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Research status of otitis media with effusion after radiotherapy

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Abstract

Objective

This brief review summarizes the efficacy of the treatments for postirradiation otitis media with effusion (OME).

Method

Literature review.

Results

Studies suggest that tympanocentesis is recommended for patients with postirradiation OME. The efficacy of balloon dilatation eustachian tube for postirradiation OME remains unclear.

Conclusion

The efficacy of different treatments for postirradiation OME is unclear. Therefore, there are no recognized clinical guidelines, and long-term clinical research with a large sample size is needed.

Key words

Nasopharyngeal carcinoma, Radiation therapy, Otitis media with effusion, Eustachian tube, Balloon dilation of eustachian tube.

Nasopharyngeal carcinoma (NPC) occurs in all countries in the world, but there is an obvious regional differences, 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 etiology of NPC is still uncertain, but it is currently considered to be a

SUMMARY

- The treatment of otitis media with effusion after radiotherapy, which is a common ear complication of nasopharyngeal carcinoma 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 eustachian tube is a new treatment method, which can improve the function of eustachian tube after radiotherapy in the short term, but whether it is really suitable for otitis media with effusion after radiotherapy needs further discussion.

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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 recognized 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 getting higher and higher. 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 them, otitis media with effusion (OME) is a common ear complication of NPC after radiotherapy. About 30.3%-40% of NPC patients had secondary OME, and the prevalence of OME increased significantly after radiotherapy, reaching 50%-78.3%[2]. Postirradiation OME is more specific and cannot achieve as good results as the treatment of ordinary OME, and there are still no treatment guidelines.

As for the etiology of OME before radiotherapy of NPC, current studies have mainly focused on the effect of tumor on eustachian tube dysfunction (ETD). Tumor compression and tumor invasion of the tensor veli palatini muscle (TVPM), levator velum palatini muscle (LVPM) or other corresponding nerves causing paralysis, or the tumor invaded the eustachian tube (ET) cartilage, and the wall of the cartilage segment collapsed, resulting in the eustachian tube opening dysfunction[3].

During the 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 ETD, 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 eustachian tube (BET), 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 summarizes the efficacy of tympanocentesis, myringotomy with grommet insertion and balloon dilatation eustachian tube for postirradiation 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 edema at 6 months after radiotherapy, and edema subsided at 6-12 months. OME usually appears 3 to 6 months after radiotherapy[7].

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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% and 15%, the incidence of external ear canal infection or persistent otorrhea was 1% and 6.4%, and the incidence of tympanic adhesion was 1% and 1.5%.And the recurrence rates of tympanocentesis and myringotomy with ventilation tube insertion were 23% and 6%, respectively[9, 10].

Patients with NPC are more difficult to treat otorrhea after ventilation tube insertion due to their decreased resistance, so the effect of short-term hearing improvement is often offset by long-term otorrhea[11]. Some scholars even believe that grommet insertion should be prohibited for postirradiation 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[9] believes that myringotomy with grommet insertion is desirable and complications can be controlled through prevention and treatment of middle ear infection. A study have suggested that the earlier the grommet insertion of OME after NPC radiotherapy, the faster the functional recovery of eustachan tube, and the better the efficacy of postirradiation OME[13].

Some studies have proposed that the ventilation tube insertion time be shifted forward. Xian[14] conducted grommet insertion in NPC patients without OME before radiotherapy and followed them up for 12 months, and found that it could reduce the occurrence of OME after radiotherapy. Grommet insertion can not only help drain fluid, but also reduce the burden of eustachian tube, so that the 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.

The methods each have advantages and disadvantages. The 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 have significantly improved the symptom remission of patients. Although there are no guidelines for the treatment of OME after radiotherapy, lots of studies recommend that a step by step approach should be used when choosing the treatment method for postirradiation OME. And controlling the radiation-induced inflammation in areas such as the ears, nose, sinuses, and nasopharynx is also important.

Balloon dilatation eustachian tube (BET)

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, ETD is still a hidden danger of recurrence. In 2010, Ockerman[16] first reported the use of BET in the treatment of obstructive ETD. Subsequently, a large number of clinical experimental studies related to

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BET were carried out, and the operation was gradually recognized, which brought hope for the treatment of refractory OME. The BET operation was performed using nasal endoscopy. Under the guidance of a guide wire, the balloon was placed into the ET isthmus at a depth of about 2cm and the balloon pressure was 10bar for 2min. Silvola believed that the BET has the following mechanisms: (1) Expanding ET and improving ET function; (2) The reduction of inflammation can promote tissue regeneration. Under the condition that the underlying etiology is controlled, the damaged mucosa and submucosal tissues are crushed and scour away by surgery, creating conditions for tissue regeneration.[17].

Randrup and Ovsen[18] conducted quality evaluation and risk assessment on BET, pointing out that the current research has confirmed the safety and feasibility of BET, and provided some help for the improvement of patients' symptoms. Some studies on postirradiation OME suggest that BET can not only improve the eustachian tube function and hearing status, but also improve clinical efficacy with good safety[19,20]. However, other studies suggested that the ETS-7 score was the highest at 6 months after surgery, and then dropped sharply from 6 months to 24 months after surgery, suggesting that BET could only significantly improve the ET function of NPC after radiotherapy for a period of time[21]. On the contrary, Wong have compared the surgical effects of NPC patients with non-NPC patients , suggesting that BET does not show any benefit for eustachian tube dysfunction in NPC patients after radiotherapy[22]. A Consensus on treatment of obstructive ET dysfunction with BET published in Spain in 2020 lists radiation therapy in the Eustachian tube area as a contraindication for balloon dilation[23]. BET is helpful for the improvement of symptoms in OME patients after NPC radiotherapy in the short term, but the long-term effect is still unknown. Whether the application of BET in such patients is recommended or whether it is in line with social and economic benefits needs further discussion[18,24,25]. Table 2 and Table 3 show the pros and cons using BET in postirradiation OME. Therefore, rigorous and long-term RCTs or randomized controlled studies are necessary.

With the deepening of the research, we have a new understanding of the anatomy, physiology and diagnosis of ET. However, the standard of ETD etiology is still unclear, and there are no effective and reliable ETD functional tests. At present, there are no recognized 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 believe 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. Strengthen the management of postoperative complications. At the same time, the pathological mechanisms of OME can be further explored to explore new ways to improve the 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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Table 1. Studies of Grommet insertion and Tympanocentesis for postirradiation OME

Authors	year	No. of patients （ears）	Mean age	Study design	Intervention	follow-up	Result
C Y Chen[26]	2001	67（100）	46	Retrospective cohort	Grommet insertion and Tympanocentesis	11y	The prevalence of middle ear complications in the tympanocentesis group (33%) was less than that in the grommeted group (90%)
Paninee Charusripan[27]	2017	43(43)	49.6	Prospective randomized controlled trial	Grommet insertion and Observation	6m	70% patients in the intervention group without suffering otorrhea. And hearing improvement was more obvious in the intervention group.
Kai-Li Liang[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
Yao-Dong Xu[9]	2008	96(135)	48.8	Prospective quasirandomized clinical trial	Grommet insertion and Tympanocentesis	2y	A step by step approach should be used when choosing the treatment method for postirradiation OME. That is, first apply tympanocentesis
Y H Young[12]	1995	18(18)	52	Retrospective cohort	Grommet insertion and Tympanocentesis	5y	Tympanocentesis may be preferable to insertion of a ventilatory tube in patients with nasopharyngeal carcinoma who have otitis media with effusion.

Table 2. Pros of BET for postirradiation OME

Authors	year	No. of patients（ears）	Mean age	Study design	follow-up	Result
Maomao Ai[29]	2024	36(51)	53.58	Comparative Study	12m	BET plus Grommet insertion is an effective treatment method for postirradiation OME
Pan HS[19]	2022	124(167)	48.56	Prospective randomized controlled trial	12m	BET in the treatment of postirradiation OME could improve clinical efficacy and improve eustachian tube function and hearing function condition, so it is recommended to use.
Zhu SR[20]	2023	92	51.93	Prospective randomized controlled trial	6m	BET in the treatment of postirradiation OME can improve the total effective rate of treatment and reduce the threshold, the ear effusion infammatcry factor levels, the ETD0-7 scores and the complication rate

Table 3. Cons of BET for postirradiation OME

Authors	year	No. of patients（ears）	Mean age	Study design	follow-up	Result
Hongcun Sun[21]	2020	58(74)	50.1	Retrospective	24m	BET can not significantly improve efficacy of refractory OME after radiotherapy for NPC for long term.
M S L Wong[22]	2021	12(14)	39.1	cohort pilot study	24w	BET was not shown to be beneficial for post-radiotherapy ETD in NPC patients
Guillermo Plaza[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

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