Tx of CMV-Related Hearing Loss May Expand

Availability of valganciclovir could help infants with leading nongenetic cause of deafness.

BY M. ALEXANDER OTTO

SEATTLE — If an infant fails a hearing test, think cytomegalovirus infection, advised Dr. Kathleen Sie.

Congenital cytomegalovirus (CMV) infection is now known to be the leading nongenetic cause of deafness in children, said Dr. Sie, clinical director of Seattle Children's Hospital's childhood communication center.

In infants with nongenetic hearing loss—at least 25% of cases—she recommended doing cytomegalovirus (CMV) screening by shell vial urine culture if the infant is within the first 6 weeks of life. Past that, the diagnosis must be made by polymerase chain reaction (PCR) testing of the neonatal blood spot.

If an infant is positive for CMV, treatment with valganciclovir, an oral antiviral agent, might halt or reverse hearing loss, Dr. Sie said at a conference sponsored by the North Pacific Pediatric Society.

Although not the standard of practice now, she said screening and treatment for pediatric CMV-related hearing loss will become increasingly common over the next 10 years. CMV will become the treatable cause of hearing loss in children because of promising results from small, early studies and because of the availability of valganciclovir, the active metabolite of ganciclovir, the drug used in those early studies.

In a small, randomized clinical trial published in 2003, the hearing of 25 infants born with symptomatic CMV infections and treated with ganciclovir did not deteriorate by 6 months; hearing deteriorated in 41% (7 of 17) of untreated infants. At or beyond age 1 year, hearing deteriorated in 21% (5 of 24) of ganciclovir-treated patients, compared with 68% (13 of 19) of controls (J. Pediatr. 2003;143:16-25).

The study did not lead to widespread use of ganciclovir for CMV hearing loss, however, because the results came only after the drug was given for 6 weeks through a central line, and because 63% of those treated developed grade 3 or 4 neutropenia.

Drug administration drawbacks, at least, will be avoided with the oral agent valganciclovir, she said.

An ongoing National Institutes of Health–funded study could shed light on the use of the drug; a 6-week course of valganciclovir is being tested against a 6-month course for CMV-related hearing loss and developmental delays.

About 1% of newborns are born with congenital CMV infections in Washington state, Dr. Sie noted. Nationwide, National Institutes of Health estimates range from 0.5% to 1.5%.

Between 22% and 65% will have hearing loss if they are born with CMV symptoms; the percentage is 6%-23%, if the infants are born asymptomatic (J. Clin. Virol. 2006;35:226-31).

CMV hearing loss can be either unilateral or bilateral, and vary in the severity and frequencies affected, Dr. Sie said. It is unclear how the virus damages hearing, but CMV has been detected in the perilymphatic spaces of the inner ear and the spiral ganglion, the location of the nerve endings in the inner ear.

The reason shell vial urine cultures can be done at or before 6 weeks of age is that an infected newborn will likely be shedding virus. Later, a neonatal blood spot PCR must be done to rule out postnatal infection, which is not thought to carry the same risk of hearing loss.

Although infants with hearing loss are not yet typically screened and treated for CMV, when they are, treatment is usually initiated only when the infection is caught by 6 months of age, Dr. Sie said. That misses later-onset CMV hearing loss.

Dr. Sie said he expects that in coming years, treatment will be initiated even if the diagnosis comes later. "We do know that [CMV-related] damage can continue for the first few years of life. So it's reasonable to think the window for treatment might extend beyond 6 months," she said. ■

Disclosures: *Dr. Sie reported that she had no conflicts of interest to disclose.*

Dried Blood Spot PCR Lacks Sensitivity to Newborn CMV

BY MARY ANN MOON

Real-time polymerase chain reaction assays of dried blood spots are not sensitive enough to reliably identify cytomegalovirus infection in newborns, according to a recent report.

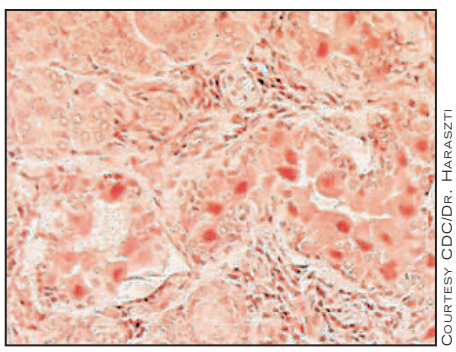
Two such methods missed approximately two-thirds of the CMV infections in a prospective cohort study of 20,448 newborns, said Dr. Suresh B. Boppana of the University of Alabama at Birmingham and associates (JAMA 2010;303:1375-82).

"These results have major public health implications because they indicate that such methods, as currently performed, will not be suitable for the mass screening of newborns for congenital CMV infection," the investigators noted.

Traditional isolation of CMV from cultured saliva or urine samples is the standard method of identifying the congenital infection, but it is not amenable to mass screening. Experts had been hopeful that PCR technology would prove sensitive and specific at identifying occult CMV infection, since " it does not require tissue culture facilities and is amenable to automation with the screening of large numbers of specimens at low cost," Dr. Boppana and colleagues said.

Dried blood spots already are collected routinely for newborn metabolic screening, and there has been "considerable" enthusiasm for using PCR assays for CMV on such samples, but their diagnostic accuracy had never been directly compared with that of standard tissue culture methods.

The researchers compared standard saliva culturing with dried blood spot sampling in infants born at seven U.S. medical centers in 2007-2008. Two different PCR techniques, a single-primer and a double-primer assay, were assessed.



COURTESY CDC/DR. HARASZTI

Traditional isolation from saliva (above) is not amenable to mass screening.

A total of 92 infants (0.45%) were found to have congenital CMV infection.

Saliva screening correctly identified 91 of the 92 affected newborns (99%). In contrast, single-primer blood spot PCR identified only 17 of the 60 infants (28%) who were tested by that method and double-primer blood spot PCR detected only 11 of the 32 infants (34%) who were tested by that method.

The sensitivity and specificity of the single-primer blood spot PCR were 28% and 99.9%. The sensitivity and specificity of the double-primer blood spot PCR were 34% and 99.9%.

"Our data indicate that as many as 80% of infants with congenital CMV infections could be missed" with the dried blood spot real-time PCR assays, Dr. Boppana and associates said. This failure probably was due to an absence of detectable CMV DNA in the peripheral blood of most newborns with congenital CMV. ■

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