

## Thyroid Metastasis of Squamous Cell Carcinoma in an Unsuspected Patient

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### Abstract

Malignancies metastasizing to thyroid are a very rare phenomenon. Out of them all, diagnosis of metastatic squamous cell carcinoma in thyroid can be difficult to establish as in thyroid there can also be a primary thyroid squamous cell carcinoma SCC.

We herein report a rare case of a 28-year old man with metastasis of oral SCC the thyroid gland. He was operated six months back, took incomplete cycles of adjuvant chemo-radiotherapy. On FDG-PET CT was found to have metabolically active lesions in right lobe of thyroid along with right paratracheal and bilateral cervical nodes.

Fine needle aspiration cytology (FNAC) smears from thyroid showed malignant squamous cells. Considering various factors like previous history, histopathology, present FDG-PET scan findings and present cytology diagnosis was concluded to be metastatic over primary thyroid SCC.

It is necessary to differentiate between primary or metastatic SCC in thyroid as they are different in clinical and prognostic behaviour. Primary squamous cell carcinoma is very aggressive with a poor prognosis.

**Keywords:** Thyroid; Squamous cell carcinoma; Immunohistochemistry; PAX8; FDG-PET CT scan

### Introduction

Tumoral metastasis to the thyroid is a rare entity with only a few cases reported in literature till date [1-5]. Metastasis to thyroid is mostly discovered on autopsy with an incidence of 0.5-24% and most of these cases have widespread tumoral metastasis at the time of presentation. Of all these cases of thyroid metastasis, patients presenting with a palpable thyroid mass or deranged thyroid function tests are less than a quarter. Tumors causing thyroid metastasis are mostly from lungs followed by bones, liver, kidney, breast, pancreas, colon, ovary, bladder and malignant melanoma.

Out of all malignancies metastasizing to thyroid, squamous cell carcinoma has an incidence of 0.2-1.1%. A squamous cell carcinoma metastasizing to thyroid commonly originates from lung, esophagus, head and neck region and cervix whereas primary thyroid SCC is extremely rare [6]. Hence presence of malignant squamous cells in thyroid FNAC should prompt a first suspicion of metastasis from an occult primary over primary thyroid. We have reported a case of SCC tongue giving metastasis to thyroid which was picked up on FDG-PET CT scan and followed on by FNAC.

### Case Report

A 26-year-old male presented with. Pain and ulceration at right border of tongue. He was operated outside for right hemiglossectomy with modified neck dissection for carcinoma tongue, 6 months. Patient took incomplete adjuvant treatment, 4 cycles of chemotherapy and 17 cycles of radiotherapy, against 6 cycles of chemo and 30 cycles of radiotherapy as advised. He had left the treatment on his own.

Histopathology of previous hemiglossectomy was: Moderately differentiated squamous cell carcinoma with focal sarcomatoid change. Tumor involving underlying muscle with perineural invasion and no lymphovascular emboli and a positive cervical node (1/29). Pathological stage was pT2pN1.

FDG-PET CT scan ordered for restaging, showed metabolically

active lesions over right tongue border, bilateral cervical lymph nodes, one sub centimetric right paratracheal lymph node. Few hypodense nodules, largest measuring 1 X 1 cm in the enlarged right lobe of thyroid were seen with abnormal FDG uptake, (SUV max 14.32) as shown in Figure 1a-1d. Extrathyroidal extension was not seen. No other abnormal FDG uptake was seen elsewhere in the body.

USG guided FNAC was performed from thyroid and right paratracheal node.

Smears were stained using May - Grönwald Giemsa staining for air dried smears and Hematoxylin and eosin and Papanicolaou staining for smears wet fixed in 95% alcohol.

The smears showed many benign thyroid follicular cells, macrophages, and colloid along with atypical cells in clusters and occasional scattered cells as shown in Figure 2a. Cells are polygonal with dense, orangeophilic cytoplasm, few with cytoplasmic tails. Nuclei are hyperchromatic, pleomorphic. No atypical mitosis, necrosis, giant cells or papillary or follicular pattern are seen in Figure 2b and 2c. Few cells were elongated, having cytoplasmic tails and with spindly nuclei as shown in Figure 2d.

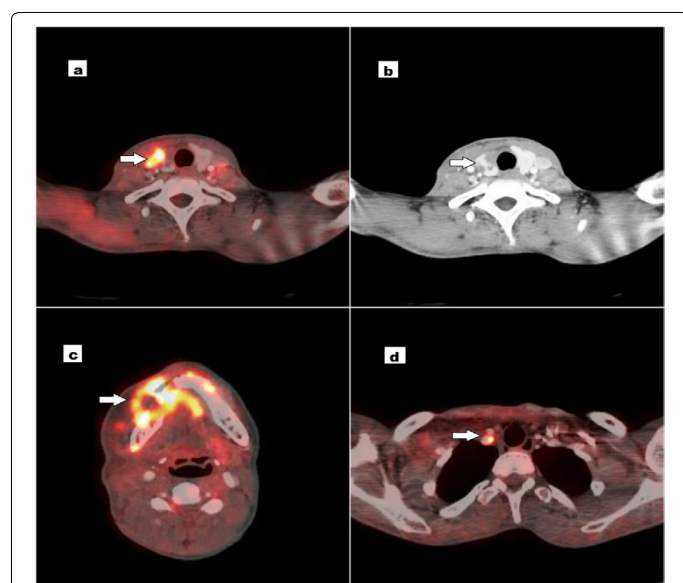
Similar tumor cells were also seen in smears from right paratracheal node. Considering previous history, histopathology, present FDG-PET scan findings and present cytology, a diagnosis of Metastatic squamous cell carcinoma-Bethesda VI was given.

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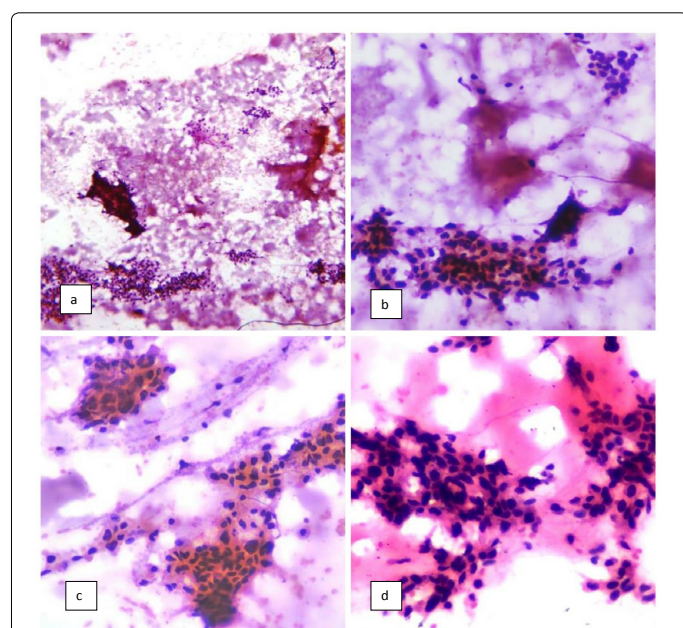
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**Figure 1:** (a and b) FDG- PET CT scan showing metabolically active lesions in (a) right lobe of thyroid (arrow), (c) right border tongue( arrow) - previous wide excision site, (d) right paratracheal node ( arrow).



**Figure 2:** (a and b) Benign thyroid follicular cells, colloid and tumor cells in clusters (PAP, 40x), (c) orangeophilic tumor cells (PAP, 40x), (d) tumor cell with cytoplasmic tails (arrow) (PAP, 40x).

Unfortunately, the patient was lost to follow up and could not be traced further.

## Discussion

Presence of squamous cells in thyroid is a very rare phenomenon. Incidence of Thyroid metastasis is more of an autopsy finding. Routes of thyroid involvement in head and neck SCC are lymphatic, hematogenous or local infiltration. Abundant, fast blood flow through the gland, high iodine content and hyperoxic environment, which prevent attachment and growth of tumor cell, are postulated to be the

probable factors which inhibit the development of metastatic tumor cells in thyroid.

Clinically thyroid SCC - primary, metastatic or local infiltration, may present as a nodule, diffuse swelling, signs due to local infiltration like dysphonia, dyspnoea, dysphagia or cough, it could be silent without any significant change or just an incidental finding on workup (as in the present case).

Main differential diagnosis on cytology are squamous metaplasia of thyroid follicular epithelial cells, papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) or anaplastic thyroid carcinoma (ATC) with squamous differentiation or primary SCC thyroid.

Presence of admixed normal thyroid follicular cells with tumor cells and absent papillary and follicular patterns favour metastasis on cytology.

However histopathology, along with immunohistochemistry is the best to form a definitive diagnosis. Immunohistochemical (IHC) analysis on FNAC material can be performed to give a diagnosis.

In identifying metastatic versus primary thyroid SCC, IHC plays a crucial role and markers can be selected based on suspected origin of tumor.

Thyroid marker, TTF1, is positive in majority of differentiated thyroid malignancies like PTC/FTC and usually negative in ATC and primary thyroid SCC. Whereas PAX-8, another nuclear marker is found to be consistently positive in all thyroid malignancies including PTC, FTC, ATC or primary thyroid SCC as well as in squamous metaplasia of thyroid follicular cells. The reason for presence of PAX 8 in all differentiated and poorly differentiated thyroid malignancies is cited as being primitive in chronological emergence when compared to TTF-1 [7,8].

On other hand, SCC of lungs, larynx, thymus, and skin will be positive for p 63 and HMW-CK whereas they barely express PAX 8.

Some common SCCs metastasizing to thyroid, eg. SCC from lung might occasionally show TTF1 positivity, there will definitely be absence of PAX -8 whereas HPV related SCCs originating from cervix or head neck region will show p16 positivity and PAX8 negativity [7-9].

PAX8 is therefore useful in distinguishing primary thyroid SCC from extrathyroidal SCC.

In cases with malignant squamous cells, distinction between primary thyroid SCC or metastatic SCC is necessary as it has both prognostic and therapeutic significance.

Primary thyroid SCC mostly occurs in 5<sup>th</sup> or 6<sup>th</sup> decade with a rapidly growing anterior neck mass and/or dysphagia/dyspnoea. Also primary SCC thyroid is associated with rapid progression, poor response to radiotherapy, even radio-resistant in some cases and poor prognosis. Several theories have been postulated regarding its etiology:

- The embryonic nest theory suggests that the squamous cells are derived from the remnants of thyroglossal duct or the epithelium of the thymus.
- The metaplasia theory suggests that these cells present as a result of environmental stimuli (inflammation and Hashimoto's thyroiditis).

Also the de-differentiation theory suggests that existing papillary, follicular, medullary and anaplastic thyroid carcinoma de-differentiate into SCC.

Radioisotope scan [FDG-PET] makes a huge difference in cases of such hidden metastases. A focal thyroid lesion with significant uptake is more malignant as opposed to diffuse uptake in other benign disorders like Graves disease, chronic thyroiditis, diffuse or multinodular goitre. Cytology is an easily available and accessible, non-invasive technique with a rapid turnaround time [10].

## Conclusion

Incidence of metastatic SCC to thyroid is much more than primary thyroid SCC. So, history of any primary tumor elsewhere, clinical presentation, radiology findings and cyto/histomorphology along with ancillary techniques (wherever possible) is necessary before finalizing any diagnosis.

Hence, in presence of malignant squamous cells in thyroid, it is known that cases of metastasis or direct invasion of SCC into the thyroid gland are more common than primary thyroid SCC.

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