

Main Article

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Cholesteatoma in children and adults: are there really any differences?

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Abstract

Background. Cholesteatoma is widely considered to be more aggressive in children than adults, yet few studies have directly compared the operative findings and surgical outcomes between these two groups. This study aimed to assess differences between childhood and adult cholesteatoma.

Methods. The operative caseload of a single consultant surgeon was reviewed between January 2006 and May 2017 using the online Common Otology Audit database. Extracted data were categorised according to patient age (children, aged below 16 years, and adults, aged 16 years or over) and compared.

Results. This study included data from 71 operations on children and 281 operations on adults, performed for cholesteatoma. Childhood cholesteatoma demonstrated significantly more extension (into the sinus tympani, mastoid antrum and mastoid air cells) and ossicular erosion (of the malleus, incus and stapes superstructure) compared to adults. No significant differences were seen in revision rates, post-operative complications or hearing gain.

Conclusion. Childhood cholesteatoma was more extensive and destructive compared to adults, representing a more aggressive disease in this cohort.

Introduction

Cholesteatoma is characterised by a benign a mass of keratinising squamous epithelium, peri-matrix and keratin, usually found in the tympanic cavity, mastoid or subepithelial connective tissue, which demonstrates destructive and inflammatory properties.^{1,2} The exact pathogenic molecular mechanisms behind the formation and propagation of cholesteatoma remain unclear. Studies examining the immunohistochemistry of the matrix and perimatrix have considerably improved the knowledge of cholesteatoma pathogenesis, although its aetiology has not been established.³ Left untreated, cholesteatoma is associated with significant morbidity through complications including recurrent ear infections, hearing loss, facial nerve paralysis and destruction of the semi-circular canals.^{4,5} Mortality is rare, but is usually related to intracranial infection.⁴

Cholesteatoma can be classified into congenital and acquired forms. Congenital cholesteatoma is mainly seen in children and presents with an intact tympanic membrane, while the acquired form is usually seen in adults and is typically associated with a defect in the tympanic membrane.⁶ Cholesteatoma is uncommon, with a reported incidence of 3–15 cases per 100 000 children^{7,8} and 9.2–12.6 cases per 100 000 adults.^{7,9} Geographical studies have identified higher rates of cholesteatoma within less developed countries¹⁰ and in areas of greater socioeconomic deprivation.¹¹ Familial tendencies have been reported, with cholesteatoma affecting several family members.^{12,13}

There have been a few studies investigating the differences between childhood and adult cholesteatoma. These have focused on various aspects of the disease, including symptom presentation, intra-operative cholesteatoma or granulation levels, hearing levels, and molecular differences. Edelstein *et al.* found increased neuro-otological symptoms in adults compared to children.¹⁴ Regarding complications, while some authors have reported fewer complications in children,¹⁵ others have not found any statistical differences between the two groups.¹⁶ Mallet *et al.* reported more aggressive cholesteatoma in children based on increased levels of the monoclonal antibody MIB1, which is thought to be responsible for epithelial hyperproliferation and hence more aggressive disease.¹⁷ This was further confirmed by Dornelles *et al.*, who reported an increased number of inflammatory markers, including cluster of differentiation 31, and matrix metalloproteinases 2 and 9, in childhood cholesteatoma compared to adult disease.¹⁸

We reviewed our experiences of cholesteatoma surgery with the aim of answering three main questions: (1) do the intra-operative findings support the notion that more aggressive disease is present in children?; (2) do the rates of revision surgery for cholesteatoma differ between children and adults?; and (3) do differences exist between the post-operative complications seen in children and adults following cholesteatoma surgery?

Materials and methods

Data were retrospectively extracted from the Common Otology Audit,¹⁹ an online database for recording ear operations. This data represented the operative caseload of a single otology consultant and his trainees for cholesteatoma between January 2006 and May 2017. All operations took place at the Norfolk and Norwich or the James Paget University Hospitals. Patient electronic health records and clinic letters were also reviewed, and these provided a valuable source of information.

Based on age, data were classified into two groups. Group 1 ($n = 58$) comprised of children aged below 16 years, while group 2 ($n = 260$) consisted of adults aged 16 years or more. Patients' demographic details were gathered, and data for specific parameters including cholesteatoma site, operative findings, revision surgery rates, audiometric results and post-operative follow-up duration were extracted.

Statistical analysis was performed on the two groups to assess for significant differences between the children and adults with cholesteatoma. This was conducted using GraphPad Prism software, version 6.00 for Windows (GraphPad Software, La Jolla, California, USA). Where appropriate, quantitative data were compared using Fisher's exact test or the student's unpaired *t*-test. A *p*-value of less than 0.05 was considered statistically significant.

Results

Demographics

In total, 352 operations were performed for cholesteatoma in 318 patients; 186 operations were for left-sided disease, while 166 were for right-sided disease. Bilateral cholesteatoma was seen in 13 patients (4.1 per cent).

In children, 71 operations were performed on 58 patients. The average age at operation was 11.0 years and the average length of recorded follow up during the study period was 16 months (range, 3–84 months). Left-sided disease was seen in 36 cases, compared to 35 on the right. Bilateral disease was seen in three children (5.2 per cent), all of whom underwent bilateral surgery. One child had revision surgery performed on the same ear twice for cholesteatoma.

In the adult group, 281 operations were carried out on 260 patients. The average age at operation was 46.0 years, while the average length of recorded follow up during the study period was 12 months (range, 3–84 months). Left-sided disease was seen in 150 cases, compared to 131 for right-sided disease. Bilateral cholesteatoma was seen in 10 adults (3.8 per cent), of which 9 (3.5 per cent) underwent bilateral surgery.

Extension of disease

Regarding the site of cholesteatoma, children had significantly higher rates of cholesteatoma behind the tympanic membrane ($p = 0.007$), and in the sinus tympani ($p = 0.001$), the mastoid antrum ($p = 0.014$) and mastoid air cells ($p = 0.003$). There was no statistical difference in cholesteatoma affecting the attic between both groups ($p = 0.559$) (Table I).

Ossicular erosion

The level of ossicular erosion was significantly higher in children compared to adults in the malleus ($p = 0.041$),

TABLE I OPERATIVE SITE OF CHOLESTEATOMA IN CHILDREN AND ADULTS

Cholesteatoma site	Children (<i>n</i> (%))	Adults (<i>n</i> (%))	<i>p</i> -value*
Under tympanic membrane	20 (28.2)	38 (13.5)	0.007
Sinus tympani	26 (36.6)	41 (14.6)	0.001
Mastoid antrum	31 (43.7)	78 (27.8)	0.014
Mastoid air cells	25 (35.2)	51 (18.1)	0.003
Attic	53 (74.6)	199 (70.8)	0.559

*Fisher's exact test

TABLE II INCIDENCE OF OSSICULAR EROSION DUE TO CHOLESTEATOMA IN CHILDREN AND ADULTS

Ossicle eroded	Children (<i>n</i> (%))	Adults (<i>n</i> (%))	<i>p</i> -value*
Malleus	17 (23.9)	37 (13.2)	0.041
Incus	50 (70.4)	159 (56.6)	0.042
Stapes superstructure	25 (35.2)	48 (17.1)	0.0016

*Fisher's exact test

incus ($p = 0.042$) and stapes superstructure ($p = 0.0016$). Cholesteatoma affecting the stapes footplate was not seen in either group (Table II).

Revision surgery

Within this study, all revision mastoid surgical procedures were performed for cholesteatoma. In adults, 225 procedures (80.1 per cent) were primary operations and 56 procedures (19.9 per cent) were revision operations. In 9 adults, both primary and revision surgical procedures were undertaken by the authors' team during the study period, with an average interval of 565.8 days between operations. In the remaining 47 adults, primary surgery was either performed outside the study period, by a different surgeon or at a different institution. The rate of revision surgery was comparable in children: 55 (77 per cent) were primary operations and 16 (23 per cent) were revision cases. Similarly, 9 children had both primary and revision surgery during the study period, with an average interval of 647.1 days between operations. There was no significant difference in the rate of revision surgery for cholesteatoma between children and adults (Fisher's exact test, $p = 0.624$).

Complications

In children, four complications (5.6 per cent) were seen in four different patients, which including facial nerve palsy (1.4 per cent), hypertrophic scarring (1.4 per cent), post-auricular fistula (1.4 per cent) and wound abscess (1.4 per cent) (Table III).

In adults, a total of 23 complications (8.2 per cent) occurred in 18 different patients. These included cerebrospinal fluid leak (0.4 per cent), dead ear (2.1 per cent), facial palsy (1.1 per cent), taste disturbance (0.4 per cent), vertigo (3.9 per cent) and wound infection (0.4 per cent) (Table IV).

No statistical difference was found between children and adults in terms of the rate of complications following cholesteatoma surgery (Fisher's exact test, $p = 0.620$).

TABLE III INCIDENCE AND OUTCOME OF COMPLICATIONS ASSOCIATED WITH CHOLESTEATOMA SURGERY IN CHILDREN

Complication	Cases (n)	Outcome
Facial palsy	1	Fully resolved
Hypertrophic scar	1	Scar present
Post-auricular fistula	1	Persistent fistula ongoing
Wound abscess	1	Drained surgically
Total	4	

TABLE IV INCIDENCE AND OUTCOME OF COMPLICATIONS ASSOCIATED WITH CHOLESTEATOMA SURGERY IN ADULTS

Complication	Cases (n)	Outcome
CSF leak	1	Repaired intra-operatively
Dead ear	6	Predictable at operation (n = 4); not predictable at operation (n = 2)
Facial palsy	3	Fully resolved (n = 2); residual weakness (n = 1)
Taste disturbance	1	Fully resolved
Vertigo	11	Symptoms fully resolved (n = 7); symptoms present (n = 4)
Wound infection	1	Treated with antibiotics
Total	23	

CSF = cerebrospinal fluid

Audiometric results

A variety of reconstructive techniques were used individualised according to the operative findings. Post-operative pure tone audiometry demonstrated an average post-operative hearing gain of 0.62 dB in adults (range, -92.5 to 42.5 dB) and 1.67 dB in children (range, -45 to 36.9 dB); the difference was not statistically significant (unpaired *t*-test, *p* = 0.8341).

Discussion

We found significant differences between childhood cholesteatoma and adult disease, the former of which was more extensive and destructive at the time of surgery. These results support the findings of other studies that have suggested cholesteatoma in children to be more aggressive.^{16,20,21} Although many studies have reviewed children and adult populations with cholesteatoma, a limited number of studies have directly compared these two groups.

An Egyptian study by Elrashidi²² divided 81 patients with cholesteatoma into age-based groups: children, adolescents and adults. The overall extent of disease was significantly higher in children; however, the rate of ossicular erosion between the groups was not significantly different. Sade and colleagues presented the findings of two separate studies that investigated untreated cholesteatoma disease in 63 children and 148 adults.^{23,24} Their results found similar levels of malleus and stapes erosion, while adult cholesteatoma was associated with higher rates of incus erosion.

Although the differences between children and adult cholesteatoma are not fully understood, studies have demonstrated differences in the histological constituents of cholesteatoma affecting these groups. Elevated levels of the monoclonal antibody MIB1,

cluster of differentiation 31, and matrix metalloproteinases 2 and 9 have all been isolated in childhood cholesteatoma cases compared to adult disease.^{17,18} The pro-inflammatory or hyper-proliferative effects of these mediators may explain why cholesteatoma in children demonstrates a greater propensity to spread and cause ossicular erosion. Other theories that may account for these differences are raised within an article by Preciado, which reviewed the biology of cholesteatoma in children. These theories include increased levels of circulating growth hormone among children, a higher incidence of childhood infectious otitis media and differences in aeration of the mastoid cavity.²⁵

- Cholesteatoma is considered more aggressive in children than in adults, but few studies have directly compared these two groups
- In this study, cholesteatoma was more extensive and destructive in children compared to adults
- Rates of revision surgery and post-operative complications were similar between children and adults
- These findings support a more aggressive disease process in children

Interestingly, despite childhood cholesteatoma behaving more aggressively, no significant differences were found in revision rates and complications associated with surgery. Around one in five patients underwent revision mastoid surgery for cholesteatoma within children and adults. Adult cholesteatoma surgery was associated with more significant complications, including six incidences of post-operative dead ear. Importantly, four cases of dead ear were predictable at the time of surgery given the extent of disease found. Further analysis of adult patients who developed significant post-operative complications extends beyond the scope of this study; however, these findings may represent a subset of more aggressive adult cholesteatoma or be a consequence of delayed surgical intervention.

Conclusion

This study found significantly higher rates of ossicular erosion and extension of cholesteatoma within the middle ear in children, suggestive of a more aggressive disease process. However, this did not translate into differences in cholesteatoma recurrence, complications or post-operative hearing gain. The study findings suggest that a more pragmatic approach to managing childhood cholesteatoma is needed, in which surgery is offered early to avoid further progression of disease. It may also inform decision making regarding the need for reconstructive surgery, although this should be assessed on a case-by-case basis.

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Competing interests. None declared.

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