Long-Term Follow-Up of Implanted Children with Cytomegalovirus-Related Deafness

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Introduction

Cytomegalovirus (CMV) is still one of the most common and important intrauterine viral infections in developed countries today, affecting approximately 0.5–2.5% of all live births [Hagay et al., 1996]. Approximately 10% of congenitally infected infants are symptomatic at birth for developing the congenital CMV syndrome [Stagno and Whitley, 1985]. The remaining 90% with asymptomatic congenital CMV appear clinically normal at birth. However, later complications such as sensorineural hearing loss (SNHL), mental retardation, delay in psychomotor development, learning disabilities and expressive language delay are reported in association with more than 90% of these patients [Stagno et al., 1977]. SNHL is a common manifestation of the congenital CMV infection, affecting 20–60% of symptomatic and 15–25% of asymptomatic infants [Fowler et al., 1999; Iwasaki et al., 2007; Grosse et al., 2008]. Several authors noticed that SNHL becomes more severe after the 1st year of life [Huygen and Admiral, 1996], with a further deterioration within the first 4 years of life (progressive hearing loss) [Hickson and Alcock, 1991; Williamson et al., 1992]. The proposed mechanism for CMV-associated SNHL appears to be the direct infection of the otic capsule. CMV antigens have been detected in the organ of Corti, the auditory nerve,
the cochlear duct, the semicircular canals and the perilymph of infected infants [Davis et al., 1981].

Although the usefulness of cochlear implantation to CMV children with profound deafness has been fully demonstrated, there is an aspect that should be considered when counseling such children, i.e. possible coexisting central disorders and learning difficulties that may influence their speech and language development. The literature investigating the postoperative cochlear implant results of congenital CMV-deafened patients is limited. Lee et al. [2005] reported that the mean speech perception scores were 4.5 (out of 6) following implantation. Ciorba et al. [2009] reported that a cochlear implant can provide useful speech comprehension to patients with CMV-related deafness, even if language development is poorer compared to a group of connexin-26-implanted children. Nevertheless, these results only investigate short-term outcomes while no long-term data are available on speech perception and language development.

This study is a retrospective review of 6 patients with CMV-related profound deafness in order to investigate speech development and speech comprehension after 10 years of using a cochlear implant.

**Methods**

A retrospective review of the pediatric cochlear implant database was performed and 6 implantees who had been diagnosed with CMV-induced profound deafness were found. The diagnosis of CMV was made when the mother was found to have either anti-CMV IgG or IgM during pregnancy and the child was found to have CMV in urine samples or positive anti-CMV IgM titers. The charts of these 6 children were reviewed for additional clinical information including current history, neonatal and past medical histories, imaging data and clinical examination findings. The presence or absence of prematurity, microcephaly, hepatosplenomegaly, seizure activity, psychomotor delay, leukoencephalitis and intracranial calcifications were considered as risk factors related to CMV infection that could influence the outcomes. All patients were implanted with Clarion devices (Advanced Bionics Corporation, Calif., USA). The patients’ characteristics are presented in table 1.

Audiological assessment (in a preoperative period, during hearing aid use and then during cochlear implant use) included auditory brainstem responses, free field audiometry and behavioral audiometry with and without hearing aids or implant.

The speech perception abilities of children with implants were described using the speech perception categories according to the Moog and Geers Scale [Geers and Moog, 1987] in order to compare subjects across different ages and varying degrees of speech development. This is a hierarchical scale of auditory skills, ranging from no detection of speech sound to open-set speech recognition. Six levels of speech perception were then used.

The language development was also described using the Nottingham classification categories [Allen and Dyar, 1997]. According to the Nottingham scale, three levels of speech development were then classified: (1) preverbal = no intentional verbal com-

<table>
<thead>
<tr>
<th>Patients (n = 6)</th>
<th>Clinical signs at birth</th>
<th>MRI calcification</th>
<th>Motor impairment</th>
<th>Prematurity</th>
<th>Visual impairment</th>
<th>Cognitive impairment</th>
<th>Hearing loss onset</th>
<th>Age at implant</th>
<th>CI use in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1 symptomatic</td>
<td>microcephaly</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>90</td>
<td>congenital profound</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>P2 asymptomatic</td>
<td>none</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>100</td>
<td>congenital profound</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>P3 symptomatic</td>
<td>seizures</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>70</td>
<td>congenital profound</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>P4 symptomatic</td>
<td>thrombocytopenia, petechiae</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>100</td>
<td>congenital profound</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>P5 asymptomatic</td>
<td>none</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>100</td>
<td>progressive</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>P6 symptomatic</td>
<td>seizures, thrombocytopenia</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>70</td>
<td>progressive</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

CI = cochlear implant.

a MRI calcification of central nervous system at birth.

b Cognitive impairment: mental retardation scale according to the DSM-IV criteria: IQ >70 = normal, IQ 50–70 = moderate, IQ 35–50 = middle, IQ 20–35 = severe, IQ <20 = profound.
communication (2) periverbal = use of words and (3) functional = use of phrases and word sequences based on morphological and syntactic rules.

The cognitive development of all patients was assessed according to the DSM-IV criteria.

Results

Included in the study were 6 children, 3 male and 3 female; 4 were symptomatic for CMV disease at birth and 2 were not symptomatic. Of the 4 children with symptomatic congenital CMV infection, 3 presented with congenital bilateral profound SNHL and 1 had progressive SNHL. Among the 2 children with asymptomatic congenital CMV infection, 1 child presented with congenital profound hearing loss and 1 had progressive hearing loss. All the patients underwent implantation with Advanced Bionic devices, all of which were fitted with digital sequential strategies (3 were fitted with continuous interleaved sampling and 3 with HiRes 90K). The mean age at surgery was 4.6 years, with a range of 2–10 years. The mean age of follow-up was 10 years with a range of 7–15 years. In regard to the results of the speech perception analysis, we noticed that patients affected by congenital profound hearing loss showed lower scores compared to patients with progressive hearing loss.

All the patients demonstrated the detection of speech sound. However, the recognition and comprehension results were adequate only for patient number 5 who developed profound hearing loss at the age of 10. Concerning auditory perceptive performance, it is evident that the patients tended mostly to advance to the 5th category and recognize the words that were presented to them with the exception of patient number 1 who received the implant later. Concerning language development, it is important to note that only 2 of the 6 patients developed a functional language with the use of phrases and word sequences based on morphological and syntactic rules. The others demonstrated the development of a preverbal or transitional language with only the use of single words (Table 2). Nonverbal IQ was within the normal values for 4 patients and slightly delayed in 2 patients.

In Figure 1 the chronological age of the patients and the corresponding age of language development are re-
ported. It is shown that language delay, expressed as a percentage of CA/LA, tended to increase with time, as though the children reached a plateau during their language development.

**Discussion**

There are no studies in the literature regarding the outcome of cochlear implantation in CMV-infected children based on long-term follow-up. Published data have shown that cochlear implantation in children with deafness resulting from CMV infection varies widely and only early hearing rehabilitation can provide good speech perception in these patients. In this study, most of the children with CMV-related deafness were found to show an improvement in language perception and production after cochlear implantation. Asymptomatic CMV children showed better results in comparison to those who were symptomatic, and patient number 5 with progressive hearing loss showed better results compared to those with congenital hearing loss. Nevertheless, progress in these children was slower compared to their non-CMV peers [Ciorba et al., 2009; Matsui et al., 2012]. This outcome might be related to central nervous system involvement since no association between duration of deafness, age at implant and speech outcomes was evident in our study group. Yoshida et al. [2009] claim that CMV children without cognitive delay manage to bridge the gap with their non-CMV peers over a 1-year follow-up. However, in our long-term study we showed how both symptomatic and asymptomatic CMV implantees still underperformed both in speech perception and language development compared to their non-CMV peers.

In our study group, 4 of the 6 children were symptomatic at birth. Nevertheless, all children – including the asymptomatic ones – showed language delay even after 10 years of using a cochlear implant, which varied consistently despite the fact that nonverbal IQ was within normal values for most of them. The prevalence of mental retardation in CMV patients varies from 40 to 54.5%, according to the study protocol and the composition of the study group [Matsui et al., 2012; Yamazaki et al., 2012]. In our study group we found slight mental retardation in 2 of the 6 patients (33.3%). This difference might be related to a different method used to assess mental retardation and a different follow-up between study groups. As far as opting for the Raven test is concerned, although some aspects might be addressed in less depth, this is a well-standardized test where nonverbal intelligence can be assessed independently from coexisting motor delay and above all from verbal linguistic competence. In our experience with deaf children, this test is the easiest to administer, even in the presence of cultural differences. Furthermore, our long-term follow-up (10 years) has enabled us to observe a positive trend in the evolution of the cognitive behavior in these children, favored by the integrative use of the hearing function.

Concerning the correlation between cognitive skills and language delay, in this study group the language delay seems to be more severe than that referred to in the literature for slight mental retardation, measured in non-CMV deaf children [Meinzen-Derr et al., 2011]. This can probably be partly related to the complex neurological situation of CMV patients, and it is indeed presented in various degrees in CMV children with progressive hearing loss and IQ scores within the normal values.

In these children, language delay tends to increase over time, reaching a plateau in language skills, widening the gap between chronological and language age even in children implanted at an earlier age. Furthermore, it is also important to remember that CMV children have poor attention control and are considered more susceptible to later complications such as learning difficulties. Hence, careful observation is required on clinical course after cochlear implantation [Yoshida et al., 2009].

All these children integrated their communication handicap via the use of the visual-gestural channel at different levels, from gesture to codified Italian signs.

Present data and evidence from the literature are valuable to set realistic expectations of parents when children with CMV and profound hearing loss are considered for cochlear implantation. Multidisciplinary rehabilitation programs following cochlear implantation are essential, and a mode of language rehabilitation should be set based on the child’s characteristics as early as possible.

**References**


