Early Primary Cytomegalovirus Infection in Pregnancy: Maternal Hyperimmunoglobulin Therapy Improves Outcomes Among Infants at 1 Year of Age

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(See the Editorial Commentary by Adler, on pages 504–6.)

Background. Primary cytomegalovirus (CMV) infection during pregnancy is the leading infectious cause of congenital neurological disabilities. Early CMV infection carries a higher risk of adverse neonatal outcome (sensorineural hearing loss or neurological deficits). Intravenous hyperimmunoglobulin (HIG) therapy seems to be promising, but its efficacy needs further investigation.

Methods. Since 2002, we have enrolled consecutively all pregnant women with early (ie, before gestational week 17) CMV infection. Beginning in 2007, all women were offered treatment with HIG (200 UI per kilogram of maternal weight, in a single intravenous administration). Outcome of infants was evaluated at the age of 1 year.

Results. Of the 592 women with early primary CMV infection, amniocentesis for CMV DNA detection was performed for 446. Of the 92 CMV-positive fetuses, pregnancy was terminated for 24, HIG was administered to mothers of 31, and no treatment was received by mothers of 37. Fetuses of treated mothers did not differ from fetuses of nontreated mothers according to mother’s age, gestational week of infection, CMV load, or detection of abnormal ultrasonography findings. At the 1-year evaluation, 4 of 31 infants with treated mothers (13%; 95% confidence interval [CI], 1%–25%) and 16 of 37 infants with nontreated mothers (43%; 95% CI, 27%–59%) presented with poor outcomes (P < .01, by the 2-tailed Fisher exact test).

Conclusions. HIG treatment improved the outcome of fetuses from women who had primary CMV infection before gestational week 17.

Cytomegalovirus (CMV) is the most common cause of congenital viral infection in the developed world, affecting 0.3%–2.3% of newborns [1]. Primary and secondary CMV infection can affect pregnant women, with the former showing a higher rate of vertical transmission [2]. During the last few years, CMV seroprevalence in the population has steadily decreased [3], thus fuelling a further increase in the incidence of primary infection. Despite the mild, often overlooked maternal symptoms, primary CMV infection is the leading infectious cause of congenital neurological morbidity [4]. Ten to fifteen percent of congenitally infected newborns present with symptoms at birth, and 15% of asymptomatic infants will develop long-term sequelae [5]. Each year in the United States,
congenital CMV infection causes an estimated 400 deaths and leaves approximately 8000 children with permanent disabilities, such as hearing deficits or mental retardation. The direct annual costs of caring for these children are estimated to be US$1–2 billion [6].

The vertical transmission rate depends on the gestational age at infection and varies from 30%–40%, during the first trimester, to 70%–90%, at the end of pregnancy [7]. Despite the lower transmission rate, early infection, defined as infection that occurs between periconception and the first months of gestation, has a higher risk of poor outcomes [8–10]. The severe prognosis warrants an effective prenatal intervention for congenital primary CMV infection, to reduce the substantial burden of social costs [6].

Currently, standard management of primary CMV infection does not exist: pregnant women might be offered a limited range of medical therapies or the option to terminate pregnancy [11]. Intravenous treatment with CMV hyperimmunoglobulin (HIG) seems a newsworthy and important option [12–16], and it has been widely tested in animals [17, 18]. There are no randomized trials ongoing that are evaluating HIG for treatment for CMV-infected fetuses [19]; so far, only a controlled nonrandomized study has demonstrated HIG to be efficacious against CMV infection in pregnant women [13]. Since this treatment is expensive and its safety in pregnancy has to be confirmed, there is a need for more evidence on the effectiveness of HIG administration that takes into account several possible confounders.

We report on a large population of CMV-infected pregnant women followed at University Hospital of Padua from 2002 to 2010. This article focuses on the efficacy of intravenous HIG treatment for early (ie, before gestational week 17) primary CMV infection by evaluating the neurological outcome of infants at a follow-up time point of 1 year of age.

**METHODS**

Since January 2002, we have performed a prospective study on vertical transmission and complications of CMV infection during pregnancy. This report focuses on women who had primary CMV infection before gestational week 17.

Beginning in January 2007, women with CMV-infected fetuses were offered HIG treatment (misoprostol [Cytotec]) at a dose of 200 U per kilogram of maternal weight, in a single administration. Detection of CMV in amniotic fluid after gestational week 20 and at least 6 weeks after infection were the main criteria for inclusion in the treatment protocol. HIG was administered during gestational weeks 20–24.

Our ethical committee approved the study, and written informed consent was obtained from the patients.

Primary maternal CMV infection was defined by seroconversion in previously seronegative mothers or by the presence of specific immunoglobulin G (IgG), immunoglobulin M (IgM), and low CMV-specific IgG avidity (<25%).

All women with documented or suspected CMV infection had serologic tests performed in the same laboratory. The virologic panel included testing for CMV DNA in blood and urine and shell vial analysis for CMV in urine.

Diagnosis of fetal infection was based on CMV DNA detection in amniotic fluid by real-time polymerase chain reaction (PCR) and was confirmed by isolation of CMV by shell vial analysis. Amniocentesis was performed at least 6 weeks after detection of maternal infection and only after verification that CMV DNA was not in maternal blood, to avoid iatrogenic infection of the fetus. The viral load was measured by quantitative TaqMan PCR and expressed in genomic copies per milliliter.

Ultrasoundography was performed before amniocentesis by 2 consultants with >10 years of experience in prenatal diagnosis, using ultrasonography equipment with a 3.5–5–MHz linear array transducer (Elegra/Antares, Siemens Medical Solutions, Mountain View, CA).

Ultrasoundography included evaluation of fetal biometric characteristics, morphologic characteristics, and well-being, to disclose any structural and/or growth abnormalities indicative of fetal infection, such as intrauterine growth restriction (defined as an estimated fetal weight below the tenth percentile), ventriculomegaly, oligohydramnios, hydrops, polyhydramnios, hydrops, brain calcifications, pleural effusion, and placental enlargement (define as placental thickness of >35 mm) [20].

Congenital infection in newborns was defined by isolation of CMV in urine ≤1 week after birth. The neonatal general evaluation included standard analyses, such as physical examination; determination of blood cell counts, platelet count, and alanine aminotransferase level; brain transfontanellar ultrasonography; ophthalmologic assessment; and evaluation of brain stem auditory evoked responses. Serologic tests for CMV-specific IgG and IgM and virologic tests by quantitative PCR for CMV DNA in blood and urine were performed soon after birth.

For women who delivered in hospitals different from ours, laboratory results were obtained from the appropriate facility.

Symptomatic congenital CMV disease included neurologic damage such as paresis, seizures, sensorineural hearing loss and deafness, chorioretinitis, cholestasis, chronic liver diseases, and microcephaly (head circumference below the fifth percentile). Periventricular calcifications, cortical dysplasia, ventricular enlargement, and cerebellar hypoplasia on brain computed tomography or magnetic resonance imaging (MRI) supported the clinical diagnosis of cytomegalic inclusion body disease. Since 2006, fetal MRI has been used for evaluating brain abnormalities in congenital CMV infection associated with CMV-positive amniotic fluid.
The audiological assessment consisted of a formal audiological follow-up, according to which all CMV-infected children underwent newborn audiological screening, using automated transient evoked otoacoustic emissions and auditory brainstem response, followed by audiological evaluations twice per year until 3 years of age and once per year until 6 years of age. This audiological assessment included pure-tone threshold evaluation by testing air conduction (250–8000 Hz) and bone conduction (250–4000 Hz). Outer hairy cell function was tested using distortion product otoacoustic emissions. Middle-ear function was assessed by tympanometry and on the basis of acoustic reflex thresholds. All tests were conducted and analyzed by audiologists with pediatric experience and in an environment that ensured reliable measurements. Sensorineural hearing loss (SNHL) was defined as a unilateral or bilateral hearing threshold of >25 dB for at least 2 of the frequencies tested (from 500 to 4000 Hz). Conductive hearing loss was diagnosed in children with normal bone conduction thresholds (<20 dB) and an air-bone gap of ≥15 dB, averaged over 500, 1000, and 2000 Hz.

Infant outcome was evaluated at the age of 1 year. The outcome was considered poor whenever the infant presented with neurological or audiological involvement (ie, hemiparesis, motor retardation, hyper- or hypotonia, seizures, spastic paraparesis, chorioretinitis, or unilateral or bilateral SNHL), necrotizing hemorrhagic enterocolitis, or chronic liver disease.

RESULTS

A total of 708 consecutive women with primary CMV infection were recruited. Of the 592 women in whom CMV infection was detected before gestational week 17, infection was identified by seroconversion in 365 patients. Amniocentesis was performed in 446 cases (5 women had twins), and CMV DNA was identified in the amniotic fluid of 92 fetuses. All patients had fetal infection confirmed by culture. No amniocentesis-related complications occurred in the present study. A total of 258 of 441 women (58.5%) received a diagnosis of CMV infection on the basis of seroconversion. Diagnosis of CMV infection was confirmed for 183 women on the basis of avidity findings. The frequency of vertical transmission did not differ significantly between women whose diagnosis was based on seroconversion and those whose diagnosis was based on immunoglobulin avidity (62 of 258 [24%] vs 53 of 183 [29%]).

A total of 24 of 92 amniocentesis-positive women (15 of 35 in 2002–2006 and 9 of 33 in 2007–2010) underwent termination of pregnancy. Autopsy results were available in 12 of 24 cases and showed brain or ocular involvement in 2 fetuses. Of the women who underwent termination of pregnancy, 19 had ultrasonography performed, and 7 had CMV-related ultrasonography abnormalities. Only 3 women underwent fetal MRI: 2 had CMV-related abnormal findings of both MRI and ultrasonography, while 1 had normal MRI findings. Of the remaining 68 amniocentesis-positive cases (2 women had twins), 31 were treated with HIG, while 36 (involving 37 babies) did not have the opportunity (ie, they were enrolled before 2007) or refused treatment (in 2 cases; see Table 1). These 2 groups did not differ with regard to age, gestational week of infection, or viral load (Table 1). At the 1-year evaluation, a greater proportion of infants born to nontreated women than those born to treated

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIG-Treated Women (n = 31)</th>
<th>Nontreated Women (n = 36)</th>
<th>Women Who Terminated Pregnancy (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>31</td>
<td>29.5</td>
<td>29</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>30.5 ± 4.8</td>
<td>29.3 ± 5.5</td>
<td>29.9 ± 4.2</td>
</tr>
<tr>
<td>Gestational age of infection, weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>10</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>9.4 ± 5.6</td>
<td>10.2 ± 6.4</td>
<td>8 ± 1.8</td>
</tr>
<tr>
<td>CMV load, DNA copies × 10⁶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>1.7</td>
<td>1.1</td>
<td>2.3</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>3.9 ± 5.4</td>
<td>2.6 ± 3.7</td>
<td>52.6 ± 204.7</td>
</tr>
<tr>
<td>Abnormal ultrasonography findings</td>
<td>4/31 (12.9)</td>
<td>5/37 (13.5)</td>
<td>7/19 (36.8)</td>
</tr>
<tr>
<td>Poor outcome</td>
<td>4/31 (12.9)</td>
<td>16/37 (43.2)</td>
<td>2/12 (16.7)</td>
</tr>
</tbody>
</table>

Data are proportion (%) of patients, unless otherwise indicated.

Abbreviations: CMV, cytomegalovirus; HIG, hyperimmunoglobulin; SD, standard deviation.

* Inclusive of twins.

† Three of 11 events (27.3%) occurred during 2002–2006, and 4 of 8 have occurred since 2007.

‡ Pathologic signs of central nervous system involvement. Both cases occurred before 2007.
women had a worse outcome (16 of 37 [43%; 95% confidence interval [CI], 27%–59%] vs 4 of 31 [13%; 95% CI, 1%–25%]; P < .01, by the 2-tailed Fisher exact test). SNHL was less frequent among infants born to treated women, compared with those born to nontreated women (3 of 31 [10%] vs 11 of 37 [30%]; P = .07, by the 2-tailed Fisher exact test). SNHL was bilateral in 10 infants (8 of whom were born to nontreated women).

In amniocentesis-positive cases, ultrasonography performed before gestational week 23 (range, gestational weeks 20–22) showed that 9 of 68 cases had abnormal findings consistent with CMV infection (liver calcifications in 3, hepatomegaly in 3, and splenomegaly, placental hyperechogeticity, bowel hyperechogenicity, monolateral ventriculomegaly, ventriculomegaly, periventricular brain calcifications, and splenic calcifications in 1 case each). These abnormal ultrasonography findings were predictive of poor outcomes at the 1-year evaluation (P < .05, by the 2-tailed Fisher exact test). The proportion of women with abnormal ultrasonography findings did not differ between women who subsequently did (4 of 31) and those who did not (5 of 37) receive HIG, whereas the proportion among women who underwent termination of pregnancy was greater than that among those who did not (7 of 19 vs 9 of 68; P < .05, by the χ² test).

Among the 349 amniocentesis-negative cases (4 women had twins), 23 newborns (7%) had a CMV-positive urine test: 2 (9%) had a poor outcome. Moreover, 3 women underwent termination of pregnancy for reasons different from CMV infection (1 because of thalassemia and 2 because of trisomy 21). Among amniocentesis-negative cases, seroconversion was significantly less frequent among women with CMV-positive newborns (7 of 23 vs 196 of 326 cases; P < .01, by the χ² test).

The proportion of infected infants who had a poor outcome was greater among those born to amniocentesis-positive nontreated women, compared with those born to amniocentesis-negative women (16 of 36 vs 2 of 23; P = .004, by the 2-tailed Fisher exact test); no difference was found in a comparison of infants born to amniocentesis-negative women and those born to amniocentesis-positive treated women (2 of 23 vs 4 of 31).

A total of 155 women did not have amniocentesis performed: 5 (3%) had a miscarriage, and 37 (24%) underwent termination of pregnancy. Of the 113 newborns, 28 (25%) had a CMV-positive urine test; 9 (32%) had a poor outcome.

Table 2 shows the outcome and the specific abnormalities observed in the subgroups described above.

**DISCUSSION**

This study focused on pregnant women with primary CMV infection detected during the first 17 weeks of gestation and showed that HIG therapy significantly improved the outcome of their infants at 1 year of age. In fact, HIG treatment reduced the rate of poor outcomes among infected newborns.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Amniotic Fluid Not Tested (n = 155)</th>
<th>CMV-Positive Amniotic Fluid</th>
<th>CMV-Negative Amniotic Fluid (n = 349)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOP or miscarriage</td>
<td>42 (24% of 176)</td>
<td>24 (25% of 92)</td>
<td>3 (2% of 153)</td>
</tr>
<tr>
<td>SNHL</td>
<td>6 (3% of 176)</td>
<td>14 (15% of 92)</td>
<td>3 (2% of 153)</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>2 (1% of 176)</td>
<td>2 (2% of 92)</td>
<td>0 (0% of 153)</td>
</tr>
<tr>
<td>Motor retardation</td>
<td>2 (1% of 176)</td>
<td>5 (6% of 92)</td>
<td>2 (1% of 153)</td>
</tr>
<tr>
<td>Hypertonia</td>
<td>1 (1% of 176)</td>
<td>1 (1% of 92)</td>
<td>1 (1% of 153)</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>0 (0% of 176)</td>
<td>1 (1% of 92)</td>
<td>0 (0% of 153)</td>
</tr>
<tr>
<td>Seizures</td>
<td>1 (1% of 176)</td>
<td>1 (1% of 92)</td>
<td>0 (0% of 153)</td>
</tr>
<tr>
<td>Spastic paraparesis</td>
<td>1 (1% of 176)</td>
<td>1 (1% of 92)</td>
<td>0 (0% of 153)</td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>1 (1% of 176)</td>
<td>2 (2% of 92)</td>
<td>1 (1% of 153)</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>0 (0% of 176)</td>
<td>2 (2% of 92)</td>
<td>0 (0% of 153)</td>
</tr>
<tr>
<td>Proportion (%) of infants with poor outcomes</td>
<td>9/113 (8.0)</td>
<td>20/68 (29.4)</td>
<td>16/37 (43.2)</td>
</tr>
</tbody>
</table>

Data are No. of infants, unless otherwise indicated. Some infants had ≥1 adverse outcome.

Abbreviations: CMV, cytomegalovirus; HIG, hyperimmunoglobulin; NHE, necrotizing hemorrhagic enterocolitis; SNHL, sensorineural hearing loss; TOP, termination of pregnancy.

a Total of 28 infants were infected with CMV.
b Denominator excludes fetuses associated with termination of pregnancy or miscarriage.
c Denominator is the no. of infants infected with CMV.
from 43% to 13%, thus confirming results from previous studies [13, 14]. Because HIG was available in our hospital from 2007 on, nontreated women clustered during 2002–2006. For this reason, we analyzed 2 subgroups—treated and non-treated women with CMV-positive amniotic fluid—to determine whether the frequency of vertical transmission, CMV load in amniotic fluid, frequency of abnormal ultrasonography findings, and frequency of termination of pregnancy might have influenced the outcome and, thus, interfered with assessment of the efficacy of HIG treatment.

The rate of vertical transmission among women with primary CMV infection ranges between 30% and 90% [7, 21, 22] and depends on several factors, such as the time of infection and the criteria used for evaluating the vertical transmission. Our study on early CMV infection showed that amniotic fluid was positive in 20% of cases, similar to what was found in previous studies of primary infections during pregnancy [23] or periconception [7]. An additional 23 of 342 newborns (7%) had CMV infection detected despite negative amniocentesis findings; previous studies would not have considered these to be cases of vertical transmission. The addition of the latter cases increased the frequency of vertical transmission in our cohort to 25% (114 of 449). Vertical transmission of CMV occurred fairly constantly during the study period, thus minimizing its effect as possible cause of selection bias in our study population. The reason for CMV-negative amniocentesis findings for newborns with proven CMV infection is unclear; false-negative findings have been attributed to recurrence of maternal infection after amniotic fluid sampling [24], suboptimal primer or probe specificity, improper transport or procession of the sample [25], and inappropriate timing of sampling (before gestational week 20). In our study, amniocentesis was performed strictly after gestational week 20 and at least 6 weeks after detection of maternal infection, to guarantee the maturity of the excretory system of the fetus and to let the virus reach and accumulate in the amniotic fluid. The infection of the fetus during the sampling procedure has also been hypothesized [26] but not confirmed in subsequent studies [23, 27]. Furthermore, studies of human placenta have shown that vertical transmission of CMV is a multistep process that might be influenced by placental receptors and maternal immunity [28, 29] and, thus, be completed over a variable period. Whatever the mechanism, it is evident that a negative amniocentesis finding does not preclude vertical transmission. Even if the frequency of poor outcomes among these subjects appears to be relatively low (9%), these findings raise some concern about restricting therapy only to women who have CMV-positive amniotic fluid and onset of primary CMV infection before gestational week 17. Indeed, an ongoing study is investigating the efficacy of HIG in preventing vertical transmission, but the results are not available yet.

CMV-positive amniocentesis is the most powerful predictor of poor outcomes among infants [13, 26]. In the group of nontreated women with positive amniocentesis findings, nearly half of the infants had severe neurological involvement at 1-year of follow up, which is comparable to findings from previous studies. The difference among the studies mostly depends on the outcome definition and the follow-up length. In a 2-year outcome study, 50% of infants had a poor outcome [13], whereas a lower proportion with poor outcomes (32%) was found in another study, which had a shorter follow-up time ranging from 2.5 months to 3 years [25].

Other studies reported CMV-related imaging abnormalities in 15%–19% of newborns [30, 31]; however, imaging abnormalities underestimate the rate of poor clinical outcomes, since sensorineural hearing loss and visual impairment might be present even with normal neuroimaging findings. Despite the discordant results of the studies mentioned above, there is general agreement that positive amniocentesis findings are associated with a worse outcome among infants, thus confirming the importance of a proper antenatal treatment.

In contrast, in our study the viral load in amniotic fluid did not predict infant outcome. This finding contradicts previous studies that showed higher DNA levels in amniotic fluid from mothers of symptomatic infants [27, 30–32] and proposed >10^5 CMV DNA copies/mL as a marker of congenital infection severity [31]. Subsequent studies [25, 33] failed to detect any correlation between infant outcome and amniotic fluid viral load. Indeed, viral load seems to be related to the time of pregnancy when the amniocentesis was performed [25]. In our study, the viral load ranged between 1000 and 896 × 10^6 DNA copies/mL. Interestingly, no woman with positive amniocentesis had less than 1000 DNA copies/mL despite our PCR quantitative technique was highly sensitive (from 50/100 copies/mL). Our data are in contrast with those of Guerra and Lazzarotto, who had a relatively high proportion of positive amniocentesis with less than 168 GE/mL (16/78, 12 without neonatal viro) [30, 31]. A possible explanation might be related to a strict adherence to the amniocentesis protocol in our study (after the 20th gestational week and after six weeks from the infection) or to technical differences in PCR method. The viral load observed in our study is consistent with what found in previous studies [25].

As expected, in our study infants born to women with CMV-negative amniotic fluid had a low risk (0.6% [2 of 346]) of poor outcomes, as shown by the presence of a few infected infants at birth despite negative results of amniocentesis. In this subgroup of infected infants, the rate of poor outcomes increased to 8.7% (2 of 23), which is far lower than the rate for infected newborns born to women with CMV-positive amniotic fluid (43%), probably because vertical transmission occurred later during pregnancy. These data confirm indirectly
the predictive value of a negative amniocentesis result when dealing with early CMV primary infection. Interestingly, receipt of HIG treatment by women with CMV-positive amniotic fluid reduced the difference in poor outcomes among infants born to women with positive (13%) and negative (8.7%) amniocentesis findings, thus neutralizing the above-mentioned predictive value of CMV-positive amniotic fluid.

In our study, abnormal ultrasonography findings were found in 16 of 87 women (18.4%) with CMV-positive amniotic fluid, which accords with results of previous studies [23, 26] that detected fetal ultrasonography anomalies in 12%–30% of women with primary CMV infection at gestational week 20.

In other studies, ultrasonography abnormalities were detected in 20%–50% of cases [13, 31]. This high percentage may be due to the fact that ultrasonography was performed after gestational week 20 and that intrauterine growth restriction, which usually is recognizable in the third trimester, is a sign of infection. Moreover, many ultrasonography findings might change during gestational age: fetal abnormalities become evident later, change, or disappear during pregnancy [23].

Abnormal ultrasonography findings are a good predictor of poor outcome [34, 35]. Interestingly, in the present study the proportion of women with abnormal ultrasonography findings did not differ between those who received and those who did not receive treatment.

Termination of pregnancy is an option frequently considered by women with CMV-positive amniotic fluid. In previous studies, frequencies of pregnancy termination ranged widely, from 18% to 91% [7, 13, 23–25, 27, 28–32, 36], probably reflecting the cultural background of the mother and the centered perspective of counseling. Besides being a key ethical topic, termination of pregnancy represents a problem in interpreting the results of treatment efficacy, since it might introduce a form of selection bias that is difficult to adjust for by means of statistical methods.

In our study, 26% of women with CMV-positive amniotic fluid underwent termination of pregnancy, especially when CMV-related ultrasonographic abnormalities were detected. Compared with women who carried out the pregnancy, a greater proportion of women who terminated pregnancy had abnormal ultrasonography findings, likely because the presence of CMV-positive amniotic fluid and ultrasonographic abnormalities led more frequently to pregnancy termination. Interestingly, frequency of ultrasonographic abnormalities did not change during the study period, nor did the frequency of pregnancy termination (3 per year), despite the introduction of treatment. Even autopsy findings did not differ before and after treatment introduction. Not even the introduction of fetal MRI, available in our center since 2006, seems to have influenced mothers’ choice: indeed, very few women underwent this test before termination of pregnancy.

CONCLUSIONS

Despite difference in the enrollment periods of women with primary infection before gestational week 17, the thorough analyses of the frequency of vertical transmission, CMV load in amniotic fluid, frequency of abnormal ultrasonography findings, and frequency of termination of pregnancy seem to confirm that treated and nontreated women did not differ significantly before treatment. Therefore, according to this study, HIG treatment affected the clinical course of newborns with congenital CMV infection by improving outcomes at 1-year and should be considered in the management of pregnant women with early primary CMV infection and CMV-positive amniotic fluid.

Notes

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References