Varicella zoster virus infection can occur in preterm infants despite “protective” maternal varicella zoster virus IgG antibodies.

Placental transfer of maternal IgG antibodies generally protects the infant against varicella zoster virus (VZV) infection during the first months of life. These maternal antibodies decrease after the age of 6 months [4]. However, it has been reported that newborns and infants can develop chickenpox before 6 months of age [2]. We describe a 10-week-old preterm infant who developed chickenpox despite VZV IgG antibodies.

A 10-week-old preterm infant was admitted to our hospital with gastroenteritis and bronchiolitis both beginning 1 day before admission. Coronavirus was found by electron microscopy in the stool and antigen of respiratory syncytial virus detected in nasopharyngeal secretion. The girl was born at 31 weeks gestational age. The post-natal period was uncomplicated. Five days before admission she developed fever and crops of erythematous maculae evolving into fluid-filled vesicles. The rash dominated on the trunk, involved the scalp and was identified as the typical rash of chickenpox. The temperature rose to 39°C on the 1st day and decreased gradually over the following 2 days. In hospital the girl presented with plenty of crusting lesions, especially on the trunk and the scalp. She was infected by a 2-year-old brother who developed chickenpox 2 weeks earlier. The mother had chickenpox as a child and no illness or rash at this time.

Antibodies against VZV were determined using an enzyme linked immunosorbent assay (Diasonin, Düsseldorf, Germany). This test calculates an immune status ratio for each specimen dividing the specimen’s optical density value by a cutoff calibrator value comparable to values obtained by different standard techniques. Immune status ratios are considered negative when below 0.9 and positive when above 1.0. The titre ratios of VZV IgM and VZV IgG of the patient and her mother are shown in Table 1. In addition, cell-mediated immunity was examined: total lymphocytes, B-lymphocytes, T-lymphocytes including HLA-DR activated lymphocytes, CD4⁺ and CD8⁺ lymphocytes and natural killer lymphocytes were normal. Functional tests of cell-mediated immunity were not performed.

During the second and third trimester of pregnancy IgG antibodies are transferred placentally. Mothers with a past history of varicella transmit antibodies against VZV to the fetus [1]. At term, newborns have antibody titres similar or higher than those of their mothers. Our patient had a lower titre of VZV IgG possibly due to prematurity [4]. Obviously, after the close contact to her brother the placentally acquired VZV IgG did not protect her from chickenpox despite “protective” maternal VZV antibody titres. Definitive cut off levels for protective VZV IgG antibodies are not documented in the literature. Two months after the infection the infant’s VZV IgG titre ratio increased from 1.7 to 2.3. This “boostering” phenomenon is well known. Seventeen months after the infection, the VZV IgG titre ratio was 2.0 indicating that the previous infection left humoral immunity against VZV. Suppressed, specific cell-mediated immunity, i.e. in individuals treated with immunosuppression, correlates with a high susceptibility to VZV infection indicating the primary importance of cell-mediated immunity in prevention of VZV infection [3]. Non-specific, non-antibody-dependent cell mediated mechanisms, such as natural killer cells, are known to have a role in controlling the extent of disease. A low T4/T8-cell ratio, a high suppressor T-cell activity and a low natural killer cell activity characterise the specific cell-mediated immunity in preterm infants. Additionally, neonatal viral infection may depress T-cell function. We tested the cell-mediated immunity in this patient and the results were normal.
Table 1 VZV IgM and IgG antibodies in the patient and her mother during and following varicella zoster infection. Titres are shown as ratios of the patient’s specimen value and the cutoff calibrator value.

|                  | Patient | Mother |
|------------------|---------|--------|
|                  | VZV IgM | VZV IgG | VZV IgM | VZV IgG |
| Day 6 of infection | Positive | 1.7 | Negative | 2.8 |
| 2 Months after infection | Negative | 2.3 | Negative | 2.7 |
| 17 Months after infection | Negative | 2.0 |         |      |

IgG antibodies against VZV do not protect all newborns and infants against VZV infection when a close and prolonged contact to an infected person exists. In children with maternal VZV IgG antibodies and normal cell-mediated immunity, the course of the disease is uncomplicated and generates persistent antibodies as documented in this patient at 19 months of age.

References

1. Asano Y, Hiroishi Y, Itakura N, Hirose S, Kajita Y, Suga S, Yazaki T (1988) Placental transfer of IgG subclass-specific antibodies to varicella-zoster virus. J Med Virol 26: 1–6
2. Bending JWA, Meurisse EV, Anderson F, Diaz H, Shankar A (1998) Neonatal varicella despite maternal immunity. Lancet 352: 1985–1986
3. Goldblatt A (1998) The immunology of chickenpox. J Infect 36(Suppl 1): 11–16
4. Linder N, Waintraub I, Smetana Z, Barzilai A, Lubin D, Mendelson E, Sirota L (2000) Placental transfer and decay of varicella-zoster virus antibodies in preterm infants. J Pediatr 137: 85–88