

Affection of the middle ear after radiotherapy for head and neck tumors

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Aim

The aim of this study is to evaluate the effect of radiotherapy (RT) as one of the modalities of treatment in patients with head and neck tumors on the Eustachian tube and middle ear.

Study design

This is a prospective study.

Material and methods

This study included 20 patients suffering from squamous cell carcinoma of the head and neck other than nasopharynx and parotid. They were treated either by surgery and postoperative radiotherapy or by primary radiotherapy alone or by concomitant chemoradiotherapy. Audiological evaluation was performed both pre-treatment and post-treatment in the form of pure tone threshold audiometry (PTA), tympanometry, stapedius acoustic reflex and eustachian tube (ET) function test.

Results

The 20 patients corresponded to 40 ears which were analyzed. Post RT tympanometry done revealed 16 (40%) ears with normal type A tympanogram and 24 (60%) ears with abnormal tympanometry findings, Post RT ET function test done revealed 7 (17.5%) ears with good ET function and 33 (82.5%) with abnormal ET function, acoustic reflex done post RT revealed 36 (90%) ears with absent acoustic reflex bilaterally and 4 (10%) ears with preserved acoustic reflex and Post RT PTA done revealed 16 (40%) ears with normal PTA, 13 (32.5%) ears with conductive hearing loss (CHL), 8 (20%) ears with sensori neural hearing loss (SNHL) and 3 (7.5%) ears with mixed hearing loss.

Conclusion

Patients with head and neck tumors given RT as one of the modalities of treatment have a high incidence of affection of middle ear function and ET dysfunction as well as development of CHL.

Keywords

tympanometry, pure tone audiometry, acoustic reflex, Eustachian tube function test.

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Introduction

Irradiation has become the therapy of choice for many malignant tumors of the head and neck and is the only treatment for some of them. However, in the application of irradiation, its effect on the adjacent normal tissues must be considered. However, no strategies have been adopted to shield the ear to minimize radiation exposure. Several studies were conducted to describe the Eustachian tube (ET) function and middle ear status in patients with nasopharyngeal carcinoma after radiotherapy (RT) [1]. In this study, we aimed to evaluate the effect of RT on the ET and middle ear in patients with head and neck tumors other than nasopharynx and parotid carcinoma and to investigate the possibility of affection of these sites in patients with the radiation field relatively distant from the ear.

Materials and methods

This study included 20 patients suffering from squamous cell carcinoma of the head and neck who were treated

either by surgery and postoperative RT or by primary RT alone or by concomitant chemoradiotherapy (CRT). The study was conducted in a prospective manner during the period from February 2012 to February 2013. Patients were selected from the otolaryngology head and neck surgery outpatient clinic of Kasr El Aini University Hospital. The surgical management was carried out in the Department of Otolaryngology Head and Neck Surgery in Kasr El Aini University Hospital and the RT or CRT were given in the Nuclear Medicine Department in Kasr El Aini University Hospital. The pretreatment and post-treatment audiological assessment were performed in the outpatient audiology unit in Kasr El Aini University Hospital.

Patient selection and pretreatment tumor work-up

Patients suffering only from head and neck squamous cell carcinoma were included in our study. Carcinomas of the parotid, nasopharynx, or temporal bone were excluded from the study. Patients were subjected to careful history-taking and complete otolaryngological

and head and neck examination. Computed tomography of the neck was performed (axial with coronal and sagittal reformatting) for assessment of the primary tumor as well as the neck nodes. Direct laryngoscopy under general anesthesia was performed for mapping the tumor and for biopsy-taking for histopathological examination. The primary tumor and the neck were classified on the basis of physical examination, computed tomography, and endoscopic findings. According to the site and TNM staging of the tumor, patients were offered either surgery and postoperative RT or primary RT alone or concomitant CRT. According to the site of the tumor, there were 16 (80%) patients with laryngeal carcinoma [12 glottic (60%) and four supraglottic (20%) carcinoma], two (10%) patients with postcricoid carcinoma, and two (10%) patients with carcinoma of the oral tongue. According to the T classification of the primary tumor, five (25%) patients were classified as T1, two (10%) patients as T2, seven (35%) patients as T3, and three (15%) patients as T4. Staging of the neck revealed that 14 (70%) patients were classified as N0, three (15%) patients as N1, and three (15%) patients as N2.

Management of the tumor

According to the site and TNM staging of the primary tumor, eight (40%) patients underwent surgery and postoperative RT, six (30%) patients were treated by primary RT alone, and six (30%) patients were treated by concomitant CRT. Of the eight patients who underwent surgery, five (25%) had en-bloc neck dissection (two bilateral and three unilateral neck dissection) for treatment of the neck.

Irradiation

RT was used in all patients either as a sole primary treatment ($n = 6$; 30%) or as an adjuvant postoperative treatment ($n = 8$; 40%) or concomitantly with chemotherapy ($n = 6$; 30%). The field of RT included the site of the primary tumor and possible areas of local spread. Inclusion of the sites of regional spread to the neck nodes in the field of irradiation was carried out according to the primary tumor characteristics, namely site, T stage, differentiation, and depth of invasion, in tongue cancer as well as histopathological examination of the neck dissection specimen was carried out. The dose of RT ranged from 60 to 70 Gy and the daily fractionation ranged from 1.8 to 2 Gy. Table 1 demonstrates patient's tumor and treatment details.

Audiological assessment

Audiological evaluation was performed both before treatment of the neoplasia and 3 weeks after finishing the full dose of irradiation. For audiological evaluation,

Table 1 Patient's tumor and treatment details

	<i>n</i> (%)
Tumor site	
Glottic	28 (70)
Supraglottic	4 (10)
Postcricoid	4 (10)
Tongue	4 (10)
Tumor stage	
T1	10 (25)
T2	10 (25)
T3	14 (35)
T4	6 (15)
Nodal stage	
N0	28 (70)
N1	6 (15)
N2	6 (15)
Treatment	
Surgery and radiotherapy	16 (40)
Radiotherapy	12 (30)
Chemoradiotherapy	12 (30)
Dose of irradiation (Gy)	
60	10 (25)
66	14 (35)
70	16 (40)

the following procedures were used: (a) pure tone threshold audiometry (PTA) with assessment of air bone gap if conductive hearing loss (CHL) was present, (b) acoustic emittance measurement including tympanometry and stapedius acoustic reflex ipsilateral and contralateral, and (c) ET function test. Only patients with normal acoustic emittance measurement and good ET function before treatment were included in our study. Before starting irradiation, the PTA revealed six patients with variable grades of sensorineural hearing loss (SNHL), five of them were with bilateral affection; however, this did not have any influence on our study as we focused on the ET function.

Statistical analysis

The statistical package of social science (SPSS) program version 16 designed for Windows was used (IBM Corporation, Chicago, USA). Descriptive statistics for all parameters was carried out. The Pearson χ^2 -test was used for statistical analysis. Significance was set at P value of 0.05 or less. Statistical analysis regarding the audiological parameters for comparison between pre-RT and post-RT was not obtained as the pretreatment audiological parameters were always constant.

Results

This study included 19 (95%) male patients and one (5%) female patient. The patients' age ranged

between 42 and 76 years with a mean of 63 years. A total of 20 patients corresponded to 40 ears that were analyzed. With respect to the acoustic emittance results (tympanometry), the 40 ears (20 patients) evaluated in this study had normal tympanometry (type A) before the initiation of irradiation. Post-RT tympanometry revealed 16 (40%) ears with normal type A tympanogram and 24 (60%) ears with abnormal tympanometry findings, 10 (25%) of them had type B tympanogram denoting the middle ear effusion and 14 (35%) had type C tympanogram denoting the ET dysfunction. In the analysis of the ET function, the 40 ears (20 patients) evaluated in this study had normal tympanometry (type A) before the initiation of irradiation and the post-RT ET function test revealed seven (17.5%) ears with good ET function, 23 (57.5%) with poor ET function, and 10 (25%) with blocked ET. Acoustic reflex performed after RT revealed 36 (90%) ears with absent acoustic reflex bilaterally and four (10%) ears with preserved acoustic reflex. Post-RT PTA revealed 16 (40%) ears with normal PTA, 13 (32.5%) ears with CHL, eight (20%) ears with SNHL, and three (7.5%) ears with mixed hearing loss. Of the ears that had CHL or mixed hearing loss, the air bone gap ranged between 5 and 35 dB with a mean of 9.95 ± 13.29 . Table 2 demonstrates the post-treatment audiological results of the 40 ears. Comparative statistical analysis regarding tumor and treatment characteristics compared with post-RT audiological findings are shown in Table 3.

Table 2 Post-treatment audiological results of the 40 ears

	n (%)
Tympanometry	
Type A	16 (60)
Type B	10 (25)
Type C	14 (35)
Eustachian tube function	
Good	7 (17.5)
Poor	23 (57.5)
Blocked	10 (25)
Acoustic reflex	
Absent	36 (90)
Preserved	4 (10)
PTA	
Normal	16 (40)
CHL	13 (32.5)
SNHL	8 (20)
Mixed hearing loss	3 (7.5)
ABG^a	
Range	5 – 35
Mean \pm SD	9.95 \pm 13.29

ABG, air bone gap; CHL, conductive hearing loss; PTA, pure tone threshold audiometry; SNHL, sensorineural hearing loss; ^aABG among the ears with CHL (13) and mixed hearing loss (3).

Discussion

Irradiation is commonly used either alone or in combination with surgery and/or chemotherapy for the treatment of malignant tumors of the head and neck. As a result of RT, the tympanic membrane may become dull, retracted, congested, or may remain normal; this change in the tympanic membrane is usually transient and reversible. Coplan *et al.* [2] in their study revealed thickening of the tympanic membrane after RT. Bhandare *et al.* [3] found erythema and opacification of the tympanic membrane as one of the signs of middle ear inflammation resulting from irradiation-induced middle ear damage. Bursary *et al.* [4] noted radiation otitis media as an early and transient change following ionizing radiation to the head and neck. They explained the mechanism by obstruction of the ET due to swelling of the mucosa following irradiation resulting first in the absorption of the oxygen then later the nitrogen from the middle ear. Because of the negative pressure in the middle ear cavity, transduction can take place, which is enhanced by the edema of the middle ear mucosa and the dilatation of the blood vessels resulting in sterile fluid collection in the middle ear cavity. In this study conducted on 20 patients with laryngeal, hypopharyngeal, and tongue cancer, post-RT tympanometry performed 3 weeks after the end of treatment revealed that 60% of the ears developed abnormal tympanometry findings: 25% had type B tympanogram and 35% had type C tympanogram. Upadhyaya *et al.* [1] conducted a similar study and reported 68% abnormal tympanometry findings among their patients, where 25% had serous middle ear effusion with type B tympanogram and 43% had ET dysfunction with type C tympanogram. They also stated that the incidence of serous middle ear effusion declined 3 months after RT, whereas ET dysfunction persisted. Bhandare *et al.* [3] found a 28.6% incidence of post-RT middle ear toxicity, which included radiation otitis media, otitis media with effusion, and ET dysfunction. They stated middle ear complication post-RT to the head and neck as the most common complication. In this study, other audiological parameters reflecting post-RT ET function revealed 57.5% patients with poor ET function and 25% with blocked ET function. Although the post-RT tympanometry findings were abnormal in 60% patients, the post-RT ET function was abnormal in 82.5%; this would point to two observations: the first is the high prevalence of ET affection among patients treated by RT in head and neck cancer and the second is the significant possibility of the presence of abnormal ET function in head and neck cancer patients treated by RT despite normal tympanometry findings. Supporting this, the acoustic reflex test results in this study revealed that 90% of the ears had an absent acoustic reflex despite that only a

Table 3 Comparative statistical analysis between tympanometry, Eustachian tube function, acoustic reflex, and development of conductive hearing loss results with respect to tumor and treatment data of the 40 ears

	Tympanogram				Eustachian tube function				Acoustic reflex			Postradiotherapy CHL		
	Type A	Type B	Type C	<i>P</i>	Good	Poor	Blocked	<i>P</i>	Present	Absent	<i>P</i>	Yes	No	<i>P</i>
Tumor site [<i>n</i> (%)]														
Glottic	11 (27.5)	7 (17.5)	10 (25)	0.37 (NS)	5 (12.5)	16 (40)	7 (17.5)	0.28 (NS)	2 (5)	26 (65)	0.041 (S)	11 (27.5)	17 (42.5)	1 (NS)
Supraglottic	1 (2.5)	1 (2.5)	2 (5)		0	3 (7.5)	1 (2.5)		0	4 (10)		1 (2.5)	3 (7.5)	
Postcricoid	2 (5)	0	2 (5)		2 (5)	2 (5)	0		2 (5)	2 (5)		2 (5)	2 (5)	
Tongue	2 (5)	2 (5)	0		0	2 (5)	2 (5)		0	4 (10)		2 (5)	2 (5)	
Tumor stage [<i>n</i> (%)]														
T1	5 (12.5)	3 (7.5)	2 (5)	0.04 (S)	1 (2.5)	6 (15)	3 (7.5)	0.4 (NS)	0	10 (25)	0.21 (NS)	4 (10)	6 (15)	0.62 (NS)
T2	3 (7.5)	3 (7.5)	4 (10)		2 (5)	5 (12.5)	3 (7.5)		2 (5)	8 (20)		3 (7.5)	7 (17.5)	
T3	8 (20)	1 (2.5)	5 (12.5)		4 (10)	9 (22.5)	1 (2.5)		2 (5)	12 (30)		5 (12.5)	9 (22.5)	
T4	0	3 (7.5)	3 (7.5)		0	3 (7.5)	3 (7.5)		0	6 (15)		4 (10)	2 (5)	
Nodal stage [<i>n</i> (%)]														
N0	12 (30)	5 (12.5)	11 (27.5)	0.55 (NS)	5 (12.5)	18 (45)	5 (12.5)	0.11 (NS)	4 (10)	24 (60)	0.21 (NS)	10 (25)	18 (45)	0.51 (NS)
N1	2 (5)	2 (5)	2 (5)		0	4 (10)	2 (5)		0	6 (15)		2 (5)	4 (10)	
N2	2 (5)	3 (7.5)	1 (2.5)		2 (5)	1 (2.5)	3 (7.5)		0	6 (15)		4 (10)	2 (5)	
Treatment [<i>n</i> (%)]														
S+RT	5 (12.5)	4 (10)	7 (17.5)	0.85 (NS)	2 (5)	10 (25)	4 (10)	0.53 (NS)	2 (5)	14 (35)	0.36 (NS)	8 (20)	8 (20)	0.31 (NS)
RT	5 (12.5)	3 (7.5)	4 (10)		1 (2.5)	8 (20)	3 (7.5)		0	12 (30)		4 (10)	8 (20)	
CRT	6 (15)	3 (7.5)	3 (7.5)		4 (10)	5 (12.5)	3 (7.5)		2 (5)	10 (25)		4 (10)	8 (20)	
Dose of irradiation (Gy) [<i>n</i> (%)]														
60	4 (10)	3 (7.5)	3 (7.5)	0.98 (NS)	2 (5)	5 (12.5)	3 (7.5)	0.94 (NS)	2 (5)	8 (20)	0.2 (NS)	5 (12.5)	5 (12.5)	0.71 (NS)
66	6 (15)	3 (7.5)	5 (12.5)		3 (7.5)	8 (20)	3 (7.5)		2 (5)	12 (30)		4 (10)	10 (25)	
70	6 (15)	4 (10)	6 (15)		2 (5)	10 (25)	4 (10)		0	16 (40)		7 (17.5)	9 (22.5)	

CHL, conductive hearing loss; CRT, chemoradiotherapy; RT, radiotherapy; S+RT, surgery and radiotherapy.

proportion of them had abnormal tympanometry and PTA findings. However, Liberman *et al.* [5] reported only 18% type B and type C tympanometry findings among 11 patients with laryngeal and hypopharyngeal carcinomas treated by CRT.

In our study, assessment of the pattern of post-RT PTA showed that CHL developed in 16 (40%) ears; of those three were mixed hearing loss, as they had SNHL before irradiation. It is worth reporting that none of our patients developed SNHL as a result of RT. Aringa *et al.* [6] reported 26.3% SNHL among patients with head and neck tumors treated with RT, but most of the patients in their study had nasopharyngeal carcinoma. In our study, all patients had laryngeal, hypopharyngeal, or tongue carcinoma as we excluded tumors that could directly affect the middle ear function, particularly nasopharyngeal carcinoma. In view of our results, we could state that irradiation given as a modality of treatment for head and neck tumors, which are relatively distant from the ear, could affect the middle ear function while sparing the inner ear. In the analysis for the influence of different tumor characteristics (site, tumor stage, and nodal stage) on the middle ear function, the only variable that had statistical influence on the tympanogram findings was the tumor stage ($P = 0.04$); this could be explained by increasing the dose and field of irradiation to include the neck with increasing tumor stage. The vast majority of our patients had laryngeal or hypopharyngeal cancer (18 patients corresponding to 36 ears) where the upper limit of irradiation was the hyoid bone, of them 14 ears developed postirradiation CHL. Only two patients had tongue cancer corresponding to four ears where the upper limit of irradiation was the soft palate, of them two ears developed postirradiation CHL. We cannot correlate between the upper level of irradiation and the development

of CHL because of the relatively low number of tongue cancer patients.

Conclusion

Patients with head and neck tumors apart from the nasopharynx and parotid have a high incidence of affection of the middle ear function namely middle ear effusion and ET dysfunction as well as development of CHL. In those tumors, the inner ear function is usually spared as the field of irradiation is relatively distant from the ear. The possibility for the development of middle ear effusion and ET dysfunction increases with increased tumor stage. Larger sample size studies with homogenous tumor sites are recommended. In addition, long-term follow-up for the middle ear function is needed to investigate the reversibility of middle ear changes following RT for the treatment of patients with head and neck cancer.

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Conflicts of interest

None declared.

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