Cartilage Shield Tympanoplasty in Children

Review of 268 Consecutive Cases

Jérôme Nevoux, MD; Gilles Roger, MD; Pierre Chauvin, MD, PhD; Françoise Denoyelle, MD, PhD; Erea Noel Garabédian, MD

Objective: To assess the efficacy of partial ossicular chain reconstruction using autologous cartilage.

Design: Prospective study (April 1, 1997, through January 1, 2008).

Setting: Tertiary academic children’s hospital.

Patients: Two hundred forty-eight children (268 ears) underwent partial ossicular chain reconstruction using a shaped block of tragal cartilage interposed between the head of the stapes and an underlay tympanic membrane reconstruction along with tragal cartilage and its perichondrium.

Main Outcome Measures: Anatomical and audiological results were evaluated according to the American Academy of Otolaryngology–Head and Neck Surgery guidelines. χ² Tests and multivariate analysis were used for statistical evaluation.

Results: Mean age at surgery was 10.9 years. Single-stage surgery was performed in 124 ears (46.3%) (62.9% for cholesteatomas and 32.3% for retraction pockets). Second-look patients (53.7%) included 93.8% of staged surgery. Audiometric results were available for 222 ears at 1 year and for 78 ears at 5 years. Closure of the average air-bone gap (ABG) to within 20 dB was achieved in 62.2% of ears at 1 year. The mean (SD) preoperative and 1-year postoperative ABGs were 25 (11.8) dB and 18.9 (10.3) dB, respectively. Anatomical results were satisfactory in 87.3%. No cases of extrusion, resorption, or displacement of the cartilage were encountered. No statistically significant difference was found between audiometric results at 1 and 5 years. Multivariate analysis showed a significant negative correlation between preoperative and postoperative ABGs and between postoperative otitis media with effusion and postoperative ABG (P < .05).

Conclusions: Cartilage ossiculoplasty is a reliable technique for partial ossicular replacement. Long-term hearing outcomes remain stable and satisfactory. Preoperative ABG and postoperative otitis media are the predictive factors of the hearing outcome.


IN SURGERY FOR DANGEROUS chronic otitis media (retraction pockets or cholesteatomas), several types of graft material are available to reconstruct the tympanic membrane, including temporalis fascia, fat, and cartilage. In children, a large cartilage plate is the most suitable.1 If the stapes superstructure is usable, ossiculoplasty material may be autologous (ossicle or cartilage)2-4 or synthetic (titanium or ceramic prostheses).5 Positioning 1 or more cartilage plates between the stapes head and the tympanic reinforcement cartilage is a simple and effective way of restoring an ossicular chain in primary or revision surgery. The few studies6-8 in the literature basically concern adult cohorts. The present prospective study analyzed the results of using cartilage for partial ossicular chain reconstruction in children and their evolution over time and sought to identify functional prognosis factors.

METHODS

PATIENTS

Between April 1, 1997, and January 1, 2008, 268 ears were operated on in 248 children with a mean (SD) age at surgery of 10.90 (3.54) years (age range, 3.33-18.91 years). All the patients underwent type III cartilaginous tympanoplasty using the Wullstein classification with the stapes heightened by 1 or 2 small cartilage plates under a large cartilage reinforcement plate. Audiograms were obtained at 1, 2, and 5 years’ follow-up and again as long as the ossiculoplasty remained unchanged. Secondary surgery concerned 93.8% of staged surgery. Nine of 144 revision procedures were due to...
failure: 2 perforations, 3 retraction pockets, and 4 recurrent cholesteatomas. The cholesteatomas and retraction pockets were localized on the edge of the cartilage for all but 1 ear, which had cartilage failure (Table 1).

**TECHNIQUE**

All the ears were operated on using a canal wall-up technique. The cartilaginous tympanic membrane repair used a large cartilage island graft of at least half the area of the tympanic membrane, with its perichondrium cover on the superficial side (Figure). We tried to preserve a part of the native tympanic membrane free of reinforcement to permit postoperative otoscopic control and tube insertion if necessary. Beneath, 1 or 2 cartilage plates were positioned, depending on the depth of the middle ear cleft. A single such plate was used in 176 cases, and 2 plates were used in 19 cases; both sides were without perichondrium.

The ossiculoplasty was performed in the primary surgery if no secondary surgery was scheduled or in patients with at least 30 dB of opposite hearing loss. In the secondary surgery, it was either staged or performed in revision for recurrence or residual lesion. The series cases were thus grouped according to whether ossiculoplasty was performed in the primary or secondary surgery.

**AUDIOMETRIC CRITERIA**

The audiometric criteria used were those of the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS). Auditory results were considered good for a postoperative, pure-tone, average air-bone gap (PTA-ABG) of 20 dB or less and excellent for a PTA-ABG of 10 dB or less. Air conduction gain rather than closure of the ABG (preoperative ABG–postoperative ABG) was used: this is the difference between preoperative and postoperative PTA for air conduction.

**ANATOMICAL CRITERIA**

The AAO-HNS guidelines considered the status of the ossicular chain, in particular of the stapes and malleus and, notably, the presence or absence of its handle. Ossicle lesions were classified into 2 groups following the Austin-Kartush classification. Ears with intact stapes and a malleus handle (including 19 cases in which the stapes superstructure showed partial lysis but remained usable for ossiculoplasty and for which no significant differences were found in a dedicated study) comprised group 1. All the cases showing lysis or absence of the malleus handle, leaving only the stapes intact at the end of surgery, comprised group 2. The incus in all the cases either showed spontaneous lysis or was removed during surgery. Likewise, lysis of the stapes superstructure, allowing only total ossicular reconstruction, was an exclusion criterion.

The AAO-HNS also recommends noting the degree of or potential aeration of the tympanic cavity. To estimate this, we con

**PREDICTIVE FACTORS**

The preoperative criteria studied were indication for surgery (primary cases: perforation, retraction pocket, or cholesteatoma; secondary cases: staged or revision for perforation, retraction pocket, residual lesion, or recurrence), type of surgery (primary or secondary), mean preoperative PTA-ABG, number of tube insertions, and opposite otoscopy. Perioperative criteria were state of the middle ear mucosa (inflammatory or not) and reconstruction of the scutum and ossicular chain status (Austin-Kartush classification): malleus handle present and intact stapes, malleus handle absent and intact stapes. Finally, the 2 postoperative criteria were postoperative OME and tube insertion.

Auditory result stability (mean postoperative PTA-ABG) was analyzed as a function of time: mean postoperative PTA-ABG was compared at each audiometric session (1, 2, 5, and 5 years) and then were backward selected to keep factors associated with success.

**STATISTICAL ANALYSIS**

Anatomical results in function of type of surgery were compared using a $\chi^2$ test ($P < .05$). Distributions of quantitative data have been compared using an analysis of variance test or a non-parametric Kruskal-Wallis test when the distributions were not normal. Associations between potential predictive factors and auditory results have been studied using the $\chi^2$ test (or the Fisher exact test when numbers were small). All the factors associated with a $P < .20$ were introduced in a logistic regression model and then were backward selected to keep factors associated with a $P = .05$.
Audiometric Results Over Time

At 1 year, 222 ears had audiograms (82.8% of 268 operated-on ears); at 2 years, 149 (55.6%); and at 5 years, 78 (29.1%). Good results were found for 62.2% of the 222 1-year audiograms, 57.0% of the 149 2-year audiograms, and 68.0% of the 78 5-year audiograms. Overall results were excellent in 21.6% of cases at 1 year (48 of 222), 20.8% at 2 years (31 of 149), and 28.2% at 5 years (22 of 78). Ninety-one of the 138 good 1-year results had a 2-year audiogram, with good results in 79.1% (72 of 91). Forty-one of the 72 good 2-year results had a 5-year audiogram, with good results in 82.9% (34 of 41). Mean (SD) air conduction gain at 1 year was 5.76 (13.59) dB (range, −30 to 49.25 dB). Mean (SD) PTA-ABG improved from 25 (11.8) dB preoperatively to 18.9 (10.3) dB at 1 year. In 35.1% of ears (78 of 222) with 1-year audiograms, surgery impaired hearing by a mean (SD) of 8.3 (6.4) dB.

The number of cartilage plates positioned between the stapes head and the subtympanic membrane cartilage had no effect on functional results. Good postoperative results did not differ between primary and secondary surgery (P = .07). We did not revise any cases for poor hearing. Concerning the revision cases due to failure, we did not notice any difference in auditory results. The mean PTA-ABG at 1 year was 19.75 dB.

**Anatomical Results**

In 14 years, there were no cases of cartilage plate extrusion or resorption; resorption was checked on follow-up otoscopy in all the cases and on computed tomographic control in some and was confirmed peroperatively in the case of secondary surgery. Secondary surgery found significantly fewer cases of middle ear inflammation, although the rate of malleus handle lysis was unchanged. Anatomical results were improved in the secondary surgery, independently of functional result (Table 4).

**Stability of Results Over Time**

Pairwise comparison of good results (overall cohort mean PTA-ABG) at each audiometric check showed no significant difference. Ears were classified according to successive audiometric results (good, bad, or missing), and evolution of hearing was studied for each ear. In 199 of the 222 ears (89.6%) with postoperative audiograms, the 1-year result, whether good or bad, was stable on subsequent controls. The other 23 cases (10.4%) showed varied patterns of evolution, but the small numbers involved precluded significant findings in one way or another in terms of improvement or degradation. It can, thus, be said that 1-year results proved stable at 5 years in most ears.

**Factors Predictive of Good Auditory Results**

Factors predictive of mean postoperative PTA-ABG were sought at 1-year follow-up. Univariate analysis of the

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**Table 2. Auditory Results and Number of Audiograms for Primary and Secondary Surgery**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Primary Surgery (n=124)</th>
<th>Secondary Surgery (n=144)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audiogram at 1 y</td>
<td>109 (87.9)</td>
<td>113 (78.5)</td>
<td>.03</td>
</tr>
<tr>
<td>Good results at 1 y</td>
<td>69 (63.3)</td>
<td>69 (61.1)</td>
<td>.21</td>
</tr>
<tr>
<td>Excellent results at 1 y</td>
<td>24 (22.0)</td>
<td>24 (21.2)</td>
<td>.57</td>
</tr>
</tbody>
</table>

**Table 3. Comparison of Auditory Results Between Primary and Secondary Surgery**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Primary Surgery</th>
<th>Secondary Surgery</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative PTA-ABG, mean (SD), dB</td>
<td>23.1 (12.3)</td>
<td>26.7 (11.2)</td>
<td>.01</td>
</tr>
<tr>
<td>Postoperative PTA-ABG at 1 y, mean (SD), dB</td>
<td>18.8 (10.3)</td>
<td>18.8 (10.4)</td>
<td>.97</td>
</tr>
<tr>
<td>ACG at 1 y, mean (SD), dB</td>
<td>3.3 (13.6)</td>
<td>8.4 (13.5)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Negative postoperative ACG at 1 y, No. (%)</td>
<td>46 (42.2)</td>
<td>32 (28.3)</td>
<td>.007</td>
</tr>
<tr>
<td>PTA-ABG degradation at 1 y, mean (SD), dB</td>
<td>7.1 (8.2)</td>
<td>3.0 (6.6)</td>
<td>.04</td>
</tr>
</tbody>
</table>

**Table 4. Comparison of Anatomical Results Between Primary and Secondary Surgery**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Primary Surgery (n=124 Ears)</th>
<th>Secondary Surgery (n=144 Ears)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfactory tympanic membrane, %</td>
<td>82.3</td>
<td>91.7</td>
<td>.03</td>
</tr>
<tr>
<td>Inflammatory mucosa, %</td>
<td>58.1</td>
<td>20.8</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Intact malleus handle and stapes vs lysis, %</td>
<td>90.3</td>
<td>84.7</td>
<td>.17</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACG, air conduction gain; PTA-ABG, pure-tone average air-bone gap.

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**RESULTS**

Audiometric Results Over Time

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For the 9 patients who underwent surgery because of failure, the mean PTA-ABG is 19.75. A nonparametric statistical analysis did not show any difference between these 9 cases and the 135 staged surgical procedures. There were 7 cases of severely decreased bone conduction or opera-

tive hearing damage (postoperative bone conduction at 4 kHz – preoperative bone conduction at 4 kHz > 20 dB), but the differences in average bone conduction threshold and mean bone conduction at 4 kHz between preoperative and postoperative at 1 year were not significant. No dead ears were encountered postoperatively. Table 2 and Table 3 present results with comparisons between primary and secondary surgery.

The number of cartilage plates positioned between the stapes head and the subtympanic membrane cartilage had no effect on functional results. Good postoperative results did not differ between primary and secondary surgery (P = .07). We did not revise any cases for poor hearing. Concerning the revision cases due to failure, we did not notice any difference in auditory results. The mean PTA-ABG at 1 year was 19.75 dB.

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Factors Predictive of Good Auditory Results

Factors predictive of mean postoperative PTA-ABG were sought at 1-year follow-up. Univariate analysis of the
1-year results identified 2 prognostic factors: mean preoperative PTA-ABG (in 10-dB steps) (P = .002) and postoperative OME or tube insertion (P = .03). No other preoperative, perioperative, or postoperative variables were predictive of auditory results.

In multivariate analysis, these 2 factors were still correlated with mean postoperative PTA-ABG at 1 year. A 10-dB increase in mean preoperative PTA-ABG reduced the probability of a good postoperative result 1.62-fold (odds ratio, 0.62; 95% confidence interval, 0.49-0.78). Independently of this, postoperative OME or tube insertion reduced the probability of a good postoperative result 3.06-fold (odds ratio, 0.33; 95% confidence interval, 0.12-0.87). Results could be extrapolated beyond that date because functional results did not significantly vary with time. Multivariate analysis results at 2- and 5-year follow-up confirmed results at 1 year, especially for the prognostic value of a preoperative PTA-ABG increase.

The present series was one of the largest to study partial ossicular reconstruction using double cartilage plates in children. Two hundred forty-eight children (268 ears) were treated and followed up in the same department. Despite the long study period, and partly thanks to lack of turnover in the surgical team, indications and techniques did not change over time. The predictive factors for the auditory results of ossiculoplasty most frequently found in the literature are basically preoperative or perioperative ossicular chain and middle ear mucosa status.

In the present study, mean preoperative PTA-ABG was predictive of mean postoperative PTA-ABG. The PTA-ABG can be seen as a combination of several items reflecting middle ear status (mucosal and ossicular chain status, etc) and, thus, sums up certain classic predictive factors. Postoperative middle ear inflammation (OME or tube insertion) was the other predictor of postoperative PTA-ABG, indicating residual pathologic abnormalities in the middle ear. Preoperative OME or tube insertion or a perioperative finding of inflammation, on the other hand, was not predictive of the auditory result. This is the first study, to our knowledge, to focus on the role of postoperative OME and to underline its major effect on functional results, which is expected to be higher in children than in adults. An isolated impact of malleus handle presence was not found, possibly because in cartilage reinforcement of the tympanic membrane it is a much less important element in tympanic membrane stabilization.

In the 2006 study by De Vos et al with 85% adult subjects, predictive factors on univariate analysis were age, malleus handle presence, and mucosal status; type of prosthesis, initial middle ear pathologic abnormality, surgery (primary vs secondary), presence of stapes superstructure, and otorrhea were not predictive. Their multivariate analysis confirmed the effect of the malleus handle and of mucosal status; the authors did not specify whether the latter was preoperative, perioperative, or postoperative, but it was doubtless preoperative mucosal status. The stability of results was shown at the cohort level. However, pairwise comparison at each audiometric control session, using mean overall cohort PTA-ABG, masks evolution over time for a given ear. The study of the evolution in auditory results for each ear confirmed stability at an individual level.

Literature reports generally involved 1-year follow-up; a few were longer, notably those of Dornhoffer at 2.7 years, Yung at 5 years, and Malafronte at 7 years. The present study provided medium- and long-term follow-up with a large number of audiograms. Studies of partial ossicular chain reconstruction using double cartilage plates are few and mainly old; there were no purely pediatric series.

Cartilage plate techniques varied from author to author, differing in whether the perichondrium was removed from 1 or both sides of the fragments and in the size of the grafts, especially in contact with the tympanic membrane, which was in all cases small compared with the present technique.

The present study used a large cartilage plate (shield tympanoplasty) to prevent recurrence given the initial pathologic abnormality in the cohort (cholesteatomas or retraction pockets). No previous study, to our knowledge, has assessed hearing in shield tympanoplasty associating ossiculoplasty in children.

The present technique consists of superimposing a cartilage fragment or fragments freed of perichondrium on both sides. The number of fragments depends on the depth of the cavity and does not affect the functional result. The advantage lies in the absence of perichondrium between the fragments, providing a more rigid assembly and, thus, less energy loss in sound transmission. In most cases, just 1 supplementary fragment is enough. The large reinforcement plate reduces cavity depth, especially between the stapes head and the tympanic membrane. There is serious risk of postoperative tympanic membrane retraction in children, further reducing cavity depth, and the choice of ossiculoplasty material needs to consider this. The advantage of cartilage is that it allows the ossiculoplasty to be tailored exactly to cavity depth. Adaptation using the incus is more difficult, with a risk of ossicular fracture during drilling. Partial prostheses, finally, have an irreducible minimum size and cannot be so easily used.

The literature analysis revealed much missing information, hindering rigorous comparison (Table 5). Cohort patient data were never complete. In 3 studies, patient age was not reported despite the fact that severity varies with age. Apart from the present study, only the study by Harvey and Lin included a substantial number of children.

It is difficult to find data about initial pathologic abnormalities, even when they are available. It seems to have been much less severe in the series of Malafronte than in that of Harvey and Lin, or the present study. Audiometric follow-up also varied. The earliest studies (Altenau and Sheehy and Luetje and Denninghoff) gave results at 6 months, which is far too early to assess stability over time. Finally, none of the studies reported mean preoperative ABG and gain or mean postoperative air conduction. Neither was the hearing threshold calculation explained except by Malafronte et al and Harvey and Lin, who followed AAO-HNS guidelines.

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**COMMENT**

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In brief, there is lack of homogeneity in the methods for reporting results of type III tympanoplasty using a cartilage plate. The study by Harvey and Lin\textsuperscript{17} was the most complete and the closest to the present findings, with, however, much shorter follow-up and a smaller cohort.

The incus, sculpted and positioned between the malleus handle and the stapes head, can be used to restore the ossicular chain. The few, and old, child studies\textsuperscript{18,19} reported results scarcely different than those for cartilage plates. The percentage of good results was nearly 60% to 65%. The mean postoperative PTA-ABG was approximately 20 dB. Inner ear impact was slight, as in the present study (approximately 3%). Extrusion rates using the incus, on the other hand, which varied from 3% to 17%, were greater than with cartilage plates, where they would seem to be zero.\textsuperscript{20,21} At 15-year follow-up, Hall and Rytzner\textsuperscript{22} found no incus resorption.

There are few studies of partial ossicular replacement prostheses (PORPs)\textsuperscript{23-25} in children, and their data are not always usable. Cohorts usually combined children and adults without distinction. Thus, the House Clinic study\textsuperscript{24} included a large number of children (25%) in a large cohort. Results reported by Daniels et al\textsuperscript{25} in 1998, in a purely pediatric cohort, were similar to those found in adults. In 1986, Silverstein et al\textsuperscript{21} reported auditory results after incus transposition comparable with those obtained with PORPs. This was not confirmed by Rondini-Gilli et al\textsuperscript{20} in 2001, who reported better results with the porous polyethylene (Plasti-pore; Plastipore, Fountain Valley, California) prosthesis than using the incus.\textsuperscript{20} Conversely, the Portmann Institute team\textsuperscript{26} reported better results with incus transposition. The auditory results in the present study were better than those reported for PORPs. In 2001, Iurato et al\textsuperscript{27} demonstrated stable hearing results over time with PORPs, as with cartilage plates in the present series. Extrusion rates when prostheses are not covered by a cartilage plate are close to those found with incus transposition at 4% to 21%.\textsuperscript{27} Extrusion with cartilage reinforcements is, in contrast, rare (1.9%).\textsuperscript{28}

The choice of ossiculoplasty material should be founded on precise criteria. Assembly time needs to be taken into account because it varies considerably between techniques; it seems to be longest in the case of the incus, which needs sculpting—shorter with cartilage and shortest with prostheses. Cartilage is readily available in large quantities and with varying thicknesses (tragus and concha) to allow precise adaptation to individual middle ear anatomy. Moreover, it is cost free, durable, and free of risk of absorption or extrusion, all combining to make it a material of choice. Furthermore, using the incus in the case of cholesteatomas entails a risk of residual lesion due to residual ossicle epidermal fragments.

In conclusion, the present study demonstrated the efficacy of type III tympanoplasty using cartilage plates to reconstruct the ossicular chain in children. Functional results were good (postoperative PTA-ABG ≤20 dB) in approximately 60% of cases, matching results reported with other materials, and there is a trend toward stability over time at more than 5 years of follow-up. Anatomical results were very satisfactory in 80% of cases.

Predictive factors for results were mean preoperative PTA-ABG and postoperative inflammation (postoperative OME or tube insertion). The prime factor determining the result of ossiculoplasty is the causal pathologic abnormality and not which material is used.

After comparison with literature reports for other materials, this study validates (1) cartilage ossiculoplasty associated with shield tympanoplasty in children, (2) the use of cartilage for ossiculoplasty where the stapes is present, and (3) stability of results in the medium and long term.

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Table 5. Comparison of Cartilage Partial Ossiculoplasty Results in the Literature

<table>
<thead>
<tr>
<th>Variable</th>
<th>Altenau and Sheehy,\textsuperscript{3} 1978</th>
<th>Luefje and Denninghoff,\textsuperscript{16} 1987</th>
<th>Harvey and Lin,\textsuperscript{17} 1999</th>
<th>Malafronte et al,\textsuperscript{4} 2008</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>NR</td>
<td>NR</td>
<td>36.1 (6-85 y)</td>
<td>NR</td>
<td>11 (3-19 y)</td>
</tr>
<tr>
<td>No. of operated ears</td>
<td>88</td>
<td>35</td>
<td>20</td>
<td>25</td>
<td>32</td>
</tr>
<tr>
<td>Secondary surgery, %</td>
<td>14</td>
<td>97</td>
<td>26</td>
<td>48</td>
<td>46.8</td>
</tr>
<tr>
<td>Initial middle ear abnormality, %</td>
<td>60 Staged</td>
<td>100 Staged</td>
<td>74 Revision</td>
<td>100 Staged</td>
<td>100 Staged</td>
</tr>
<tr>
<td>Extrusion</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Resorption</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Preoperative PTA-ABG, mean (SD), dB</td>
<td>1 Case</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>24.9 (10.96)</td>
</tr>
<tr>
<td>Postoperative PTA-ABG ≤20 dB</td>
<td>75% at 6 mo</td>
<td>80% at 6 mo</td>
<td>50% at 19.5 mo</td>
<td>80% at 1 y</td>
<td>84.3% at 1 y</td>
</tr>
<tr>
<td>ACG, mean (SD), dB</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Sensorineural hearing loss</td>
<td>1 Case</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>4.7 (13.08)</td>
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</tbody>
</table>
Financial Disclosure: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Nevoux, Roger, Chauvin, Denoyelle, and Garabédian. Acquisition of data: Nevoux. Analysis and interpretation of data: Nevoux, Roger, and Chauvin. Drafting of the manuscript: Nevoux and Roger. Critical revision of the manuscript for important intellectual content: Nevoux, Roger, Chauvin, Denoyelle, and Garabédian. Statistical analysis: Roger and Chauvin. Administrative, technical, and material support: Nevoux and Roger. Study supervision: Nevoux, Roger, Denoyelle, and Garabédian.

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