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Case Report

Multiple squamous cell carcinomas of temporal bone years after radiotherapy for malignancy glottis-report of a rare case with review of literature

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ABSTRACT

Larynx is unique in its anatomy. It is critical to map the lesions accurately so that the patient may benefit from the strategy most likely to preserve a functional larynx with the lowest likelihood of recurrence and the least morbidity. We describe a case of 60-year-old male with malignancy glottis diagnosed at the age of 43, treated with external beam radiotherapy, presented 15 years after with swelling in the right upper part of the face, lateral to the eye. Radiological investigations suggested neoplasm in the skin over the right zygomatic part of the temporal bone. Biopsy confirmed malignancy, basal cell carcinoma type. Wide local excision of the lesion with split skin grafting was done. After 2 years, he presented with right ear pain, discharge, and hard of hearing. Examination and radiological investigations confirmed a mass in the external auditory canal, infiltrating through the temporal bone. Biopsy revealed an acantholytic variant of squamous cell carcinoma (SCC). The patient was advised about treatment options and radiotherapy was chosen. Further, a literature search was conducted to detect similar cases. We describe the incidence and prevalence of radiation-induced temporal bone malignancy, an exceedingly rare and late complication of head and neck irradiation. Radiation induced SCCs are highly malignant secondary neoplasms in the head and neck region. It constitutes a therapeutic challenge because of its anatomy and the known side effects of radiation. Timely intervention with a multidisciplinary approach is necessary.

Keywords: SCC, Radiation, Head and neck malignancy

INTRODUCTION

Malignancy glottis is treated with surgery, radiotherapy, and chemotherapy. The most common long-term adverse outcome of head and neck tumor irradiation is hypothyroidism, permanent xerostomia, skin changes, decaying of teeth, osteoradionecrosis, cartilage necrosis, serous otitis media, sensorineural hearing loss, vestibular symptoms and radiation-induced malignancy.

Currently, proposed characteristics of radiation-induced temporal bone malignancy include the finding of a different histological type to the primary tumor, has developed within or adjacent to the path of the radiation beam, and a latency period ranging from 5 to 30 years. Cahan et al established criteria that needed to be fulfilled in order to make the diagnosis of radiation-induced sarcoma in bone.[1] About 50 years later, Lustig et al defined similar criteria for radiation-induced temporal

bone tumours as follows:[2] The second neoplasm must develop in the irradiated field. A latent period of at least several years must elapse between radiation exposure and the development of a second primary. The previous condition must show histological, radiographic, and microscopic evidence of neoplasia. The second tumour must be of a different histological type from that previously irradiated.

Radiation-induced tumours of the temporal bone are rare, but there are reports in the literature of tumours, such as SCC, fibrosarcoma, and osteosarcoma, which fulfill the above criteria. These tumors are aggressive and tend to metastasize early. Treatment is difficult and management of reported cases has included surgical resection, chemotherapy, and adjuvant radiotherapy. Reported outcomes are generally poor with 22-32% of patients surviving 2 years and a 5-year survival of 11-32%.[2] Overall prognosis in radiation-induced malignancy is poor.

Newer techniques such as robotic surgery may reduce the usage of irradiation for head and neckmalignancies.

Glottis malignancy is common. In 2008, 150,000 people worldwide were diagnosed with laryngeal SCC.[3] More than 50% of laryngeal SCC arise in the glottis, and such cancers tend to occur in heavy smokers who present early in the course of the disease with hoarseness.[4-6] Because of the paucity of lymphatics in the glottic region, many glottic cancers do not have regional metastasis. Untreated glottic malignancy conveys significant morbidity and mortality, with a 5-year survival rate of 65%, attributable to complications. Surgery is the standard of care first-line treatment of glottic carcinoma. The long-term local control rates for early glottic carcinomas are similar to organ preserving surgical approaches (TLM). RT is preferred in most centers in the UK and the United States, where the tumour involves Anterior commissure and in T2 glottic tumours, largely due to better functional outcomes and to a lesser extent due to the low availability of surgical expertise. This modality is also the preferred option in patients with poor access to surgery and/or high risk for general anesthesia. Medical chemotherapy may be used. Tracheostomy is indicated in stridor cases when requiring rapid requirement of airway. Although undoubtedly an effective adjunct treatment in the treatment of malignancy glottis, radiotherapy may result in potential complications including hypothyroidism, skin changes, and secondary malignancies.

CASE REPORT

We report a case of a 60-year-old male diagnosed with malignancy glottis in 2006, on the basis of clinical, radiological, and histopathological tests. Neck imaging showed a vocal cord tumour, with no signs of metastatic lesions in the chest, abdomen, and brain. The otorhinolaryngologist referredthe patient to a surgical and radiation oncologist. He then received 55 Gy of EBRT, 32 cycles. He required subsequent medical replacement therapy with thyroxine for all years with control of hypothyroidism. His other comorbidities include diabetes and hypertension for the last 4 years, forwhich he was on regular medications. He was also diagnosed with CVA on his left side 2 years back. He was a known alcoholic from 2009-2016, consuming about 180 ml/day for 2 days in a week; and not a known smoker. At the age of 57, he presented with swelling in the right upper face, lateral to the right eye. Biopsy was done and it showed malignancy involving skin over the right zygomatic part of the temporal bone (Basal cell carcinoma type) without deep extension, for which he underwent superficial excision with split skin grafting. At the age of 60, he presented to our OPD with right ear pain, discharge, and hard of hearing. No other history was significant apart from progressive lethargy.

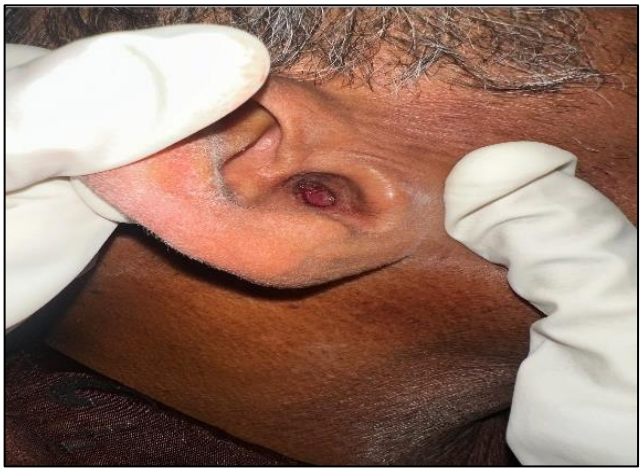

Figure 1: External appearance of right pinna.

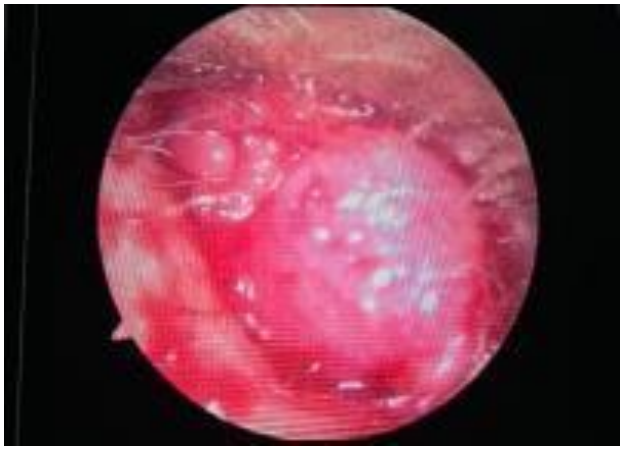

Figure 2: Endoscopic picture of polypoidal mass in external auditory canal.

Otoendoscopy on the first visit showed a friable bleeding pink mass in the right external auditory canal, covered with purulent discharge. Suction clearance was done. Basic blood routine and serology tests were done. High-resolution CT of the temporal bone on presentation

demonstrated an oblong soft tissue density lesion involving the entire length of the right external auditory canalwith erosion of the anterior wall of external auditory canal, Examination of nose throat, mouth, neck, and systemic examination was normal. All blood investigations were within normal range. Biopsy was taken from the external auditory canal mass and sent for histopathological examination.

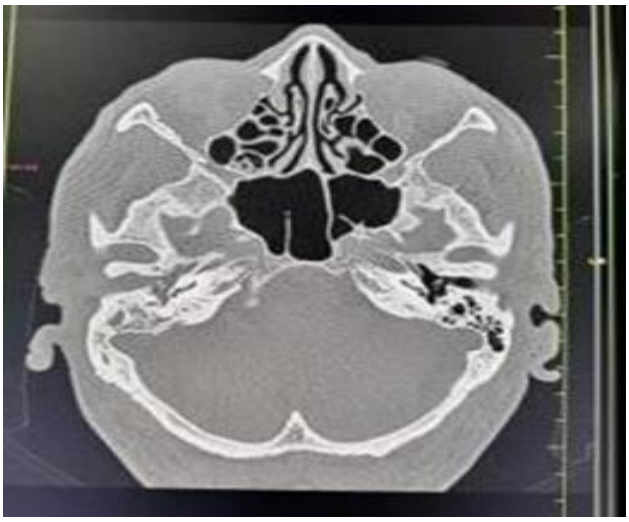

Figure 3: Axial view of HRCT temporal bone showing opacification of right external and middle ear.

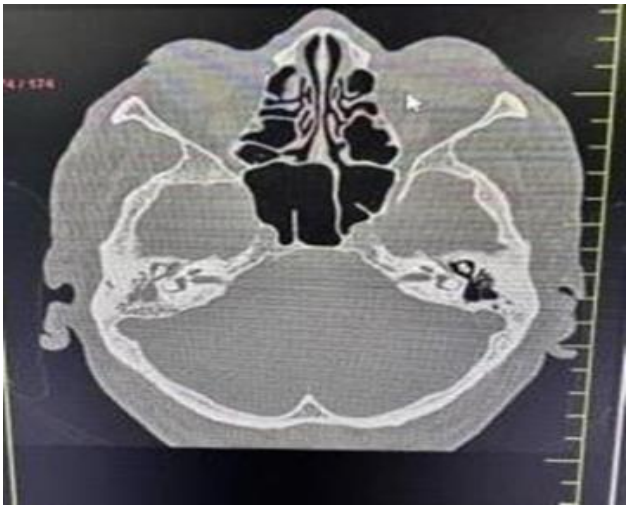

Figure 4: Axial view of HRCT temporal bone showing soft tissue opacification extending into middle ear.

On histopathological examination, the tumour was an acantholytic variant of SCC with a high-grade component. The tumour arose from the right temporal bone tympanic part and invaded anteriorly. The section studied showed infiltrating neoplasm with tumour cells arranged in nests and alveolar pattern. Tumour cells were discohesive and acantholytic scattered within the lumen. Individual tumour cells were highly pleomorphic with increased nuclear to cytoplasmic ratio, hyperchromatic vesicular nuclei, and inconspicuous nucleoli. Malignant keratin pearls were also seen. The patient was advised to undergo surgery followed by radiotherapy. Butthe patient refused to undergo surgery. Hence, he was started on radiotherapy.

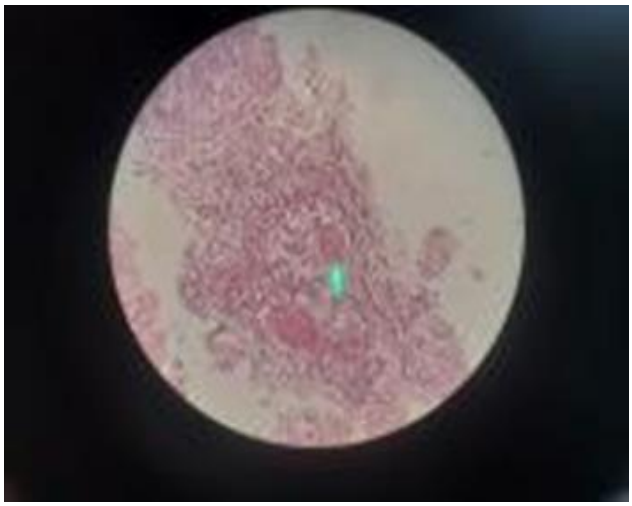

Figure 5: Microscopic picture of acantholytic variant of SCC (40x).

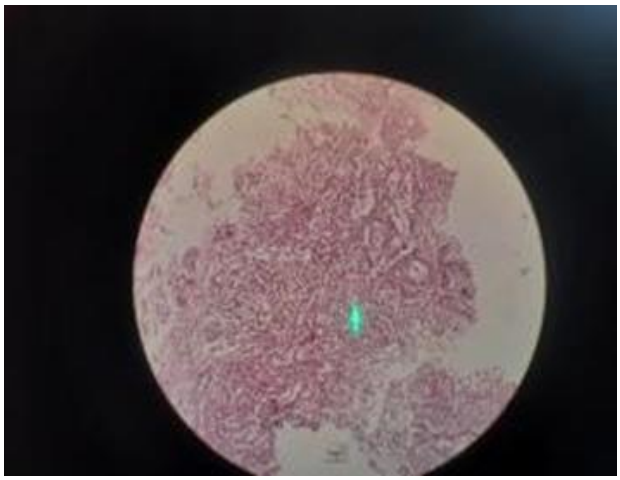

Figure 6: Microscopic picture of acantholytic variant of SCC (100x).

DISCUSSION

Radiotherapy is an effective treatment for malignancy glottis. Compared to conventional EBRT, newer techniques like LINAC, accelerated or hyper fractionated radiation using intensity-modulated radiotherapy and cyber knife stereotactic radiation have refinements in patient immobilization, imaging, and dose distribution, thus delivering more localized radiation.[7] Nevertheless, complications of modern radiotherapy include radiation sickness (loss of appetite and nausea), mucositis, xerostomia, skin reactions (erythema, dry or wet desquamation), laryngeal oedema, candida infections, hematopoietic suppression, osteoradionecrosis (mandible more than maxilla), cartilage necrosis, radiation

retinopathy and cataract, endocrine deficit (thyroid, pituitary), serous otitis media and sensorineural hearing loss and vestibular symptoms, radiation-induced malignancy (thyroid cancer, osteosarcoma of orbit) and brain injury (somnolence syndrome and brain necrosis). Ionizing radiation causes double-strand DNA damage and genomic instability, thereby increasing the risk of secondary malignancy.[8] Malignancies that occur within 6 months of 1st primary tumour are defined as synchronous while those that develop after 6-monthinterval are defined as metachronous, 2nd primary tumours are second malignancy that presents either simultaneously or after the diagnosis of index tumour.

Criteria for the diagnosis of a radiation-induced SCC has been proposed andinclude the following (a) the presence of malignancy of a different histological type before irradiation, (b) the development of carcinoma within or adjacent to the path of the radiation beam, (c) latency period of several years between irradiation and diagnosis of secondary tumour and (d) histological diagnosis of secondary carcinoma.[9] Our patient fulfilled all the criteria for a radiation- induced carcinoma, with histopathology confirming SCC. The most commonhistological subtypes of radiation-induced carcinoma of bone include SCC, fibrosarcoma, and osteosarcoma, which fulfill the above criteria. At present after surviving from a primary malignancy, 17-19% patients develop a second malignancy and observed more commonly in patients receiving radiotherapy for primary malignancy.[10] They behave more aggressively than primary temporal bone malignancy and tend to metastasize early. Although the term implies the causative role of radiation in tumorigenesis, the contributory effects of genetic predisposition or concurrent chemotherapy in oncology indications should not be undermined.[11] The risk of radiation-induced carcinomas increases with dose and field size, with the minimum and median dose of cumulative radiation thought to cause a secondary carcinoma estimated to be20 and 15 Gy, respectively.[12] Our patient received 5500 rad, equivalent to 55 Gy, through EBRT and thus the field size was significantly larger than one would expect with a modern treatment. In a study by Chung et al the crude rate of second malignancies was lower in proton beam therapy as compared to photons (5.2% vs 7.5%).[13] The use of older radiation techniques has been shown to increase the risk of radiation induced malignancies.[14]

Table 1: Depicts previous studies done related to temporal bone radiation induced malignancy.

Author	Publication name	N	Primary malignancy/ source of radiation
Sofija et al[15]	Osteosarcoma of the mastoid process following radiation therapy of muco-epidermoid carcinoma of the parotid gland	1	Parotid
Frederick et al[16]	Radiation-induced sarcoma of the skull	1	Brain (astrocytoma)
Ben Nsir et al[17]	Osteolytic clear cell meningioma of petrous bone occurring 36 years after posterior cranial fossa irradiation	1	Brain stem tumor
Applebaum[18]	Radiation-induced carcinoma of temporal bone	1	Series of radium chloride injections
Goh et al[10]	Malignancy the temporal bone and external auditory canal	7	Nasopharynx
Aub et al[19]	The late effects of internally deposited radioactive materials in man	1	Radium dial painter
Beal et al[20]	Radiation-induced carcinoma of the mastoid.	9	Radium dial painters
Lustig et al[2]	Radiation-induced tumors of the temporal bone	5	Brain tumours (astrocytoma, glomus meningioma, vestibularschwannoma)
Lim et al[21]	Malignancy of thetemporal bone and external auditorycanal	18	Nasopharynx
Darrouzet et al[22]	Radiation-induced sarcoma, apropos ofa case with cervicaland intrapetrousdevelopment	1	Cerebellar astrocytoma
Coatesworth et al[23]	Post-irradiation liposarcoma of thetemporal bone	1	Parotid-disease, benign.

Of late, there is a concern that increased use of intensity modulated radiotherapy is associated witha greater risk of radiation induced malignancy.[24] However, it should be noted that long-term follow-up data for patients receiving modern radiotherapy are shorter than that of EBRT, and thus definitive conclusions cannot be made at this stage. Reported outcomes are generally poor with 22-32% of patients surviving 2 years and a 5-year survival of 11-32%.

The prevalence of radiation induced carcinoma of the temporal bone in patients with prior radiotherapy for head and neck tumours is largely described through case reports. Secondary tumours may arise in bone at the borders of the radiation field, where the radiation dose was sufficient to cause malignant transformation but insufficient to cause cell death.[25] As far back as 1917, it was recognized that up to 85% of patients with this

disease had an associated purulent chronic otitis media.[26] It is not infrequent that patients may undergo excision of polyps and/or granulation tissue which are not submitted for histopathology thus further delaying the definitive diagnosis.

The risk of radiotherapy induced secondary temporal bone tumours in individuals with malignancy head and neck region has been reported variably in literature. Goh et al reported seven patients with temporal bone malignancy, all of whom were initially treated by radiotherapy for head and neck disease.[10] In 1952, Aub et al presented a case of epidermoid carcinoma of the middle ear in a radium dial painter.[19] This tumour appeared 31 years following exposure. Beal in 1965 described another case of epidermoid carcinoma of the middle ear and mastoid in a radium dial painter and mentioned that there have been eight other similar cases.[20] In 1997, Lustig et al did a retrospective case review comprising 5 patients with radiation induced tumours involving the temporal bone.[2] All 5 temporal bone tumours occurred in individuals that had previously received >5000 Gy radiation. There wasan average latency period of 15 years (range 7-23) between completion of radiation and diagnosis of malignancy. The prognosis was poor, with a survival time of 7-14 months after the diagnosis of radiation induced tumours. Complete surgical excision, while the treatment of choice, was often ineffective due to tumour adherence and invasion of surrounding structures.[27] Applebaum reported a case of a patient in whom carcinoma of the right temporal bone developed 39 years after a series of injections of radium chloride is presented. Carcinomas of the temporal bone and paranasal sinuses are a complication of radium administered therapeutically or ingested accidentally by watch dial painters. Acantholytic SCC (ASCC) is frequently considered to be a more aggressive variant with a worse prognosis than other SCC subtypes. ASCC represents 2-4% of all cutaneous SCC, developing mainly in elderly persons, as it can be seen in our study too, with a male predominance. It conserves the same risk factors as in the category it belongs, such as ultraviolet lights and radiation therapy, and for the oral, pharyngeal, and larynx location, alcohol, and smoking. Clinically, ASCC appears as an ulcerated papule with a slow-growing pattern. The lesions typically arise on the head and neck as a nodule or ulcer on sun-exposed skin, particularly on and around the ears and face, de novo, or may develop from an actinic keratosis.

CONCLUSION

Our case highlights a rare but devastating long-term complication of head and neck tumor irradiation. The fact that the tumor developed after radiation to glottic carcinoma makes it a distinct one, as no other case of temporal bone carcinoma that developed following radiation to glottic carcinoma has been reported in literature. These tumours by definition occur years after primary irradiation with a dose-dependent increase in risk. Management consists of surgical resection, radiotherapy although patients often present with advanced disease unamenable to treatment, with poor outcomes.

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