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Hepatitis B vaccine: Immunogenicity in an extremely low-birthweight infant

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From 2013, infants born to mothers carrying serum hepatitis B (HB) surface antigen (HBsAg) receive HB immunoglobulin at birth and HB vaccine at birth, and at 1 and 6 months of age in Japan (prevention protocol for mother-to-child HB virus infection).[1] Due to immature immune response to HB vaccine, the American Academy of Pediatrics and Japan Pediatric Society recommend that infants <2,000 g birthweight are given an additional HB vaccination at 2 months of age.[2,3] No previous case report, however, has described the trajectory of the immunogenic response for this prevention protocol, including an additional dose at 2 months of age, in extremely low-birthweight (ELBW) infants. The present case is reported with informed consent.

The present patient was born to a 29-year-old Chinese mother (gravida 0, para 0) with HBsAg. At 20 weeks of gestational age, serum HBsAg, HB envelope antigen, HB virus core-related antigen, and HB virus DNA were positive (67 878 IU/mL, 1,531.9 sample relative light units/cut-off, >7.0 log U/mL, and 9.7 log copies/mL, respectively). Both serum HB surface antibody (HBsAb) and HB envelope antibody were negative. The HB virus genotype was type C. A male newborn weighing 918 g was born at 25 weeks and 4 days of gestational age via cesarean section due to fetal distress.

He was admitted to the neonatal intensive care unit due to ELBW. Along with respiratory and circulatory treatment, i.v. immunoglobulin (IVIG; 500 mg/10 mL, Venoglobulin IH™, Japan Blood Products Organization, Tokyo, Japan) was administered soon after birth because of hypoimmune globulinemia (serum total IgG, 280 mg/dL). At 11 h after birth, a total of 200 U/mL HB immune globulin (Dried HB globulin Nichiyaku™; Nihon Pharmaceutical, Tokyo, Japan) was injected i.m. in the right and left femoral muscles (100 U/0.5 mL in each side), and HB vaccine (0.25 mL, Bimmugen™; Kaketsuken, Kumamoto, Japan) was injected s.c. in the left upper arm. No side-effects, such as redness, swelling, or induration were observed. HB vaccine was again administered at 1 and at 2 months of age. The infant was reared on breast milk and was discharged at 4 months of age. The fourth HB vaccine was injected at 6 months of age.

The HBsAb titer reached a peak at 1 month of age, and decreased to the lowest level at 4 months of age, but HBsAb was >10 mIU/mL (Fig. 1). Then, the HBsAb titer gradually increased, and after the fourth HB vaccine, it finally increased to >100 mIU/mL at 12 months of age. Serum HBsAg was negative at 12 months of age.

We herein report the HBsAb titer in an ELBW infant who received four doses of HB vaccine. In the present case, the prevention protocol for mother-to-child HB virus infection with an additional dose at 2 months of age (0, 1, 2, and 6 months of age) achieved sufficient seropositivity of HBsAb at 12 months of age. The infant had an HBsAb titer of 47 mIU/mL at the time of discharge, even with an additional vaccine at 2 months of age. Because ELBW infants are usually discharged from hospital at 3–4 months of age, and are

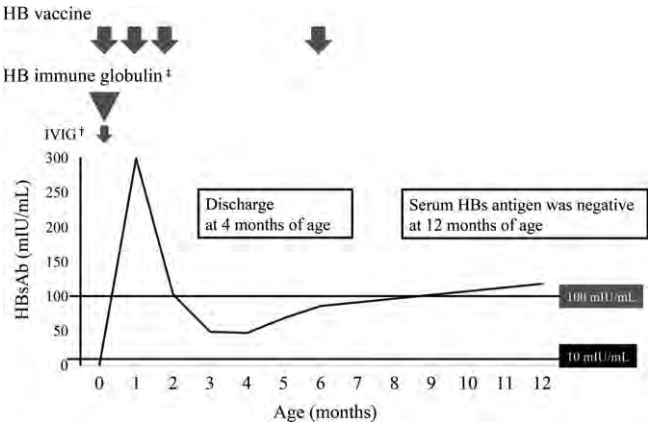

Fig. 1 Trajectory of serum hepatitis B surface antibody (HBsAb) titer. †Effect of i.v. immunoglobulin (IVIG) on HBsAb titer: the patient received 500 mg/10 mL Venoglobulin IH™ (Japan Blood Products Organization), which has an HBsAb titer of approximately 100 mIU/mL. Assuming that the circulating blood volume is 72 mL (80 mL/kg bodyweight) and the bioavailability of IVIG is 100%, IVIG treatment might have increased HBsAb titer by 14 mIU/mL. Given, however, that the half-life of Ig is 27 days,[4] the effect is limited. ‡Effect of HB immune globulin on HBsAb titer: the titer at 4 months of age (47 mIU/mL) can be explained only by the HB immune globulin at birth because the half-life of HB immune globulin is 23 days.[5]

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then in close contact with their mother who are HB virus carriers, it is important for the ELBW infant to have a sufficient HBsAb titer at that time.

The seroprotection level is usually defined as HBsAb titer ≥10 mIU/mL.[6,7] Although all infants ≥2,000 g birthweight who received three doses of HB vaccine at 0, 1, and 6 months of age at the present hospital had sufficient HBsAb (median, 210 mIU/mL; range, 21–898 mIU/mL; n = 12), in a previous study, ELBW infants who received three doses of HB vaccinations at birth and at 1–3 and at 6–8 months of age had only a 52% seropositivity rate.[6] And in another study, 98.4% of preterm infants vaccinated using another four-dose HB vaccine protocol (0, 1, 2, and 12 months of age) had a protective level.[7] Four doses of HB vaccine may be needed to obtain a sufficient rate of seropositivity in ELBW infants as recommended by the Japan Pediatric Society.

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Disclosure

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Author contributions

K.Y. and I.M. drafted the initial manuscript. K.Y. and S.I. collected the clinical data. K.Y., I.M. and K.F. interpreted the data. K.I. revised the article critically for important intellectual content. All authors contributed to the intellectual content of this manuscript and approved the final manuscript as submitted.

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