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Granulation tissue after otologic surgeries: a cross-sectional report on the incidence and management

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Abstract

Background Granulation tissue (GT) formation is a complication of otologic surgeries. We aimed to assess the rate of GT formation following these procedures and their outcome.

Methods This cross-sectional study was performed from 2015 to 2019. Patients who underwent tympanomastoidectomy (either CWD or ICW) and stapedotomy were included. Demographic and other related data were gathered. Four weeks after surgery, patients were assessed for any sign of granulation tissue formation. If present, they were managed topically and were followed every 2 months until complete resolution.

Results Of 1045 included cases, 200 underwent Canal Wall Down (CWD) mastoidectomy, 568 underwent Intact Canal Wall (ICW) mastoidectomy, and 277 experienced stapedotomy. Four weeks after surgery, 180 participants were diagnosed with GT (17.22%). The incidence rate of GT formation following tympanomastoidectomy and stapedotomy is 23.44% and 0%, respectively. This measure is 43% and 16.5% for CWD, and ICW approaches. Following treatment for 2 months, we found 164 (91.1%) participants with complete resolution at the second visit. Of the remaining 16 cases, 10 and 6 were cured at the third and fourth visits. Males developed GT significantly more ($p < 0.001$).

Conclusion Those with CWD mastoidectomy are more likely to develop GT than ICW and stapedotomy surgeries. It has a favorable response to conservative topical management.

Keywords Granulation tissue, Otologic surgeries, Mastoidectomy

Background

Granulation tissue (GT) formation is a possible complication of all ear surgeries including Canal Wall Down (CWD), Intact Canal Wall (ICW) tympanomastoidectomy and stapes surgeries [1]. In the process of surgical wound healing, in the first day, polymorphonuclear cells migrate to the margins of surgical incision and fibrin clot form. In 3 days, macrophages appear and PMN leave the tissue and in 5 days granulation tissue fill the space. In the form of large skin defect or wound infection the granulation tissue proliferate beyond the margin and can cause otorrhea [2].

The data regarding predisposing factors, associations, etiology, and treatment are scarce. CWD procedure secondary to cholesteatoma or other chronic ear conditions could cause GT with varying reported rates of 9–57.7% [3–7]. We found no estimation of GT occurrence in ICW and stapes surgery; however, more limited surgical interventions like tympanostomy tube placement may also be complicated with GT in 5–13.8% of patients [8, 9].

Herein, we aimed to evaluate GT formation incidence and the potential contributing factors following tympanomastoidectomy and stapedotomy surgeries.

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Methods

Patient population

We performed a cross-sectional study on patients referred to our tertiary university hospital for tympanomastoidectomy and stapedotomy from 2016 to 2020; patients were included regardless of their age. The first author performed all surgeries. After taking the consent, we filled out a checklist of demographic characteristics, chief complaint, accompanying symptoms (including pain, otorrhea, hearing loss, etc.), body mass index (BMI), previous history of middle ear infections, and past medical history of other diseases and comorbidities. Then the type of surgery performed, its approaches and procedures, and pathologic data of the surgical samples were also gathered. All the patients with active otorrhea at the time of surgery were excluded from the study. We did not prescribe antibiotic postoperatively. The canal wall down patients that needed obliteration at the time of surgery were excluded from the study. Four weeks after the surgery, the participants were examined by microscope. In case of GT formation, the management included local debridement, topical steroid and antibiotics, and chemical cauterization by Trichloroacetic acid 25%. The second visit would be scheduled 3 months after surgery; and this process was repeated until the complete resolution of the symptoms. One surgeon performed all the post-operational visits.

The Ethical Committee of the University approved the present research protocol under the code of IR.mums.fm.rec.1396.217. Written informed consent was obtained from all patients regarding participation and the anonymous publication of the results.

Statistical analysis

The data of this study were analyzed via SPSS software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). The p-value of less than 0.05 was considered statistically significant. The quantitative variables were reported as mean ± standard deviation and qualitative variables as numbers and percentages. The Independent t test and chi-square tests were used where appropriate.

Results

A total of 1045 patients were included. Two hundred underwent CWD mastoidectomy, 568 underwent ICW mastoidectomy, and 277 had stapedotomy. Four weeks after surgery, 180 (17.22%) participants were detected to have GT in the external ear (Fig. 1). These cases were managed as described in the "Methods" section and re-visited within 2 months. We found 164 (91.1%)

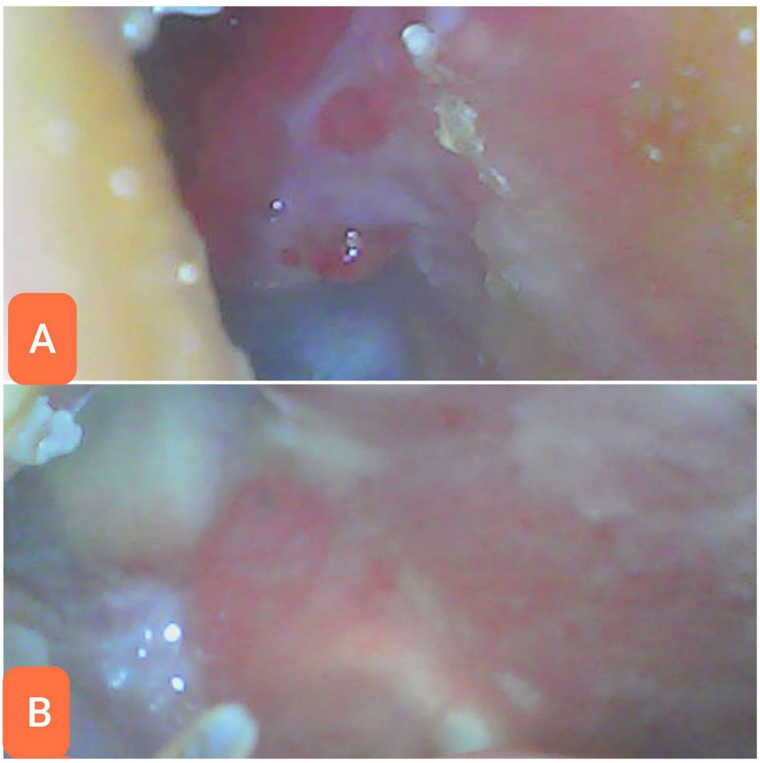

Fig. 1 Granulationtissue in tympanomastoidectomy (**A**) canal wall up (**B**) canal wall down 1 month after surgery

Table 1 Comparison of sex and age variables between cases with and without GT formation

Variables	GT development ($N = 180$) N (%)/Mean ± SD	No GT development ($N = 865$) N (%)/Mean ± SD	P value*
Sex			
Male	109(60.6%)	289(33.4%)	0.001 >
Female	71(39.4%)	576(66.6%)	
Age (year)	36.40 ± 17.00	38.62 ± 15.42	0.109

*Independent *t* test were used for age; chi-square test were used for sex

participants with complete resolution of the GT. Only 16 (8.9%) cases still had GT on month 3 examination.

The comparisons between participants with and without granulation tissue development are presented in Table 1. GT growth was detected significantly more among men ($p < 0001$; chi-square). The mean age of the two groups did not differ significantly. We found that of 200 cases who underwent CWD tympanomastoidectomy, 86 (43%) had GT occurrence after four weeks (first visit), while of 568 ICW performed, 94 (16.5%) patients detected to have GT formation in the first visit. No GT was observed in 277 cases that underwent stapedotomy. These three types of surgery were significantly different in terms of GT development ($p = 0.001$; chi-square).

The demographic data of participants who developed GT after surgery are presented in Table 2. Of 180 GT cases, 71 (39.4%) were female. These cases' mean age and BMI were 36.40 ± 17.00 years and 25.50 ± 5.24 kg/m^2, respectively. The location of GT development, type of surgery, the status of diabetes, anemia, smoking, previous otic surgery, and other otic diseases are also presented in the table.

Table 3 demonstrates the differences between cases who responded to the GT treatment at the second visit versus those who did not. Of those participants with (164 cases) and without (16 cases) resolution of granulation tissue, 64 (39%) and 7 (43.8%) cases were female, respectively. No statistical significance was found between the two groups. Insignificant associations were also observed between these two groups regarding BMI, smoking, diabetes, anemia, steroid use, history of any otic surgery, location of the granulation tissue, and type of surgery.

In the second visit, 16 participants were diagnosed with GT, treated with chemical cauterization, and continued local betamethasone and ciprofloxacin if necessary. Ten cases improved completely in the third visit (after 2 months of the additional treatment), and six experienced total resolution of GT at the fourth visit (additional 2 months of treatment).

Table 2 Pre-operative demographic features of cases with GT in the first visit

Demographics	$N = 180$ N (%)/Mean ± SD
Age (year)	36.40 ± 17.00
BMI (kg/m^2)	25.50 ± 5.24
Sex	
Male	109 (60%)
Female	71(39.4%)
Smoking	
Yes	55(30.60%)
No	125(69.4%)
Diabetes	
Yes	23(12.8%)
No	157(87.2%)
Anemia	
Yes	53(29.4%)
No	127(70.6%)
Steroid use	
Yes	9(5%)
No	171(95%)
Previous ear surgery	
Yes	55(33.9%)
No	125(66.1%)
Primary ear disease	
COM	88(48.9%)
Cholesteatoma	69(38.3%)
Otosclerosis	23(12.8%)
Type of surgery	
CWD	86(47.8%)
ICW	94(52.2%)
Stapedotomy	0(0%)
Location of GT	
Tympanic membrane + canal	62(36.7%)
In the canal	107(63.3%)

BMI Body mass index, *COM* Chronic otitis media, *ICW* Intact canal wall, *CWD* Canal wall down

Discussion

Due to the scarcity of data on this complication, we designed a cross-sectional study to evaluate the associations and incidence rate of GT formation following tympanomastoidectomy and stapedotomy surgeries. Of 180 (17.22%) participants with GT diagnosis, none was from the stapedotomy group; thus, GT formation incidence in tympanomastoidectomy cases was 23.44%. The incidence rate of GT development for CWD and ICW approaches were 43% and 16.5%, respectively. Females were significantly less likely to develop GT ($p < 0.001$). Those with CWD mastoidectomy were more likely to develop GT than ICW and stapedotomy surgeries ($p = 0.001$). We

Table 3 Pre-operative demographic features of cases with GT in the first visit classified based on their response to the treatment at the second visit versus the third visit

Demographics	Responded at second visit ($N = 164$) *N* (%)/Mean ± SD	No response at second visit ($N = 16$) *N* (%)/Mean ± SD	*P* value*
Age (year)	36.24 ± 16.94	38.06 ± 17.68	0.884
BMI (kg/m^2)	25.42 ± 5.03	26.30 ± 7.20	0.183
Sex			
Male	100(61.0%)	9(56.2%)	0.454
Female	64(39.0%)	7 (43.8%)	
Smoking			
Yes	53(32.3%)	2(12.5%)	0.081
No	111(67.7%)	14(87.5%)	
Diabetes			
Yes	20(12.2%)	3(18.8%)	0.334
No	144(87.8%)	13(81.2%)	
Anemia			
Yes	47(28.7%)	6(37.5%)	0.316
No	117(71.3%)	10(62.5%)	
Steroid use			
Yes	8(4.9%)	1(6.2%)	0.576
No	156(95.1%)	15(93.8%)	
Previous ear surgery			
Yes	55(33.5%)	6(37.5%)	0.473
No	109(66.5%)	10(62.5%)	
Primary ear disease			
COM	79(48.2%)	9(52.6%)	0.808
Cholesteatoma	64(39.0%)	5(31.2%)	
Otosclerosis	21(12.8%)	2(12.5%)	
Type of surgery			
CWD	87(53.0%)	7 (43.8%)	0.237
ICW	77 (47.0%)	9(52.6%)	
Stapedotomy	0(0%)	0(0%)	
Location of GT			
Tympanic membrane + canal	58 (37.2%)	4 (30.8%)	0.445
In the canal	98(62.8%)	9(69.2%)	

*Independent *t* test were used for age and BMI; chi-square test were used for the rest

BMI Body mass index, *COM* Chronic otitis media, *ICW* Intact canal wall, *CWD* canal wall down

found 164 (91.1%) participants with complete resolution after 2 months of treatment at the second visit. The remaining 16 patients, were all CWD cases and 10 and 6 were cured at the third (2 months later) and fourth visits, respectively.

GT manifests as a granulomatous mass, and the pathologic studies usually report granular tissue with epithelioid histiocytes, fibroblast proliferation, dense vasculature with ingrowing capillaries, and inflammatory cells like lymphocytes, plasma cells, and neutrophils [10].

Granulation tissue grows in the areas which lack suitable epidermal coverage. This is part of the reparative process in the secondary wound repair. So, it is not strange to have higher incidence of GT in CWD cases where the secondary repair is expected, in contrast to ICW cases where canal skin defects happen rarely [2].

While we found a significantly higher incidence of GT formation in males following tympanomastoidectomy, we found no similar article to compare our results. Despite the rarity of research on GT formation, granular myringitis, a similar but localized condition, gained more attention in the literature. It is a chronic inflammation manifesting on the external surface of the tympanic membrane but restricted to the squamous epithelium of the ear [11]. We found no significant sexual predominance regarding the incidence of granular myringitis in our database search [10, 11]. Future prospective studies are needed to elucidate the possible role of sex (and subsequently sexual hormones) in developing GT and granular myringitis.

CWD approach accompanied a higher rate of GT formation. As the procedures explained in the method section, the surgical intervention's complexity and extent might play a pivotal part in GT growth; This is consistent with proposed inciting events of granular myringitis, which signify traumatic injury and surgical ear interventions as possible factors [12, 13]. Faramarzi et al. used amniotic membrane and temporalis fascia to cover the musculoperiosteal flap in the CWD approach [5]. They concluded that the epithelialization time is significantly shorter in the amniotic membrane group and GT development was three times less than in the temporalis fascia group. The graft success rates were over 92% in both groups. Additionally, these patients did not experience recurrence of the cholesteatoma.

There is no consensus on the standard management of the GT. Our study showed about 91% (164 of 180 cases) complete resolution of GT with well-timed diagnosis and triple treatment with otic ciprofloxacin and betamethasone ear drops, plus chemical cauterization with Trichloroacetic acid 25% solution. Of note, the rest of the patients were cured completely by continuing this regimen and timely visits. This signifies the importance of surveillance over surgical treatment. Our study was empowered by its relatively high sample size. However, we did not use culture and staining studies on otorrhea secretions for the GT Group to determine a potential microbial etiology. Future studies should be designed prospectively to gain more confident results and assess whether routine follow-up of patients after otologic surgeries to diagnose GT in time is beneficial.

Another limitation of our study was that tympanoplasty and myringoplasty cases were not included in the study because all the surgeries in this study was done by the first author and tympanoplasty and myringoplasty as minor surgeries was mostly done by junior surgeons. Hence, we do not include them in the study.

Conclusion

The incidence rate of GT formation following tympanomastoidectomy and stapedotomy is 23.44% and 0%, respectively. This measure is 43% and 16.5% for CWD, and ICW approaches. A timely-manner diagnosis could warrant a favorable response to conservative treatment (otic ciprofloxacin, betamethasone, and trichloroacetic acid drops).

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Authors' contributions
MR: Designed the study, interpreted the patient data, managed the patient, supervised the research and revised the manuscript. PN: Interpreted the patient data, managed the patient and co-wrote the paper. MA: Interpreted the patient data, managed the patient and co-wrote the paper.

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Availability of data and materials
The data used to write this article is available by sending a request to the corresponding author.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethical Committee of Mashhad University of Medical Sciences under the ethical code of IR.mums.fm.rec.1396.217. Consent to participate: Written informed consent was obtained from all patients regarding the participation.

Consent for publication
Written informed consent was obtained from all patients regarding the anonymous publication of the results.

Competing interests
The authors declare that they have no competing interests.

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