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Research status of otitis media with effusion after radiotherapy

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Abstract

Objective. This brief review summarises the efficacy of the treatments for post-irradiation otitis media with effusion.

Method. Literature review.

Results. Studies suggest that tympanocentesis is recommended for patients with post-irradiation otitis media with effusion The efficacy of balloon dilatation Eustachian tube for post-irradiation otitis media with effusion remains unclear.

Conclusion. The efficacy of different treatments for post-irradiation otitis media with effusion is unclear. Therefore, there are no recognised clinical guidelines, and long-term clinical research with a large sample size is needed.

Review Article

Peng Li takes responsibility for the integrity of the content of the paper

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Introduction

Nasopharyngeal carcinoma (NPC) occurs in all countries in the world, but there are obvious regional differences (e.g. China and Southeast Asian countries have a high incidence). The incidence of NPC in other ethnic populations worldwide is relatively low, at around 1.0 per 100,000.[1] The aetiology of NPC is still uncertain, but it is currently considered to be a polygenic disease with ethnic susceptibility and a high familial tendency. It often involves interactions between multiple genes or between genes and the environment. At present, the more certain pathogenic factors are Epstein–Barr virus infection, chemical carcinogenic factors or environmental factors and genetic factors.

The recognised and effective radical treatment for nasopharyngeal carcinoma is radiation therapy, or a combination therapy based on radiation therapy. With the application of new radiotherapy techniques, the 5-year overall survival rate of patients after radiotherapy is increasing. The extension of survival time has gradually attracted clinical attention to the side effects caused by radiotherapy, such as pharyngoxerosis, radiation brain damage, radiation ear damage, etc.

Among the side effects caused by radiotherapy, otitis media with effusion (OME) is a common ear complication of NPC after radiotherapy. About 30.3–40 per cent of NPC patients had secondary OME, and the prevalence of OME increased significantly after radiotherapy, reaching 50–78.3 per cent.[2] Post-irradiation OME is more specific and cannot achieve results as good as the treatment of ordinary OME, and there are still no treatment guidelines.

As for the aetiology of OME before radiotherapy of NPC, current studies have mainly focused on the effect of tumours on Eustachian tube dysfunction. Tumour compression and tumour invasion of the tensor veli palatini muscle, levator velum palatini muscle or other corresponding nerves causing paralysis, or tumour invasion of the Eustachian tube cartilage and collapse of the cartilage wall segment, resulting in Eustachian tube dysfunction.[3]

During treatment of NPC, important structures such as the Eustachian tube, middle ear, soft palate, nasal cavity and sinuses are exposed to the irradiation target. These structures are inevitably damaged to some extent after radiotherapy, and such exposure can cause Eustachian tube dysfunction, leading to OME, which is a very common problem during or after radiotherapy and can persist for many years after treatment.[4]

Clinically, OME induced by radiotherapy is initially treated conservatively with drugs to control the radiation-induced inflammation in the ears, nose, sinuses and nasopharynx. If there is no obvious effect, surgical intervention is considered, which is usually performed by tympanocentesis, myringotomy with ventilation tube insertion, balloon dilatation of the Eustachian tube, etc. The management of OME in patients who have undergone radiation therapy for nasopharyngeal cancer has been a subject of controversy, with no clear consensus on the most

effective treatment approach. This review summarises the efficacy of tympanocentesis, myringotomy with grommet insertion and balloon dilatation Eustachian tube for post-irradiation OME.

Tympanocentesis and myringotomy with grommet insertion

Tympanocentesis and myringotomy with grommet insertion are the two most commonly used methods in clinical application. Histopathological studies have found that the acute phase within 3 months after radiotherapy will cause inflammation of the middle ear mucosa, epithelial cell desquamation and cilia injury, thus leading to middle ear dysfunction.[5,6] NPC showed local oedema at six months after radiotherapy, and oedema subsided at 6–12 months. OME usually appears 3–6 months after radiotherapy.[7]

A meta-analysis suggested that tympanocentesis was less prone to complications than tube insertion. A step-by-step approach should be used when selecting a treatment for OME due to radiotherapy for NPC. Priority should be given to tympanocentesis for less risk of complications. However, the advantage of myringotomy with grommet insertion over tympanocentesis is that it has a lower recurrence rate.[8] The incidence of complications in tympanocentesis and myringotomy with ventilation tube insertion was as follows: the incidence of tympanic perforation was 4 per cent and 15 per cent, the incidence of external ear canal infection or persistent otorrhoea was 1 per cent and 6.4 per cent, and the incidence of tympanic adhesion was 1 per cent and 1.5 per cent. The recurrence rates of tympanocentesis and myringotomy with ventilation tube insertion were 23 per cent and 6 per cent, respectively.[9,10]

Patients with NPC are more difficult to treat otorrhoea after ventilation tube insertion due to their decreased resistance, so the effect of short-term hearing improvement is often offset by long-term otorrhoea.[11] Some scholars even suggest that grommet insertion should be prohibited for post-irradiation OME.[12] However, due to the relatively high recurrence rate of tympanocentesis and repeated symptoms, grommet insertion can continue to relieve ear swelling, tinnitus and other symptoms, thereby improving the quality of life of patients. Moreover, repeated auripuncture brings inconvenience to patients and reduces treatment compliance to a certain extent. Therefore, Xu *et al.*[9] judged that myringotomy with grommet insertion is desirable and complications can be controlled through prevention and treatment of middle-ear infection. A study has suggested that the earlier the grommet insertion of OME after NPC radiotherapy, the faster the functional recovery of the Eustachian tube, and the better the efficacy of post-irradiation OME.[13]

Some studies have proposed that the ventilation tube insertion time should be shifted forward. Xian *et al.*[14] conducted grommet insertion in NPC patients without OME before radiotherapy and followed them up for 12 months and found that grommet insertion could reduce the occurrence of OME after radiotherapy. Grommet insertion not only can help drain fluid, but also reduce effects on the Eustachian tube, so that Eustachian tube function can be repaired. If OME is left untreated for a long time, it may cause adhesive otitis media, suppurative otitis media, radiation otitis media, tympanosclerosis and even sensorineural hearing loss.

Each method has advantages and disadvantages. Table 1 lists relevant studies on tympanocentesis and myringotomy with grommet insertion. The long-term efficacy of invasive interventions for OME after NPC radiotherapy remains unclear. However, different intervention methods significantly improved the symptom remission of patients. Although there are no guidelines for the treatment of OME after radiotherapy, many studies recommend that a step-by-step approach should be used when choosing the treatment method for post-irradiation OME. And controlling radiation-induced inflammation in areas such as the ears, nose, sinuses and nasopharynx is also important.

Balloon dilatation of Eustachian tube

For refractory OME, tympanocentesis and grommet insertion can relieve ear symptoms, but the long-term effect is not good,[15] because once the eardrum heals, Eustachian tube dysfunction is still a hidden danger of recurrence. In 2010, Ockerman *et al.*[16] first reported the use of Eustachian tube balloon dilatation in the treatment of obstructive Eustachian tube dysfunction. Subsequently, numerous clinical experimental studies related to balloon dilatation of the Eustachian tube were carried out,[29,30] and the operation was gradually recognised, which brought hope for the treatment of refractory OME. The Eustachian tube balloon dilatation operation was performed using nasal endoscopy. Under the guidance of a guide wire, the balloon was placed into the Eustachian tube isthmus at a depth of about 2 cm and the balloon pressure was 10 bars for 2 minutes. Silvola *et al.*[17] reported that balloon dilatation of the Eustachian tube has the following advantages: (1) expanding the Eustachian tube and improving Eustachian tube function; and (2) reduction of inflammation, which can promote tissue regeneration. Under the condition that the underlying aetiology is controlled, the damaged mucosa and submucosal tissues are crushed and scoured away by surgery, creating conditions for tissue regeneration.[17]

In 2015, Randrup and Ovsen[18] conducted quality evaluation and risk assessment on Eustachian tube balloon dilatation, pointing out that the current research at that time had confirmed the safety and feasibility of balloon dilatation of the Eustachian tube, and provided some help for the improvement of patients' symptoms. Some studies on post-irradiation OME suggest that balloon dilatation of the Eustachian tube not only improves the Eustachian tube function and hearing status, but also safely improves clinical efficacy.[19,20] However, other studies suggested that the Eustachian tube-7 score was the highest at six months after surgery, and then dropped sharply 6–24 months after surgery, suggesting that balloon dilatation of the Eustachian tube could only significantly improve the Eustachian tube function of NPC after radiotherapy for a period of time.[21]

On the contrary, Wong and Prepageran[22] compared the surgical effects of NPC patients with non-NPC patients and suggested that balloon dilatation of the Eustachian tube does not show any benefit for Eustachian tube dysfunction in NPC patients after radiotherapy. A consensus on treatment of obstructive Eustachian tube dysfunction with Eustachian tube balloon dilatation published in Spain in 2020 lists radiation therapy in the Eustachian tube area as a contraindication for balloon dilation.[23]

Balloon dilatation of the Eustachian tube is helpful for the improvement of symptoms in OME patients after NPC radiotherapy in the short term, but the long-term effects are still unknown. Whether the application of balloon dilatation Eustachian tube in such patients is recommended or whether it is in line with social and economic benefits needs further discussion.[18,24,25] Tables 2 and 3 show the pros and cons using balloon dilatation of the Eustachian tube in post-irradiation OME. Therefore, rigorous and long-term RCTs or randomised controlled studies are necessary.

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Table 1. Studies of grommet insertion and tympanocentesis for post-irradiation otitis media with effusion (OME)

Authors	Year	No. of patients (ears)	Mean age	Study design	Intervention	Follow-up	Result
Chen *et al*.[26]	2001	67 (100)	46	Retrospective cohort	Grommet insertion and tympanocentesis	11 years	The prevalence of middle-ear complications in the tympanocentesis group (33%) was less than that in the grommeted group (90%)
Charusripan & Khattiyawittayakun [27]	2017	43 (43)	49.6	Prospective randomised controlled trial	Grommet insertion and observation	6 months	70% patients in the intervention group without suffering otorrhoea; hearing improvement was more obvious in the intervention group
Liang *et al*.[28]	2011	85 (124)	46.1	Prospective cohort	Grommet insertion, tympanocentesis and observation	842.1days	There was no significant difference in the resolution rates of OME among patients who received conservative treatment, those who underwent tympanostomy with aspiration or those who received grommet insertion
Xu *et al*.[9]	2008	96 (135)	48.8	Prospective quasirandomised clinical trial	Grommet insertion and tympanocentesis	2 years	A step-by-step approach should be used when choosing the treatment method for post-irradiation OME (i.e. first apply tympanocentesis)
Young *et al*.[12]	1995	18 (18)	52	Retrospective cohort	Grommet insertion and tympanocentesis	5 years	Tympanocentesis may be preferable to insertion of a ventilatory tube in patients with nasopharyngeal carcinoma who have OME

Table 2. Pros of BET for post-irradiation otitis media with effusion (OME)

Authors	Year	No. of patients (ears)	Mean age	Study design	Follow-up	Result
Ai *et al.*[31]	2024	36 (51)	53.58	Comparative study	12 months	BET plus grommet insertion is an effective treatment method for post-irradiation OME
Pan & Wang[19]	2022	124 (167)	48.56	Prospective randomised controlled trial	12 months	BET in the treatment of post-irradiation OME could improve clinical efficacy and improve Eustachian tube function and hearing function, so its use is recommended
Zhu & Sun[20]	2023	92	51.93	Prospective randomised controlled trial	6 months	BET in the treatment of post-irradiation OME can improve the total effective rate of treatment and reduce the threshold, ear effusion inflammation factor levels, ETDO−7 scores and the complication rate

Table 3. Cons of BET for post-irradiation otitis media with effusion (OME)

Authors	Year	No. of patients (ears)	Mean age	Study design	Follow-up	Result
Sun *et al.*[21]	2020	58 (74)	50.1	Retrospective	24 months	BET cannot significantly improve efficacy of refractory OME after radiotherapy for NPC in the long term
Wong & Prepageran [22]	2021	12 (14)	39.1	Cohort pilot study	24 weeks	BET was not shown to be beneficial for post-radiotherapy Eustachian tube dysfunction in NPC patients
Plaza *et al.*[23]	2020	Consensus on treatment of obstructive Eustachian tube dysfunction with balloon Eustachian tuboplasty				A history of radiotherapy in the Eustachian tube region is a contraindication of BET

- Treatment of otitis media with effusion after radiotherapy is more difficult than that of ordinary chronic otitis media with effusion
- Tympanocentesis and myringotomy with grommet insertion are the conventional treatments for otitis media with effusion after radiotherapy
- Tympanocentesis is recommended as the preferred treatment because it has fewer complications
- Balloon dilatation of the Eustachian tube is a new treatment method, which can improve the function of Eustachian tube after radiotherapy in the short term, but it is not known whether it is really suitable for otitis media with effusion after radiotherapy

With the deepening of research, we have a new understanding of the anatomy, physiology and diagnosis of the Eustachian tube. However, the standard of Eustachian tube dysfunction aetiology is still unclear, and there are no effective and reliable Eustachian tube dysfunction tests. At present, there are no recognised clinical guidelines, and long-term clinical research with a large sample size still needs the joint efforts of otology physicians and scientists. But there is reason to anticipate that with the further development of clinical research, these problems will eventually be resolved. In further research, we can focus on the indications and timing of different treatments and strengthen the management of post-operative complications. At the same time, the pathological mechanisms of OME can be further explored for new ways to improve function of the Eustachian tube after radiotherapy in the long term.

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Conflicts of interest. The authors declare none.

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