CASE REPORTS

Horizontal In Utero Acquisition of Cytomegalovirus Infection in a Twin Pregnancy

Liliana Gabrielli,1 Tiziana Lazzarotto,1 Maria Pia Foschini,2 Marcello Lanari,3 Brunella Guerra,4 Vincenzo Eusebi,2 and Maria Paola Landini1*

Section of Microbiology, Department of Clinical and Experimental Medicine,1 Section of Anatomic Pathology, Department of Oncology,2 Department of Preventive Pediatrics and Neonatology,3 and Department of Obstetrics and Gynecology,4 University of Bologna, Bologna, Italy

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It is generally accepted that viral infections can be transmitted horizontally by direct or indirect contact with virus-excreting persons, and some viral infections can be transmitted vertically, either prenatally or perinatally, from mother to child. This report presents data strongly supporting a prenatal horizontal acquisition of human cytomegalovirus infection in a twin pregnancy.

CASE REPORT

A 24-year-old primipara with a twin pregnancy (two female fetuses) had a 6-day illness during the 15th week of pregnancy characterized by nausea, anorexia, fever, headache, and muscle weakness. Biochemical tests detected raised blood transaminase levels; serological tests disclosed both anti-cytomegalovirus (CMV) immunoglobulin M and low-avidity immunoglobulin G, indicating a recent primary infection (4). In addition, viral antigenemia (2 pp65-positive cells/2 × 10^5 polymorphonuclear leukocytes [PMNL]) and DNAemia (1.7 × 10^5 copies/10^5 PMNL) were detected. The urine culture was CMV negative. Amniotic fluid was collected from the two gestational sacs by transabdominal amniocentesis at 21 weeks of gestation. At the time of amniocentesis, maternal DNAemia was CMV negative. While the left-side twin was antigenemia negative and had a low viral DNAemia (7.8 × 10^2 copies/10^5 PMNL), the right-side twin had 2 pp65-positive cells/2 × 10^5 PMNL and a DNAemia of 2.5 × 10^5 copies/10^5 PMNL, suggesting an infection of the left-side twin after the time of amniocentesis.

Further clinical studies revealed no cranial ultrasonography abnormalities and no evidence of chorioretinitis. However, auditory brain stem-evoked responses were absent at 80 dB in the right-side twin, indicating a severe hearing impairment caused by infection early in pregnancy. The other infant had normal auditory brain stem-evoked responses.

Interestingly, placenta examination showed a fused placenta (Fig. 1a). In the portion separating the two amniotic sacs (dividing membranes), one amnion on either side and two chorions in the middle, separated by a thin trophoblastic rim, were histologically identified, thus indicating the diamniotic-dichorionic (DiDi) nature of the placenta (Fig. 1b). At submicroscopic examination, performed with a stereomicroscope (Fig. 1c) and by assessment of histology (Fig. 1d), blood vessels crossing the two placentas were detected. Both placentas were CMV positive, as detected by in situ hybridization (ISH) (Fig. 1e and f).

This case supports the hypothesis that initial (15 weeks of gestation) maternal viremia caused infection of the right-side twin. As the placenta is a dynamic organ whose structure and function change throughout pregnancy, twin placentas (even if dichoral) may fuse together to create vascular anastomoses (2). Therefore, placental fusion can lead to the transmission of a hematogenous virus from the infected fetus to the uninfected twin.

This report provides plausible evidence of horizontal in utero transmission of CMV. The possibility that our findings are due to a late intrauterine viral transmission from the mother to the second fetus is very unlikely for the following...
reasons. (i) The route of CMV transfer from mother to fetus is presumed to be hematogenous, with placenta infection following maternal viremia, and the viremia phase in immunocompetent subjects is short (less than 30 days) (5). (ii) In our case, at the time of amniocentesis, maternal DNAemia was CMV negative. (iii) Third-trimester trophoblasts are much more resistant to CMV infection than are early pregnancy trophoblasts (3). (iv) Under our experimental conditions, a negative result in prenatal diagnosis indicates the absence of an infection of the fetus or newborn (4).

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FIG. 1. Placenta examination. (a) Macroscopic view of DiDi twin placenta, with the two sacs separated by the dividing membranes. Note the close approximation of the two placental disks with a partial fusion. (b) At histology, the membrane dividing the two placental sacs was composed of two layers of fetal membranes separated by a thin rim of trophoblastic tissue (hematoxylin and eosin stain). Magnification, ×225. (c) A stereomicroscopic examination of the DiDi fused placenta demonstrated anastomosing vascular channels at the point of fusion. Magnification, ×3.6. (d) Histology confirmed the presence of communicating blood vessels between the two placental disks at the point of fusion (hematoxylin and eosin stain). Magnification, ×36. (e) Right-side placenta. CMV positivity was detected in stromal cells by ISH (arrow). Magnification, ×225. (f) Left-side placenta. The arrow indicates an endothelial cell showing nuclear positivity for CMV (ISH). Magnification, ×112.5.
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REFERENCES