

ORIGINAL ARTICLE

Predictive Factors of Recurrence in Pediatric Cholesteatoma Surgery

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OBJECTIVE: This study aims to analyze factors influencing the recurrence of acquired pediatric cholesteatoma that has impact on operative plan decision.

PATIENTS AND METHODS: Retrospective review of 62 children (68 ears) with acquired middle ear cholesteatoma who underwent surgery from 1995 to 2006. Age distribution at initial operation ranged from 3 to 16 years with mean age of 11.2 years. Surgical removal of acquired cholesteatoma using ICWT (22%) or CWD (78%) was performed. The median observation period was 30 months (~~+SD?~~).

RESULTS: The recurrence rate was estimated at 22%. In univariate analysis, higher rate of recurrence was correlated with age, cholesteatoma extent, mucosa state, ossicular chain state and operative technique. When multivariate analysis was performed to verify the independent correlation of the above four variables, only ossicular chain state, mucosa state, and cholesteatoma extent remained associated with recurrence.

CONCLUSION: Pediatric acquired cholesteatoma is known to be an aggressive disease associated with a higher rate of recurrence than adults. Thus, this disease should be managed as early as possible for better anatomic and hearing results. To define the best therapeutic strategy, it is necessary to consider many factors such as total eradication of the disease, preservation of auditory function, and predictable follow up period. This study shows that ossicular chain state, mucosa state and cholesteatoma extent were found to be independently associated with recurrence. For the final decision, all factors should be properly considered and analyzed.

Pediatric cholesteatoma is a potentially dangerous disease with many challenges concerning diagnosis and treatment. There are no universally accepted opinions about the course, consequences and outcome of surgery for cholesteatoma in pediatric patients. While a number of surgeons prefer the open technique, others opt for the closed one.

The main goal of pediatric cholesteatoma surgery is to eradicate the disease, with a possible improvement or preservation of the hearing. Unfortunately, recurrent cholesteatoma, developing from retraction and adhesion of the tympanic membrane, is still frequent; it occurs in 5% to 23% of patients. This recurrence leads to more frequent re-operations and even conversion to open techniques.

The aim of this work is to study the rate and predictive factors of pediatric acquired cholesteatoma recurrence after first surgery.

PATIENTS AND METHODS

Patients:

Our study concerned 62 children with middle ear acquired cholesteatoma. All patients above 16 years, as well as those with congenital cholesteatoma (normal tympanic membrane) and whose follow up period was under 3 months were excluded. Bilaterally involvement was seen in 6 cases. In total, 68 ears were operated primarily during 1995 to 2006 in our department. The mean follow-up period was 30 months(\pm), with a range of 3 months up to 7 years. The mean age was 11.2 years(\pm) (range 3-16 years). There were 37 (59.7%) boys and 25 (40.3%) girls; with a 1.48 gender ratio. Initially, 4.4% of patients presented polyp in the middle ear, 29.4% had their perforations in pars tensa and 22% in pars flaccida. 44.1% had fixed retraction pockets and the bottom of the pocket could not be visualized in 63.3% of cases. 8 patients (12.9%) had consulted in emergency with mastoiditis.

Further complementary investigations revealed intracranial complications: temporal abscess (one

case); temporal abscess and lateral sinus thrombosis (one case); meningitis and lateral sinus thrombosis (one case); cerebellar abscess (one case). Because being uncooperative in younger age, audiometry could be undertaken in 59 ears (86.7%).

Hearing loss varied from 26 dB to 72 dB with a mean threshold of 41dB(\pm).

53 ears (78%) underwent canal wall down tympanoplasty or radical mastoidectomy (CWDT), 15 ears (22%) underwent intact canal wall tympanoplasty (ICWT).

The postoperative hearing gain was measured, for 59 ears, by calculating the difference between the air conduction thresholds before and after the operation. Hearing improvement (defined as 5 dB gain) was found in 45.8% of the operated ears. The hearing was not changed in 30.5% and decreased in the remaining 23.7% of the cases. Hearing improvement was significant in ICWT (53.3% in ICWT versus 35.8% in CWDT).

Our study was focused on patients with only recurrent cholesteatoma. Residual cholesteatoma cases were not included. Recurrent cholesteatoma was defined as the presence of a new developed cholesteatoma that appeared following the complete surgical removal of a previous one.

Variables analyzed:

The rate of cholesteatoma recurrence was analyzed according to age at the first operation, symptom duration, presence of complicated cholesteatoma, hearing loss before surgery, cholesteatoma aspect (cyst / diffuent) and extent (extension to the mastoid or not), state of tympanic cavity mucosa (intact / pathologic), state of ossicular chain (intact / eroded) and stapes (intact / eroded), and finally the operative surgery technique chosen.

Statistical analyzes:

The data were analyzed using the SPSS software. For univariate analysis, qualitative and quantitative variables were studied using respectively the χ^2 statistics and the t-Student test. Statistical significance was determined at the $p < 0.05$ level. Variables with

significant difference at univariate analysis were analyzed by using multivariate logistic regression analysis to determine independent variables.

RESULTS

Recurrence was observed in 15 ears (22%) of the 68 primarily operated cases. The mean duration for recurrence was 27 months(± 18.3 SD) and ranged from 6 months to 5 years. Most of the cases with recurrence were detected later than 3-year.

Among the patients operated with ICWT, 14 ears (93 %) underwent second look surgery. Recurrent cholesteatoma was detected in 8 cases (53.3% of ICWT operated ears).

The period of time following the primary surgery for the recurrent cholesteatoma that were detected during follow-up are represented in table 1. Oto-microscopic examination showed re-retraction in 5 cases. Re-perforation was evident in one case. 50 % of cases with recurrent cholesteatoma were converted to CWDT. (26.6% of ICWT surgeries).

Among the cases operated with CWDT recurrent cholesteatoma was evident in 7 cases (13.2%). There were no recurrent cholesteatoma detected later than 5 years among the patients operated with CWDT (Table1).

In univariate analysis, the extent of cholesteatoma, the state of mucosa, the state of ossicular chain and the operative technique were shown to be significantly associated with cholesteatoma recurrence (Table 2).

But when multivariate analysis was performed to verify the independent correlation of the above four variables, only ossicular chain state, mucosa's state, and cholesteatoma extent remained associated with recurrence. Cholesteatoma rate of recurrence was multiplied by 23 when these three factors were associated (Table 3).

Table 2: Predictive factors of cholesteatoma recurrence in univariate analysis.

Baseline variable	p
Age	0.41
< 7 years / \geq 7 years	
Symptoms duration	0.681
< 2 years / \geq 2 years	
Complication	0.538
Yes / No	
Hearing loss	0.339
< 40 dB / \geq 40 dB	
Cholesteatoma aspect	0.942
Cyst / Diffuent	
Cholesteatoma extent	0.031
In / Out of the Tympanic cavity	
Tympanic cavity mucosa's state	0.004
Intact / Pathologic	
Ossicular chain	0.001
Intact / Eroded	
Stapes aspect	0.453
Intact / Eroded	
Operative technique	0.001
ICWT / CDWT	

Table 1: Cholesteatoma recurrence according to detection time and surgery technique.

Detection time	Reviewed patients	Recurrent cholesteatoma	Technique	
			ICW	CWD
3 months	62	0%	0%	0%
6 months	51	4%	0%	5.5%
1 year	42	12%	14.3%	10.7%
3 years	26	23%	44.5%	11.8%
5 years	18	11%	25%	0%

Table 3: Predictive factors of cholesteatoma recurrence in multivariate analysis.

Baseline variable	OR	p
Cholesteatoma extent	2.06	0.032
In / Out of the Tympanic cavity		
Tympanic cavity mucosa's state	3.08	0.003
Intact / Pathologic		
Ossicular chain	3.7	0.001
Intact / Eroded		
Operative technique	1.7	0.061
ICWT / CWDT		

OR: odds ratio

DISCUSSION

Acquired cholesteatoma of the middle ear in child is a potentially dangerous disease. It can be associated with intracranial complications, a high rate of hearing loss, language delay and even later social handicap if not diagnosed in time. Thus, cholesteatoma should be diagnosed as early as possible, mainly to eradicate the disease and preserve hearing^[1]. Unfortunately, recurrence rate after surgery is not negligible: it is reported to occur in 5% to 23% of operated children^[2,3]. A higher recurrence rate of cholesteatoma has been reported in pediatric patients than in adults^[4,5]. Ahn et al reported 19% of recurrence among children aged under 16 years (4% among adults)^[6]. De Corso and colleagues^[7] estimated 26.6% for risk of recurrence after CWDT (6.8% among adult). Observing these results several studies were carried on trying to understand why cholesteatoma recurrence rate was higher among children under 16 and to identify delays and predictors of recurrence during the follow up period after surgery.

Children middle ear cholesteatoma is well known to have a higher proliferative activity, with a tendency to grow rapidly. Bujia and colleagues^[8] found a significantly higher proliferation of cholesteatoma keratinocytes in children than in adults. Hildmann and Sudhoff^[9], using MIB1 antibody, studied the growth

characteristics of cholesteatoma and confirmed a significantly higher proliferative rate of cholesteatoma matrix in children, if compared to adults. This high rate of proliferation, associated with scant symptoms, uneasy examination and Eustachian tube dysfunction associated with adenoid hyperplasia - usually found in children - may explain the aggressive behavior of this disease in pediatric patients and then the higher rate of recurrence compared to adults^[5]. Silvola and Palva^[10] demonstrated the aggressiveness of pediatric cholesteatoma through the higher number of extensive cholesteatomas and cases with ossicular discontinuity, compared to adults.

A review of the literature on follow up studies after acquired cholesteatoma surgery identified various predictors of recurrence. Most of recurrences were observed in younger patients aged less than 8 years^[3,7] with a mastoid involvement^[3]. Shirazi and colleagues^[11] found that extensive disease on presentation associated with ossicular chain involvement were significant predictors of patients with a high risk for recurrent disease. The cholesteatoma extension has been shown, by Stangerup and colleagues^[12], to be the main predictor of recurrence followed by age, ear discharging, ossicular chain resorption and preoperative Eustachian tube dysfunction. Vartiainen^[4] showed that recurrent cholesteatoma in children was associated with initial invasion of the posterior middle ear, presence of ossicular erosion and preoperatively discharging ears. In our current study, ossicular chain erosion was the most predictive factor of a late recurrence followed by pathologic middle ear mucosa and cholesteatoma extension to the mastoid. In other words, the more aggressive the cholesteatoma, the higher the risk of postoperative recurrence. The difficulties of evaluating the Eustachian tube function in these cases is well known.

Silvola and Palva^[10] found that recurrent cholesteatoma was independent from the cholesteatoma size, mastoid status, stapes erosion and cholesteatoma extension to the windows niches. But the presence of infection and persistent Eustachian

Table 4: Predictive factors of pediatric cholesteatoma recurrence cited in the literature.

	Ahn ⁽⁶⁾	Stangerup ⁽¹²⁾	Silvola ⁽¹⁰⁾	De Corso ⁽⁷⁾	Our study
Age	P	P	–	P	P
<7 years / ≥ 7 years					
Otorrhea	N	P	–	–	–
Symptoms duration	N	–	–	–	N
Valsalva maneuver	N	P	P	–	–
Audiometric data	N	–	–	–	N
Cholesteatoma extent	–	P	N	P	P
Mastoid involvement	P	–	N	–	P
Tympanic cavity mucosa's state	–	–	–	–	P
Ossicular chain state	N	P	–	–	P
Stapes aspect	N	–	N	–	N
Operative technique	N	–	N	N	N

P : positive association ; N: non significant association ; - : not studied.

tube function are closely related with the recurrence of cholesteatoma.. (Table 4)

Although surgical strategy was not found to be a predictor of recurrence in our study, many authors found a higher rate of recurrence after ICWT than CWDT^[3,13]. Some authors, who preferred CWDT, thought that this technique allowed not only a low incidence of recurrence but also acceptable hearing results^[7]. Others, to avoid cavity problems after open tympanoplasty, preferred closed tympanoplasty whenever possible^[13]. To minimize recurrence risk, some opted for preplanned stage operations^[3,13], and others for canal wall window tympanoplasty (CWWT)^[14].

The management of pediatric cholesteatoma requires a highly individualized approach that takes into account anatomic, clinical and social factors to determine the most successful surgical treatment paradigm. According to our study the selection of the procedures was based on the type and extension of cholesteatoma, the preoperative auditory assessment, presence of associated complications, contra-lateral ear status and the level of mastoid pneumatization. The hearing improvement should not be the main surgeon's

priority. In fact in pediatric group, surgeons usually tried to opt for closed technique with the aim to preserve a larger middle ear space and autogenous materials for ossicular chain reconstruction. They even tried to manage a primarily ossicular chain reconstruction for optimal hearing results^[15]. One stage surgery could lead to a higher rate of recurrent cholesteatoma through new retraction pockets^[3]. Thus surgical effort to preserve or to restore hearing could indirectly increase the recurrence rate.

We think that ICWT, if conditions allow to plan it preoperatively, will be the most appropriate approach in case of pediatric cholesteatoma. It allows an anatomical restoration of the ear structures; better hearing and it avoids a life-long post-operative care. However, after observing the results described above, CWDT could be the most prudent and adequate strategy for extensive cholesteatoma with a middle ear pathologic mucosa and damaged ossicular chain, especially when patients would not come for later follow up.

The average time for the recurrent cholesteatoma to be diagnosed during the postoperative period is longer

than the residual cholesteatoma detection. According to Stangerup and colleagues^[2] the detection time was 1.5 years for the residual cholesteatoma and 1.3 to 7.1 years (mean 2.5 years) for the recurrent. Arsović and colleagues^[16] reported that recurrent cholesteatoma is developed in the majority of cases during the first two years after the primary surgery. According to Pflaiderer and colleagues^[17], the mean time for recurrences to be detected was mentioned as 21.1 months. Waiting too long increased the risk that a recurrent cholesteatoma would damage the middle ear.

Compared to adults^[1,5], pediatric cholesteatoma is rarely associated to complications, despite its higher aggressiveness. In developing countries, the frequency of intracranial and extracranial complications of middle ear pediatric cholesteatoma remains significant: 45.5% in the series of Cruz and colleagues^[18] from Brazil. However, complicated cholesteatoma seldom exceeds 3% in developed countries^[19]. This difference is attributed to the disparity of the disease duration in children before presentation and treatment, rather than to the less aggressive nature.

In our study 8 children (12.9%) had consulted in emergency with mastoiditis. This relatively high percentage of complicated cholesteatoma could partly explain the high number of patients with extensive cholesteatoma as well as the importance of hearing loss that we reported. More effort should alert both general practitioners and pediatrics in order to familiarize them with such a disease in terms of diagnosis and potential risks. This would allow an early diagnosis and treatment with better functional results and a lower risk of recurrence.

CONCLUSION

Pediatric acquired cholesteatoma is known to be an aggressive disease associated with a higher rate of recurrence compared to adults. Delay in detection of cholesteatoma is often reported as a result of the lack of parent awareness, scant symptoms, and difficult

microscopic examination. The therapeutic strategy should focus on total removal of the disease and preservation of auditory function. All predictive factors of recurrence should be properly considered and analyzed in order to take the final decision. We found in the current report that the more aggressive the cholesteatoma, the higher was the risk of postoperative recurrence. Therefore the selection of the surgical approach should be selected individually. This study shows that ossicular chain state, mucosa state and cholesteatoma extent were found to be independently associated with recurrence. Even if ICWT, is the preferable approach in pediatric cholesteatoma, after observing the results above, CWDT could be the most prudent strategy for extensive cholesteatoma with a middle ear pathologic mucosa and damaged ossicular chain. Longer regular follow-up should be considered for early detection and management of recurrent disease.

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