Role of PET-CT scan in synchronous primary cancers of the upper aerodigestive tract: a case report

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Oral field cancerization though not a new concept, has time and again, proven to be a challenge to the clinician, in terms of diagnosis and management. Prolonged exposure of the aerodigestive tract to carcinogens causes multifocal cancers. Intraepithelial migration of dysplastic or clonal cells becomes the seed for different primaries in the same field. The probability of synchronous malignancies should be borne in mind while evaluating a patient with head and neck cancer. With the advent of highly specific diagnostic tools like the PET scan, the chances of missing a second primary are eliminated/negligible. This is a case report on a patient who was found to have multiple primaries on clinical and radiological evaluation. Patient underwent multimodality treatment with chemoradiotherapy followed by surgery and is currently under follow-up. We aim to highlight the role of PET scanning in the evaluation of head and neck cancer to prevent missing a second primary.

Keywords:
head and neck, PET scan, synchronous primary

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Introduction

Patients with cancers in the head and neck region are at an increased risk of developing second primary cancers. Tumours occuring simultaneously or within 6 months of the index (primary) tumour are termed as synchronous primaries and those occurring after 6 months are termed metachronous [1].

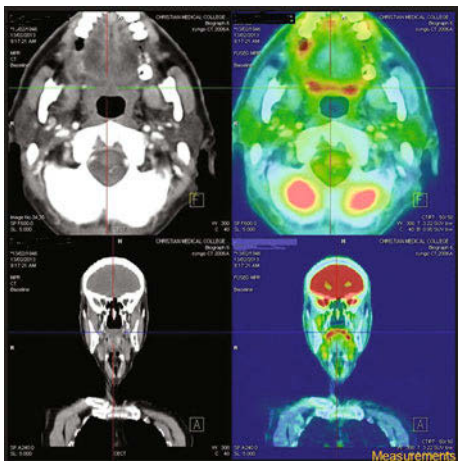
Multiple primaries are seen in about 9.7% of head and neck cancer patients including metachronous and synchronous malignancy of which 46.9% presents as synchronous [2]. The occurrence of multiple primary cancers in the aerodigestive tract has been explained by the concept of field carcinogenesis. Combined exposure to alcohol and tobacco has a multiplicative effect on carcinogenesis of upper aerodigestive tract [3]. With the advent of ^{18}F-fluorodeoxy-D-glucose PET-computed tomography (^{18}F-FDG PET-CT), the diagnosis of synchronous primary malignancies has become easier. This rare case report of a patient with a second and third primary tumour highlights the usefulness of PET-CT in pretreatment staging, radiotherapy planning, treatment response assessment and post-therapy follow-up.

Case report

A 67-year-old gentleman, a known smoker and tobacco chewer, was presented to the ENT outpatient department of Christian Medical College, Vellore, Tamil Nadu, India with complaints of swelling inside the mouth of 2 months duration which was rapidly progressive associated with mild pain. He did not have any nasal complaints or dysphagia.

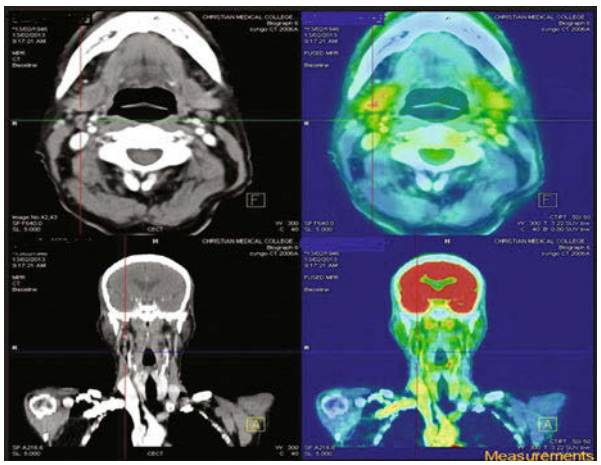
On examination, there was a 2 × 2 cm proliferative lesion on the right side of the soft palate with induration on palpation. There was no cervical lymphadenopathy. A routine flexible nasopharyngolaryngoscopy showed irregular mucosa in the left pyriform sinus but there was no definite lesion. Nasopharynx and larynx were normal. General and systemic examination was normal. Biopsy of the oral lesion was reported as moderately differentiated squamous cell carcinoma. In view of the irregular mucosa in scopy, a diagnostic PET-CT scan (Figs. 1–3) was done which showed increased metabolic activity over the right side of the soft palate [standardized uptake value (SUV) = 3.65 g/ml], right side of nasopharynx (SUV = 3.70 g/ml) and left pyriform sinus (SUV = 3.66 g/ml). Subsequently, he was posted under general anaesthesia and biopsy was taken from the nasopharynx as well as from the pyriform sinus, both of which were reported as moderately differentiated squamous cell carcinoma. The case was discussed in the Head and Neck Tumour

Figure 1



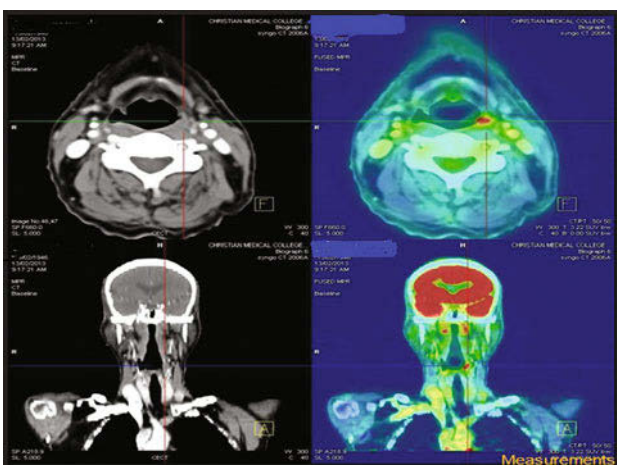
A linear band of increased ^{18}FDG uptake [standardized uptake value (SUV) = 3.65] is noted in the soft palate. Corresponding computed tomographic (CT) images show mild soft tissue thickening in the region of the soft palate.

Figure 2



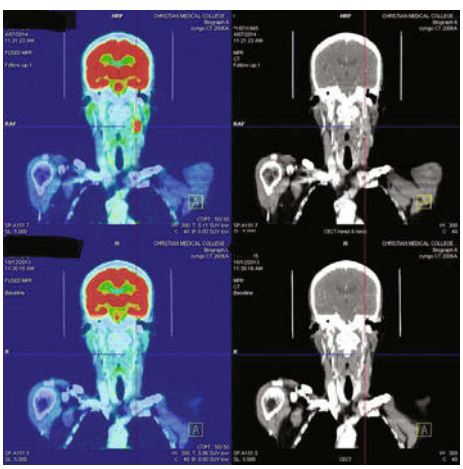
A focus of increased ^{18}FDG uptake [standardized uptake value (SUV) = 3.66] is noted in the left pyriform fossa. Corresponding computed tomographic (CT) images show mild mucosal thickening with partial obliteration of the left pyriform fossa.

Figure 3



Abnormal ^{18}FDG uptake [standardized uptake value (SUV) = upto 3.70] is noted in the nasopharynx with mild asymmetry.

Figure 4



Metabolically active lesion [standardized uptake value (SUV) = 31.95 g/ml] in the left level 2A cervical lymph node.

Board and in view of his ischaemic heart disease status for which he underwent percutaneous transluminal coronary angioplasty in 2001, it was decided that he was a high risk candidate for chemotherapy. The patient was explained regarding the risks involved and he did not consent for chemotherapy. Hence he received intensity modulated radiotherapy of 66 Gy in 33 cycles.

Following radiotherapy, he was on regular follow-up and a PET-CT scan after 1 year did not show any residual/recurrent disease. Eighteen months later, he was presented with a left neck swelling. PET-CT (Fig. 4) revealed a metabolically active lesion (SUV = 31.95 g/ml) in the left level 2A cervical lymph node. The nasopharynx, soft palate and pyriform fossae were normal. Fine needle aspiration cytology of the nodal swelling was reported as poorly differentiated squamous cell carcinoma. He was again discussed in the Tumour Board. The patient was again counselled regarding the treatment options and he gave consent for surgery followed by chemotherapy. He underwent a left modified radical neck dissection. Postoperatively, he was given four cycles of adjuvant chemotherapy with cisplatin and paclitaxel which had to be stopped because of poor tolerability. Eight months later, he presented with another metabolically active swelling in left neck (SUV = 23.95 g/ml). Fine needle aspiration cytology (FNAC) revealed metastatic squamous cell carcinoma. Presently he is on palliative chemotherapy.

Discussion

Despite the advances in therapy, long term survival of head and neck cancer patients has not improved significantly over the years. An important reason for this is the development of second primary tumour. Patients with early stage disease are at greatest risk.

Before the advent of PET-CT, Pan endoscopy (nasal endoscopy, direct laryngoscopy, oesophagoscopy and bronchoscopy) as a part of pretherapeutic work-up used to be the gold standard for the identification of synchronous malignancy of the upper aerodigestive tract especially in high-risk patients.

With the availability of PET-CT in more and more centres, it has become an important noninvasive diagnostic tool for the evaluation of head and neck squamous cell carcinomas. It has a high negative predictive value and a relatively lower positive predictive value for detection of second primary lesions and can impact both the treatment choice as well as the overall survival [4]. It also assesses treatment response, identifying viable tumour within residual masses, thus overcoming the known limitations of morphological imaging modalities [5]. The reported increase in sensitivity of PET-CT over conventional techniques has been attributed to the ability of PET-CT to detect metabolic abnormalities that precede the morphologic changes seen by CT [6].

The optimum time for PET-CT after treatment is 8–12 weeks which reduces both false positive and false negative findings [4].

Compared with MRI scan, which is noninvasive, PET scan is the modality of choice for staging of patients with advanced head and neck squamous cell carcinoma (HNSCC) in view of its greater sensitivity for the detection of metastatic lesions including nodal metastasis. Also for post-treatment follow-up, because of the anatomical distortion due to surgery, a metabolic scan may be better [7].

An area of active research today is fused PET and MRI images for better anatomic delineation. Huang *et al.* [8] found ^{18}F-FDG PET-MRI to be more reliable for focal invasion assessment and tumour size delineation in advanced squamous cell carcinoma (SCC) compared with PET-CT, MRI, and CT.

The disadvantage of PET scan is that it is an invasive procedure (needs intravenous contrast injection plus radiation exposure) when compared with other noninvasive imaging modalities like diffusion-weighted MRI. The cost of reimaging patients in the follow-up period is significant.

Slaughter *et al.* [5], in 1953 proposed the theory of 'field cancerization' whereby multiple tumours could originate independently as a result of independent mutations in the upper aerodigestive tract epithelium preconditioned to cancer development by long-term exposure to carcinogens like tobacco and alcohol. An alternative view (clonal theory) is that a single cell can get transformed giving rise to a large extended premalignant field by clonal expansion and gradual replacement of normal mucosa. With the accumulation of additional genetic alterations, separate tumours can develop [9].

Warren and Gates [10] proposed the criteria for diagnosis of multiple primary cancers.

(1) Each of the tumours must be malignancy confirmed by histology.
(2) Each must be geographically separate and distinct. The lesions should be separated by normal mucosa.
(3) Probability of one being the metastasis of the other must be excluded.

Disagreement exists regarding the application of the second and third criteria. For example, when both tumours appear in the same anatomic subsite, there is no agreement on the distance that should exist between the tumours, with some investigators favoring 1.5 cm and others requiring 2 cm.

Some authors suggest that when dealing with two lesions within the same anatomic subsite, molecular profiling techniques can be employed to identify relationships between lesions, rather than relying on a distance between lesions or time elapsed between detection of tumours.

If molecular profiles of the tumours are completely different, the second tumour is classified as a second primary tumour [11].

The reported incidence of second primary tumour ranges between 0.734 and 11.3% [12] Meta-analyses show the frequency of second primary tumor to be 3–5%, a third primary tumor to be 0.5% and a fourth primary tumor as 0.3% [13].

Smokers have been statistically shown to be a high-risk group of patients in the development of synchronous primaries. Our patient was a smoker as well as a tobacco chewer. The concept of 'field cancerization' in the head and neck epithelial cancer with the use of tobacco in both smoke and smokeless forms can be accounted as the single most important risk factor in the development of synchronous primary in the head and neck regions [2].

Current management of second primary tumours is site specific. Controversies exist whether patients with an extensive visible mucosal defect should be subjected to chemotherapy, radiotherapy or chemoprevention. Chemoprevention with 13-cis retinoic acid has been postulated to prevent recurrence after the primary modality of treatment. It has been shown to upregulate the retinoic acid receptor-b leading to a good clinical response. Other agents like COX-2 inhibitors are also being studied. Some have said that definitive therapy for genetically altered fields of mucosa ultimately consist of targeted ablation of altered clonal populations, and repair of genetic damage in affected cells [14]. Photodynamic therapy has also been tried.

Conclusion

^{18}F-FDG PET-CT may be considered to be useful for staging, restaging and radiotherapy planning as well as for assessment of treatment response in head and neck squamous cell carcinoma patients, due to its superior accuracy over clinical examination and conventional anatomic imaging especially in the diagnosis of second primary tumours.

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Conflicts of interest

There are no conflicts of interest.

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