


# Histopathological evaluation and long-term results of soft tissue preservation technique in cholesteatoma surgery

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**Abstract** The goal of cholesteatoma surgery is total removal of the cholesteatoma matrix and prevention of recurrence. Preservation of soft tissue in the attic is reported to improve post-operative middle ear aeration, and thus prevents recurrence. However, the histology and nature of the preserved tissue have rarely been reported. The aim of this study is to clarify the histology of the preserved soft tissue in cholesteatoma surgery, and to show its relationship to the clinical course. Surgical specimens were obtained from ten patients with pars flaccida-type cholesteatoma. In these patients, cholesteatoma occupied the attic and the mastoid cavity. The cholesteatoma was removed so as not to expose the bone in the attic. After the removal of the lesions, soft tissue was harvested from the floor of the attic, using cupped forceps. The specimens were fixed with 10 % formalin, and stained with hematoxylin–eosin. The

patients were followed-up for 8 years after the surgery. No patients showed post-operative inner ear disturbance or facial nerve palsy. In one patient, residual lesion was found during the revision surgery. The area of residual lesion was not explored during the first operation. Two other patients showed recurrent cholesteatoma in the pars tensa; one of these patients had accompanying otorrhea. The other seven patients showed no residual or recurrent cholesteatoma 8 years after the surgery. The histological examination showed that the harvested tissue was mainly composed of collagen fiber and fibroblasts. Ciliary epithelial cells were found in one patient. In three patients, cysts of mucosal remnants (glandular cysts), were embedded in the connective tissue. Two of these three patients experienced recurrent cholesteatoma, while the other seven patients were without recurrence at follow-up. Preservation of soft tissue behind the cholesteatoma matrix is a safe technique if the surgical field is fully visible. In most cases, the preserved tissue was fibrous connective tissue and lacked the characteristics of mucosa. The glandular cysts in the preserved soft tissue seem to be related to the recurrence of cholesteatoma.

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## Introduction

The aim of cholesteatoma surgery is to remove the cholesteatoma matrix totally, and to preserve or partially restore hearing. After the total removal of the cholesteatoma, however, a percentage of patients experience recurrence. One factor affecting recurrence is the ventilatory function of the middle ear. Middle ear aeration is obtained

by two mechanisms. One is direct ventilation via the Eustachian tube. The other is the gas-exchange through the middle ear mucosa [1]. The middle ear space is lined with mucosa, and the mucosa performs a gas-exchange function. To achieve aeration of the space after the surgery, therefore, preservation of mucosa is very important. Tanabe and his colleagues reported that the preservation of mucosa in the attic is highly related to good post-operative middle ear aeration [1]. However, the attic is usually occupied by the matrix in patients with cholesteatoma, and the preserved tissue may have lost the mucociliary function of normal mucosa. In addition, the cholesteatoma matrix has to be carefully separated from the underlying soft tissue to preserve the soft tissue. The potential risk of this technique is residual lesion. In this study, we examined the histopathology of the soft tissue in the attic, preserved during the removal of the cholesteatoma, and related the histology to the cholesteatoma recurrence rate 8 years after the surgery.

## Material and methods

Between November 2007 and May 2008, 32 adult patients underwent tympanoplasty for cholesteatoma at Kyoto University Hospital. Among them, patients with inner ear fistula, a pars tensa lesion, or a history of radical operation were excluded. The patients underwent the removal of keratin debris and were prescribed topical antibiotics to control infection; patients with persistent infection were also excluded. In the end, ten patients were included in the study: four males and six females. The range in age at the time of the operation was 21 to 78 years (average 52.8 years). All the subjects had pars flaccida-type cholesteatoma. They gave informed written consent to participation in the study. In all ten cases, cholesteatoma occupied the attic and the mastoid cavity. All underwent tympanoplasty with canal wall up or canal wall reconstruction mastoidectomy. After the mastoidectomy, the cholesteatoma was removed en bloc. We developed a cleavage plane between the cholesteatoma matrix and the underlying soft tissue. By carefully following this plane, the cholesteatoma matrix was totally removed without exposing cortex of the bone in the floor of the attic. After the removal of the cholesteatoma, the remaining soft tissue was harvested from the bed of the cholesteatoma in the attic, using cupped forceps. The specimens were fixed with 10 % formalin and stained with hematoxylin–eosin. A planned two-staged surgery was conducted 1 year after the operation in seven cases with advanced lesion, while one-stage surgery was adopted in three cases. All patients were followed-up for 8 years, to check for residual and recurrent disease, through regular otoscopic examination

and regular CT scan imaging 1, 3, 5, and 7 years after the operation.

This study was approved by the Ethics Committee of Kyoto University Hospital (Protocol No. E569).

## Results

In all patients, it was possible to preserve soft tissue behind the matrix of cholesteatoma in the attic. The post-operative course was uneventful, with no patient experiencing any serious post-operative complication, including facial nerve palsy or inner ear disturbance. During the 8-year follow-up, two patients showed the retraction of the pars tensa. One of them had otorrhea. In this patient, the retraction formed cholesteatoma again, 1 year after the initial operation. In the other patient, the retraction was dry and clean. Nevertheless, this patient also developed cholesteatoma 4 years after the original operation. In another patient, residual lesion was found during the revision surgery. The residual lesion was situated between the anterior crus of the stapes and the cochleariform process, where cholesteatoma invasion was not noted during the first operation. The other seven patients showed no residual or recurrent cholesteatoma 8 years after the surgery.

The histopathological findings are summarized in Table 1. The histological examination showed that the harvested tissue was mainly composed of collagen fiber and fibroblasts. Small capillaries were present in the collagenous tissues. No residual lesions of the cholesteatoma matrix were found in any patient. In one patient, the preserved tissue was lined with ciliary epithelial cells. In three patients, including the patient with ciliary epithelial cells, cysts of mucosal remnants were embedded in the connective tissue. All three of these patients experienced recurrent or residual cholesteatoma during the follow-up. In the other seven patients, the harvested tissues comprised of fibrous connective tissue only (Fig. 1). They did not show any sign of recurrent disease during the follow-up.

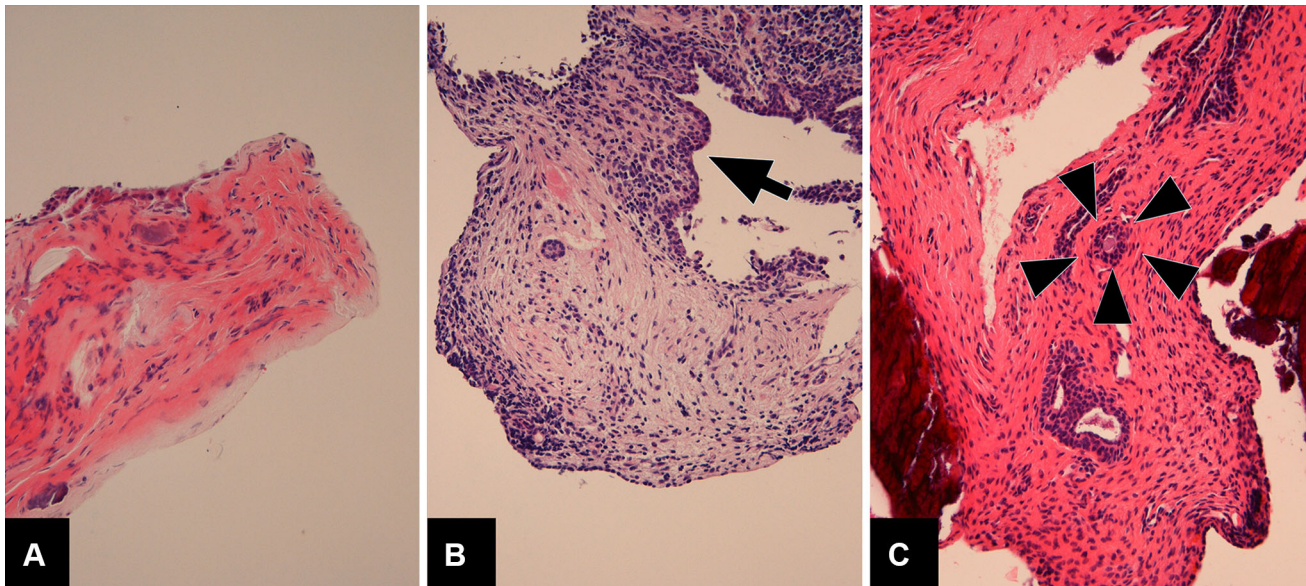
## Discussion

In the current study, we showed that the matrix of the cholesteatoma can be safely removed without exposing the cortical bone. With the use of fine tools, including a needle knife and sharp hook, the cholesteatoma matrix was easily and safely elevated from the bed, without disrupting it. No patients experienced injury to the facial nerve or the inner ear. Despite the cholesteatoma matrix sometimes infiltrating subepithelial tissues [2], residual lesion was not found in the attic with our technique. In one case, the residual lesion was found between the anterior crus of the stapes

**Table 1** Histopathological findings of the preserved soft tissue

Nos.	1	2	3	4	5	6	7	8	9	10
Ciliary epithelium	–	+	–	–	–	–	–	–	–	–
Glandular cyst	–	+	+	+	–	–	–	–	–	–
Results	NED	Rec	Rec otorrhea	Residual	NED	NED	NED	NED	NED	NED

*NED* no evidence of disease, *Rec* recurrence, *Residual* residual lesion



**Fig. 1** Preserved tissue was composed of collagen fiber and fibroblasts (a). In case 2, ciliary epithelium (arrow) was found covering the fibrous connective tissue (b). In three patients, glandular cysts (arrowheads) were embedded in the fibrous tissue (c)

and the cochleariform process. In the mesotympanum, we adopted the conventional technique in removing the cholesteatoma: total removal of the pathology. In this case of residual lesion, therefore, cause was not attributable to the surgical technique but to insufficient inspection of the surgical field during the original surgery. These results indicate that soft tissue preservation is a safe technique for the removal of cholesteatoma in the attic.

In the current study, however, the preserved tissue lacked the characteristics of normal mucosal tissue and was identified, in the majority of cases (90 %), as purely fibrous connective tissue. The significance of preserving fibrous connective tissue over the cortical bone is not proven yet. Exposed cortical bone is covered by regenerated mucosa in time [3, 4]; nevertheless, the delay in mucosal regeneration may lead to poor ventilatory function in this area and result in the recurrence of the cholesteatoma [1]. Recent advancement in the field of tissue engineering has proven that collagen-coating enhances the regeneration of mucosa [5]. In addition, the stimulatory effects of fibroblasts in the preserved tissue may enhance epithelial cell migration, proliferation, and differentiation, and reduce the time required for the regeneration of normal mucosal tissue [6]. In these ways, the preservation of soft tissue over the

cortical bone may enhance the regeneration of the mucosa in the attic. These functions are not obtained by the implantation of free collagenous tissue [7]. On the other hand, the preserved tissue may lead to persistent inflammation. In three patients, cysts of mucosal remnants, consistent with glandular cysts [8, 9], were found in the connective tissue. Despite the uncertain pathological significance of the glandular cysts, it is postulated that they may cause persistent inflammation [10]. In our case series, two of three patients with glandular cysts showed the recurrence of the cholesteatoma. On the other hand, none of the other seven patients experienced recurrent lesion. Nagai and his colleagues reported that the rupture of the glandular cysts causes inflammation in the perimatrix, and leads to the formation of cholesteatoma [10]. Although the examined tissue in the current study is only a sample of the preserved soft tissue, the finding suggests that the residual glandular cysts caused persistent inflammation in the middle ear, and resulted in the recurrence of the cholesteatoma. Therefore, it may be preferable to remove all tissue in the mastoid, and conduct canal wall down mastoidectomy in such cases. Unfortunately, we did not find any observable difference between patients with and without glandular cysts before or during the surgery. When

one considers the comparatively low rate of recurrence (20 %), soft tissue preservation is a safe and acceptable procedure. To improve the surgical result using this technique, it may be necessary to develop a new instrument that visualizes glandular cysts during the surgery.

In closing, we would like to describe some limitations of this study. The most serious one is the limited number of patients in this study. Our protocol included histopathological evaluation and regular follow-up CT, which are not economically encouraged [11]. In addition, one purpose of this study is to see the safety of the surgical technique. From these reasons, we included only ten cases. Based on the results of the current study, a clinical study with large cases should be conducted. The other problem of this study is that we may have overlooked a small recurrence. We have followed-up the patients and no retraction of the ear drum that was found other than two cases of recurrent lesion. Repeated CT scans did not prove any pathological lesions. Despite the fact that cholesteatoma can recur after a very long interval, we believe that the risk of relapse is low.

## Conclusion

Soft tissue preservation is a safe technique in cholesteatoma surgery. In most of the cases studied, the preserved tissue was fibrous connective tissue; complete mucosal tissue was found in one of the ten cases. Glandular cysts in the preserved soft tissue seem to be responsible for the recurrence of the cholesteatoma.

## Compliance with ethical standards

**Conflict of interest** There have been no conflicts of interest in the drafting of this manuscript. Dr. Hiraum, Dr. Kanemaru, Dr. Miura, Dr. Yamamoto, Dr. Sakamoto, and Dr. Ito declare that they have no conflict of interest.

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**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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