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Temporal bone tumours in patients irradiated for nasopharyngeal neoplasm

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Abstract

Radiation-associated tumours are rare complications of radiotherapy. This study seeks to highlight and discuss the clinically challenging problem of radiation-associated tumours (RATs) in the temporal bones of seven patients previously irradiated for nasopharyngeal neoplasm.

Seven patients (six males and one female) with radiation-associated temporal bone tumours are presented (five squamous cell carcinomas, one osteogenic sarcoma and one chondrosarcoma). The initial nasopharyngeal disease for which radiotherapy was indicated was nasopharyngeal carcinoma (six patients) and nasopharyngeal lymphoma (one patient). The latency period between radiotherapy and presentation of temporal bone tumours ranged from five years to 30 years with a mean of 12.9 years. All the patients underwent surgical tumour resection. Three patients had post-operative radiotherapy and one patient underwent pre- and post-operative chemotherapy. Two patients died from the disease within three months of treatment with one patient surviving 36 months at the time of writing. One patient died from an unrelated medical condition three months after surgery.

With refinement in radiotherapy techniques and the resultant increase in patient survival, there may be more patients with radiation-associated tumours in the future. It remains imperative for clinicians to be vigilant when patients previously irradiated for nasopharyngeal carcinoma present with otological symptoms as the key to the successful management of this condition lies in the early detection and expedient treatment of this difficult disease.

Key words: Temporal bone; Neoplasms, radiation induced; Radiation; Nasopharyngeal neoplasms

Introduction

Radiation therapy is an important modality of treatment in the management of patients with head and neck cancers. Although its usefulness was exploited to the extreme during the early years (Modan *et al.*, 1974), the increasing realization of the potentially persistent and debilitating complications of therapeutic radiation has restricted the use of this powerful tool. Radiation to the head and neck region is now reserved almost exclusively for the treatment of malignancies and certain benign neoplasms that can result in severe morbidity or mortality if treated with surgery alone. This modality of therapy is particularly important for nasopharyngeal cancers which are common in our part of the world.

Temporal bone complications after irradiation to the nasopharynx are frequently encountered with otitis externa (Lederman, 1985), otitis media (Elwany, 1985) sensorineural deafness being a common post-irradiation sequela and radiation-associated tumours of the temporal bone being rare complications. Although the radiation-associated tumours of the temporal bone have been reported sporadically, there has not yet been, to the best of our knowledge, any report of such tumours after irradiation specifically to the nasopharynx. This is a retrospective study of seven patients who were treated for radiation-associated temporal bone tumours in our institution, each having received radiation to the nasopharynx years before. The clinical presentations, treatment outcome and the difficult issues involved in the management of this complication are presented and discussed.

Materials and methods

Patients who had been previously irradiated for nasopharyngeal neoplasm and who subsequently developed temporal bone tumours were studied. These were consecutive patients treated in the Department over a three and a half year period (1 January 1994 to 31 June 1997). The case records of these patients were examined and the demographic data of the patients analysed.

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Results

A total of seven patients were identified. The details of each are summarized below.

Case 1

A 56-year-old Chinese man presented 10 years after radiotherapy for nasopharyngeal carcinoma with the complaint of left peri-auricular swelling and otorrhoea of seven months duration. The original nasopharyngeal carcinoma was staged T1N3M0 with a total of 5500 cGy of radiation rendered for the malignancy. The patient was disease-free in the nasopharynx after irradiation although his otherwise uneventful post-radiotherapy period was complicated two years later by the diagnosis of carcinoma of the bladder for which transurethral resection of bladder tumour (TURBT) was done. Five years after TURBT, the patient underwent injection sclerotherapy of oesophageal varices that was associated with alcoholic liver cirrhosis. In the same year, excision of a retroperitoneal small cell neuroectodermal tumour (of uncertain malignant potential) was undertaken without complications. The patient subsequently defaulted medical follow-up.

Three years later i.e. ten years after radiotherapy, patient returned to the Accident and Emergency department for the complaint of left periauricular swelling and otorrhoea of seven months duration. Physical examination showed a large fluctuant swelling in the left peri-auricular region with purulent material in the external auditory canal. Computerized tomography (CT) scan of the temporal bone and brain (Figure 1) demonstrated the presence of a large abscess cavity with extensive left temporal bone destruction and displacement of the left temporal lobe. Drainage of temporal abscess and debulking of an extensive temporal bone tumour was promptly undertaken and histology of tumour tissue showed squamous cell carcinoma. The patient was subsequently given 6600 cGy of radiation to the temporal bone but unfortunately died three months after surgery.

Case 2

A 64-year-old Chinese man had been treated with radiotherapy (6600 cGy) for nasopharyngeal carcinoma six years previously. A further course of radiotherapy was given for tumour recurrence a year later. He presented with right facial nerve paralysis and right bloody otorrhoea of two weeks duration. Examination showed lower motor neuron paralysis of his right facial nerve with a large friable polypoidal growth from the right external auditory canal. Biopsy of the canal growth showed malignant stromal chondrosarcoma (high grade). CT scan of the temporal bone (Figure 2) demonstrated the presence of an extensive destructive tumour involving the right mastoid bone, the posterior wall of the petrous temporal bone, the middle ear and the dura of the posterior cranial fossa. The patient subsequently underwent right mastoidectomy/debulking of tumour and post-operative radiotherapy (6600 cGy). The residual turmour was unfortunately unresponsive to radiotherapy. The patient died two months after surgery.

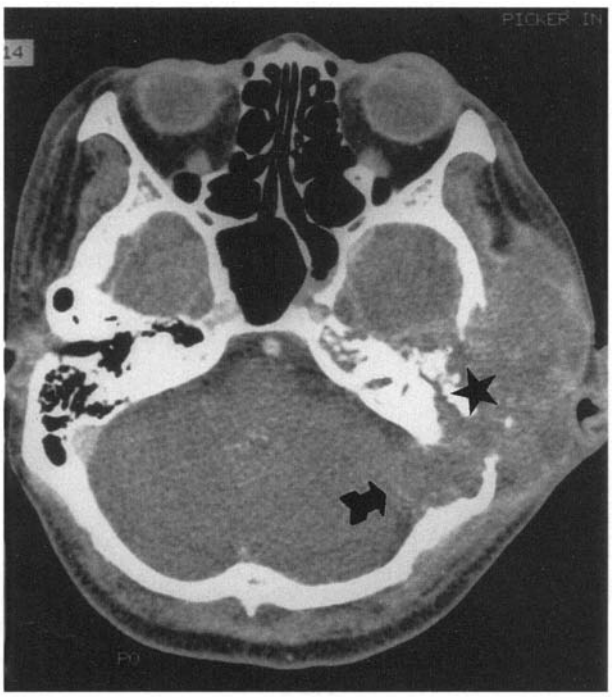

FIG. 1
Axial contrast-enhanced CT shows destruction of the left temporal bone and associated extracranial mass (star). Note the intracranial component (arrow).

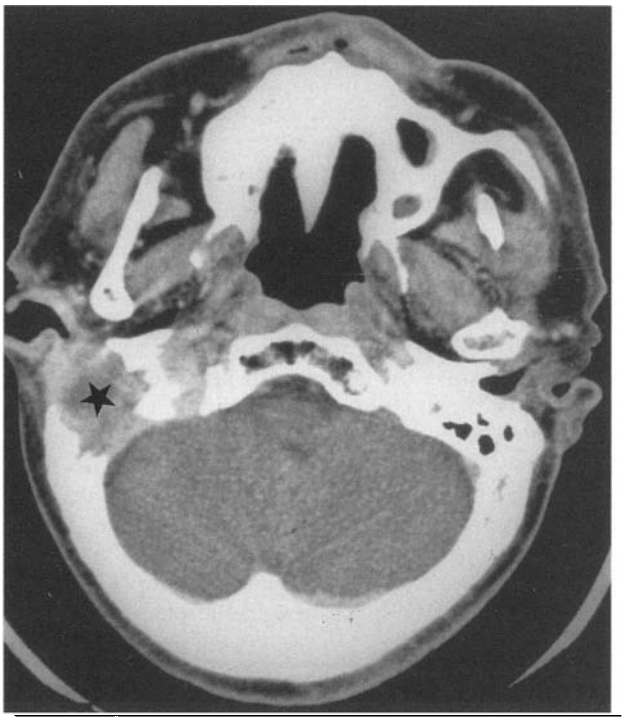

FIG. 2
Axial contrast-enhanced CT shows a mass eroding the right temporal bone (star).

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Case 3

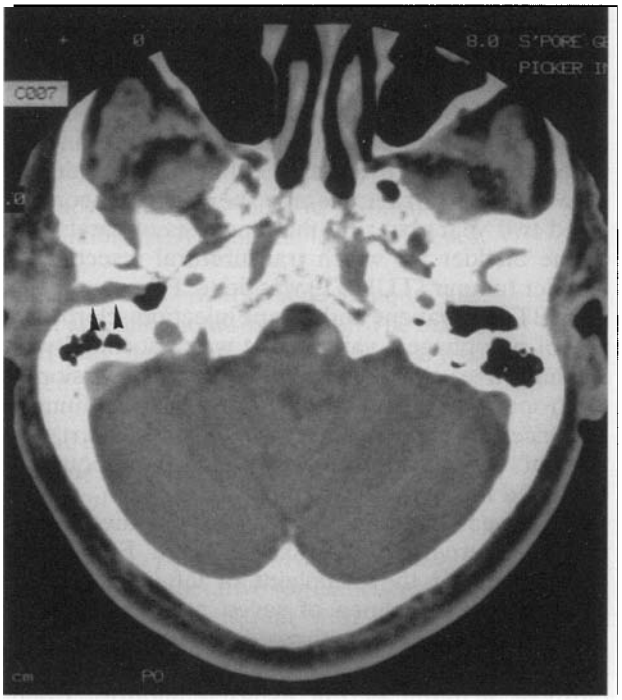
A 71-year-old Chinese man received radiotherapy for nasopharyngeal carcinoma in an overseas centre 20 years before he presented with right bloody otorrhoea of one month's duration. Otoscopy showed a small mass in the right external auditory meatus that was later shown to be a moderately differentiated squamous cell carcinoma on biopsy. CT scan of the temporal bone showed the presence of a soft tissue filling the entire external auditory meatus with no evidence of erosions of the bony walls. The man subsequently underwent right lateral temporal bone resection. All macroscopic disease was removed and random sampling biopsies of resection margins were free of tumour. A year later, he represented with a small external auditory canal nodule. Biopsy of the nodule showed differentiated squamous cell carcinoma on biopsy. The patient finally underwent wide excision of the external canal tumour and has been free of disease seven months after the second surgery.

Case 4

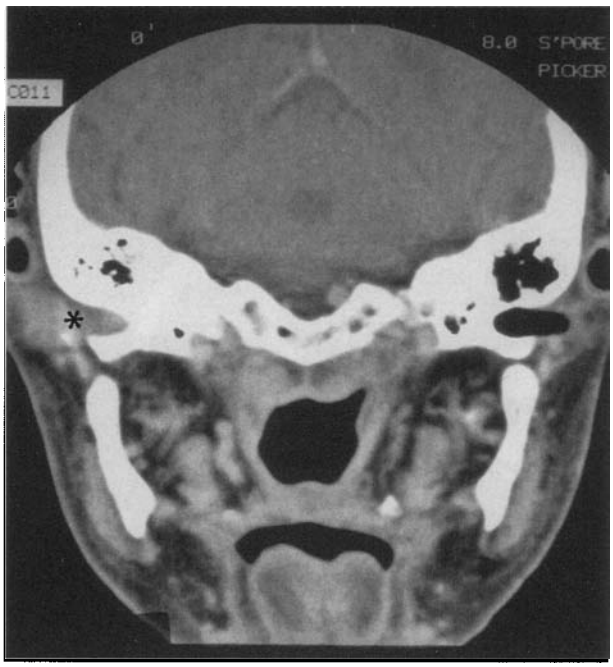
A 57-year-old Chinese man presented with the complaint of right bloody otorrhoea six years after his first course of radiotherapy for nasopharyngeal carcinoma. He gave a history of having received a second course of radiotherapy to the nasopharynx, two years after his first treatment, when his tumour recurred. The patient also underwent right radical neck dissection for right cervical nodal metastasis (NPC) two years after his second radiotherapy. As the patient was treated in an overseas centre no information on the type and dose of radiotherapy was available. Physical examination showed the presence of a small right external auditory meatus mass that showed moderately differentiated squamous cell carcinoma on biopsy. Magnetic resonance imaging (MRI) of the temporal bone showed a well-localized right external auditory canal tumour with no evidence of bony erosion. The patient subsequently underwent excision of this localized tumour. Three months later he underwent a further excision of the ear mass when his right ear tumour recurred. Two years later, the patient represented with multiple cutaneous metastasis (squamous cell carcinomata) over a large anterior portion of his neck. An excision of the skin lesion with pectoralis myocutaneous flap reconstruction and split skin graft of the residual defect was undertaken. The cutaneous metastasis unfortunately resurfaced along the margins of resection within a month of skin excision. The patient was subsequently given palliative radiotherapy to his neck and is presently alive 27 months after treatment for his temporal bone tumour. He is free of disease in the ear.

Case 5

An 82-year-old Chinese man presented with right otalgia and bloody otorrhoea of three weeks duration and gave a history of having received radiotherapy for nasopharyngeal carcinoma 30 years before in an overseas centre. He had not been on follow-up soon after his radiotherapy. Physical examination revealed a right external auditory canal tumour that showed squamous cell carcinoma on biopsy. CT scan of the temporal bone (Figure 3a and b) confirmed the presence of a



(a)



(b)

FIG. 3

a. Axial contrast-enhanced CT shows a mass in the right EAM (arrowheads) extending laterally. The middle ear cavity is normal.

b. Coronal contrast-enhanced CT shows mass in EAM and lateral extension (star).

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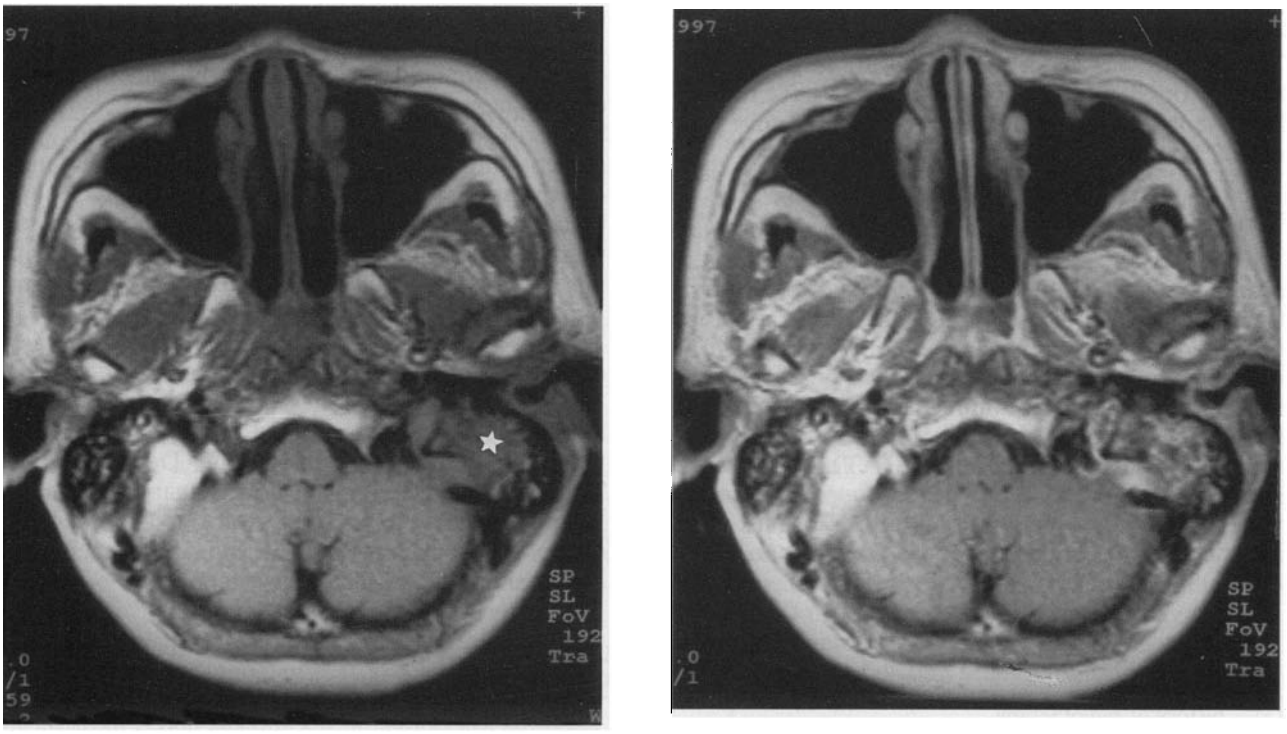
localized right external auditory canal mass involving the tympanic membrane but without any evidence of bony erosion. The patient then underwent right lateral temporal bone resection; intra-operative assessment of the tumour interestingly showed tumour erosion of the anterosuperior portion of the external auditory canal that was not demonstrated in the CT scan. The patient unfortunately died three months later after failing to recover from severe bronchopneumonia which developed after he underwent truncal vagotomy and pyloroplasty for a bleeding duodenal ulcer. A small right external auditory canal tumour recurrence was noted on review shortly before his demise.

Case 6

A 49-year-old Chinese lady presented five years after receiving radiotherapy (6600 cGy) for nasopharyngeal carcinoma with the complaint of left facial nerve paralysis of a few days duration. Apart from the lower motor neuron lesion of the left facial nerve, her physical examination and CT scan of the brain and temporal bone was unremarkable. The provisional diagnosis of Bell's palsy was made and the patient was given an appointment date for review. Unfortunately, this lady returned only four months later with worsening symptoms of left bloody otorrhoea and persistent left facial weakness. Physical examination then showed a large parotid and external auditory canal mass. Biopsy of the ear mass showed osteogenic sarcoma. CT scan (Figure 4a and b) confirmed the presence of an extensive temporal bone tumour abutting the skull base and infiltrating the mastoid bone and the parotid gland. The patient underwent three cycles of adriamycin and cisplatin with dramatic tumour shrinkage before undergoing lateral temporal bone resection, wide excision of tumour, and radical neck dissection with trapezius myocutaneous flap reconstruction. A further two cycles of cisplatin and adriamycin was administered after surgery. The resected specimen showed tumour-free margins of resection with no evidence of cervical nodal metastasis. This lady is, at present, free of disease four months after surgery.

Case 7

A 62-year-old Chinese man presented 10 years after his first course of radiotherapy (4000 cGy) for lymphocytic lymphoma of the nasopharynx. He also gave a history of previous radiotherapy (3000 cGy) to the thorax for Hodgkin's lymphoma 13 years prior to his nasopharyngeal irradiation. The detailed histology was unfortunately not available for review. During consultation he complained of a left ear growth which was seen occluding the entire external auditory canal on examination. CT scan of the temporal bone (Figure 5) showed a large mass filling the external auditory canal with infiltration into the middle ear. Magnetic resonance imaging (MRI) further demonstrated extensive tumour infiltration into the left eustachian tube, left internal auditory meatus, left middle cranial fossa and the left parotid gland. The patient subsequently underwent subtotal



(a) (b)

FIG. 4

a. Axial T1-weighted MRI shows an intermediate signal intensity mass in the left temporal bone (star).
b. Axial contrast-enhanced MRI shows enhancement of the tumour.

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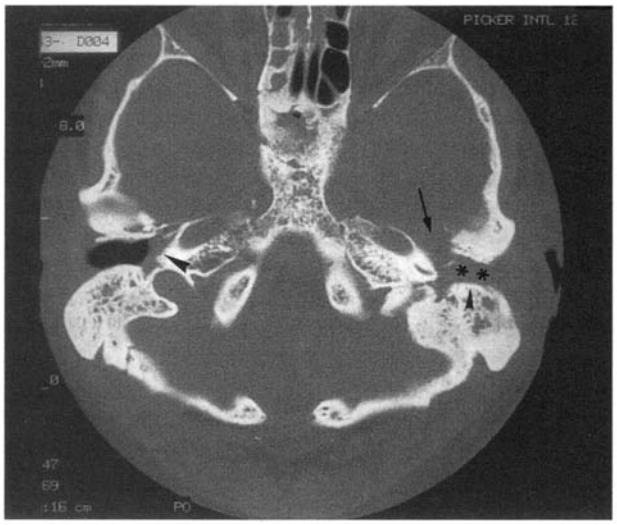

FIG. 5

Axial CT (bone window) shows mass in left EAM and middle ear cavity (asterisks). Note erosion in anterior wall of middle ear cavity (solid arrow) and posterior EAM wall (small arrowhead). Note soft tissue lesion in right middle ear cavity (large arrowhead).

petrosectomy, parotidectomy with left trapezius myocutaneous flap reconstruction of the ear defect and post-operative radiotherapy (5000 cGy).

The patient was well after surgery except for a small discharging fistula that started to develop seven months after surgery. A repeat CT scan of the temporal bone did not show any evidence of tumour recurrence and patient was lost to follow-up until 18 months later when he returned for review. Biopsy of the fistula opening then confirmed the presence of squamous cell carcinoma recurrence. The patient was given the option for further radiotherapy or chemotherapy but elected to have the no-treatment option instead. He is presently alive and active 37 months after initial surgery.

Discussion

The carcinogenic potential of ionizing radiation is a well recognized albeit poorly understood feature of therapeutic radiation. Although the term radiation-induced tumours is used frequently by many to describe second tumours within previously irradiated fields, that the second tumour is a direct product of irradiation is, at best, speculative. Better termed radiation-associated tumours (RAT), this entity should be regarded more as a group of tumours which arise after irradiation and that must also satisfy a set of criteria proposed by Cahan *et al.* (1948).

The importance in the recognition of RAT lies in the need to distinguish this from tumours that may have arisen without radiotherapy – an increasingly important issue in the evaluation of long-term effects of radiotherapy. Cahan *et al.* (1948), based on a study of 11 patients with post-radiation sarcoma proposed a set of criteria for the diagnosis of radiation-associated sarcoma. Based on his original proposal, the following modifications have been made to cater to diagnosis of other types of RAT (Table I): (a) history of radiotherapy, (b) the second neoplasm ***must*** occur within the field of radiation, (c) the histology of the second neoplasm must be distinctly different from the primary tumour, (d) a latency period of many years, ***arbitrarily*** taken to be at least five years, must have lapsed between radiotherapy and the occurrence of the second tumour. All our seven cases satisfied these criteria (Table II).

The true incidence of head and neck radiation-associated tumours is unknown although it has been estimated to occur between 0.4 per cent (Steeves and Bataini, 1981) to 0.7 per cent (van der Laan *et al.*, 1995) of patients who received therapeutic radiation. Depending on the initial site of radiation, the types of RAT that have been reported varies and includes sarcomas (Mark *et al.*, 1993), meningiomas, schwannomas (Rubinstein *et al*, 1989), gliomas (Burkey *et al.*, 1990; Bernstein and Laperriere, 1991), thyroid tumours and squamous cell carcinomas. Although much has been reported on radiation-associated tumours to the head and neck region, to our knowledge there are at present no specific reports on radiation-associated temporal bone tumours in patients who received radiation to the nasopharynx. Because of its strategic location, the bulk of the temporal bone lies well within the radiation field during nasopharyngeal irradiation and bears the brunt of radiation injury during treatment. The susceptibility of the temporal bone to radiation complications is evident from the various reports (Jackson, 1901; Skinner *et al.*, 1991) that estimated that more than 40 per cent of patients with nasopharyngeal radiation have temporal bone complications.

Nasopharyngeal carcinoma is the fifth commonest cancer in Singapore with an age standardized rate of 14.8 per 100 000 in males and 6.2 per 100 000 in females. The incidence being highest amongst the Chinese (Lee *et al.*, 1992). The Department of Therapeutic Radiology in the Singapore General Hospital treats the majority of the patients with nasopharyngeal carcinoma in Singapore each year (approximately 350–400 per year).

TABLE I

MODIFIED CAHAN'S CRITERIA FOR RADIATION-ASSOCIATED TUMOURS

(a)	history of radiotherapy,
(b)	the second neoplasm *must* occur within the previous field of radiation,
(c)	the histology of the second neoplasm must be distinctly different from the primary tumour,
(d)	a latency period of many years, *arbitrarily* taken to be at least five years, must have lapsed between radiotherapy and the occurrence of the second tumour.

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TABLE II
SUMMARY OF PATIENT DATA

S/No	Age/Race/Sex	Initial Naso-pharyngeal Disease	Radiation (cGy)	Latency (years)	RAT	Treatment Outcome
1	56/Ch/M	NPC	5500	10	SCC	Died 3 months after surgery and post-operative radiotherapy
2	68/Ch/M	NPC	6600	6	Chondro sarcoma	Died 2 months after surgery and post-operative radiotherapy
3	71/Ch/M	NPC	Unknown	20	SCC	Underwent two surgeries (recurrent disease). Presently alive and free of disease 7 months after second surgery
4	58/Ch/M	NPC	Unknown	6	SCC	Disease free in the temporal bone 29 months after surgery Has cutaneous metastasis of SCC
5	82/Ch/M	NPC	Unknown	30	SCC	Died of unrelated disease Noted to have tumour recurrence at the time of death 3 months after surgery
6	49/Ch/F	NPC	6600	5	Oesteogenic sarcoma	Treated with surgery and pre- and post-operative chemotherapy. Presently free of disease 5 months after treatment
7	62/Ch/M	Lymphocytic Lymphoma	4000	13	SCC	Tumour recurrence 7 months after surgery and post-operative radiotherapy. Decided on expectant treatment Presently alive and active 26 months after diagnosis of recurrence

Between 1991 to 1997, our Department managed 20 patients with temporal bone tumours (18 squamous cell carcinoma and two sarcomas), amongst whom seven had a history of radiation to the nasopharynx. Of the seven patients in this study, five patients had squamous cell carcinomas, one had chondrosarcoma and one other had osteosarcoma of the temporal bone. The latency period between radiotherapy and presentation of temporal bone tumours ranged from five years to 30 years with a mean of 12.9 years – a finding which is in keeping with other major reports (Steeves and Bataini, 1981; Burkey *et al.*, 1990; van der Laan *et al.*, 1995). Unusual in this review, however, is the relatively low incidence of sarcomas amongst the RAT and high incidence of squamous cell carcinoma. Lustig *et al.* (1997) reported four patients with sarcomas (two osteosarcomas and two fibrosarcomas) in his series of five patients with radiation-associated temporal bone tumours while Steeves and Bataini (1981) similarly reported that all the RAT in their 22 year review were sarcomatous in nature. The overwhelming amount of literature on post-irradiation sarcomas has to a certain extent made radiation-associated tumours almost synonymous with sarcomas (Steeves and Bataini, 1981; Burkey *et al.*, 1990; Mark *et al.*, 1993; van der Laan *et al.*, 1995) although it is clear that the spectrum of RAT is variable and is dependent on the site of origin of the second tumour. It is interesting that of the seven patients in this report, five patients had squamous cell carcinomas of the temporal bone – by itself a rare neoplasm which represents less than one per cent of all head and neck neoplasms (Crabtree *et al.*, 1976). One possible reason which might account for this observation is that chronic ear infections are common after radiotherapy to the nasopharynx. The resultant chronic irritation together with the effects of radiation could have resulted in the development of squamous cell carcinoma.

Although the second tumours were most probably by-products of radiation, one must be reminded that the presence of an aberrant tumour suppressor gene may also be an important factor which facilitated the development of the second malignancies especially in cases one and seven who have multiple neoplasms.

This series also revealed that local recurrence after surgical excision is common, even though tumour resection appeared complete during surgery. Possible reasons for this are a) removing tumours en-bloc in the temporal bone is often difficult if not impossible without compromising safety b) surgery in irradiated tissue is generally more difficult c) local immunity may have been compromised by previous radiotherapy and d) hesitation to give high doses of post-operative radiotherapy to irradiated tissues because of potential morbidity. It is also apparent from this series that with large tumours, the inability to remove all macroscopic disease resulted in patients dying within three months after surgery (*Cases 1* and *2*) whereas with small tumours where all macroscopic disease can be completely cleared, patients can survive for much longer periods (*Cases 3* and *4*). Testa *et al.* (1997) confirmed that tumour stage was indeed an important factor which determined survival. Hence, the importance of early diagnosis of this tumour.

To diagnose this tumour early, a high index of suspicion is required. The presence of chronic ear infections may mask the disease resulting in delayed diagnosis. Furthermore, the differential diagnoses of osteoradionecrosis (Birzgalis *et al.*, 1993) and even metastasis from a distant second tumour (Nelson and Hinojosa, 1991) may need to be considered in an irradiated patient with a mass in the temporal bone.

In our experience, soft tissue lesions in the external acoustic canal shows non-specific features on CT and MRI. As CT is superior to MRI in demonstrating cortical bone erosion, CT is the

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preferred method in the initial assessment of tumour arising in the external acoustic meatus. Large tumours can spread into the adjacent parotid and masticator spaces. Malignant infiltration may extend intracranially or into the jugular foramen. These large tumours are best evaluated by MRI.

In the treatment of RATs, specific clinical issues may need to be addressed. Since post-operative healing of tissue may be compromised by previous radiation, the use of perioperative antibiotics and delayed suture removal may be more relevant in these cases than in surgery of other types of tumours. To put the patient under general anaesthesia for the surgery, the presence of trismus (a common sequelae of radiotherapy to the nasopharynx) may necessitate endoscopic intubation or tracheostomy. In recurrent RATs, diagnosis and treatment can be clinically challenging (as in *Case 4*) as previous radiotherapy and neck dissections could have violated the lymphatic fields.

The progressive improvement and refinement in radiotherapy techniques has, over the years, contributed to an increase in patient survival for patients with nasopharyngeal malignancies. With this improvement in survival, we can expect to see more long-term complications of ionizing radiation like RATs. Over a short three and a half year period, we have already managed seven of such tumours that were previously regarded as rare. It remains imperative for clinicians to be vigilant when patients previously irradiated for nasopharyngeal malignancies present with otological complaints as survival appears to be dependent on the early detection and expedient treatment of this difficult disease.

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