Available online at www.sciencedirect.com
SciVerse ScienceDirect
ELSEVIER
Journal of the Chinese Medical Association 75 (2012) 329–334
www.jcma-online.com

Original Article

New therapeutic strategy for treating otitis media with effusion in postirradiated nasopharyngeal carcinoma patients

Chin-Lung Kuo [a,b,c], Mao-Che Wang [a,b], Chia-Huei Chu [a,b], An-Suey Shiao [a,b,c,*]

[a] Department of Otorhinolaryngology - Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
[b] National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC
[c] National Defense Medical Center, Taipei, Taiwan, ROC

Received November 15, 2011; accepted February 22, 2012

Abstract

Background: Postirradiation otitis media with effusion (OME) is the most common radiotherapy-associated otologic complication associated with nasopharyngeal carcinoma (NPC). This study's aim was to evaluate the efficacy of laser myringotomy followed by intratympanic steroid injection (LMIS) for treating OME in postirradiated NPC patients.
Methods: From August 2002 to January 2006, 27 newly diagnosed NPC patients who developed OME after a full course of radiotherapy were enrolled. Laser myringotomy was performed followed by once-weekly administration of steroids (0.5 mL dexamethasone at a concentration of 5.0 mg/mL) into the middle ear for 3 consecutive weeks. The success rate of dry eardrum perforation and the prognostic factors associated with OME resolution were analyzed.
Results: The procedure was performed on 44 ears of 27 patients. The mean follow-up period was 37 weeks. Of the 44 ears, 23 (52.3%) developed persistent eardrum perforation, 18 (40.9%) developed recurrent OME, and three (6.8%) were disease-free on follow-up. Of the 23 ears with persistent eardrum perforation, 18 (78.3%) were diagnosed as dry perforation. The absence of pretreatment mastoiditis was an independent factor associated with OME resolution ($p < 0.001$).
Conclusion: LMIS is a quick, minimally invasive, office-based technique that can be repeatedly performed to treat highly recurrent postirradiation OME, and it results in relatively slight pain to NPC patients. Long-lasting dry eardrum perforation allows for adequate middle ear ventilation and drainage and guarantees sustained relief from symptoms. The absence of preoperative mastoiditis is a favorable prognostic factor associated with OME resolution.

Keywords: CO2 laser; irradiation; nasopharyngeal cancer; otitis media with effusion; tympanostomy

1. Introduction

Nasopharyngeal carcinoma (NPC) is a widely prevalent malignancy in Southeast Asia. The mainstay of treatment is definitive radiotherapy.[1] Although recent advances in imaging and therapeutic techniques have reduced radiotherapy-associated complications, the exposure of nontarget organs during head and neck irradiation is often inevitable. Of the various otologic complications, postirradiation otitis media-with effusion (OME) is the most common problem,[2] and this significantly impairs the quality of life of postirradiated NPC patients with symptoms such as conductive hearing loss, ear discomfort, and muffling. The conventional treatments of postirradiation OME include simple tympanic aspiration, incisional myringotomy, and ventilation tube insertion. Unfortunately, simple tympanic aspiration and incisional myringotomy provide no meaningful therapeutic effects due to their short healing times of only 1–2 days.[3,4] On the other hand, ventilation tube insertion may cause adverse effects,

* Corresponding author. Dr. An-Suey Shiao, Department of Otorhinolaryngology, Head and Neck Surgery, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: asshiao@gmail.com (A.-S. Shiao).

1726-4901/$ - see front matter
doi:10.1016/j.jcma.2012.04.016

such as tube otorrhea which has an incidence that varies from 29–64%.[5–7] Thus, conventional approaches often fail to provide satisfactory relief of otologic symptoms.

Laser myringotomy has been used to treat conventional nonirradiation-related OME.[8,9] Recently, the use of laser myringotomy has been proposed by Hwang et al as an alternative approach for treating NPC patients with OME.[6] The duration of relief from otologic symptoms using this method is longer than that of simple tympanic aspiration. In addition, the efficacy and complication rates of laser myringotomy are similar to those of simple myringotomy. However, the study by Huang et al enrolled both pre- and postirradiated NPC patients; thus, the clinical utility of using laser myringotomy to treat postirradiation OME remains unknown. On the other hand, radiation-compromised inflammation of the middle ear plays an important role in the pathogenesis of postirradiation OME, while Eustachian tube dysfunction is the major cause of nonirradiation-related OME.[2,5,10–13] This may partly explain the poor outcomes of postirradiation OME treated using conventional approaches.

In the present study, a new therapeutic strategy was developed that uses laser myringotomy followed by intratympanic steroid injection (LMIS) to treat postirradiation OME in NPC patients due to its distinct pathogenesis. The goal of LMIS is to create a long-lasting dry eardrum perforation that achieves immediate symptom relief and provides a long-term satisfactory outcome. This study's aim was to evaluate the efficacy of LMIS for the treatment of postirradiation OME in NPC patients.

2. Methods

From August 2002 to January 2006, 27 patients with newly diagnosed primary NPC who were being treated at Taipei Veterans General Hospital were enrolled. None of these patients had been diagnosed with OME before NPC, and they only developed OME after a course of radiotherapy. Patients with recurrent OME after radiotherapy were excluded. Postirradiation OME was defined as the accumulation of effusion in the middle ear without signs of acute infection. Diagnosis was clinically confirmed by the use of video telescopy, audiometry, and tympanometry (type B tympanogram). The hospital's institutional review board approved this study, and all of the patients provided written informed consent.

Temporal bone computed tomography (CT) and Eustachian tube function tests were performed on 21 patients prior to LMIS, while six did not complete these examinations. Evidence of mastoiditis by CT imaging included: (1) clouding of the air cells or destruction of the mastoid outline; (2) loss of or a decrease in the sharpness of the bony septa within the air cells; (3) loss of the bony septa between the air cells (coalescence of mastoid air cells); and (4) hypoaeration of the mastoid. Patients with all these features on CT were diagnosed with "positive mastoiditis," otherwise they were diagnosed with "negative mastoiditis." The pressure equalization test was used to evaluate Eustachian tube function. Positive and negative pressures were applied to the middle ear, and the residual pressure was measured after several deglutinations. If equilibration of the middle ear pressure was successfully achieved, Eustachian tube function was considered "good," otherwise function was considered "poor."

In terms of the therapeutic strategy, the surgical procedure began by anesthetizing the eardrum using 10% topical lidocaine for 15 minutes. The solution was then suctioned from the ear canal. Circular laser myringotomy was performed using a CO_2 flash-scanner laser (OtoLAM; Lumenis Ltd., Yokneam, Israel) that was applied to the lower anterior or lower posterior quadrant of the eardrum according to the patient's external ear canal anatomy. The power of the CO_2 laser was set to 15 W, the spot size was 1.9 mm, and single-pulse duration of 0.2 seconds was applied. Middle ear fluid was obtained for culturing using a sterile nonrefluxing suction bottle. Steroids (0.5 mL dexamethasone at a concentration of 5 mg/mL) were injected directly through the myringotomy into the middle ear as the patient was lying on his side for 30 minutes. An intratympanic injection of dexamethasone was administered once per week for 3 consecutive weeks. The pre- and post-LMIS otoscopic findings are shown in Fig. 1.

Following treatment, the patients received follow-up examinations once per week for 3 weeks and then once every 2–4 weeks thereafter. OME resolution (i.e., disease-free status) was defined as the disappearance of aural fullness, normal findings on video telescopy, and type A tympanogram. Data on sex, age at surgery, NPC stage according to the 2002 American Joint Committee on Cancer (AJCC) staging system,[14] radiation dose, eardrum condition, perforation healing time, recurrent disease, complications, mastoiditis, and Eustachian tube function were collected and analyzed in order to build a statistical model that could be used to investigate the prognostic factors associated with treatment outcomes.

Univariate cross-tabulation analysis and Pearson's Chi-square test were used to assess associations between pretreatment variables (e.g., mastoiditis and Eustachian tube function) and treatment outcomes. All statistical comparisons and descriptive statistics were performed using the SPSS statistical software package (version 18.0; SPSS, Inc., Chicago, IL, USA). A p value of < 0.05 was considered statistically significant.

3. Results

The patient characteristics are summarized in Table 1. Laser myringotomy was performed on 44 ears of 27 patients. Of these 27 patients, 12 (44%) were female and 15 (56%) were male. Seventeen patients (63%) had experienced bilateral postirradiation OME. Eleven patients were classified as AJCC 2002 stage I–II disease and 16 patients were classified as stage III–IV disease. The mean age at the time of surgery was 53 years (range: 33–79 years). The mean radiation dose was 70.28 Gy. The mean follow-up period was 36.7 weeks (range: 4–112 weeks). The fluid content of the middle ear effusions was serous in all patients. There were no postoperative complications such as sensorineural hearing loss, nystagmus, or vertigo.

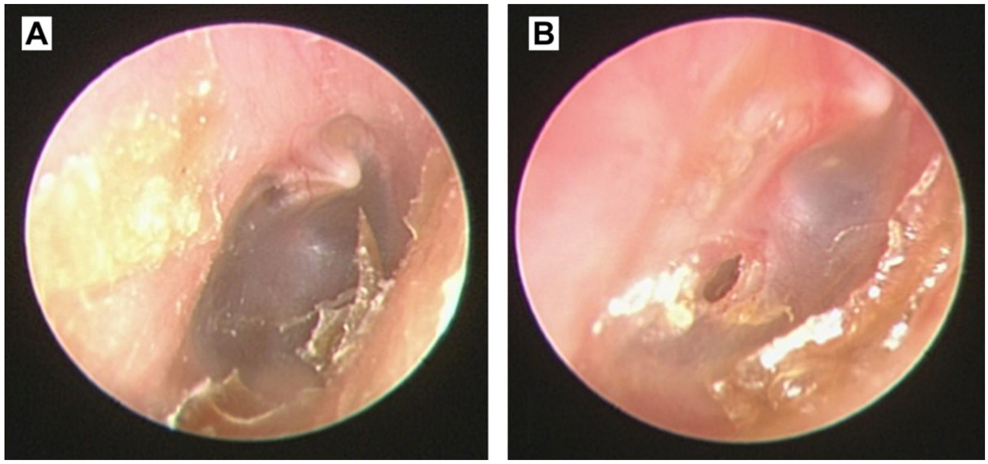

Fig. 1. Otitis media with effusion of the right ear **(A)** before and **(B)** after laser myringotomy followed by once-weekly intratympanic steroid injection for 3 consecutive weeks. Dry perforation of the eardrum resulted and was maintained for adequate middle ear ventilation and drainage, allowing the immediate and sustained relief of otologic symptoms.

The clinical outcomes of LMIS for the treatment of post-irradiation OME in NPC patients are shown in Table 2. Of the 44 ears that were treated, 23 (52.3%) were diagnosed as persistent eardrum perforation, 18 (40.9%) were diagnosed as recurrent OME, and three (6.8%) were disease-free. Of the 23 ears with persistent eardrum perforation, 18 (up to 78.3%) demonstrated dry perforation and only five (21.7%) demonstrated persistent otorrhea. The mean follow-up period for the 18 ears with dry eardrum perforation was 36.7 weeks (range: 16–89 weeks). The mean healing time following laser myringotomy of the 21 ears (18 recurrent OME ears and 3 disease-free ears) was 6.5 weeks (range: 1–24 weeks). OME recurred in 18 ears with intact eardrums about 3–4 months after LMIS, and all of these ears were treated using repeated LMIS. No NPC recurrence was observed in the 18 patients with recurrent OME, as shown on follow-up magnetic resonance imaging (MRI) examinations of the head and neck regions. Following repeated LMIS, some patients were lost on follow-up and some required even more additional LMIS.

The bacteriological isolates obtained from the middle ear effusions during surgery are shown in Table 3. Repeated cultures were performed using samples from patients with residual effusion in the middle ear. In total, 62 culture samples were obtained from 44 ears of 27 patients, yielding 22 isolates. The positive culture rate was only 35.5% (22 isolates from 62 culture samples). The predominant organism was *Staphylococcus aureus*, which accounted for 59.1% of all isolates (13 of 22 isolates).

Temporal bone CT was performed on 33 ears of 21 patients (Table 4), indicating that 23 ears were complicated by mastoiditis prior to LMIS. None of these patients were disease-free at the end of the follow-up period. Of the other 10 ears that were not complicated by pre-LMIS mastoiditis, three (30%) were disease-free at the end of follow-up. Post-irradiation OME patients without mastoiditis demonstrated a significantly higher resolution rate of OME (i.e., disease-free status) than patients with mastoiditis ($p < 0.001$).

Similarly, Eustachian tube function testing was performed on 33 ears of 21 patients (Table 4). Of these 33 ears, 24 ears demonstrated good Eustachian tube function prior to LMIS and two ears (9%; 2 of 24 ears) were disease-free at the end of the follow-up period. Of the other nine ears with poor Eustachian tube function, one (11%; 1 of 9 ears) was disease-free at the end of the follow-up period. There was no significant difference in terms of the OME resolution rate between the ears with good and poor Eustachian tube functions ($p = 0.637$).

Table 1
Patient demographics.

Parameter	No.
Ears	44
Patients	27
Sex	
Male	15
Female	12
Mean age (y)	53 (33–79)
NPC stage	
Stage I–II	11
Stage III–IV	16
Average radiation dose (Gy)	70.28

Abbreviations: NPC, nasopharyngeal carcinoma.

Table 2
Clinical outcomes.

Clinical outcome	Ears	Percentage
Persistent eardrum Perforation ($n = 23$)		
Dry	18	40.9%
Wet	5	11.4%
Intact eardrum ($n = 21$)		
Recurrent OME	18	40.9%
OME resolution	3	6.8%
Total	44	100%

Abbreviations: OME, otitis media with effusion.

Table 3
Bacteriological isolates from middle ear effusions obtained during surgery.

Organism	No. of cultures	Percentage
No growth	40	64.5%
Staphylococcus aureus	13	21.1%
MRSA	3	4.8%
Enterococcus	1	1.6%
Gram-positive *bacilli*	1	1.6%
Klebsiella pneumonia	1	1.6%
Micrococcus sp.	1	1.6%
Pseudomonas aeruginosa	1	1.6%
Mold	1	1.6%
Total	62	100%

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus.*

4. Discussion

OME is the most common otologic toxicity that presents in NPC patients after radiotherapy. Its morbidity rate has been reported to be as high as 53%.[13] Nelson et al reported that 23% of NPC patients in their study developed OME within 2 years of completing radiotherapy.[7] The pathogenesis of postirradiation OME is quite different from that of nonirradiation-related OME, which is commonly caused by Eustachian tube dysfunction.[2,15,16] Furthermore, patients with nonirradiation-related OME usually demonstrate favorable results following conventional treatment.[2] The complete resolution of effusion can even be achieved after the restoration of tubal functions. In contrast, in postirradiation OME, the generally acknowledged etiologies are associated with direct radiation damage,[2,16] including scarring of the Eustachian tube opening, poor mucociliary function of the Eustachian tube, and fibrosis of the tensor veli palatini muscle. However, an important but frequently ignored cause is radiation-compromised inflammation of the middle ear.[2,5,10−13,15,16]

There are controversies regarding the potential benefits of the conventional approaches used to treat postirradiation OME due to disappointing long-term treatment results.[2,6,16] However, there may be several explanations for these poor outcomes. First, the recurrence rate of postirradiation OME is high (range: 77.8−88.9%), whereas the cure rate is low (range: 8.7−18.2%).[2,6,16] This may be due to irreversible radiation damage to the Eustachian tube and middle ear mucosa. Second, simple tympanic aspiration or incisional myringotomy alone is ineffective due to the short duration of the perforation healing time (usually only 1−2 days).[3,4] In fact, 3 weeks is regarded as the shortest time required for transtympanic ventilation.[6,17] The ventilation tube, in comparison, requires an indwelling period of 4−6 months[4,6] and is usually associated with a high incidence of postoperative middle ear infection and otorrhea, which are often refractory to local or medical treatment.[6,7,13] Thus, the effectiveness of conventional methods of the treatment of postirradiation OME remains questionable.

To solve the troubling problems associated with postirradiation OME, many otologists have shifted their focus to alternative approaches, and laser myringotomy seems to be a promising alternative choice. Laser myringotomy was first applied to the human eardrum in 1982 by Goode,[18] who reported that myringotomy using a CO2 laser provides more prolonged eardrum perforation than incisional myringotomy using a knife. In the past decade, laser myringotomy has generated increased interest in its clinical applications for the treatment OME.[3,4,19−23] Advocates claim that its advantages over conventional treatments include the avoidance of general anesthesia, convenience of an office-based model, time and cost effectiveness, and reduced eardrum damage.[19,23] Accordingly, laser myringotomy is considered a safe and practical procedure for treating OME.

Unfortunately, the use of laser myringotomy for treating postirradiation OME in NPC patients is rarely discussed in the literature, usually because NPC patients are intentionally excluded as a separate entity from OME. To date, only one study, which was conducted by Hwang et al in 2005, has been conducted on the effectiveness of using laser myringotomy to treat NPC patients.[6] However, both pre- and postirradiated NPC patients were enrolled in that study; thus, the usefulness of laser myringotomy for treating radiation-related OME remains uncertain.

In response to the complex and delicate process of OME formation in postirradiated NPC patients, this study proposes a new therapeutic strategy—LMIS—that can not only provide ventilation to the middle ear but also treat radiation-compromised inflammation of the middle ear. This study is the first analysis of the effectiveness of laser myringotomy for treating postirradiation OME in NPC patients. Radiation can cause irreversible damage to the Eustachian tube and middle ear mucosa, inevitably resulting in a high recurrence rate (77.8−88.9%) and a low cure rate (8.7−18.2%).[2,6,16] Therefore, the therapeutic goal of LMIS is to provide sustained relief of otologic symptoms instead of a cure. In other words, LMIS is designed to create a long-lasting dry perforation of the eardrum, which allows the maintenance of middle ear ventilation and long-term relief of tubal dysfunction-related symptoms such as ear discomfort and muffling.

In the current study, the rate of persistent dry eardrum perforation is 41% (18 of 44 ears). In contrast, Liang et al reported a relatively low rate of dry eardrum perforation (4%; 1 of 23 ears) with ventilation tube insertion for the treatment of postirradiation OME in NPC patients.[16] Xu et al also reported low rates of dry eardrum perforation using conventional approaches (e.g., auripuncture, auripuncture with

Table 4
Association between clinical factors and treatment outcomes.

Factors	Disease status[b]	Disease-free status	p
Mastoiditis ($n = 33$)[a]			< 0.001
Positive ($n = 23$)	23 (100%)	0	
Negative ($n = 10$)	7 (70%)	3 (30%)	
Eustachian tube function ($n = 33$)[a]			0.637
Good ($n = 24$)	22 (91%)	2 (9%)	
Poor ($n = 9$)	8 (89%)	1 (11%)	

Abbreviations: OME, otitis media with effusion; CT, computed tomography.
[a] Thirty-three ears of 21 patients underwent temporal bone CT and Eustachian tube function tests before treatment.
[b] Disease status included persistent eardrum perforation and recurrent disease.

cauterization, and myringotomy plus grommet insertion) for treating OME in postirradiated NPC patients (11%, 5 of 45 ears; 16%, 7 of 45 ears; and 11%, 5/45 ears, respectively).[2] Compared with the results of the conventional approaches reported in the literature, LMIS demonstrates a significantly higher success rate of dry eardrum perforation (all $p < 0.01$). Using the same laser myringotomy technique as the current study, Hwang et al reported a 24% rate (16 of 68 ears) of dry eardrum perforation when treating NPC patients with OME.[6] Furthermore, the results of the current study show a long-lasting period of dry eardrum perforation (mean: 36.7 weeks; range: 16−89 weeks). Therefore, LMIS may be effective for treating postirradiation OME in NPC patients, as evidenced by the higher rate of dry eardrum perforation over a longer period of time.

Dry eardrum perforation or a dry middle ear is indicative of a restored mucosal immune system and complete remission of otorrhea, which are the most common results of ventilation tube insertion.[5−7] Immune system restoration in the middle ear mucosa may result from the administration of topical steroids. The proposed mechanisms for the actions of steroids on OME include direct anti-inflammatory actions on the middle ear and Eustachian tube, improved tubal function due to increased Eustachian tube surfactant concentration and shrinkage of peritubal lymphoid tissue, reduced middle ear fluid viscosity via mucoprotein effects, downregulation of inflammatory cytokine production by glucocorticoids, and the upregulation of sodium transport in the middle ear epithelia resulting in increased fluid clearance.[24−26] By reducing inflammation and epithelial repair of the middle ear mucosa, LMIS can accelerate the resolution of postirradiation OME and provide long-lasting and significant relief of symptoms.

Intratympanic injection of dexamethasone is a safe and simple intervention that significantly delays the healing of eardrum perforation without long-term perforations.[27−29] Antonelli et al reported a transtympanic ventilation time of at least 4 weeks through delayed-healing perforation.[27] However, this study was conducted using an animal model and the topical agent was prepared from ciprofloxacin-dexamethasone solutions. The true effect of dexamethasone on the healing process of human eardrum perforation remains uncertain. Among the 21 ears that demonstrated complete healing in the current study, the mean perforation healing time was 6.5 weeks (range: 1−24 weeks). This may be the first human model to estimate the effect of steroids on delaying healing following eardrum perforation.

The 40.9% recurrence rate determined in the current study is lower than those reported in previously published studies (77.8−88.9%),[2,16] although the cure rate (6.8%) is similar to those previously published in the literature (8.7−18.2%).[2,16] The recurrence rate determined here is not inconsequential, and even if only three ears (6.8%) attained the complete resolution of OME, this is balanced by the advantages of LMIS: namely, this quick, minimally-invasive, office-based technique allows for repeated procedures with minimal patient pain.

Although the fluid content of the middle ear effusions was serous in all patients, all of the middle ear discharge samples were sent for culturing. The positive culture rate was not high (35.5%; 22 isolates recovered from 62 culture samples) and *S aureus* was the predominant organism, which accounted for 59.1% of all of the recovered isolates. Thus, in cases of serous discharge, the use of pre- and postoperative topical and oral antibiotics may be controversial.

To identify the potential risk factors associated with the clinical outcomes (i.e., OME resolution), patients were further investigated in terms of the clinical factors of mastoiditis (positive vs. negative) and Eustachian tube function (good vs. poor). Information on the effects of these risk factors is genuinely beneficial for predicting treatment outcomes. Mastoiditis before LMIS was shown to be an independent factor associated with clinical outcome: i.e., a good mastoid status predicts a good clinical outcome ($p < 0.001$). However, pretreatment Eustachian tube function was not associated with treatment outcome ($p = 0.637$).

This study has several limitations. First, it is limited by the small number of patients that were enrolled. Thus, it is difficult to evaluate the impact of the stage or the total dose of radiation on the outcomes of LMIS. There may also be unavoidable selection bias, and some unnoticed confounding factors may not have been included in the univariate analysis used to prove the independent correlations with clinical outcomes. This study is also limited by the short-term results. Lastly, further prospectively randomized research with a control group is required to investigate the potential benefits of applying the newly proposed therapeutic strategy.

In conclusion, the preliminary results of this study provide further supportive evidence of the use of LMIS to treat post-irradiation OME in NPC patients. This new therapeutic strategy may provide both short- and long-term relief of symptoms. This convenient and minimally invasive treatment, which does not require general anesthesia, allows for repeated procedures with little pain in patients with OME recurrence. Therefore, LMIS may be a practical alternative to conventional approaches for treating NPC patients with postirradiation OME.

References

1. Leung TW, Tung SY, Sze WK, Wong FC, Yuen KK, Lui CM, et al. Treatment results of 1070 patients with nasopharyngeal carcinoma: an analysis of survival and failure patterns. *Head Neck* 2005;**27**:555−65.
2. Xu YD, Ou YK, Zheng YQ, Chen Y, Ji SF. The treatment for post-irradiation otitis media with effusion: a study of three methods. *Laryngoscope* 2008;**118**:2040−3.
3. Prokopakis EP, Lachanas VA, Christodoulou PN, Bizakis JG, Karatzanis AD, Velegrakis GA. Implications of laser assisted tympanostomy in adults. *Otol Neurotol* 2005;**26**:361−3.
4. Sedlmaier B, Jivanjee A, Gutzler R, Huscher D, Jovanovic S. Ventilation time of the middle ear in otitis media with effusion (OME) after CO2 laser myringotomy. *Laryngoscope* 2002;**112**:661−8.
5. Ho WK, Wei WI, Yuen AP, Hui Y, Wong SH. Otorrhea after grommet insertion for middle ear effusion in patients with nasopharyngeal carcinoma. *Am J Otolaryngol* 1999;**20**:12−5.
6. Hwang CF, Chien CY, Lin HC, Peng JP, Chang HW, Su CY. Laser myringotomy for otitis media with effusion in nasopharyngeal carcinoma patients. *Otolaryngol Head Neck Surg* 2005;**132**:924−7.
7. Tang NL, Choy AT, John DG, van Hasselt CA. The otological status of patients with nasopharyngeal carcinoma after megavoltage radiotherapy. *J Laryngol Otol* 1992;**106**:1055−8.

8. Kuo YL, Wang MC, Chu CH, Shiao AS. Re-evaluation of CO laser myringotomy for managing children with persistent acute otitis media. *J Chin Med Assoc* 2011;**74**:413–8.
9. Chang CW, Yang YW, Fu CY, Shiao AS. Differences between children and adults with otitis media with effusion treated with CO2 laser myringotomy. *J Chin Med Assoc* 2012;**75**:29–35.
10. Lau SK, Wei WI, Sham J, Hui Y, Choy D. Effect of irradiation on middle ear effusion due to nasopharyngeal carcinoma. *Clin Otolaryngol Allied Sci* 1992;**17**:246–50.
11. Wei WI, Engzell UC, Lam KH, Lau SK. The efficacy of myringotomy and ventilation tube insertion in middle-ear effusions in patients with nasopharyngeal carcinoma. *Laryngoscope* 1987;**97**:1295–8.
12. Young YH, Lu YC. Mechanism of hearing loss in irradiated ears: a long-term longitudinal study. *Ann Otol Rhinol Laryngol* 2001;**110**:904–6.
13. Young YH, Sheen TS. Preservation of tubal function in patients with nasopharyngeal carcinoma, post-irradiation. *Acta Otolaryngol* 1998;**118**:280–3.
14. Greene FL, Page DL, Id F. *AJCC cancer staging manual*. 6th ed. New York: Springer; 2002.
15. Yang TL, Young YH. Radiation-induced otitis media—study of a new test, vestibular-evoked myogenic potential. *Int J Radiat Oncol Biol Phys* 2004;**60**:295–301.
16. Liang KL, Su MC, Twu CW, Jiang RS, Lin JC, Shiao JY. Long-term result of management of otitis media with effusion in patients with post-irradiated nasopharyngeal carcinoma. *Eur Arch Otorhinolaryngol* 2011;**268**:213–7.
17. Bluestone CD. Role of surgery for otitis media in the era of resistant bacteria. *Pediatr Infect Dis J* 1998;**17**:1090–8. discussion, 1099–1100.
18. Goode RL. CO2 laser myringotomy. *Laryngoscope* 1982;**92**:420–3.
19. Silverstein H, Kuhn J, Choo D, Krespi YP, Rosenberg SI, Rowan PT. Laser-assisted tympanostomy. *Laryngoscope* 1996;**106**:1067–74.
20. Cohen D, Shechter Y, Slatkine M, Gatt N, Perez R. Laser myringotomy in different age groups. *Arch Otolaryngol Head Neck Surg* 2001;**127**:260–4.
21. Koopman JP, Reuchlin AG, Kummer EE, Boumans LJ, Rijntjes E, Hoeve LJ, et al. Laser myringotomy versus ventilation tubes in children with otitis media with effusion: a randomized trial. *Laryngoscope* 2004;**114**:844–9.
22. Lin SH, Lai CC, Shiao AS. CO2 laser myringotomy in children with otitis media with effusion. *J Laryngol Otol* 2006;**120**:188–92.
23. Szeremeta W, Parameswaran MS, Isaacson G. Adenoidectomy with laser or incisional myringotomy for otitis media with effusion. *Laryngoscope* 2000;**110**:342–5.
24. Rosenfeld RM. New concepts for steroid use in otitis media with effusion. *Clin Pediatr (Phila)* 1992;**31**:615–21.
25. Butler CC, van Der Voort JH. Steroids for otitis media with effusion: a systematic review. *Arch Pediatr Adolesc Med* 2001;**155**:641–7.
26. Son EJ, Kim SH, Park HY, Kim SJ, Yoon JH, Chung HP, et al. Activation of epithelial sodium channel in human middle ear epithelial cells by dexamethasone. *Eur J Pharmacol* 2009;**602**:383–7.
27. Antonelli PJ, Winterstein AG, Schultz GS. Topical dexamethasone and tympanic membrane perforation healing in otitis media: a short-term study. *Otol Neurotol* 2010;**31**:519–23.
28. Buyten J, Kaufman G, Ryan M. Effects of ciprofloxacin/dexamethasone and ofloxacin on tympanic membrane perforation healing. *Otol Neurotol* 2007;**28**:887–90.
29. Yazici A, Naiboglu B, Oysu C, Toros SZ, Noseri H, Karaca CT, et al. Effect of ototopical ciprofloxacin-dexamethasone on myringotomy in a rat model. *Int J Pediatr Otorhinolaryngol* 2009;**73**:301–5.