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PCR Detection of Cytomegalovirus DNA in Serum as Test for Congenital Cytomegalovirus Infection

Cytomegalovirus (CMV) is the most common cause of congenital infections throughout the world. Only ~5% of the infants with congenital CMV infections have typical cytomegalic inclusion disease, another 5% have atypical involvement, and the remainder (90%) are asymptomatic at the time of delivery. Even for those asymptomatic at birth, 5 to 17% will develop progressive sensorineural hearing loss or other neurodevelopmental difficulties within the first 4 years of life (4). We have studied the incidence of congenital CMV infection in Japan as reported previously (3). Currently, of 7,995 Japanese neonates, 31 (0.39%) were identified as having congenital CMV infections on the basis of viuria detectable at birth. Three of 31 infants had clinically severe disease resulting in death during the neonatal period. The remainder were asymptomatic at the time of delivery.

Recently, Nelson et al. (5) suggested that serum PCR for CMV provided a rapid, sensitive, and specific method for diagnosing congenital CMV infections in infants who were symptomatic at birth. This conclusion is in general agreement with previously studies (2), as viral DNA is present in the sera and/or plasma of selected groups of patients infected with CMV. However, we detected human CMV (HCMV) DNA in $CD3^+$, $CD4^+$, and $CD8^+$ T lymphocytes from infants with hepatitis due to primary HCMV infection by PCR assay (6). Nelson et al. also suggested that the role of commercially available CMV immunoglobulin M (IgM) assays in the diagnosis of congenital infection with CMV needed further study in using larger populations of affected infants (5).

The diagnosis of congenital CMV infection can be established by isolating the virus from urine and other clinical specimens obtained during the first 3 weeks of life. Although the presence of serum anti-CMV IgM antibody from a newborn is diagnostic evidence of congenital CMV infection, the methods often used to detect CMV IgM antibody are variable in their sensitivity (30 to 89%) compared with isolation of the virus as reported previously (4). More sensitive and specific methods of diagnosis for congenital CMV infection, particularly isolation of the virus, have allowed prospective longitudinal study of both symptomatic and asymptomatic infants at birth (1).

The diagnosis of congenital CMV infection is almost always suspected with symptomatic infants, but the presence of asymptomatic infection can be only established if newborns are routinely screened (4). Prospective studies of children born with asymptomatic congenital CMV infections also have revealed a wide but significant spectrum of neurologic complications. If the infants were identified at birth, parents of infants with asymptomatic congenital CMV infections would receive the proper anticipatory guidance, including instructions on early detection of hearing loss and neurodevelopmental problems.

Nelson et al. (5) detected CMV DNA in the serum of one of two infants with an asymptomatic congenital CMV infection. The role of PCR detection of CMV in the diagnosis of congenital infection with CMV also needs further study using larger populations of infants with asymptomatic congenital CMV infections. It was also unclear that serum PCR for CMV DNA provided a rapid, sensitive, and specific method to diagnose congenital infection only in infants who are symptomatic at birth.

REFERENCES

1. **Alford, C. A., S. Stagno, R. F. Pass, and W. J. Britt.** 1990. Congenital and perinatal cytomegalovirus infections. Rev. Infect. Dis. **12:**S745–S753.
2. **Brytting, M., W. Xu, B. Wahren, and V.-A. Sundqvist.** 1992. Cytomegalovirus DNA detection in sera from patients with active cytomegalovirus infections. J. Clin. Microbiol. **30:**1937–1941.
3. **Chiba, S., M. Kamada, H. Yoshimura, M. Hiraki, T. Nakao, and A. Komori.** 1984. Congenital cytomegalovirus infection in Japan. N. Engl. J. Med. **310:**50.
4. **Demmler, G. J.** 1994. Congenital cytomegalovirus infections. Semin. Pediatr. Infect. Dis. **5:**52–55.
5. **Nelson, C. T., A. S. Istas, M. K. Wilkerson, and G. J. Demmler.** 1995. PCR detection of cytomegalovirus DNA in serum as a diagnostic test for congenital cytomegalovirus infection. J. Clin. Microbiol. **33:**3314–3318.
6. **Numazaki, K., H. Asanuma, N. Nagata, and S. Chiba.** 1994. Analysis of human cytomegalovirus-infected peripheral blood mononuclear cells from infants with liver dysfunction by flow cytometry and the polymerase chain reaction. J. Leukocyte Biol. **56:**187–191.

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Authors' Reply

We thank Dr. Numazaki and Dr. Chiba for their interest in our article on PCR detection of CMV DNA in the sera of infants with congenital CMV infections (2). These gentlemen have pveviously described the epidemiology of congenital CMV infection in Japan (3) and have used PCR successfully to detect CMV DNA in T lymphocytes from infants with liver dysfunction associated with perinatally acquired CMV infection (3).

The aim of our study was to determine the sensitivity and specificity of PCR to detect CMV DNA in the sera of infants with symptomatic congenital CMV infections. To this end we successfully detected CMV DNA in the sera of 18 of 18 infants with symptomatic congenital CMV infections and 0 of 32 controls. Although urine viral culture remains the "gold standard" diagnostic test for congenital infection with CMV, our study showed serum PCR to be a rapid, sensitive, and specific method to diagnose congenital infections with CMV in those infants who are symptomatic at birth.

We agree with Dr. Numazaki and Dr. Chiba that the role of PCR detection of CMV DNA in the diagnosis of congenital CMV infection needs further study using larger populations of infants, especially those with asymptomatic congenital CMV infections.

REFERENCES

1. **Chiba, S., M. Kamada, H. Yoshimura, M. Hiraki, T. Nakao, and A. Komori.** 1984. Congenital cytomegalovirus infection in Japan. N. Engl. J. Med. **310:**50.

2. **Nelson, C. T., A. S. Istas, M. K. Wilkerson, and G. J. Demmler.** 1995. PCR detection of cytomegalovirus DNA in serum as a diagnostic test for congenital cytomegalovirus infection. J. Clin. Microbiol. **33:**3317–3318.
3. **Numazaki, K., H. Asanuma, N. Nagata, and S. Chiba.** 1994. Analysis of human cytomegalovirus-infected peripheral blood mononuclear cells from infants with liver dysfunction by flow cytometry and the polymerase chain reaction. J. Leukocyte Biol. **56:**187–191.

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