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Management of hearing loss in Apert syndrome

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Abstract

Background: Apert syndrome is one of the craniosynostosis syndromes, with a birth prevalence estimated to be between 9.9 and 15.5/million, and accounts for 4.5 per cent of craniosynostoses. Although conductive hearing loss is common in Apert syndrome there are contradicting reports regarding the cause of this hearing loss. There is also no detailed information available on the management of hearing loss in Apert syndrome.

Materials and methods: A retrospective analysis of case notes of Apert syndrome patients seen between 1970 and 2003 at Great Ormond Street Children's Hospital, London, was undertaken.

Results: Seventy case notes were obtained. The incidence of congenital hearing impairment was between 3 and 6 per cent. Almost all patients had otitis media with effusion (glue ear), which tended to persist into adult life. More than 56 per cent of cases developed permanent conductive hearing loss by 10–20 years. Repeated grommet insertion was common; even though 35 per cent had trouble with ear discharge and persistent conductive hearing loss. Statistically, grommets made no difference to the risk of developing permanent hearing loss.

Conclusion: This study, of the largest number of Apert syndrome cases assembled to date, showed that early optimization of hearing with possible hearing aids needs to be considered. Repeated grommet insertion does not help in optimizing hearing, especially if ear discharge complicates the picture.

Key words: Apert Syndrome; Hearing Loss; Otitis Media with Effusion; Hearing Aids

Introduction

Apert syndrome is an easily identifiable, syndromic type of craniosynostosis. It has a birth prevalence estimated at between 9.9 and 15.5/million and accounts for about 4.5 per cent of all cases of craniosynostosis.[1,2] It is characterized by craniosynostosis, midfacial malformations and syndactyly of the hands and feet, which minimally involves digits two, three and four.[3] The description and discovery of this syndrome is credited to French paediatrician Eugene Apert, although Wheaton and others had previously reported it and Apert acknowledged this in his case report.[4] As the characteristic feature of the syndrome is acrocephaly and syndactyly it is referred to as acrocephalosyndactyly.

Apert syndrome patients have a variety of clinical signs, with the craniofacial features being the most prominent. Bifid uvula and cleft of the soft palate is seen in 76 per cent, with the soft palate longer and the hard palate shorter than normal.[5,6] A variety of otologic and auditory findings have been described in Apert syndrome (Table I).[7] Hearing loss is common but tends to be overlooked because of preoccupation with other problems.

A variety of explanations have been postulated to explain the hearing loss in Apert syndrome. Initially, it was felt that hearing loss could be due to compression of the VIIIth nerve within the internal acoustic meatus.[8] It is now believed that abnormal functioning of the eustachian tube is the most important cause for the development of otitis media with effusion (glue ear) and its persistence into adulthood.[9] Hearing loss is therefore a sequelae of persistent otitis media with effusion. Eustachian tube dysfunction is possibly secondary to malformation

TABLE I

OTOLOGIC AND AUDITORY MANIFESTATIONS OF APERT SYNDROME

Low-set ears
Microtia, macrotia
Abnormal surface configuration of pinna
Posteriorly rotated external ears
Eustachian tube dysfunction
Constricted external canal
Conductive hearing loss
Chronic middle-ear effusion or recurrent otitis media
Ossicular fixation (stapes footplate fixation)
Wide cochlear aqueduct

Reproduced with permission from Phillips and Miyamoto, 1986.[7]

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and/or compression of the nasopharyngeal space, which accompanies the multiple craniofacial abnormalities of Apert syndrome.[10] Another possible explanation for hearing loss is the developmental theory. Apert syndrome patients show branchial arch abnormalities (mandibular and maxillary) and since the ossicular chain and footplate originate from the branchial arches and otic capsule it is possible these patients could also have ossicular chain abnormalities.[7]

A summary of the literature on hearing loss in Apert syndrome shows a confusing and contradictory picture. This is probably due to the fact that Apert syndrome is an uncommon condition, with small numbers of patients being seen at any one centre. Isolated case reports or reports studying only a few patients seem to contain a high proportion of Apert patients with ossicular chain fixation resulting in congenital conductive hearing loss.[7,8] However the two studies involving relatively large samples, by McGill (35 patients) and Gould and Caldarelli (17 patients), seem to indicate that otitis media with effusion is more common than congenital ossicular abnormality.[9,10] These two studies also seem to show contradicting results with regard to the incidence of congenital hearing loss. Thus in Apert syndrome the incidence of congenital hearing loss, and the main cause of hearing loss in general, remains to be clarified.

The aim of this study was to determine the best way to manage hearing loss in Apert syndrome patients, based on the type of hearing loss seen in Apert syndrome.

Materials and methods

Great Ormond Street Children's Hospital, London, is a specialized centre for craniofacial syndromes, including craniosynostoses. Apert syndrome patients from the whole of the UK have been monitored and treated here and have had audiological assessments carried out. A retrospective analysis of these patients' case notes with regard to audiological findings was undertaken.

A list of patients with Apert syndrome was prepared from the speech and language therapy database and from the database available in the craniofacial unit. Eighty-two Apert syndrome patients were identified from these databases in the time period between January 1970 and September 2003. This list was used to identify the relevant case notes or, in the case of older patients, their microfilmed notes. All the available case notes and microfilms were studied for information regarding the patient's audiological status. Those patients who did not have any audiological assessment were excluded from the study. An analysis was undertaken to determine the type, degree and nature of hearing loss and also to test for any association between the audiological findings and cleft palate. For this purpose patients were classified into three groups with regard to presence and severity of cleft palate. The groups were: no cleft palate; presence of bifid uvula/submucous cleft palate; and obvious cleft palate. Serial audiometric results were also analysed to determine if there was fluctuation in the hearing thresholds and whether normal hearing has been proved on at least one occasion. If normal hearing thresholds were obtained on at least one occasion for each ear it was taken as an indication of absence of congenital hearing impairment. Radiological reports (computed tomography (CT) and magnetic resonance imaging (MRI)) were also analysed with regard to whether any inner-ear malformations or nerve compression were seen in patients exhibiting sensorineural hearing loss.

In order to determine whether Apert syndrome patients suffered from the long-term effects of otitis media with effusion, resulting in an acquired hearing loss, only children above the age of 10 years were included. All the patients in the study group were therefore between the ages of 10 and 20 years. The degree of acquired hearing loss was classified into two categories based on British Society of Audiology (BSA) guidelines.[11] If the average hearing loss in the frequencies of 250, 500, 1000, 2000 and 4000 Hz was between 20 and 40 dBHL then it was classified as a mild hearing loss. However if the average hearing loss was between 41 and 70 dBHL it was classified as moderate hearing loss, and hearing loss between 71 and 95 dBHL was classified as severe hearing loss.

Information was also gathered on how the hearing loss was managed and, if grommets were inserted, the number inserted and whether there were any complications from this. Statistical tests using the Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows were also carried out to analyse whether repeated grommet insertions contributed to permanent hearing loss in Apert syndrome patients.

Results

Of the 82 Apert syndrome patients identified, 74 case notes were obtained. The case notes of most of the older children, born prior to 1982, were available in the form of microfilm. The eight case notes that could not be identified were for children born prior to 1985 and were all in microfilm format. Four case notes/microfilms from the 74 that were obtained had to be excluded as they did not appear to have any audiological findings. Seventy case notes/microfilms were therefore taken up for study (comprising the largest series analysing audiological findings to date).

The oldest patient included in the study was born in 1971 and the youngest in 2003. Most patients were followed up at the hospital until the age of about 16 years (as Great Ormond Street Hospital is a children's hospital), after which further follow up was arranged locally. Therefore no information was generally available beyond the age of 16 years.

Out of the 70 patients included in this study, 41 were male (59 per cent) and 29 were female (41 per cent). The majority of the patients (46 cases, 66 per cent) did not have cleft palate. Five had either a bifid uvula and/or a submucous cleft palate. Nineteen had

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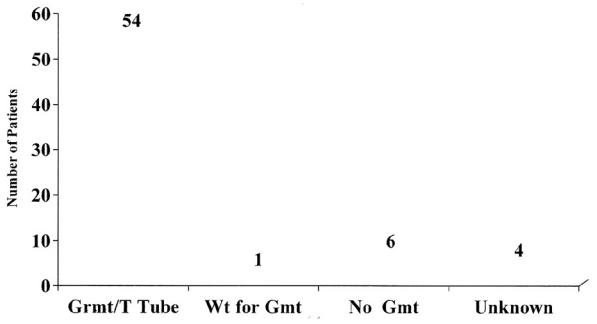

FIG. 1
Management of middle-ear effusion with grommets.

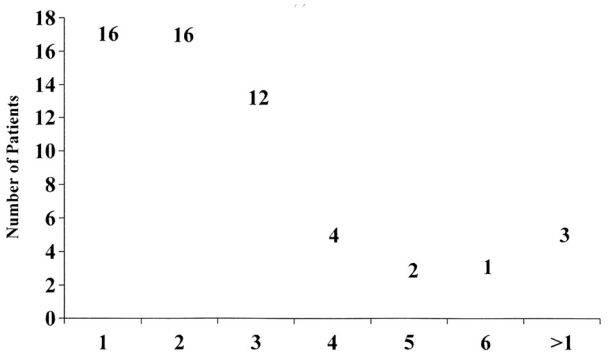

FIG. 2
Number of grommets/T-tubes inserted for each patient. Total number of patients = 54.

cleft of the palate, which appeared to mainly involve the soft palate.

Serial audiological analysis showed that 57 out of the 70 Apert patients had no congenital hearing impairment. Two of them had persistent conductive hearing impairment even after the insertion of ventilation tubes and two had sensorineural hearing loss. These two cases with sensorineural hearing loss also had predisposing causes for hearing loss, such as very low birth weight, asphyxia and early neonatal problems. In nine others it was not possible to determine whether there was any congenital hearing impairment as they were either lost to follow up after the insertion of ventilation tubes or had persistent glue ear and did not have ventilation tubes inserted. The two patients with sensorineural hearing loss were also found to have normal radiological reports (CT/MRI) with no evidence of inner-ear malformations.

In this study of 70 patients, 65 had at least one documented occurrence of otitis media with effusion. Only three patients had no documented otitis media with effusion. Information was not available on two other patients.

Of the 65 patients with otitis media with effusion, 54 were managed by insertion of ventilation tubes. This was either in the form of a grommet or T-tube. Only six did not have any history or documentation of ventilation tube insertion. While carrying out the study one patient was on the waiting list for grommet insertion and in another four patients documentation was insufficient to determine whether or not they had been managed by insertion of ventilation tubes (Figure 1). Only 10 patients received hearing aids at some point during the first 16 years of life. This included two patients with otitis media with effusion whose parents preferred treatment with hearing aids rather than grommets.

The number of grommets/T-tubes used to manage otitis media with effusion in these 54 patients was analysed, showing that several patients received multiple grommet insertions (Figure 2). The majority of the Apert syndrome patients (32 patients) received only one or two sets of grommets/T-tubes. Twelve received three sets of grommets, four received four sets, two received five sets and one received six sets of grommets. It was also noted that 19 of the 54 patients (35 per cent) had significant problems with ear discharge following grommet insertion, which certainly compromised their hearing.

Of the 34 children above the age of 10 years selected to study the development of acquired hearing loss, 19 developed a conductive hearing loss while only eight did not develop any long-standing hearing loss. It was not possible to confirm whether there was any residual hearing loss in the other seven patients. Eleven patients (58 per cent) had a mild acquired hearing loss while eight (42 per cent) had a moderate degree of acquired hearing loss. None had a severe or profound hearing loss (i.e. >70 dBHL).

The commonest cause of acquired hearing loss was atelectasis/retraction, which was present in eight of the 19 patients with acquired hearing loss. The other main causes were persistent middle-ear effusion (found in five patients) and perforation of the eardrum (found in four patients). Two of the patients had an *in situ* T-tube but persistent hearing loss; as they had been previously documented as having normal hearing, this would indicate acquired middle-ear pathology.

An analysis of variance (ANOVA) was carried out using SPSS 11.0 for Windows to study the relationship between the number of grommet insertions and hearing loss. There was no statistically significant difference ($p > 0.1$) seen between the groups of patients with no hearing loss, mild hearing loss and moderate hearing loss, with regard to the number of grommet insertions. However, as can be seen from Figure 3, as the number of grommet insertions increased so too did the likelihood of developing a hearing loss.

An ANOVA was also carried out using SPSS 11.0 for Windows to study the relationship between grommet insertions, type of cleft palate and the degree of hearing loss. Statistically, no significant difference ($p > 0.1$) was seen, which indicated that cleft palate did not influence the development of acquired conductive hearing loss. There was also no statistically significant difference ($p > 0.1$) seen with regard to whether Apert syndrome patients with cleft palate received a higher number of grommets.

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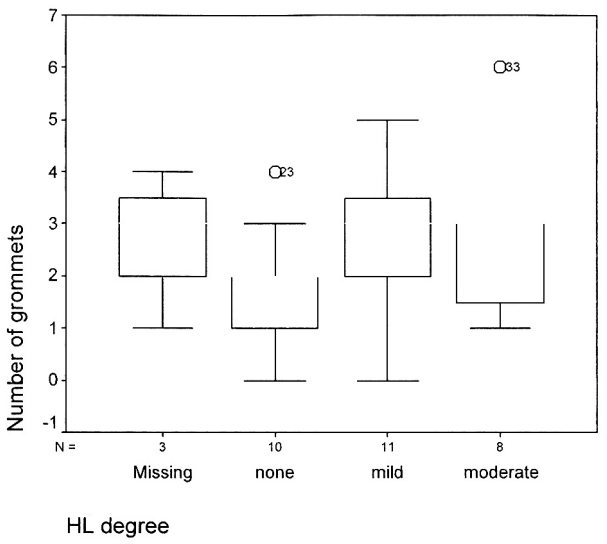

FIG. 3
Box plot of relationship between presence or absence of hearing loss, its degree and number of grommet insertions.

Discussion

The incidence of congenital hearing loss in Apert syndrome has never been established in earlier studies. In our study only two Apert syndrome patients had congenital conductive hearing loss while two others had sensorineural hearing loss which was severe in nature (i.e. >70 dBHL). The two patients with sensorineural hearing loss also had other risk factors for developing a hearing loss. As the radiology of the inner ears was also normal in these two patients the hearing loss is more likely to be due to those other risk factors rather than to Apert syndrome. Sensorineural hearing loss has not been reported in the literature with regard to Apert syndrome except for isolated reports of mixed hearing loss.[12] The two patients with congenital conductive hearing loss had persistence of hearing loss even after insertion of ventilation tubes. It is therefore likely that the aetiology of the conductive hearing loss was ossicular in origin, but as these patients did not have any surgical exploration and their tympanograms were normal it is not possible to say this with certainty. The degree of congenital conductive hearing loss was moderate in both patients and affected all the frequencies. Thus, it can be concluded that the incidence of congenital hearing loss in Apert syndrome is between 3 and 6 per cent.

Otitis media with effusion is the most important cause of hearing loss in Apert syndrome. Gould and Calderelli reported that otitis media with effusion and its sequelae was the cause of hearing loss in Apert syndrome, while McGill reported that all Apert syndrome patients had otitis media with effusion but in the same paper stated that 37 per cent had middle-ear anomalies.[9,10] In this study 65 children (93 per cent) out of the 70 had otitis media with effusion. In two Apert syndrome patients there was no information in the notes to ascertain whether they suffered from otitis media with effusion or not. Three children had no evidence of any effusion but all these three children were below the age of four years and it is quite likely that they would suffer from otitis media with effusion in the future. It can therefore be said that almost all children with Apert syndrome suffer from otitis media with effusion and that this is the most important cause of hearing loss in early childhood in Apert syndrome patients. Presence or absence of cleft palate does not alter the risk of development of otitis media with effusion.

Ventilation tubes were evidently the preferred management option for otitis media with effusion in Apert syndrome. Of the 65 patients with middle-ear effusion, 55 (85 per cent) were managed by insertion of ventilation tubes (this includes the single patient who was on a waiting list for grommet insertion). Ventilation tubes were not inserted in only six patients (9 per cent). These included the two children whose parents had opted for hearing aids instead of ventilation tubes and the children who had effusion which did not appear to persist. Although most of the children managed with ventilation tubes had only one or two sets inserted there were a few in the study group who received up to six sets of grommets. Another interesting effect of grommet insertion was that nearly 35 per cent of patients were troubled with ear discharge following the procedure. This ear discharge was noted to persist until the grommets were extruded or removed. This is significant as these children's hearing would have remained compromised despite the grommets. This has important implications for the management of hearing loss in Apert syndrome patients as use of hearing aids in the presence of aural discharge is more difficult and complicated. As the middle-ear effusion tended to persist into adulthood it would also explain why some of these patients had multiple sets of grommets inserted.

Hearing loss in Apert syndrome during early childhood is therefore due to persistent otitis media with effusion in most cases. In order to study whether persistent middle-ear effusion resulted in sequelea such as adhesions, perforations and ossicular erosion, only children with Apert syndrome over the age of 10 years were studied. There were thus 34 patients, of whom 19 (56 per cent) had acquired conductive hearing loss. Only eight (24 per cent) showed no residual effects of middle-ear effusion and grommet insertion. Seven patients (20 per cent) were lost to follow up so it was not possible to determine whether acquired hearing loss had developed. Even taking the most optimistic view that none of that group developed any acquired hearing loss, the fact would still remain that at least 56 per cent of the children with Apert syndrome would develop an acquired conductive hearing loss by the age of 10–20 years.

The question arises whether it is the repeated grommet insertion which is responsible for the Apert syndrome patients developing an acquired hearing loss, rather than the middle-ear effusion. Although a statistically significant difference was

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not seen there was a tendency towards development of hearing loss with grommets. This would indicate that it is the persistent middle-ear effusion, secondary to Apert syndrome facial anomalies, that is the most likely cause for the development of acquired conductive hearing loss. It would also mean that repeated grommet insertion does not prevent the development of acquired hearing loss and furthermore could accentuate the tendency to develop an acquired hearing loss. The two children whose parents opted for hearing aids instead of grommets were aged less than five years at the time of writing; it will be interesting to know if these children develop an acquired hearing loss. The commonest causes of acquired conductive hearing loss in this study were atelectasis/retraction of the eardrum and perforations.

The use of hearing aids in Apert syndrome patients appeared to be minimal. This may be due to the different type of therapeutic practice prevalent during the early part of the study period. Only 10 patients had hearing aids at some point during the first 16 years of life and this included the two children whose parents opted for hearing aids instead of ventilation tubes. This, combined with a high incidence of ear discharge following grommet insertions, raises the question of whether these patients' hearing was optimized to the best possible extent. As there is at least a 56 per cent chance of developing conductive hearing loss between the ages of 10 and 20 years, the use of hearing aids as an alternative needs to be considered. It was also noticed that most of the children who were issued with hearing aids were treated during the 1990s and later, in contrast to those seen during the 1970s and 1980s. It would therefore appear that lately there has been a shift towards early issue of hearing aids. This may well be due to better developed audiology services.

This study also raises the question as to which is the best way to manage hearing loss due to middle-ear effusion in patients with Apert syndrome. As some children benefited from grommet insertions and had no problems with ear discharge following grommets, it would be worth considering grommets on at least one and maybe even two occasions. If after grommet insertion there is trouble with ear discharge or if the grommets tends to extrude easily with quick re-accumulation of fluid in the middle ear, then hearing aids need to be considered as an option. Early optimization of hearing levels in these patients is important as doubts have also been raised recently as to whether Apert syndrome patients do indeed have a high degree of learning difficulties or whether this effect is due to a combination of poorly optimized hearing and poor manual dexterity.[13]

This study is not without its limitations. In addition to the limitations of a retrospective study it reflects a view from a tertiary centre. Clinical practice would also have been quite variable during the study period, spanning three decades, and this needs to be kept in mind when interpreting the results.

Conclusion

The main cause of hearing loss in Apert syndrome is otitis media with effusion and it tends to be persistent into adulthood. Most Apert syndrome patients with otitis media with effusion have been managed by multiple grommet insertions. Thirty-five per cent of Apert syndrome patients with grommets are likely to have significant ear discharge. At least 56 per cent develop acquired conductive hearing loss by the age of 10–20 years as a consequence of otitis media with effusion; this hearing loss is generally mild to moderate in degree. Early optimization of hearing with hearing aids needs to be considered, as repeated grommet insertion does not prevent the development of acquired conductive hearing loss.

- **Apert syndrome is a syndromic type of craniosynostosis**
- **Hearing loss in Apert syndrome is characterized by otitis media with effusion persisting into adult life**
- **Early optimization of hearing with hearing aids is recommended, rather than surgical middle-ear ventilation**

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