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Middle Ear Effusion in Children With Congenital Cytomegalovirus Infection

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Abstract

Background: Sensorineural hearing loss (SNHL) is well described in children with congenital cytomegalovirus (CMV) infection, but limited data are available on middle ear effusion (MEE) occurrence in this population. We assessed the prevalence of MEE and the degree of transient hearing change associated with MEE among children with congenital CMV infection.

Methods: Children with congenital CMV infection enrolled in a longitudinal study received hearing and tympanometric testing during scheduled follow-up visits annually up to 6 years of age. We used a generalized linear mixed-effect logistic regression model to compare the odds of MEE, defined as type B tympanogram (normal ear canal volume with little tympanic membrane movement) among patients categorized as symptomatic or asymptomatic based on the presence of congenital CMV-associated signs in the newborn period.

Results: Forty-four (61%) of 72 symptomatic and 24 (28%) of 87 asymptomatic patients had ≥1 visit with MEE. After controlling for the number of visits, symptomatic patients had significantly higher odds of MEE (odds ratio: 2.09; 95% confidence interval: 1.39–3.14) than asymptomatic patients. Transient hearing decrease associated with a type B tympanogram ranged from 10 to 40 dB, as measured by audiometric air-bone gap in 11 patients.

Conclusions: Among children with congenital CMV, MEE can result in transient hearing decrease, which can reduce the efficacy of a hearing aid in those with SNHL. It is warranted that children with congenital CMV infection and SNHL receive routine audiologic and tympanometric testing to better manage hearing aid amplification levels.

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The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Keywords

congenital cytomegalovirus infection; middle ear effusion; tympanometry; hearing loss

In the United States, congenital cytomegalovirus (CMV) infection is estimated to occur in about 4.5 per 1000 live births.[1] Approximately 10% of infected infants are symptomatic at birth, with a clinical spectrum that ranges from transient and mild signs such as hepatomegaly and jaundice, to severe manifestations such as microcephaly, brain abnormalities and chorioretinitis. Sensorineural hearing loss (SNHL) is estimated to affect about 30% of symptomatic and 10% of asymptomatic patients.[2–5]

Although SNHL has been well documented in children with congenital CMV infection, limited data are available on the prevalence of middle ear effusion (MEE) in this population. In the general pediatric population, about 10%–30% of children have MEE leading to transient conductive hearing loss at some time before their third birthday.[6] MEE can result in transient conductive hearing loss, impairing speech and language development in children with recurrent MEE episodes.[7] We assessed the prevalence of MEE and associated degree of transient hearing change among children with congenital CMV infection during follow-up audiologic visits.

MATERIALS AND METHODS

Study Population

Our study included patients with congenital CMV infection enrolled in the Congenital Cytomegalovirus Longitudinal Study at Texas Children's Hospital: 87 of 92 asymptomatic case patients identified through hospital-based newborn CMV screening from 1982 to 1992, and 72 symptomatic patients identified through referrals from 1983 to 2005. Diagnosis of congenital CMV infection was made by culturing urine samples collected within 3 weeks of life. We classified infants as symptomatic if one or more of the following CMV-related signs were present in the newborn period: purpura, petechiae, jaundice, hepatosplenomegaly, microcephaly, unexplained neurological abnormality, elevated liver enzymes (alanine aminotransferase >100 IU), hyperbilirubinemia (total bilirubin >3 mg/dL, hemolytic anemia or thrombocytopenia (platelet count <75,000/mm^3). Infants who were small for gestational age or had congenital SNHL without the above CMV-related signs were classified as asymptomatic.[4] The study protocol was approved by the Institutional Review Board for Human Subject Research of the Baylor College of Medicine and affiliated hospitals.

Study Evaluations and Definitions

Evaluations were performed annually up to age 6 years and at least once during elementary, middle and high school years and included otoscopy, tympanometry and hearing tests. Patients were not under continuous surveillance for abnormal middle ear conditions. Clinical data such as ear pain, fever or abnormal appearance of the tympanic membrane suggesting inflammation were not systematically collected during follow-up visits. Thus, we were unable to differentiate whether patients with MEE had acute otitis media or otitis media with effusion.

To assess MEE, we relied on tympanometry test results. Tympanometry measures the ear canal volume, the peak middle ear pressure and the amount of tympanic membrane mobility (ie, compliance). The audiologists used these 3 indexes to determine and categorize the middle ear status on the day of the testing. MEE was defined as normal ear canal volume with no detectable tympanic membrane movement due to effusion (ie, type B tympanogram result).[8] In addition to MEE, patients could have perforation or a pressure equalization (PE) tube inserted in the tympanic membrane to drain fluid. Both conditions result in a large ear canal volume value in the tympanometric result. Otoscopy was performed to assess the integrity of the tympanic membrane, presence and the position of the PE. We classified the presence of a PE tube as type B-tube. Only 1 patient was found to have a tympanic membrane perforation. Therefore, this condition was excluded from the analysis. Two independent audiologists further reviewed the tympanometry test results before data analysis.

Audiologic evaluations included auditory brainstem response and behavioral audiometry. The auditory brainstem response testing protocol included the use of a broadband click, where the sound energy was concentrated between 2 and 4 kHz, and frequency-specific tone-burst stimuli from 0.5 to 8 kHz. Behavioral audiometry included pure-tone air- and bone-conduction testing for audiometric frequencies 0.25–8 kHz. We assessed the degree of transient hearing change associated with MEE (type B tympanogram) using frequency-specific air-bone gap.[8] The pure-tone bone-conduction hearing thresholds were subtracted from the pure-tone air-conduction hearing thresholds obtained on the same visit when type B tympanogram was documented. Transient hearing change was defined as an air-bone gap of ≥15 decibel hearing level (dBHL) in any frequency or ≥10 dBHL in 2 or more frequencies.

Statistical Analysis

We assessed the prevalence of both type B and B-tube tympanograms, overall and by age. We used the Fisher exact test to compare the age distribution of first and last visits with a type B tympanogram result in symptomatic versus asymptomatic patients. To assess whether symptomatic patients were more likely to have any of the 2 tympanogram types compared with asymptomatic patients, we used a generalized linear mixed-effect logistic regression model to estimate the odds ratio (OR) and 95% confidence interval (CI), adjusted for age. We used PROC GLIMMIX to account for multiple audiologic visits for the same patient and for varying intervals in which visits occurred across patients. We used Excel and SAS version 9.4 (SAS Institute Inc., Cary, NC) for data analysis.

RESULTS

The median age at first audiologic evaluation was 36 days (interquartile range: 10–116 days) and 75 days (interquartile range: 48–103 days) for symptomatic and asymptomatic patients, respectively; 144 (91%) were first evaluated within 6 months of birth.[3,4,9] The median age of first and last audiologic visit with tympanometry results was 0 (0–9) years and 12 (0–18) years for symptomatic patients and 1 (0–17) year and 17 (0–18) years for asymptomatic patients. The median number of audiologic visits with tympanometry results was 7 (range: 1–20) for 72 symptomatic patients and 6 (range: 1–16) for 87 asymptomatic patients. Forty-

six (64%) symptomatic patients and 27 (31%) asymptomatic patients had ≥1 follow-up visit with either type B or B-tube tympanograms (Table 1). The first documented MEE (ie, type B tympanogram) was at a median age of 1 year for both symptomatic and asymptomatic case patients ($P > 0.05$).

Overall, 44 (61%) symptomatic patients and 24 (28%) asymptomatic patients had MEE; 19% and 11%, respectively, had undergone surgical insertion of a PE tube in the tympanic membrane. The prevalence of MEE was highest at age 1 year for both groups (Fig. 1, bar graph). By age 6 years, the proportion of symptomatic patients who experienced at least 1 visit with MEE was almost twice that of asymptomatic patients. Symptomatic patients had significantly higher odds of having either type B or B-tube tympanograms (OR: 1.74; 95% CI: 1.23–2.46; $P = 0.002$) and MEE (type B tympanogram only) (OR: 2.09; 95% CI: 1.39–3.14; $P = 0.0005$) (Table 1). In 11 patients with MEE, for which we could measure the air-bone gap, the transient hearing change was in the range of 10–40 dBHL.

DISCUSSION

In this study, MEE was more common in children with symptomatic congenital CMV disease than in children with asymptomatic congenital CMV infection. By age 1 year, about half of symptomatic and one-third of asymptomatic patients had at least 1 visit with either MEE or a PE tube in the tympanic membrane. The prevalence of MEE decreased with age in both symptomatic and asymptomatic patients consistent with findings from other studies in the general population.[7,10,11]

Limited information is available on the frequency of MEE in children with congenital CMV infection. Published studies typically excluded type B tympanogram data to assess hearing loss progression or fluctuation in children with congenital CMV infection. By age 1 year, we found about half of symptomatic case patients had at least 1 visit with MEE. Other studies with more frequent (ie, monthly or bimonthly) assessments of the middle ear status reported abnormal middle ear findings in 77%–91% of healthy children at 1–2 years of age.[10–12] However, studies with less frequent (ie, annual or bi-annual) follow-up visits, such as ours, reported abnormal middle ear findings in 29%–38% healthy children at 1 year of age.[13–15] Thus, our study likely underestimated the prevalence of MEE.

In our study, half of the symptomatic patients had at least 1 visit with MEE by 1 year of age compared with one-third of asymptomatic patients. This finding suggests that children with symptomatic congenital CMV disease may have a higher risk of MEE. In our cohort, 43% of the symptomatic patients had intellectual disability.[4] Children with developmental disabilities may have more frequent upper respiratory tract infections and persistent Eustachian tube dysfunction, which can allow fluid reflux and bacteria from the nasopharynx into the middle ear cavity, contributing to higher risk of MEE.[16–18] Studies with a specific protocol designed to assess type and prevalence or incidence of MEE, including acute otitis media and otitis media with effusion, in children with congenital CMV infection are needed.

We found that patients with MEE could have a transient hearing decrease of up to 40 dBHL, consistent with the 18–35 dBHL hearing loss reported in a systematic review assessing the effects of otitis media with effusion on children's listening abilities.[7] A recent study further indicated that a history of otitis media can negatively affect various auditory processing abilities such as processing speech in background noise, and integration of auditory inputs from 2 ears later in life.[19] In children with SNHL, transient conductive hearing loss caused by MEE can compromise the amplification adequacy of a hearing aid.[20] In our cohort, 58% of the symptomatic patients and 10% of the asymptomatic patients had congenital/early-onset SNHL.[3] Transient hearing loss resulting from MEE can impose an added disadvantage on the hearing ability of children with congenital CMV-associated hearing loss and potentially lead to speech and language delays. The American Academy of Otolaryngology–Head Neck Surgery practice guideline recommends identifying at-risk children to optimize their conditions for hearing, speech and language development.[21–23] Because children with congenital CMV-associated SNHL are at risk for speech, language or learning problems, regular audiologic and hearing aid amplification assessment, tympanometric testing and screening for speech and language delay are warranted.[20,24]

Our study had limitations. Study children had on average 1 annual scheduled follow-up visit for hearing evaluation. Clinical data such as fever and ear pain were not systematically collected and pneumatic otoscopy was not performed to further categorize MEE into acute otitis media or otitis media with effusion. We assessed MEE using tympanometry data (ie, type B tympanogram). Although tympanometry yields quantitative results, such as ear canal volume, peak middle ear pressure, tympanic membrane compliance, artifacts may occur and the categorization into tympanogram types is subject to an audiologist's interpretation. Nonetheless, the sensitivity of tympanometry for diagnosing MEE is as high as that of pneumatic otoscopy (94%).[25]

CONCLUSIONS

Our findings suggest that MEE may be more frequent among children with symptomatic congenital CMV disease than those with asymptomatic infection or in a general population of healthy children. Studies assessing the prevalence or incidence of otitis media in children with congenital CMV infection may be helpful to document the burden of otitis media in this population and to inform hearing monitoring protocols. In addition, because of the potential transient hearing change associated with MEE, future studies assessing the efficacy of antiviral interventions should ensure the integrity of the middle ear (absence of MEE) at baseline and follow-up visits to avoid misclassification of hearing changes, either improvement or worsening of a hearing loss.

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APPENDIX: The Congenital Cytomegalovirus Longitudinal Study Group

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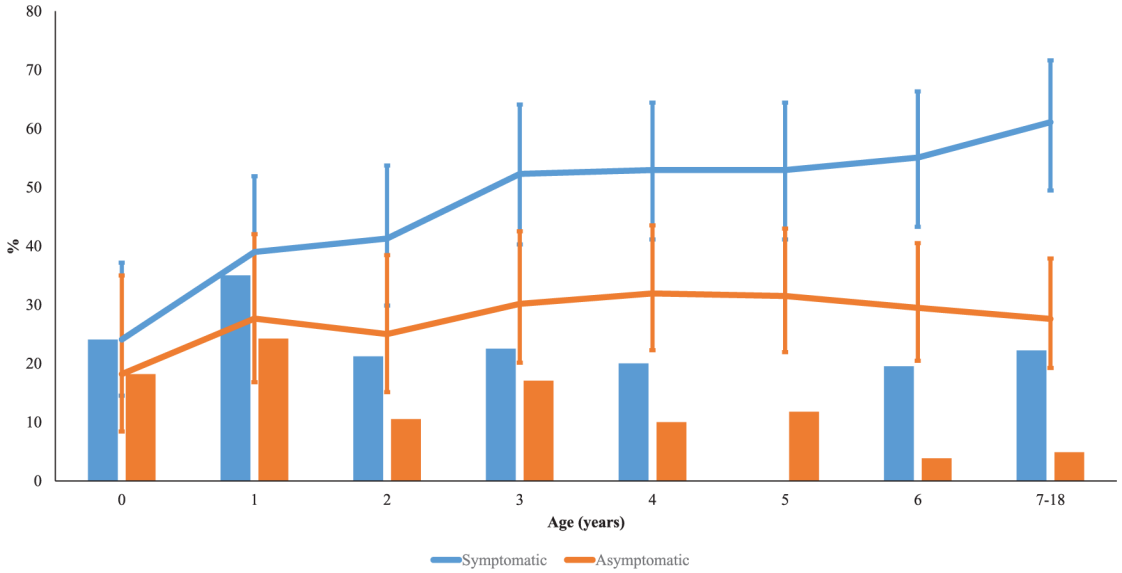

FIGURE 1.

Proportion of patients with middle ear effusion (type B tympanogram) by age and patient status. Bar graph: proportion with ≥1 visit with middle ear effusion (ie, type B tympanogram) at each age. Line graph: proportion with ≥1 visit with middle ear effusion (ie, type B tympanogram) by age.

TABLE 1.

Tympanogram Types by Patient Status and by Visits

Tympanogram Result	Overall Prevalence* Symptomatic cCMV N = 72 No. (%)	Overall Prevalence* Asymptomatic cCMV N = 87 No. (%)	Adjusted OR (95% CI)†	*P*†‡	Frequency by Visit Symptomatic cCMV N = 562 No. (%)	Frequency by Visit Asymptomatic cCMV N = 548 No. (%)
Normal tympanic membrane movement at expected pressure level	72 (100%)	87 (100%)	NA	NA	445 (79%)	472 (86%)
Either type B or B-tube tympanogram	46 (64%)	27 (31%)	1.74 (1.23–2.46)	0.002	118 (21%)	58 (11%)
Type B tympanogram only (MEE)	44 (61%)	24 (28%)	2.09 (1.39–3.14)	0.0005	88 (16%)	36 (7%)
Type B-tube tympanogram (presence of PE tube)	14 (19%)	10 (11%)	1.08 (0.60–1.94)	0.795	30 (5%)	20 (4%)
Age distribution of first type B tympanogram (y)‡	-	-	-	0.0452	-	-
0	10 (23)	6 (25)	-	-	-	-
1–2	16 (36)	7 (29)	-	-	-	-
≥3	18 (41)	11 (46)	-	-	-	-
Age distribution of last type B tympanogram (y)‡	-	-	-	0.0129	-	-
0	7 (16)	3 (13)	-	-	-	-
1–2	11 (25)	6 (25)	-	-	-	-
3–6	16 (36)	11 (46)	-	-	-	-
≥7	10 (23)	4 (17)	-			

*Frequencies by patient: number of case patients with at least 1 visit with type B tympanogram.

†We used a generalized linear mixed-effect logistic regression model to estimate the OR and 95% CI, adjusted for age. We used PROC GLIMMIX to account for multiple audiologic visits for the same patient and for varying intervals in which visits occurred across patients.

‡We used the Fisher exact test to compare the age distribution of the first and last visit with type B tympanogram in symptomatic vs. asymptomatic patients. Analysis restricted to the 44 symptomatic and 24 asymptomatic patients With ≥1 type B tympanogram during the study period.

cCMV indicates congenital cytomegalovirus.