International Journal of Otorhinolaryngology and Head and Neck Surgery
Gandla S et al. Int J Otorhinolaryngol Head Neck Surg. 2019 Mar;5(2):391-395
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: http://dx.doi.org/10.18203/issn.2454-5929.ijohns20190767

Original Research Article

Role of PET CT in the detection of second synchronous primary tumors and distant metastasis in head and neck cancers at initial presentation

Sowjanya Gandla*, Vishal Rao

Department of Head and Neck Surgical Oncology, HCG Hospital, Bangalore, Karnataka, India

Received: 27 October 2018
Revised: 10 December 2018
Accepted: 12 December 2018

***Correspondence:**
Dr. Sowjanya Gandla,
E-mail: sowjanya233@gmail.com

ABSTRACT

Background: The patients with the head and neck cancer are strongly at risk of developing a second primary tumor which can be related to share etiological factors such as tobacco, alcohol and smoking. The aim of the study is to evaluate the percentage of synchronous second primaries and distant metastasis that are identified on PET CT imaging in head and neck cancer patients at initial presentation.
Methods: This study is a retrospective observational study. A total of 503 patients with histological confirmation of head and neck cancer and who had undergone 18F FDG PET CT imaging from 2007 to 2013 were included in the study. The PET CT scan images of all 503 patients were reviewed. The patients with PET CT scan images indicating the presence of abnormal metabolic uptake suggestive of additional primary malignant lesion or distant metastasis were identified.
Results: Out of the total 503 patients with histological confirmation of head and neck cancer, 34 patients were excluded due to non-availability of complete details, among the 469 patients of head and neck cancer, 7 patients (1.49%) were diagnosed with synchronous primary tumors and 33 patients (7.03%) were diagnosed with distant metastasis in PET CT imaging at the time of initial presentation.
Conclusions: PET CT imaging is a useful tool to detect distant metastasis and second primary synchronous tumors in advanced head and neck cancers. The incidence of distant metastasis is a much more valid indication for the PET CT imaging in advanced head and neck cancers.

Keywords: PET CT, Synchronous second primary tumors, Distant metastasis, Head and neck cancers

INTRODUCTION

Head and neck cancer is the one of the commonest cancer in India and consists of about one-third of all cancers. The patients with the head and neck cancer are strongly at risk of developing a second primary tumor commonly in esophagus and lung which can be related to shared etiological factors such as chewing tobacco, alcohol and smoking.[1] By definition, the tumor found simultaneously or within 6 months of diagnosis of primary index tumor is considered as synchronous primary tumor. The detection of distant metastasis and second primary tumors at the time of initial evaluation changes the prognosis and influences the selection of treatment modality in patients with head and neck cancer. The role of PET CT scan is being increasingly realized for metastasis of unknown origin, recurrent tumors and as a staging modality. Compared to anatomical imaging modalities like CT or MRI, PET CT has an advantage of assessing the primary tumor, regional spread, distant metastasis and second primaries in a single sitting in advanced head and neck cancer patients. But in a developing country like India, PET CT scan has several limitations in the routine practice like cost, availability etc.[2] The purpose of this study is to evaluate the percentage of synchronous second primaries and distant metastasis that are identified on

PET CT imaging in head and neck cancer patients at initial presentation.

METHODS

This is a retrospective observational study conducted at HCG (Health Care Global Enterprises), Bangalore, a tertiary cancer centre. A total of 503 patients with histological confirmation of head and neck cancer and who had undergone 18F FDG PET CT imaging from 2007 to 2013 were included in the study. The PET CT scan images of all 503 patients were reviewed. The patients with PET CT scan images indicating the presence of abnormal metabolic uptake, suggestive of additional primary malignant lesion or distant metastasis were identified. The synchronous primary lesion was considered when the lesion was newly discovered on PET CT imaging and has not been previously detected by other modalities and was confirmed histologically. The presence of synchronous second primary and distant metastasis was noted in the PET CT imaging which was done in patients with head and neck cancers at initial presentation.

RESULTS

Out of the total 503 patients with histological confirmation of head and neck cancer, 34 patients were excluded due to non-availability of complete details, among the 469 patients of head and neck cancer, 7 patients (1.49%) were diagnosed with histologically confirmed synchronous primary tumors and 33 patients (7.03%) were diagnosed with distant metastasis in PET CT imaging at the time of initial presentation. In PET CT imaging, the lung lesion was interpreted as synchronous second primary, when the spiculated solitary FDG positive mass was present and as metastasis when multiple peripheral non-spiculated well demarcated solid nodules were present. Among the 469 patients, 367 patients are males (78.25%) and 102 patients are females (21.74%) and out of 7 patients with synchronous primary, 3 were females (42.85%) and 4 were males (57.14%) and out of 33 patients of distant metastasis, 27 were males (81.8%) and 6 patients were females (18.18%) (Table 1).

Table 1: Sex distribution.

Sex distribution	Total patients N %	No of Patients with synchronous primary N %	Patients with distant metastasis N %
Male	367 (78.25)	4 (1.089)	27 (7.3)
Female	102 (21.74%)	3 (2.9%)	6 (5.8%)

The distribution of primary site in patients with synchronous second primary seen in decreasing order is as follows: the primary site was hypopharynx in 3 patients, oral cavity in 2 patients, salivary gland in 1 patient and nasopharynx in 1 patient (Table 2). In our study, we found that synchronous primary was common in hypopharynx 3/7 patients. Out of 70 patients of hypopharyngeal malignancies, 3 patients had synchronous primary (4.28%), the sites of synchronous second primaries in hypopharyngeal malignancies were lung cancer, colon carcinoma and carcinoma of base of tongue. Out of 205 patients of oral cavity carcinoma, 2 patients (0.97%) had synchronous primary. The primary subsites in the oral cavity were tongue and retromolar trigone and the sites of synchronous second primary were lung cancer and gastric carcinoma respectively. 1 patient of carcinoma nasopharynx (2.29%) had developed carcinoma of the breast and the other patient of adenoid cystic carcinoma of parotid gland (4.16%) had developed lung cancer (Table 3).

Table 2: Distribution of index primary site in patients with synchronous second primary and distant metastasis.

Primary malignancy site	Number of patients	No of patients with synchronous primary N %	No of patients with distant metastasis N%
Oral cavity	205	2 (0.97)	11 (5.36)
Oropharynx	49	-	4 (8.16)
Hypopharynx	70	3 (4.28)	9 (12.8)
Nasopharynx	44	1 (2.27)	2 (4.5)
Larynx	49	-	2(4.08)
Salivary glands	24	1 (4.16)	4(16.6)
Maxilla	13	-	
Nasal cavity & PNS	10	-	1 (10)
Miscellaneous	5	-	

In our study, we found that, among the patients of head and neck carcinoma with synchronous primary tumors, 42.8% (3/7) of patients with synchronous second primary were of hypopharyngeal malignancies, 28.57% (2/7) of patients were of oral cavity carcinoma, 14.28% (1/7) of patients were of nasopharyngeal carcinoma and the rest 14.28% (1/7) were parotid.

In our study, we found that among the 469 patients, 33 patients (7.03%) had distant metastasis on PET CT scan at initial presentation. Among these 33 patients of distant metastasis, 33.3% (11/33) patients were of oral cavity carcinoma, 12.1% (4/33) patients were of oropharyngeal carcinoma, 27.2% (9/33) patients were of hypopharyngeal cancer, 6.06% (2/33) were of nasopharyngeal cancer, 6.06% (2/33) patients were of laryngeal cancer, 12.1% (4/33) patients were of salivary gland origin, 3.03% (1/33) patients were of nasal cavity (Figure 1). The sites of distant metastasis were lung, adrenal gland,

liver and skeletal metastasis (Figure 2). In our study, the distant metastasis was common in oral cavity carcinoma followed by hypopharyngeal cancer.

The clinical staging of head and neck cancer patients with synchronous second primary is described in Table 4.

Table 3: Distribution of primary tumour site and synchronous primary tumour site.

Primary tumor site	Synchronous primary tumor site
Adenoid cystic carcinoma of parotid	Lung cancer
Carcinoma pyriform fossa	Lung cancer
Carcinoma pyriform fossa	Base of tongue carcinoma
Carcinoma retromolar trigone	Gastric carcinoma
Carcinoma pyriform fossa	Carcinoma of colon
Carcinoma tongue	Lung cancer
Carcinoma nasopharynx	Breast carcinoma

Table 4: Staging of index primary site in patients with synchronous second primary tumour.

Site of index primary	Clinical staging
Carcinoma pyriform fossa	T3N1
Carcinoma pyriform fossa	T3N1
Carcinoma pyriform fossa	T2N2
Carcinoma retromolar trigone	T4N1
Carcinoma tongue	T4N1
Carcinoma nasopharynx	T3N2
Adenoid cystic carcinoma of parotid	T2N0

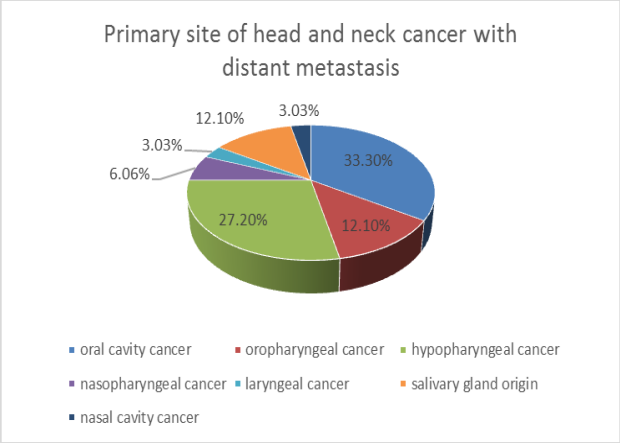

Figure 1: Primary site of head and neck cancer with distant metastasis.

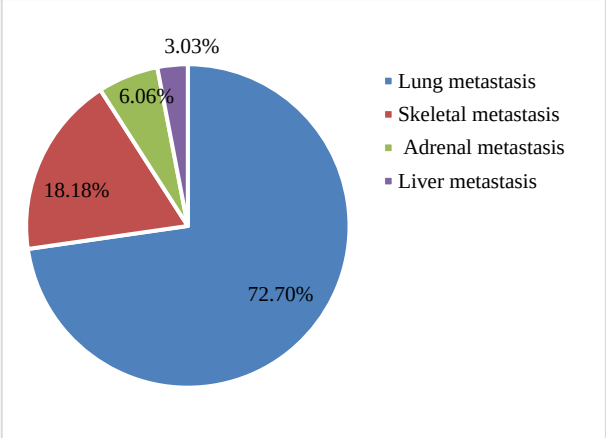

Figure 2: Site of distant metastasis.

DISCUSSION

PET CT imaging is now frequently being used in advanced head and neck cancer for staging, to detect distant metastasis, synchronous second primary tumors and for treatment planning. PET-CT scan can also be used as baseline imaging for follow up of the disease. PET provides metabolic information and CT complements the PET with anatomical information[3]. The functional imaging obtained by PET which depicts the spatial distribution of metabolic activity in the body can be more precisely correlated with the anatomical imaging obtained by CT scan. This unique quality confers on PET CT scan in providing the crucial information over and above routine examination and investigations. PET CT imaging has shown to alter and guide the management plan in patients with advanced head and neck malignancies.

A second primary tumor detected simultaneously or within 6 months of the initial primary tumor is defined as synchronous second primary. Emergence of a second primary lesion more than 6 months after the diagnosis of the index primary tumor is referred to as metachronous primary. The criteria used to identify the second primary cancer was originally described by Warren and Gates were as follows: 1) Each neoplasm must be geographically separate and distinct (it is considered as multicentric primary if the intervening mucosa shows dysplasia). The second primary had to be separated from the first primary by at least 2 cm of normal epithelium. 2) The possibility that the second primary representing the metastasis or relapse must be excluded. 3) The index tumor and the second primary tumors should be histologically confirmed.[4] Even though the incidence of synchronous second primary and distant metastasis is low, PET CT imaging could be a simple test rather than multiple diagnostic modalities like diagnostic panendoscopy, chest CT imaging and USG abdomen in detecting synchronous second primary and distant metastasis.

The incidence of second primary tumors can be explained by the field cancerization theory. Field cancerization theory was proposed by slaughter and colleagues in 1953. They hypothesized that in patients of upper aero-digestive tract carcinomas, the entire epithelial surface of the upper aero-digestive tract has an increased risk of second primary tumors and premalignant lesions. This increased risk could be due multiple genetic abnormalities in the whole upper aero-digestive tract secondary to exposure to common carcinogens present in tobacco, alcohol.[5] The occurrence of multiple tumors can be explained by two hypothesis, monoclonal theory and polyclonal theory. In monoclonal theory, a single cell is transformed to cancer cell and through the mucosal spread, these cells can give rise to multiple genetic related tumors. In polyclonal theory, the multiple transforming genetic events in the upper aero-digestive tract can give rise to genetically unrelated second primary tumors.[6]

In a retrospective study by Singa et al, the PET CT scans of 1522 patients were reviewed.[3] Out of 1522 patients, 68 patients were suspected to have a synchronous second primary tumour, in which 8 cases were histologically confirmed. Seven (0.4%) of them were malignant and 1 was a benign tumor. In their study, the prevalence of double primary malignant tumors was 0.4%. In another retrospective study, the PET CT scans of 1912 patients were reviewed, 1.2% (22 patients) of their patients were found to have second primary malignancy.[7] The above 2 studies have included patients of all malignancies. In a study by Strobel et al, PET CT images of 589 head and neck cancer patients were reviewed for the presence of synchronous primary and they have concluded that PET CT scan detects a considerable number of synchronous primaries (8% prevalence) at initial staging.[8] Lee et al, conducted a prospective study on 314 patients.[9] In their study, synchronous second primary in the head and neck cancers was identified in 8 patients (2.5%) and they found that the sensitivity and specificity of 18F-FDG PET/CT for identification of second primaries were 75.0% and 98.7%, respectively. In our study, 7 (1.49%) patients were found to have incidental synchronous second primary on PET CT imaging which is in keeping with the previous literature.

In a study by Krishnatreya et al, data of 4184 patients with head and neck cancer was retrospectively analyzed for the presence of second primary.[10] All their patients were worked up with endoscopy, imaging modality (computed tomography, chest x-ray). PET CT imaging was not used in their study either in the initial workup or in the subsequent follow-up. In their study, multiple primaries were seen in about 9.7% of head and neck cancer patients (both synchronous and metachronous malignancies, of which 46.9% presented as synchronous second primary).

In our study, majority of the index primary tumors in synchronous cancers were seen in hypopharynx. In the present study, out of 469 patients with histological confirmation of head and neck cancer, 7 patients (1.49%) had synchronous primary cancer at the initial presentation. The distribution of primary in the head and neck synchronous cancers was seen highest in hypopharynx. The site of synchronous second primary site in the head and neck cancer was highest in lung. In our study, the presence of distant metastasis at the initial presentation in the PET CT imaging was 7.03% and the common site of distant metastasis was lung followed by bone metastasis. The diagnosis of distant metastasis at the initial presentation adversely affects the survival, prognosis and treatment planning. Conventionally the tests detecting for distant metastasis and second primary tumors in patients with head and neck carcinomas include chest radiography, chest computed tomography, ultrasonography of the abdomen and the bone scan. In our study, the clinical staging of all head and neck cancer patients with distant metastasis are stage III/IV. This indicates that distant metastasis is common in patients with advanced head and neck cancer. Based on our results, PET CT can be considered in advanced stages of head and neck cancer patients at the initial presentation. In one of the largest published series of 73, 247 head and neck squamous cell carcinoma patients registered between 1988 to 2003, the distant metastatic rate of 2.82% at presentation was reported. They have concluded that there is a relationship between the tumor size, site, nodal status and distant metastatic rate.[11] In General, if distant metastasis is not present at initial presentation, it usually becomes apparent within 2 years.[12] The metastatic pattern of head and neck squamous cell carcinoma seems to be consistent with the distribution. In general, the reported frequency of metastasis in head and neck squamous cell carcinoma is approximately 70-85% in lungs followed by bone metastasis and liver metastasis.[12]

CONCLUSION

PET CT imaging is a useful tool to detect distant metastasis and second primary synchronous cancers in advanced head and neck cancers. The incidence of distant metastasis is a much more valid indication for the PET CT imaging in advanced head and neck cancers. PET CT imaging can be considered in advanced head and neck cancers at the initial presentation

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Jegu J, Foucard FB, Borel C, Velten M. Trends over three decades of the risk of second primary cancer among patients with head and neck cancer. Oral Oncol. 2013;49:9-14.

2. Strobel K, Haerle SK, Stoeckli SJ. Head and Neck Squamous cell carcinoma: detection of synchronous primaries with 18F-FDG-PET/CT. Eur J Nucl Med Mol Imaging. 2009;36:919-7.
3. Sing WC, Jie GN, Ching CY. Prevalence of synchronous second primary malignancy: Identification using whole body PET/CT imaging. Clin Imaging. 2013;38(2):179-86.
4. Warren S, Gates DC. Multiple primary malignant tumors: a survey of the literature. Am J Cancer. 1932;16:1358-414.
5. Slaughter DP, Southwick HW, Smejkal W. Field cancerization in oral stratified squamous epithelium: clinical implication of multicentric origin. Cancer. 1953;6(5):963-8.
6. Alok A, Singh ID, Panat SR, Singh S, Kishore M. Oral field cancerization: A Review. Int J Dent Med Res. 2014;1(3):98-104.
7. Ishimori T, Patel PV, Wahl RL. Detection of unexpected additional primary malignancies with PET CT. J Nucl Med. 2005;46(5):752-7.
8. Strobel K, Haerle SK, Stoeckli SJ, Schrank M, Jon D Soyka. Head and Neck Squamous cell carcinoma (HNSCC) -detection of synchronous primaries with 18 FDG PET CT. Eur J Nucl Med Mol Imaging. 2009;36:919-27.
9. Lee HS, Kim JS, Roh JL, Choi SH, Nam SY, Kim SY. Clinical values for abnormal 18F-FDG uptake in the head and neck region of patients with head and neck squamous cell carcinoma. Eur J Radiol. 2014;83(8):1455-60.
10. Krishnatreya M, Rahman T, Kataki AC, Das A, Das AK, Lahkar K. Synchronous primary cancers of the head and neck region and upper aero digestive tract: Defining high risk patients. Indian journal of cancer. Indian J Cancer. 2013;50(4):322-6.
11. Kuperman D, Auethavekiat V, Adkins DR, Nussenbaum B, Collins S, Boonchalermvichian C, et al. Squamous cell carcinoma of the head and neck with distant metastasis at presentation. Head Neck Surg. 2011;33:714-8.
12. Takes RP1, Rinaldo A, Silver CE, Haigentz M JR, Woolgar JA, Triantafyllou A, et al. Distant metastasis from head and neck squamous cell carcinoma. Part 1. Basic aspects. Oral Oncol. 2012;48(9):775-9.

Cite this article as: Gandla S, Rao V. Role of PET CT in the detection of second synchronous primary tumors and distant metastasis in head and neck cancers at initial presentation. Int J Otorhinolaryngol Head Neck Surg 2019;5:391-5.