Int. Adv. Otol. 2010; 6:(1) 201-205

ORIGINAL ARTICLE

Histopathological Evaluation of the Polyps with and without the Presence of Cholesteatoma*

Muzeyyen Yildirim Baylan, Ersar Evren Koc, Nihal Kilic, Faruk Meric

Dicle University Department of Otolaryngology, Diyarbakir, Turkey, (MB, FM)
Department of Otolaryngology, Veni Vidi Hospital, Diyarbakır, Turkey, (EK)
Canakkale Onsekizmart University, Department of Otolaryngology, Canakkale, Turkey. (NK)

Objective: To determine if there were any differences between the histopathological structures of the polyps with or without cholesteatoma

Materials and Methods: In our study, 41 patients underwent operation with complaints of chronic otitis media with polyp. The patients were divided into those who had cholesteatoma and those who did not, so that discriminatory features were identified. Chronic otitis media with polyp was associated with cholesteatoma in 21 patients. Cholesteatoma was not found in 20 patients with chronic otitis media with polyp. Specimens removed from the both of patients groups were evaluated and compared between the groups in according to histopathologic features.

Results: We observed that specimens of polyps with cholesteatoma were comprised of keratinized masses, keratinized tissue layers, and abundant immature granulation tissue, whereas, specimens of the polyps without cholesteatoma consisted of copious glandular stroma bordered by smooth epithelium ($p<0,05$).

Conclusion: Our study showed that histopathologic features of the polyps suggest the presence or absence of cholesteatoma.

Submitted : 03 September 2010 *Accepted : 03 January 2010*

Introduction

Cholesteatoma once established in the middle ear, mastoid or petrous bone, is a destructive lesion that gradually expands and leads to complications due to the destruction of adjacent structures. Erosion caused by bone resorption of the ossicular chain and otic capsule may result in hearing loss, vestibular dysfunction, facial paralysis, and intracranial complications.[1]

Cholesteatoma is a serious disorder of the middle ear cleft that is comprised a sac filled with keratin and lined by keratinizing squamous epithelium. Once the diagnosis is certain the standard treatment is surgery.[2] Extensive surgery may not be necessary in patients with chronic otitis media with isolated polyp. A more limited surgery can be adequate. However, the scope of the surgery may need to be extended if there is cholesteatoma present. Previous studies have shown that radical surgery is not necessary except in cases of chronic otitis media with polyp which contains tumor and cholesteatoma.[3-5] Recent improvements in the magnetic resonance imaging (MRI) techniques have made diagnosing cholesteatoma easier. In recent studies MRI has been found to be capable of high sensitivity and specificity in diagnosing cholesteatoma.[6,7] Prasannaraj et al.[8] showed that underlying cholesteatoma tissues were diagnosed in 11 (35%) of the 31 patients that underwent exploration for chronic otitis media with polyps. Only 5 (12%) of the patients were diagnosed preoperatively by using clinical and radiologic methods. Thus several predictive factors are necessary for detecting the underlying disease in the patients with aural polyp. The histopathology of the polyps may be important as an additional factor to other preoperative diagnostic tools such as MRI, to precisely plan the extent of the surgery. We aimed to assess whether or not the histopathologic features of the polyps suggest the presence of cholesteatoma.

Materials and Methods

Our study included 41 (25 male and 16 female) patients who underwent mastoidectomy because of polyps between the years of 2000 and 2002. Ages of the patients ranged from 3 to 63 years. The patients

Corresponding address:
Muzeyyen Yildirim Baylan
Dicle University Faculty of Medicine, Department of Otolaryngology Diyarbakir, Turkey
Phone: 90- 412-2488001/ 4543 - GSM: 90 536 798 04 97; Fax: 90- 412-2488440; E-mail: muzeyyenyldrm@hotmail.com

*This paper was presented at 8th National Otolaryngology Head and Neck Surgery Congress in Ankara, TURKEY

that were previously diagnosed with cholesteatoma or suspected malignancy were excluded from the study. The patients that underwent a second operation for cholesteatoma were also not included the study. Polyps were removed during the ear surgery. Specimens were fixed in 10% formaldehyde. The samples were paraffin embedded, cut in 4 μm-thick sections and stained with hematoxylin, eosin, and 0.5% toulidin blue, then examined by light microscope.

Polyps were divided into 3 groups and 13 histopathologic features were assessed due to: histopathologic features of polyps (epithelial tissue surrounding polyp, fibrosis, mucous glands, granulation tissue); features of inflammatory cells (lymphocytes, plasmocytes, lymphoid aggregates, multinuclear giant cells); and special findings observed in polyps (keratinization, cholesterol granuloma, cholesterol fissures, hemosiderin deposits, calcification)

Associations between the variables were evaluated using Chi-square (χ^2) test with Yates' Correction and Fischer exact test. Two-sided p values were considered statistical significant at $p<0.05$.

Results

Biopsy samples removed from 41 patients with chronic otitis were examined histopathologically. There were 25 males and 16 females. Ages of the patients ranged from 3 to 63 ages. Cholesteatomas were present in 21 of the patients.

Cholesteatoma fissures ($\chi^2=0.228$, $\chi^2=0.633$) and cholesteatoma sac ($p=0.5328$) were observed rarely and findings were not statistically significant. Although calcifications were more frequently observed with the cholesteatoma there was no statistical significance ($\chi^2=1.66$, $p=0.197$).

Hemosiderin deposits were also uncommon histopathologic features and have no statistical significance ($\chi^2=0.15$, $p=0.7002$). Even though multinuclear giant cells were observed in some cases, there was no statistical significance (p=0,387).

Keratinization was observed in the majority of the polyps with cholesteatoma and the findings were statistically significant ($\chi^2=10.587$, $p=0.0005$), (Table 1) (Figure 2).

In regard to distribution of the inflammatory cells, lymphocytes were observed in many of the cases. However, there was no statistical significance as a predictor. Even though plasmocytes were more commonly found in polyps without cholesteatoma,

Table 1. Special findings observed in polyps

	With cholesteatoma (n=21)	Without cholesteatoma (n=20)
Cholesterol fissures	1	3
Cholesteatom sac	1	0
Hemosiderin deposits	3	1
Calcification	6	1
Keratinization	26	5
Multinuclear giant cells	6	5

Table 2. Features of inflammatory cells

	With cholesteatoma (n=21)	Without cholesteatoma (n=20)
Plasmocytes	7	17
Lymphocytes	10	13
Lymphoid aggregates	1	5

Table 3. Histopathologic features of polyps

	Polyp with cholesteatoma (n=21)	Polyp without cholesteatoma (n=20)
Epithelial tissue surrounding polyp	7	15
Fibrous nucleus	2	14
Mucous glands	2	10
Granulation tissue	14	3

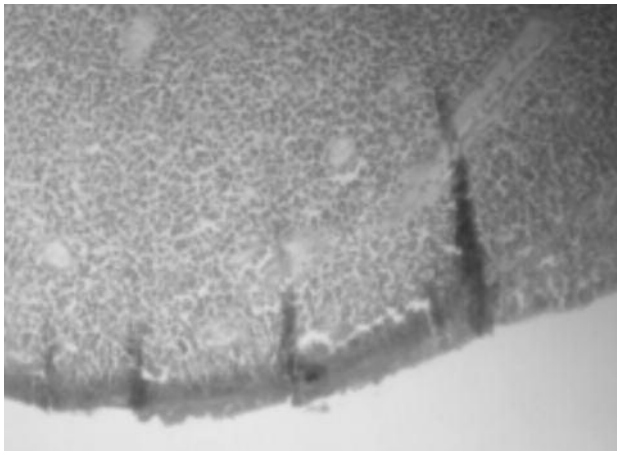

Figure 1. Aural polyp comprising granulation tissue (100×H&E)

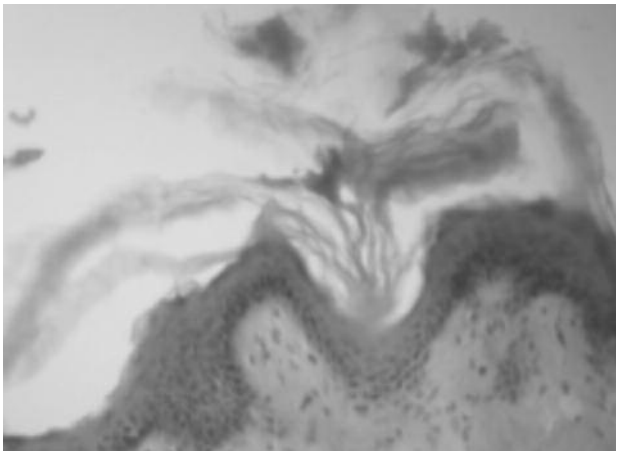

Figure 2. Aural polyp containing keratin (100×H&E)

there was no statistical significance (p=0.387).

Although lymphoid aggregates were more commonly noted in the polyps without cholesteatoma there was no statistical significance due to the limited area on the polyps. Thus it could not be helpful for discrimination (p=0.387).

We observed that polyps with fibrous tissue were usually associated with cholesteatoma and this histopathologic feature was noted as a significant predictive factor for the presence of cholesteatoma (χ^2=10.097, p=0.006), (Table 2).

We also noted that the presence of immature granulation tissue in polyps might be a predictive factor for differentiating the polyps (χ^2=10.587 p=0.0005), (Table 3) (Figure 1).

We determined that the coexistence of the granulation tissue with keratinized strata in polyps was the best indicator for cholesteatoma, whereas, cholesteatoma was not found in isolated polyps composed of fibrous nucleus covered with epithelium, abundant glandular tissue, and lymphoid aggregates.

Discussion

Cholesteatoma is a poorly understood disease. Studies have shown that locally produced cytokines such as interleukin 1α, TNF-α, vascular endothelial growth factor, and epidermal growth factor play a role in the initiation and maintenance of this chronic inflammatory process [9,10]. These cytokines are related to epithelial proliferation and keratinization of the matrix in the cholesteatoma. Due to the effect of these cytokines, we would expect the histopathological structure of the polyps with no cholesteatoma to differ from those polyps with the presence of cholesteatoma. Starting with this premise, we tried to determine if there were any differences between the histopathological structures of the polyps with the presence of cholesteatoma and those without the cholesteatoma.

Cholesteatoma is usually associated with inflammatory reactions in the middle ear cavity. The inflammatory process may mimic aural polyps, which are a soft reddish mass lined by pseudostratified columnar, cuboidal, and occasionally squamous epithelium.[11] Formation of aural polyps can be frequent and is not a clinical dilemma. However it may not be easy to assess its relation with cholesteatoma.[12] Prassannaraj et al.[8] noted 11 (35%) cholesteatoma in 31 patients that underwent mastoidectomy for aural polyp. Only 5 (45%) of those patients could be diagnosed preoperatively, whereas 6 cholesteatoma cases were overlooked clinically and radiologically. In this study, we observed external ear canals entirely filled with epithelial tissue in all cases. We also observed underlying cholesteatoma in 21 (51%) patients intraoperatively. Predictive factors are usually necessary for detecting underlying cholesteatoma in patients with chronic otitis media with polyp. Although the relationship between cholesteatoma and aural polyp is well known, there is no definitive method to predict the cholesteatoma. The clinical diagnosis of cholesteatoma can be difficult sometimes. Computerized tomography (CT) is commonly used in the evaluation of cholesteatoma; however, this imaging method plays a limited role in differentiation

of cholesteatoma.[13] Recently, improvements in MRI techniques have led to a more accurate diagnoses of cholesteatoma using delayed contrast enhanced T1-weighted imaging and diffusion-weighted imaging. Studies showed that the Diffusion-weighted (DW) magnetic resonance imaging (MRI) is useful for cholesteatoma identification and evaluation. With the use of turbo-spin echo (TSE)-DW MRI, the diagnosis of cholesteatoma can be fairly easy. In addition, the TSE-DW MRI can be very useful in preventing the patient from undergoing any unnecessary surgery and in determining the scope of surgery that is required.[6,7,14,15] DW MRI is capable of high sensitivity and specificity in diagnosing cholesteatoma.[6,7] In this study we have found that the histopathological structure of the polyps can change depending on the presence of cholesteatoma. Hence, we believe that the histopathological structure of the polyps might be used to determine the presence of cholesteatoma, along with the use of new diagnostic equipment.

Rhys Williams et al.[3] reported that the area of the perforation and origin of polyps could arouse the suspicion for presence of cholesteatoma. He also noted cholesteatoma beneath the tissue of polyp in 24.6% of 65 patients, whereas, cholesteatoma had not been found in patients with tubotympanic perforations. It is clear that the incidence of cholesteatoma is not possible in canals which are completely filled with polyp. In our studies, polyps occluded the canals entirely and the condition of the tympanic membrane could not be evaluated. Studies have also shown that symptoms, duration of the illness, and the degree of hearing loss could not be predictive for underlying disease. Gliklich et al.[16] reported that cholesteatoma were found in 29% of 35 pediatric patients with chronic otitis media with polyp and noticed that there was no correlation between conductive type of hearing loss and cholesteatoma. Contrary to our findings, they suggested that there was no significant correlation between the histopathologic appearance of polyps and cholesteatoma.

It has been shown that cytokines, fibroblast growth factor (FGF), and fibroblast growth factor receptors (FGRF) may play an initiating role in epithelial proliferation that results in cholesteatoma. Thus fibroblast growth factor and the frequency of its receptors were sought in the mucosa of the polyps. However, it has been recorded that there was no significant difference between the ratios of FGF and FGFRs.[17] Milroy et al.[18] tried to predict the presence of cholesteatoma relating to histopathologic features of polyps. They also suggested that there is a high (70% or 80%) probability of the presence of cholesteatoma in the polyps if they consisted of immature granulation tissues or keratinized mass, whereas, the possibility of the presence of cholesteatoma is very low in polyps consisting of fibrous nucleus covered with epithelium, and glandular or lymphoid tissues. Thus they concluded that surgical strategy could be planned according to the histopathologic features of polyps. Our findings are consistent with these findings. In our studies, the histopathologic features of polyps which were assessed included: type and rate of inflammatory cells, polyps covered with epithelial tissue, fibrosis, mucous glands, glandular tissue, keratinization, cholesterol granuloma, hemosiderin and calcification. There was no significant difference in the presence of histopathologic features such as type and count of inflammatory cells, cholesteatoma sac, hemosiderin, and calcification. Similar to findings previously reported, we observed that particularly the presence of granulation tissue and the depositing of keratin might indicate the underlying cholesteatoma. However in the absence of underlying cholesteatoma, epithelial and glandular tissues were widespread.

Gaafar et al.[19] designed a study to evaluate the polyps according to the histochemical and histopathologic features of polyps. It has been demonstrated that polyps with a stroma consist of increased inflammatory cell infiltration, smooth epithelial surface, and increased vascularization. It has also been suggested that increased permeability, demonstrated histochemically, comprises the baseline of polyp formation. The results of Gaafar et al.[19] did not show interactions between polyps and cholesteatoma, but demonstrated that inflammatory cells in polyp tissue have increased phagocyte and metabolic activity, whereas glandular tissues did not change.

As a result, the histopathological structure of the polyps can suggest the presence or absence of cholesteatoma. The polyps with cholesteatoma contain more granulation, keratinization, and fibrous tissue.

References

1. Olszewska E, Wagner M, Sperkelsen MB, Ebmeyer J, Dazert S, Hildmann H, et al. Ethiopathogenesis of cholesteatoma. Eur Arch Otorhinolaryngol 2004; 261:

6–24

2. Browning GG, Merchant SN, Kelly G, Swan IRC, Canter R, McKerrow WS. Chronic otitis media. In: Gleeson M ed. Scott-Brown's Otorhinolaryngology Head and Neck Surgery. 7th ed. London: Hodder Arnold, 2008; 3395-3445

3. Williams SR, Robinson PJ, Brightwell AP. Management of the inflammatory aural polyp. J Laryngol Otol 1989; 103:1040-2

4. Hussain SS. Conservative treatment in the management of inflammatory aural polyp. J Laryngol Otol 1992; 106:313-5

5. Veitch D, Brockbank M, Whittet H. Aural polyps and cholesteatoma. Clin Otolaryngol Allied Sci 1998; 13: 395-7

6. Plouin-Gaudon I, Bossard D, Fuchsmann C, Ayari Khalfallah S, Froehlich P. Diffusion-weighted MR imaging for evaluation of pediatric recurrent cholesteatomas. Int J Pediatr Otorhinolaryngol. 2010; 74:22-6

7. Jindal M, Doshi J, Srivastav M, Wilcock D, Irving R, De R. Diffusion-weighted magnetic resonance imaging in the management of cholesteatoma. Eur Arch Otorhinolaryngol. 2010; 267:181-5

8. Prasannaraj T, Narajit S.D, Narasimhan I. Aural polyps: safe or unsafe disease? Am J Otolaryngol 2003; 24:155-8

9. Sudhoff H, Bujia J, Holly A, Kim C, Fisseler-Eckhoff A. Functional characterization of middle ear mucosa residues in cholesteatoma samples. Am J Otol 1994; 15: 217-21

10. Yetiser S, Satar B, Aydin N. Expression of epidermal growth factor, tumor necrosis factor- alpha, and interleukin-1 alpha in chronic otitis media with or without cholesteatoma. Otol neurotol 2002; 23:647-52

11. Tay HL, Hussain SS. The management of aural polyp. J Laryngol Otol 1997; 111:212-4

12. Browning GG: The unsafeness of safe ears. J Laryngol Otol 1984; 98: 23-26

13. Alzoubi FQ, Odat HA, Al-Balas HA, Saeed SR. The role of preoperative CT scan in patient with chronic otitis media. Eur Arch Otorhinolaryngol 2009; 26: 807-809

14. Rajan GP, Ambett R, Wun L, Dhepnorrarat RC, Kuthubutheen J, Chow Z, et al. Preliminary outcomes of cholesteatoma screening in children using non-echo-planar diffusion-weighted magnetic resonance imaging. Int J Pediatr Otorhinolaryngol. 2010; 74:297-301

15. Vercruysse JP, De Foer B, Somers T, Casselman J, Offeciers E. Magnetic resonance imaging of cholesteatoma: an update. B-ENT. 2009; 5:233-40

16. Gliklich RE, Cunningham MJ, Favey RD. The cause of aural polyps in children. Arch Otolaryngol Head Neck Surg 1993; 119:669-71

17. Nair S, Watts S, Flood L. Fibroblast growth factor receptor expression in aural polyps: predictor of cholesteatoma. J Laryngol Otol 2004; 118: 338-342

18. Milroy CM, Slack R W, Maw AR, Bradfield JW. Aural polyps as predictors of underlying cholesteatoma. J Clin Pathol 1989; 42:460-465

19. Gaafar H, Maher A, Al-Ghazzawi E. Aural polyp: