest and hydration, her symptoms improved without a fulminant course. She was discharged on the 10th hospital day. Three months after the onset, her tests revealed seroconversion. Eventually, at 8 years of age, she was declared HBsAg negative, and virological remission was achieved (Table 1).

Case 2

The second patient was a 2-year-7-month-old girl and was an older sibling of the first patient. She was born with a low birth weight of 2,272 g. She had neither medical history nor vaccination against HBV. Although she had no symptoms when the first patient was diagnosed with acute hepatitis B, her laboratory findings revealed mild liver dysfunction, with an ALT level of 87 U/L and an AST level of 79 U/L. She was HBsAg positive, hepatitis B envelope antigen (HBeAg) positive, and hepatitis B envelope antibody negative. Her HBV DNA (PCR) was high (>8.2 log IU/L), and the HBV genotype was type B. Simultaneously, she was diagnosed as an HBV carrier. Since then, she had been followed up for inactive chronic hepatitis, and seroconversion was detected at the age of 3 years and 8 months (Table 2). To date, she is being followed up

in an outpatient clinic as an inactive carrier of HBV. When the first patient developed acute hepatitis, her father was HBeAg positive, whereas her mother was HBsAg negative and anti-hepatitis B surface antibody positive. Therefore, HBV infection of these siblings was considered to be transmitted from their father. Their father was an asymptomatic HBV carrier; however, the source of infection was unknown.

Discussion

In this report, we observed different clinical courses of horizontal HBV infection in siblings, transmitted from their father. HBV is detected not only in blood but also in urine, saliva, nasopharynx, and tears, which may be sources of infection.[1] Therefore, the risk of HBV horizontal infection in daily life exists. In the literature, the prevalence of HBsAg carriage among children of 1 year or older has been reported to be higher than that among those aged under 1 year.[2] This pattern of age distribution suggests that horizontal infection is an important route of HBV infection during early childhood.[2] Vaccine failure of mother-to-child infection is the major cause of chronic HBV infection in Japanese children, with paternal infection being the second most common mode of transmission.[3] Although the incidence of paternal infection has been reported to be lower than that of mother-to-child infection, 19.2% of HBeAg-positive fathers have been reported to transmit HBV infection to their children.[4] In our report, the HBV genotype of the sibling's father was not examined, but we diagnosed that the route of HBV transmission of the siblings was paternal, as no other HBV-infected person, except their father, was detected as a possible contact. Infants are susceptible to chronic persistent HBV infection owing to poor cytotoxic T-cell (CTL) response.[5] Therefore, the CTL response of the second patient might have been weaker than that of her sibling. In addition, genetic variants in the HLA-DP locus, including HLA-DPA1 and HLA-DPB1, are associated with the chronicity of hepatitis B in literature.[6] Therefore, the second patient may have genetic variants in the HLA-DP gene.

To prevent mother-to-child HBV infection, HBV screening and preventive measures for pregnant women have been created. In contrast, HBV screening of fathers and other family members is necessary to prevent horizontal infection.[7] The World Health Organization recommends universal vaccination to eradicate HBV.[8]Despite routine immunization of infants with HBV vaccine being initiated in 2016 in Japan, many children are unvaccinated. Therefore, we must remember that some children do not benefit from the HBV vaccine, especially those who are out of their routine vaccination age.

In conclusion, we reported a case of paternal HBV infection that resulted in varying clinical presentations of HBV infection in the offspring. Our findings suggest that we should encourage the administration of HBV vaccination for all children and screening of HBV infection to all family members, including fathers. These measures are expected to minimize horizontal infection of HBV.

Conflicts of interest

None declared

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Author Contributions:

YS wrote the manuscript. HK critically reviewed the manuscript. All authors read and approved the final manuscript.

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Table legends

Table 1. Laboratory results of the first patient

HBsAg: Hepatitis B surface antigen, *Anti-HBs:*Anti-hepatitis B surface antibody, *IgM anti-HBc:* Immunoglobulin M antibody to hepatitis B core antigen, *HBeAg:* Hepatitis B envelope antigen, *Anti-HBe:* Anti-hepatitis B envelope antibody, *HBV DNA:* Hepatitis B virus-deoxyribonucleic acid, *ALT:* alanine aminotransferase, *AST:* aspartate aminotransferase, blank: no result available, neg: negative, pos: positive, N.D: not detected

Table 2. Laboratory results of the second patient

HBsAg: Hepatitis B surface antigen, *Anti-HBs:*Anti-hepatitis B surface antibody, *IgM anti-HBc:* Immunoglobulin M antibody to hepatitis B core antigen, *HBeAg:* Hepatitis B envelope antigen, *Anti-HBe:* Anti-hepatitis B envelope antibody, *HBV DNA:* Hepatitis B virus-deoxyribonucleic acid, *ALT:* alanine aminotransferase, *AST:* aspartate aminotransferase, blank: no result available, neg: negative, pos: positive, N.D: not detected

Table 1. Laboratory results of the first patient

	HBsAg	Anti-HBs	IgM anti-HBc	HBeAg	Anti-HBe	HBV DNA (Log IU/L)	ALT (IU/L)	AST (IU/L)
Age								
1-year-4-month	pos.	neg.	pos.	pos.	neg.	> 8.2	583	406
1-year-7-month			neg.	neg.	pos.	N.D.	11	29
8-year-0-month	neg.	pos.				N.D.	13	25

HBsAg: Hepatitis B surface antigen*, Anti-HBs:* Anti-hepatitis B surface antibody*, IgM anti-HBc:* Immunoglobulin M antibody to hepatitis B core antigen*, HBeAg:*Hepatitis B envelope antigen, Anti-HBe*:* Anti-hepatitis B envelope antibody*, HBV DNA:* Hepatitis B virus-deoxyribonucleic acid*, ALT:* alanine aminotransferase*, AST:* aspartate aminotransferase*, blank:* no result available*, neg:* negative*, pos:* positive*, N.D:* not detected

Table 2. Laboratory results of the second patient

	HBsAg	Anti-HBs	IgM anti-HBc	HBeAg	Anti-HBe	HBV DNA (Log IU/L)	ALT (IU/L)	AST (IU/L)
Age								
2-year-7-month	pos.	neg.	neg.	pos.	neg.	> 8.2	87	79
3-year-10-month			neg.	neg.	pos.	N.D.	44	55
15-year-10-month	pos.	neg.	neg.	neg.	pos.	3.27	10	17

HBsAg: Hepatitis B surface antigen*, Anti-HBs:* Anti-hepatitis B surface antibody*, IgM anti-HBc:* Immunoglobulin M antibody to hepatitis B core antigen*, HBeAg: Hepatitis B envelope antigen, Anti-HBe:* Anti-hepatitis B envelope antibody*, HBV DNA:* Hepatitis B virus-deoxyribonucleic acid*, ALT:* alanine aminotransferase*, AST:* aspartate aminotransferase*, blank:* no result available*, neg:* negative*, pos:* positive*, N.D:* not detected