IMAGING

Fetal cerebral periventricular halo at midgestation: an ultrasound finding suggestive of fetal cytomegalovirus infection

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OBJECTIVE: The objective of the study was to identify a cerebral ultrasound finding indicative of fetal cytomegalovirus (CMV) infection at midgestation.

STUDY DESIGN: All fetuses of 218 patients with primary CMV infection underwent prospective transvaginal neurosonographic examination at 20-22 weeks' gestation.

RESULTS: Transvaginal sonography identified a periventricular echogenic halo with well-defined borders in 6 infected fetuses at a mean gestational age of 20.5 weeks. Transabdominal axial views of the fetal head were normal in all cases. All patients opted for termination of pregnancy. Autopsy in 2 fetuses showed changes compatible with subacute white matter injury resembling telencephalic leukomalacia.

CONCLUSION: A fetal cerebral periventricular halo disclosed by transvaginal sonography at midgestation in pregnant patients with recent CMV infection is suggestive of fetal infection and may be associated with white matter lesions.

Key words: congenital cytomegalovirus, fetal brain, telencephalic leukomalacia, transvaginal ultrasound

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Cytomegalovirus (CMV) is the most common cause of intrauterine infection. Although the difficult counseling in case of congenital CMV infection is based mainly on prenatal imaging, several studies have demonstrated that ultrasound abnormalities are seen in a small proportion of CMV-infected fetuses.[1]

We recently published the results of a 10-year retrospective cohort study on the ability of ultrasound to predict symptomatic congenital CMV infection once primary maternal infection has been proven serologically.[2] That study showed an abnormal ultrasound finding yielded a sensitivity of 15% and a specificity of 94% in predicting congenital CMV infection. In addition, a relatively low positive predictive value of 45% was obtained when all abnormal ultrasound findings were examined, indicating that the anomalies could be tied to CMV in less than half the cases.

Among the abnormalities encountered in our infected fetuses, it was difficult to pinpoint ultrasound features pathognomonic for CMV infection. The most common abnormal findings, hyperechogenic bowel and cerebral ventriculomegaly detected in about 30% of infected fetuses, were also seen in uninfected cases.

The presence of fetal brain abnormalities at ultrasound examination, such as microcephaly or lissencephaly, is currently the most specific predictor of poor prognosis, but such anomalies are usually diagnosed late in pregnancy or, more frequently, after birth. Other more subtle or nonspecific ultrasound features of CMV infection are likely to escape detection.

Because transvaginal sonography gives a much better resolution of the fetal brain, allowing detailed study of the periventricular parenchyma,[3] this prospective study performed a targeted transvaginal neurosonographic examination in all fetuses of patients with primary CMV infection to disclose any cerebral ultrasound findings indicative of fetal infection at midgestation.

Materials and Methods

Between January 2007 and December 2008, all pregnant women referred to our Maternal-Fetal Medicine Unit for primary CMV infection (patients seroconverted to CMV immunoglobulin [Ig] G positivity or with anti-CMV IgG of low avidity combined with true IgM) prospectively underwent targeted transvaginal neurosonographic examination (GE Voluson 730; GE Healthcare, Milan, Italy) between 20 and 22 weeks' gestation. Ultrasound examinations were performed by experienced operators and included serial transverse, sagittal, and coronal views obtained through the fontanelle.

As is usual at our institution, women with primary CMV infection acquired

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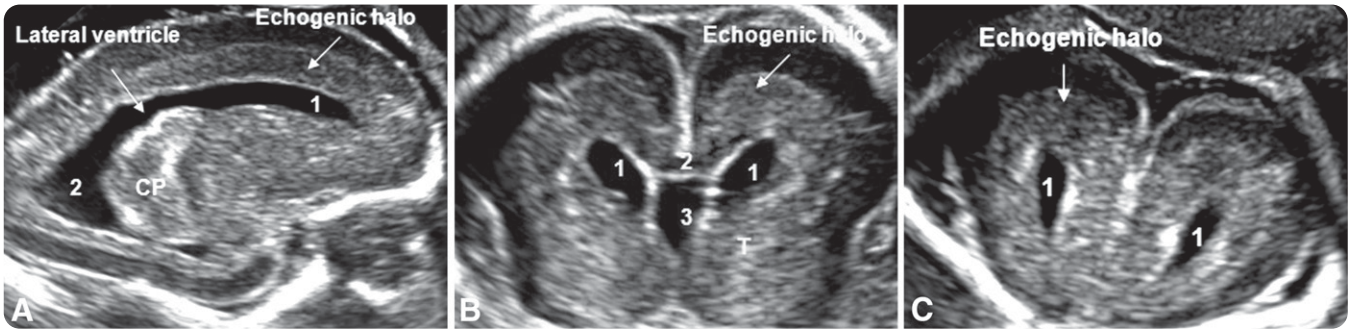
FIGURE 1
Transvaginal views of the fetal brain



Transvaginal views of the fetal brain show periventricular echogenic halo with well-defined borders. **A,** Parasagittal plane showing the lateral ventricle (*arrow*), echogenic halo (*arrow*), frontal horn (1), occipital horn (2), and the choroid plexus (CP). **B,** Coronal transthalamic plane showing both frontal horns of the lateral ventricles (1), corpus callosum (2), cavum septi pellucidi (3) and thalamus (T), and echogenic halo (*arrow*). **C,** Coronal transfrontal plane slightly anterior to the transthalamic plane showing both frontal horns of the lateral ventricles (1) and echogenic halo (*arrow*).

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early in gestation were also counseled about the possibility of the diagnosis of fetal infection by amniocentesis at 20-21 week's gestation, in all cases at least 6 weeks after seroconversion.[4,5] Diagnostic performances of viral isolation, polymerase chain reaction (PCR), and quantitative PCR on amniotic fluid with respect to the presence or absence of CMV infection in the fetus were described in previous studies.[4]

According to our protocol, if a high likelihood of fetal injury is recognized (ultrasound abnormalities and/or high viral load in the amniotic fluid), the couple may opt to terminate the pregnancy within the time frame currently provided by Italian legislation that does not allow late termination. If test results show a low viral load in the amniotic fluid and there are no ultrasound abnormalities, serial ultrasound scans are scheduled at 28 and 33 weeks' gestation throughout continued pregnancy to evaluate the fetal anatomy along with magnetic resonance imaging (MRI) in the third trimester.

Information concerning fetal and neonatal outcomes was obtained directly when the mothers had terminated their pregnancies or given birth at our hospital. If the mothers had received care elsewhere, this information was elicited by questionnaire or telephone interview or both.

Ethics

The study was carried out following the ethical rules of St Orsola-Malpighi General Hospital (Bologna, Italy).

Results

Between January 2007 and December 2008, 218 women with primary CMV infection were referred to our division. Of these, 135 underwent amniocentesis to diagnose fetal infection (including 2 sets of twins, for a total of 137 fetuses). Low viral load (<500 copies/mL) in the amniotic fluid was found in 103 cases; the viral load was high in the remaining 32 cases (34 fetuses).

No abnormal sonographic brain findings were diagnosed in fetuses with low viral load in the amniotic fluid (103/218). One of these fetuses presented multiple extra-central nervous system (CNS) malformations and the pregnancy was terminated as requested by the parents. At autopsy, the fetus was classified as uninfected on the basis of macroscopic and histologic examination. Follow-up was not available in 9 pregnancies; 83 newborns were uninfected at birth on the basis of viral isolation from urine or saliva within the first 2 weeks after delivery; 7 were infected but asymptomatic at birth and/or at subsequent follow-up visits; in 3 cases the parents did not follow recommended neonatal tests.

Abnormal sonographic brain findings were found in 8 cases with high viral load in the amniotic fluid, all of them at 20-22 weeks of gestation, including 6 cases of periventricular echogenic halo and 2 cases showing patterns of abnormal sulcation associated with parenchymal foci of increased echogenicity consistent with calcifications. Hypoplastic corpus callosum was present in 1 of these 2 fetuses. All these patients opted for termination of pregnancy, but postmortem examination was available for only 2 cases with periventricular echogenic halo. Extra-CNS abnormal findings, namely a hyperechogenic bowel, were found in 4 fetuses, including 2 cases with periventricular echogenic halo and a set of twins (9 pregnancies, 10 fetuses).

Of the remaining 23 pregnancies (24 fetuses, because of a set of twins) with high viral load in the amniotic fluid and normal ultrasound findings at 20-22 weeks at gestation or later, follow-up is available for 21 fetuses: 11 fetuses were terminated, 1 fetus died in utero at 24 weeks, and 11 newborns were delivered. Among the delivered babies, 9 were infected but asymptomatic and 2 infected and symptomatic.

No abnormal sonographic findings were found in 83 patients who declined amniocentesis. Follow-up was available in 76 cases: 12 pregnancies were terminated in the first trimester, 11 newborns