Ototoxic Effects of Irradiation

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Abstract In this study ototoxic effect of ionizing radiation was studied in 70 ears with minimum follow up of 6 months post radiotherapy. Patients of nasopharyngeal carcinoma and with conductive deafness pre radiotherapy were excluded from the study to eliminate mechanical obstruction that may play role in Eustachian tube dysfunction. We found that Eustachian tube dysfunction and conductive deafness were reversible where as Sensorineural hearing loss was an irreversible effect of radiotherapy. Dose of radiation was directly proportional to ototoxicity, minimum 60 Gys of total radiation dose was required to produce significant ototoxicity.

Keywords Sensorineural hearing loss · Eustachian tube · Conductive hearing loss · Radiotherapy

Introduction

Irradiation is commonly used either alone or in combination with surgery for the treatment of malignant tumors of head and neck. It has become the therapy of choice for many lesions and is the only treatment for some lesions. However, in the application of irradiation to any disease process, its effect on adjacent normal tissues must be considered as an integral part of the therapy from the view point of both morbidity and mortality. Certain strategies

have been developed to minimize radiation exposure to vital structures including spinal cord, brainstem, optic chiasm, pituitary gland, and eyes, but none of them has been adopted to shield the ear. Therefore, the hearing apparatus is invariably included in the radiation field. The effects of ionizing radiation on different organs and tissue elements have been widely studied, but the data concerning the ototoxic effects of radiation are rather meager. Majority of the studies conducted describe Eustachian tube function and middle ear status in patient with nasopharyngeal carcinoma after radiotherapy. Nasopharyngeal carcinoma itself causes mechanical dysfunction of the Eustachian tube due to blockage of pharyngeal opening of the Eustachian tube. So results are biased that is why we excluded patients of nasopharyngeal carcinoma in this study.

Material and Method

This is a prospective study of 58 patients carried out at Department of ENT-HNS, Government Medical College, New Civil Hospital, Surat. Total 58 patients of histologically proven carcinoma of head and neck who were advised external beam radiotherapy and who had normal Eustachian tube function and middle ear status were included in this study. None of the patients were exposed to chemotherapy before and during the study period. All the patients were subjected to a detailed history taking of ear, nose and throat symptoms, ENT examination, diagnostic nasal endoscopy. Only those patients who had normal diagnostic endoscopy were subjected to pure tone audiometry and impedance audiometry and those with normal impedance audiometry were included in the study. They were exposed to this protocol total 4 times i.e. pre-radiotherapy, immediately post-radiotherapy, 3 months post radiotherapy and

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6 months post radiotherapy. From these 58 patients 12 patients received bilateral radiotherapy due to midline disease. So this study comprised of total 70 ears.

All the patients received radiotherapy at Lions Cancer Detection Centre, Surat. External beam radiotherapy was given by Cobalt-60 with Theratron 780c machine. None of the patients undergoing radiotherapy were provided any shield to protect hearing apparatus as such facility is not available in this institute. The treatment protocol for curative radiotherapy was 2 Gy per fraction and five fractions per week for 6 weeks, i.e. conventional fractionation. The protocol for palliative radiotherapy was one sitting of 6 Gy per week for 6 weeks. The details of the location of the tumors were as under (Table 1).

Observation and Discussion

Maximum number of patients suffering from head and neck carcinoma were in the age group of 51–70 years indicating that head and neck carcinomas mostly occur in 5th and 6th decade of life.

With male: Female ratio of 8:2. The reason for this may be more prevalence of consumption of tobacco products and alcohol in males as compared to females as tobacco and alcohol are the most common etiologic agents in head and neck carcinoma.

Common complaints experienced by the patients after irradiation was ear heaviness, earache, decreased hearing, tinnitus and dizziness. All these were acute and transient complaints which may start as early as immediately after the radiotherapy, may appear later, might last till 6 months. Bohne et al. [1] in their study have mentioned slight pain or discomfort in the ear as well as tinnitus as symptoms of serous otitis media resulting due to ionizing radiation of the ear. They attributed tinnitus to acute changes consisting of edema of the middle ear mucosa, radiation otitis media and transient vasculitis of the vessels of the inner and middle ear. Borsanyi et al. [2] and Evans et al. [3] found that

tinnitus was one of the symptoms of radiation otitis media and was an occasional, early and temporary complaint in the affected ear.

As a result of radiotherapy tympanic membrane may become dull, retracted, bulged, congested or may remain normal. This change in the appearance of the tympanic membrane is transient and reversible. Coplan J et al. [4] in their study of hearing loss after radiotherapy revealed thickening of the tympanic membrane while Bhandare et al. [5] found erythema (congestion), or opacification of the tympanic membrane as one of the signs of middle ear inflammation resulting from radiation induced middle ear damage (Table 2).

“A” type Tympanogram suggests normal middle ear status while “B” type of Tympanogram is suggestive of serous otitis media and “C” type of Tympanogram is suggestive of Eustachian tube dysfunction. Above table shows that following radiotherapy serous otitis media and Eustachian tube dysfunction can occur as temporary and reversible side effects. These can occur as early as immediately following radiotherapy to up to 6 months following radiotherapy. At 6 months post radiotherapy number of patients with serous otitis media and Eustachian tube dysfunction decreased significantly as compared to immediate post-radiotherapy. Bhandare et al. [5] concluded that radiotherapy toxicity is observed in all parts of the auditory system with median doses varying between 60 to 66 Gy. They found 28.6% incidence of middle ear toxicity which included radiation otitis media or otitis media with effusion, Eustachian tube dysfunction and tympanic membrane sclerosis or perforation. Amongst these, radiation otitis media has been reported as the most common middle ear complication immediately post-radiotherapy or 3 months after radiotherapy suggestive of transient and reversible nature of this condition after irradiation of the ear. Coplan J et al. [4] revealed reduced compliance in tympanometry following irradiation of the auditory apparatus of the same side. Borsanyi J S et al. [2] noted ‘radiation otitis media’ as an early and transient change following ionizing radiation of the ear, they explained mechanism of its occurrence as follow:

Obstruction of the Eustachian tube, due to swelling of the mucosa following irradiation, resulted 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, transudation took place which was enhanced by the edema of the middle ear mucosa and the dilatation of the blood vessels resulting in the sterile fluid collection. L F Wang et al. [6] concluded that post-radiotherapy otitis media with effusion is considered to be a result of Eustachian tube dysfunction after radiation and plays a major part in conductive hearing loss after radiotherapy (Table 3).

Table 1 Primary site of malignancy versus number of cases

Primary site of malignancy	Number of cases
Laryngopharynx	23
Oropharynx	08
Oral cavity	17
Neck (nodes with unknown primary)	01
Maxillary sinus	04
Parotids	03
Thyroids	02
Total	58

Table 2 Impedance audiometry

	Impedance audiometry	Immediate post RT Number/% of patients	3 months post RT Number/% of patients	6 months post RT Number/% of patients
RT radiotherapy	A type tympanogram	22/31.42	27/38.57	43/61.42
	B type tympanogram	18/25.71	11/15.71	4/5.71
	C type tympanogram	30/42.85	32/45.71	22/31.42

Table 3 Average hearing threshold and average air-bone gap

	Pre RT (dB)	Immediately after RT (dB)	3 months post RT (dB)	6 months post RT (dB)
RT radiotherapy	Average hearing threshold	22.74	25.21	26.12
	Average air bone gap	9.22	18.09	19.29

Table 4 Sensory neural hearing loss

	Pre RT	Immediately after RT	3 months post RT	6 months post RT
RT radiotherapy, SNHL sensory neural hearing loss	No of cases/% of cases with SNHL	9 (New)+9 (Worsening of deafness)/25.71%	11 (New) + 10 (Worsening of deafness)/30%	11 (New) + 11 (Worsening of deafness)/31.43%

Table 5 Dose of RT versus impact on hearing

	Number of patients	Total dose of RT received (Gy)	Duration of RT (weeks)	Dose of RT per sitting (Gys)	Protocol	SNHL at 6 months post RT
RT radiotherapy, SNHL sensory neural hearing loss	47	60	6	2	5 days/week	22/47 (46.80%)
	11	36	6	6	1 day/week	0/11 (0%)

In our study, patients developed around 2.47 dB average hearing loss immediately post radiotherapy, 3.38 dB average hearing loss 3 months post radiotherapy, 2.96 dB average hearing loss 6 months post radiotherapy. Here average hearing threshold is average of hearing threshold at 500, 1000, 2000 and 3000 Hz frequencies. In Novotny's [7] research hearing impairment of 8.4 dB was noted after 12–72 Gys radiation dose which was more than our study. In Kozlov's [8] study on 10 guinea pigs, 8.9–9.1 dB hearing loss was demonstrated while Dias [9] noted average 9.9 dB deterioration of hearing threshold after 10–180 Gys radiation dosage which was also much more than our study.

In our study pre-radiotherapy only 5 (7.14%) cases were having conductive hearing loss and rest 65 (92.86%) cases were having no conductive deafness. Among these 65 cases, 32 (45.71%) cases developed conductive deafness immediately post-radiotherapy. 2 new cases developed conductive deafness at 3 months post-radiotherapy. But total number of cases with conductive deafness at 3 months post-radiotherapy remained same (32) as compared to immediate post-radiotherapy because 2 of them regained normal hearing. Number of cases with conductive deafness

at 6 months post-radiotherapy was 14 (20%). Out of these 14, 5 cases were those who developed conductive deafness only after 6 months of radiotherapy, while rest 9 cases were those who continued having conductive deafness. This means that total 20 (28.57%) cases regained normal hearing within 6 months of radiotherapy i.e. conductive deafness resulting from effects of radiotherapy is reversible in 28.57% of cases within 6 months following radiotherapy (Table 4).

From above table it is obvious that due to irradiation of the ear total 22 (31.43%) cases developed SNHL within 6 months of completion of RT. Among these 22 cases, 18 cases developed SNHL immediate post-RT, 3 cases developed SNHL 3 months post RT and 1 more case was added at 6 months post RT. Anteunis LJ et al. [10] (1994) concluded that at the end of 2 years up to 50% of patients developed a clinically relevant hearing loss both conductive and/or Sensorineural while in our study conductive hearing loss and SNHL are calculated separately. There are many studies which mention hearing loss as a consequence of irradiation of the hearing apparatus. Bohne et al. [1] found that conductive impairments occur during therapy but these usually disappear after completion of treatment

and resolution of the radiation otitis media. L F Wang et al. [6] concluded that hearing deterioration may begin as early as 3 months post RT.

In this study all the cases that developed any ototoxic effects after irradiation had received curative RT i.e. total 60 Gys, while none of the cases who received palliative RT i.e. total 36 Gys, developed any ototoxic effect indicating that minimum 50–60-Gys total radiation dose is required to produce noticeable ototoxic effects. Thibadoux et al. [11] found no statistically significant hearing loss in his study of 61 patients receiving 24 Gys of total radiation dosage. He concluded that the reason for this was low dosage of radiation and he found that at least 30 Gys of radiation is minimum requirement for producing hearing effects. Evans et al. [3] also did not find any statistically significant hearing loss in his study of 18 patients with total 55–60 Gys radiation dosage in daily fraction of 2–2.2 Gys. He concluded that hearing loss is unlikely if daily fraction is less than 2 Gys and total dose is less than 60 Gys.

Six patients out of 58 received palliative RT on weekly basis every week 6 Gys for total 6 weeks. None of them developed any kind of hearing loss. This means to have SNHL minimum 60 Gys of radiation exposure is required as rest 47 patient received 60 Gys, 46.80% of them developed SNHL (Table 5).

The fields and type of RT used in both groups i.e. curative and palliative were the same.

Conclusion

Otitis media with effusion and Eustachian tube dysfunction are temporary and reversible side effects of the irradiation of the ear.

Conductive hearing loss develops as a reversible side effect of radiation of the ear.

Sensorineural hearing loss is noticed after RT in total 22 (31.43%) of cases at 6 months post RT.

Dose of the radiation is proportional to development of ototoxicity. Total radiation dose of minimum 60 Gys is required to produce noticeable ototoxic effects.

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Competing interest None.

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