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Synchronous Lung and Thyroid Cancers Our Experience and Review of Literature

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Abstract

The occurrence of multiple neoplasms is not rare. They can be either synchronous or metachronous. However primary lung and associated synchronous thyroid cancer is rare. We present our experience of 3 patients who were diagnosed and treated for synchronous lung and thyroid malignancies. PET- CT was an important diagnostic modality in detecting the synchronous second malignancy. All the patients underwent surgery for the lung and thyroid cancer simultaneously and had an uneventful postoperative recovery. 2 patients developed distant metastases secondary to the lung carcinoma in the follow up whereas 1 patient is disease free at 6 years follow-up. A high index of suspicion at the time of initial diagnosis of the primary cancer, relevant investigations and detailed genetic profiling helps in finding out the probable cause for such synchronousneoplasms.

Keywords*: synchronous; metachronous; lung; thyroid; PET-CT.*

Abbreviations:

UADT: upper aerodigestive tract

SCC:squamous cell carcinoma

FNAC: fine needle aspiration cytology

TTF-1: thyroid transcription factor-1

FVPTC: follicular variant off papillary thyroid cancer

NSCLC: non small cell lung cancer

HPE: histopathological examination

LVE: lymphovascular emboli

DFI: disease free interval

WBRT: whole brain radiotherapy

Introduction:

Bilroth in 1889 described a patient with multiple primary lesions in the upper aerodigestive tract (UADT).**[1]** Since then, many reports have described the association between squamous cell carcinoma (SCC) of the UADT and a second primary in the UADT. They can either be synchronous or metachronous. Incidence of multiple primary malignancies has progressively increased over time. Commonly occurring malignancies accompanying primary lung cancer are found in the lung, upper respiratory tract, breast, oesophagus, colon, rectum, stomach and cervix. **[**2**]** Thyroid malignancies have been linked with other cancers such as breast, prostate, kidney, salivary, scrotal, neural and leukemia **[**3,4**]**. Double primary thyroid and lung cancers have rarely been reported. **[**5,6**]** Here we describe 3 cases of synchronous lung and thyroid cancers each of which had a varied presentation.

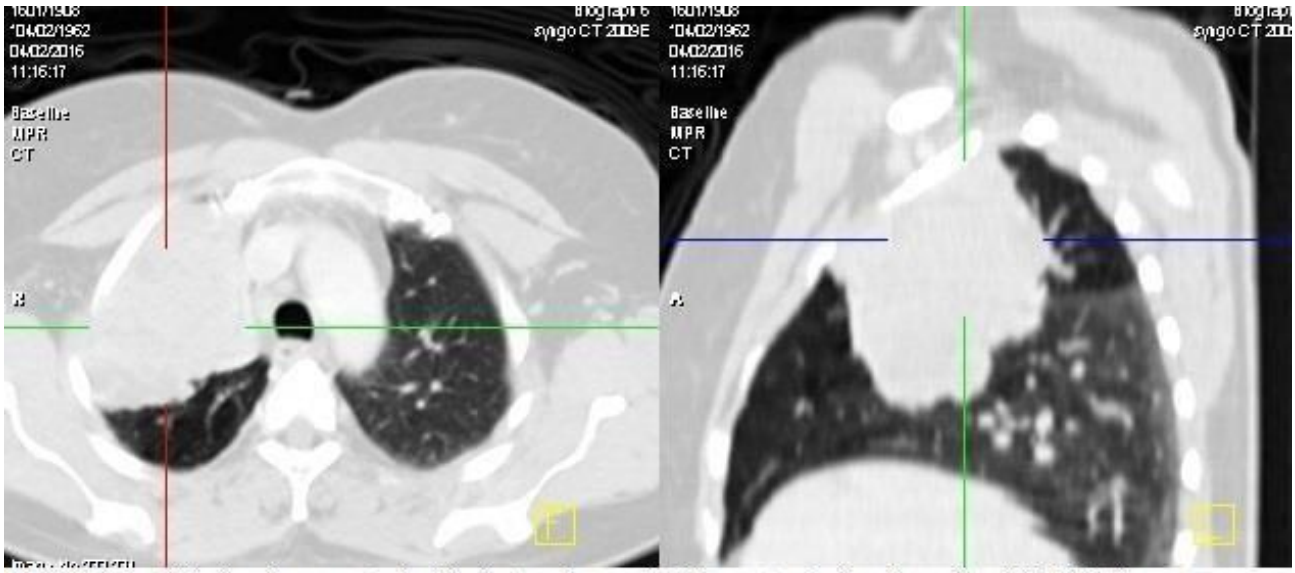

Fig 1: 54 year old lady who presented with chest pain, cough & hemoptysis since 2 months. (a) CECT shows a heterogenously enhancing mass in right UL extending laterally to the pleural surface

Figure 1 a

Fig 1(b): FDG avid mass (SUV Max 9.70) in upper lobe of right lung with another FDG avid nodule (SUV Max 4.05) in left lobe of thyroid gland

Figure 1 b

Case Reports:

Case 1: A 54 year old lady with no comorbidities presented with right sided chest pain, cough and hemoptysis since 2 months with an undocumented weight loss. CECT (Thorax) showed a heterogeneously enhancing irregular marginated soft tissue lesion in right upper lobe extending laterally to the pleural surface with multiple enlarged right upper and lower paratracheal nodes (Fig 1 [a]). PET- CT revealed a large hypermetabolic FDG avid mass lesion in the upper lobe of right lung (SUVmax: 9.70) with few hypermetabolic mediastinal lymph nodes,most likely metastasis. There was a hypermetabolic nodule in the lower pole of the left lobe of thyroid. (Fig 1[b]) No distant metastases were seen. MRI Brain was normal. CT guided FNAC of lung lesion was adenocarcinoma. FNAC of the thyroid lesion was suspicious for malignancy (Bethesda Cat V). She was planned for neoadjuvant chemotherapy followed by reassessment for surgery. She received 3 cycles of Permetrexed and Cisplatin which she tolerated well. She had good radiological and clinical response to the neoadjuvant chemotherapy. She underwent right upper and middle lobectomy with systematic mediastinal lymph node dissection with total thyroidectomy with central compartment clearance with bilateral selective neck dissection (level II-IV). The HPE report revealed mixed adenocarcinoma (acinar:50%, papillary:45% and solid:5%) of lung with invasion of visceral pleura and lymphatics with superior mediastinal nodes being positive. Final stage: pT3N2, Stage-IIIA.IHC was positive for CK-7, Napsin and TTF-1. The left hemithyroidectomy came out to be the follicular variant of papillary carcinoma(FVPTC) (max. tumour size: 3.5 cm) with no capsular or vascular invasion. The right hemithyroidectomy also showed FVPTC (max. tumor size 0.6cm). Both the central and lateral compartment node did not show any metastasis. IHC confirmed the diagnosis with positive reaction to Thyroglobulin, CK-19, Galectin-3 and HBME-1 [pT2N0Mx]. She received adjuvant chemotherapy and radiotherapy for her stage IIIA NSCLC. After a DFI of 5years, she presented with a solitary pubic bone metastasis and 2 brain metastases. She is planned for liquid biopsy and PDL- 1 testing followed by WBRT and chemotherapy or targetedtherapy.

Case 2: 49 year old lady with no comorbidities presented with backache and neck pain since 3 years. MRI spine showed age related changes in the spine with an incidental finding of a solid cystic lesion at the inferior pole of right lobe of thyroid. USG showed a small hypoechoic nodule in right lobe of thyroid with few areas of calcification. FNAC was suspicious for malignancy (Bethesda Cat.V). PET-CT showed a FDG avid lesion in right lobe of thyroid (SUV Max 10.2). Incidentally a small well defined spiculated FDG avid lesion was noted in lower lobe of left lung (SUV Max 3.24). CT guided FNAC of the left lower lobe mass was adenocarcinoma. She underwent total thyroidectomy with central and bilateral selective neck dissection (level II-V) with video assisted left lower lobectomy with systematic mediastinal lymph node dissection. The HPE of the lobectomy showed invasive mixed adenocarcinoma (lepidic:60%, acinar:35%,solid:5%). Max. tumor size is 2cm. No unequivocal LVE/PNI noted. Tumor involves the visceral pleura. No nodal metastases noted. Final stage: pT2aN0Mx. The right hemithyroidectomy

proved to be classical papillary carcinoma (max. tumor size 2.7cm) extending to the perithyroidal soft tissue with LVE+. Left thyroid lobe was unremarkable. 8/8 central compartment nodes show metastatic papillary carcinoma with PNI.8/15 right lateral compartment nodes show metastatic papillary carcinoma without PNI. Left lateral compartment (0/13 nodes) showed no metastases. Final stage: pT3N1bM0. Radio-iodine scan was done 1-month post-surgery showed focal uptake in the neck for which she was treated with high dose radio-iodine ablative therapy (100mCi). In view of early stage NSCLC, no adjuvant therapy but regular follow up was advised. She has now been disease free for 6 yrs.

Case 3: 60 year old lady, diabetic hypertensive on routine health check up was found to have a well defined shadow in left mid zone with a bulky left hilum. CECT Thorax showed a mildly enhancing partly necrotic lesion in the lower lobe of left lung with mildly enlarged mediastinal nodes. It also showed a heterogeneously enhancing nodule in left lobe of thyroid.

CT guided biopsy of the lung nodule was pulmonary adenocarcinoma (TTF-1+). PET-CT showed a FDG avid lobulated lesion in the lower lobe of the left lung (SUV Max 8.2) with hypermetabolic mediastinal lymph nodes (SUV Max 5). Thyroid gland was enlarged with increased metabolic activity seen in nodules in both lobes (SUV Max 3.5). FNAC of thyroid nodule was suspicious for malignancy (Bethesda Cat.V). She was planned for neoadjuvant chemotherapy. She took 2 cycles of Permetrexed and Carboplatin. Post neoadjuvant chemotherapy PET-CT showed good response to the therapy. She underwent a left pneumonectomy in view of the hilar nodes densely adherent and infiltrating into the MPA & SPV with systematic mediastinal lymph node dissection and total thyroidectomy with central compartment clearance. The HPE report showed invasive mixed adenocarcinoma (max tumor size 3cm) with invasion of visceral pleura and lymphatics with nodal metastases. Final stage: pT2N2aMx. The left hemithyroidectomy showed FVPTC (max tumor size 1.1cm). Tumor present over thyroid capsule and infiltrates the adjacent parathyroid. The right thyroid shows adenomatous colloid nodule. The central compartment nodes did not show any metastasis. Final stage being pT1N0Mx. The lung tumor was positive for Exon 19 deletion in EGFR. She was started on Tab. Geftinib 250 mg once a day. She had a disease free interval of (DFI) of 1year following which she developed liver and skeletal metastases. She was planned for T790M mutation studies followed by palliative chemotherapy.

Discussion:

Double primary thyroid and lung carcinomas have been reported rarely in the literature **[**5,6**]**. Shinozaki et al **[**7**]** reported that thyroid carcinoma occurred in 9.7% of patients with multiple primary malignancies, and the most frequent sites for the associated cancers were the breast, uterine cervix and uterine body in women, and the stomach and larynx in men. However, thyroid carcinoma was found with a higher rate of second malignancy (22.7%) than average (4.2%) in autopsy findings, and follicular carcinoma was more frequent among the cancers associated with another tumor (12 out of 20 cases), while in general papillary carcinoma was the most frequent (48 out of 88 cases). **[**8**]**

The most common associated malignancy in women is breast occurring in 36% of second cancers.[3,9] A review of literature did not find a consensus on the incidence of synchronous lung and thyroid cancer. Ronckers et al. had found decreased number of observed cases to expected cases of lung carcinoma with concurrent differentiated papillary thyroid carcinoma in the US

surveillance, epidemiology, and end result database.[3] However, smaller single center studies, like the one by Ömür et al. had found that lung carcinoma was the second most common malignancy occurring in 3 of 15 cases with synchronous thyroid carcinoma. **[**9**]** Differential diagnosis for these cases included pulmonary metastasis from the thyroid cancer or vice versa, and both the situations have been reported previously. **[**10**]** In our series, all our patients were females with a median age of 54 years. They presented with wide array of symptoms however none of the patients had any thyroid related complaints and were euthyroid at presentation. There was no family history of cancer, history of past head and neck radiation, smoking , and unhealthy environmental or work exposure and no other risk factors associated with either of these malignancies.

Hence it is hard to propose a theory for the development of these two primary malignancies. However considering the concurrent nature of these cancers, genetic counselling and hereditary cancer testing should be advised to find out any variances that could have led to their condition.

Incidental thyroid nodules were picked up in all of these patients who underwent PET-CT as the staging investigation for carcinoma lung. Incidental positive lesions are diagnosed while staging cancer patients with Whole body FDG PET at the rate of about 4.1-12% **[**1,11,12**]**. Incidental PET positivity in the thyroid can be either diffuse or focal. Diffuse positivity is linked with benign conditions like thyroiditis **[**13**]**. Focal positivity is less common with a rate of 0.8-4.9% **[**13,14,15**]** but carries a high risk of thyroid cancer with a rate of about 34-39.6% **[**14,15**]** .

Conclusion:

Synchronous lung and thyroid carcinomas have rarely been reported in literature. Diagnostic modalities like PET-CT help in diagnosis of synchronous cancers and was an extremely valuable diagnostic tool in our study. In our series all 3 patients were detected with a synchronous cancer with a PET-CT and underwent surgery for both cancers either upfront or post neoadjuvant chemotherapyin the same sitting with good postoperative recovery.

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