



Metachronous nasopharyngeal carcinoma in a case of carcinoma of the larynx- A rare entity

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Abstract:

Introduction: Second primary tumour (synchronous or metachronous) is increasingly being reported but in most of the cases lung and oral cavity or oropharyngeal carcinomas have been described in association with carcinoma of the larynx.

Case report: The occurrence of nasopharyngeal carcinoma as a metachronous second primary in a case of carcinoma of the larynx is very uncommon. This is a rare case of such an association. **Conclusion:** This case highlights the need of long term follow up of all head & neck malignancy patients. A very high degree of suspicion should be maintained to initiate thorough examination including nasopharyngeal examination either by endoscopy or clinically in order to expedite the diagnosis of second primary.

Key words: Carcinoma of the larynx, Head Neck carcinoma, Metachronous carcinoma, Nasopharyngeal carcinoma, Second primary

Introduction

Head and neck malignancies comprises a heterogenous group of tumors involving varying subsites with different causative factors [1]. The collective term head and neck squamous cell carcinoma (HNSCC) encompasses more than 95% of all head and neck malignancies [2]. The incidence of second primary malignancy (SPM) occurring as synchronous or metachronous tumour is increasing and reported as high as 10% whereas further meta-

analyses show the frequency of a third tumour (TT) as 0.5%, and a fourth tumour (QT) as 0.3% [3,4]. Here we represent an unusual case of metachronous nasopharyngeal carcinoma arising in a case carcinoma of the larynx. Occurrence of such a combination is extremely rare as only one study highlighting such association was found after thorough search of English literature available in Medline & PubMed using keywords 'metachronous

carcinoma, second primary, carcinoma of the larynx, carcinoma nasopharynx'.

Case Report

A 50 year old male presented with hoarseness of voice, insidious in onset 12 years back in 1999. He used to smoke homemade cigarette (20 per day for 30 years) which he stopped after onset of symptoms. At that time his left vocal cord showed only mucosal irregularities at middle 3rd with normal mobility, which on microlaryngoscopic biopsy was reported as carcinoma in situ. Patient was advised for microlaryngeal surgery for complete stripping of the lesion & regular follow-up. But the patient lost to follow-up. After 9 years he presented to emergency with stridor in March 2008 and was tracheostomised. On direct laryngoscopic (DL) examination huge ulceroproliferative transglottic growth was found involving left vocal cord, aryepiglottic fold, left vestibular fold, anterior commissure and extending onto anterior half of right vocal cord with fixation of left hemilarynx & there was no palpable neck node. Contrast enhanced computerised tomographic (CECT) scan of neck confirmed large ill-defined heterogeneously enhancing soft tissue mass occupying glottis having supraglottic & subglottic extensions but no involvement of laryngeal cartilages (figure 1) & the patient's carcinoma of the larynx was staged as T3N0M0 (Stage III). Histopathological study revealed moderately differentiated infiltrating squamous cell carcinoma; so the options were total laryngectomy with bilateral neck dissection or concomitant chemoradiation [5]. The patient opted for laryngeal preservation. He was treated with external beam radiotherapy (EBRT) with Cobalt 60 (Theratron 780E, Ottawa, ON, Canada) 63 Gy in 28 fractions (2.25 Gy per fraction) over 5.5 weeks with CT scan based planning with Theraplan Plus planning software. Concomitant chemotherapy with Cisplatin (40 mg/m² iv weekly) for 6 cycles was used [6].

On regular two monthly follow up, no recurrence or residual growth was noted till 1 year after completion of radiotherapy, but then the patient dropped out from follow up. Again in May 2010 he presented with symptoms of neck pain, cough with occasional blood stained foul smelling discharge from tracheostome. On DL examination large supraglottic ulceroproliferative mass with areas of necrosis, covering whole of the laryngeal inlet and obscuring the anatomical details was found. CECT scan of neck corroborated with it showing large

supraglottic mass with transglottic extension, about 1cm below the level of lower margin of vocal cords, but without any cartilage involvement. There was no palpable neck node. In spite of cardiological compromise, we had no other salvage option other than to perform total laryngectomy which was done in June 2010 along with type 3 modified radical neck dissection in view of post-radiotherapy tumor recurrence and a near impossibility of re-radiating the patient. Histopathology proved moderately differentiated squamous cell carcinoma with resection margin free from involvement with histologically negative neck nodes, no lymphovascular or perineural invasion.

In post-operative period parenteral nutrition was administered in order to maintain patient's nutritional status. But unfortunately the patient developed a very small pharyngocutaneous fistula about 2 weeks post-operatively, which we expected to heal by regular dressing, but were dwindled by the recurrence of fistula thrice in a span of 3 months. During this period patient was being maintained on Ryle's tube feeding which was obstructed at choana during second time of insertion. Hence we performed a diagnostic nasal endoscopy which surprisingly revealed a proliferative mass occupying left side of nasopharynx arising from Fossa of Rosenmuller (figure 2). CECT scan of nasopharynx showed 22mm X 17mm mass extending to the nasal cavity with no neck nodes (T2aN0M0, Stage IIA) (figure 3). An endoscopic biopsy in September 2010 was reported histopathologically as poorly differentiated infiltrating squamous cell carcinoma of nasopharynx. The nasopharyngeal second primary tumor was treated with 3D conformal radiotherapy, 50.4Gy in 28 fractions for 5 ½ weeks to neck & 70.2Gy in 39 fractions over 7 ½ weeks to the GTV (Gross tumour Volume) as nasopharyngeal boost with concomitant chemotherapy using Cisplatin (100mg/m² iv day 1) & 5-FU (750mg/m² iv bolus day 1-5) for 3 cycles i.e. on day 1, 22 & 43 over 6 weeks. Three cycles of adjuvant chemotherapy with Cisplatin (80mg/m² iv day 1) & 5-FU (750mg/m² iv bolus day 1-5) was also given every 21 days [7]. The patient achieved complete response (CR) post radiotherapy. During this period the pharyngocutaneous fistula healed on regular local dressing. The patient was followed up every 2 months. No recurrence at site of second primary was noted on 6 months follow-up after radiotherapy.

Discussion

The criteria for classifying a tumor as a second primary malignancy (SPM) has remained consistent since it was first proposed in 1932 [8]:

- i) Both the index and secondary tumors should be malignant, with histologic confirmation.
- ii) There should be at least 2 cm of normal mucosa between the two tumors. If the tumors are in the same location, then they should be separated in time by at least five years.
- iii) Metastatic tumor should be excluded. For example, a lesion in the lung should be solitary and histologically different from the primary head and neck tumor.

'Metachronous' carcinoma has been defined as second carcinoma developing more than 6 months after the index cancer being diagnosed whereas 'synchronous' cases develop within 6 months [9]. Literature review shows varied incidence of SPM, ranging from 8% incidence of synchronous to 20% metachronous tumors (including tumors of lung and esophagus) [10]. The probable factors implicated are persistent exposure to environmental carcinogens, genetic instability, field cancerization, increasing use of systemic chemotherapy or high dose radiotherapy, hormonal manipulation, targeted/genetic therapy, immune suppression, tissue transplantation, and improved survival after index primary carcinoma [11]. Tian SZ et al reported occurrence rate of multiple primary cancers (MPC) in 81 patients with squamous cell carcinoma of the larynx as 7.4% (81/1101). Oral cavity carcinoma and nasopharyngeal carcinoma were the most common MPC in 29 cases (35.8%) in head and neck regions. MPC in head and neck regions were more often seen among patients who had been treated with radiotherapy ($\chi^2 = 5.7$, $P = 0.017$). Fourteen cases (17.3%) were synchronous MPC, the median time interval was 2 months.

Other 67 cases (82.7%) were metachronous MPC, the median time interval was 28 months. Squamous cell carcinoma (66.7%) was the most common pathologic type among all MPC in 81 cases, which was more often seen among patients who had smoked and drunk. The MPC of oral cavity cancers and nasopharyngeal carcinoma and lung carcinoma were more often seen among patients of glottic index cancer presentation [12]. Our case corroborated with the above mentioned results in development of nasopharyngeal squamous cell carcinoma within 2.5 years after radiotherapy for transglottic squamous cell carcinoma of the larynx in a smoker, but the combination is rare in occurrence as even after

thorough search of English literature available in Medline & PubMed using keywords 'metachronous carcinoma, second primary, carcinoma of the larynx, carcinoma nasopharynx' no other case reports were available depicting such association. Rather Tandon DA et al reported oropharynx as the most common location for SPM in review of 900 patients with squamous cell carcinoma in the head and neck during a nine year period [13]. Stanley RE et al found carcinoma of the lung was the most common second primary tumour in carcinoma of the larynx (46.7%) followed by tumors of oropharynx or oral cavity [14]. The case discussed here is also unique in the fact that there was no clinical features of natural presentation of nasopharyngeal carcinoma (eg. no palpable neck node, aural symptoms, nasal obstruction, epistaxis, ophthalmo-neurological features) & the tumor was noticed incidentally as it caused obstruction to passage of Ryle's tube.

Conclusion

This case highlights the need of long term follow up of all head & neck malignancy patients. A very high degree of suspicion should be maintained to initiate thorough examination including nasopharyngeal examination either by endoscopy or clinically in order to expedite the diagnosis of second primary. Only this can help us to start early & proper management of second primary tumor in curative intent and can considerably improve the survival of patients with multiple primary tumors.

Consent:

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Conflict of Interest: None

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Authors' contributions:

KDB prepared the manuscript. SD maintained records of the data & necessary information. SG retrieved the pictures & did the necessary formatting. AS performed the histological examination of biopsy samples. RS edited the manuscript & have given final approval of the version to be published. All authors read and approved the final manuscript & agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figure 1: Contrast enhanced computed tomography scan of neck, axial section, showing completely lumen occluding laryngeal mass in glottic region.

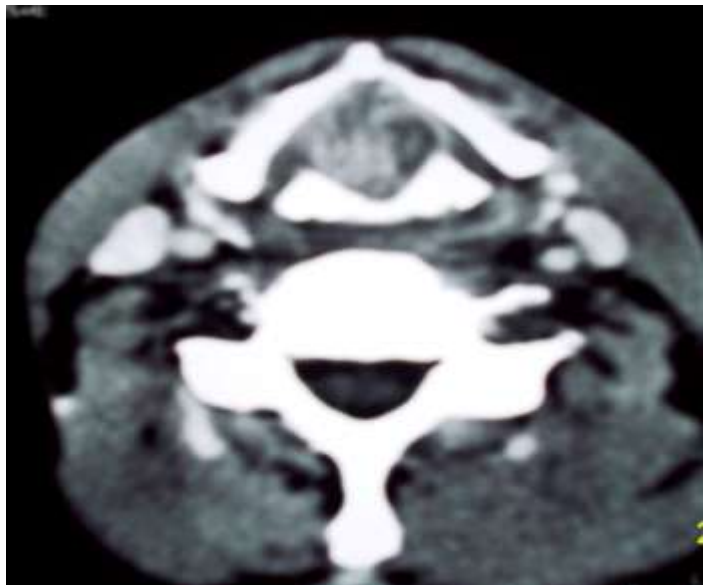


Figure 2: Endoscopic view of the mass in nasopharynx through left nasal cavity occluding the choana



Figure 3: Contrast enhanced computed tomography scan of nasopharynx, axial section, showing an enhancing growth in left lateral wall of nasopharynx, occluding the fossa of Rosenmuller.

