Surgery for Isolated Metachronous Thyroid Metastasis in a Non-small Cell Lung Carcinoma Patient with Hashimoto’s Thyroiditis: A Case Report

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Abstract

Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer deaths in Western population. Chemotherapy with platinum-based regimens is the first line management for majority of advanced NSCLC. Distant metastasis in lung cancer commonly involves the adrenal glands, liver, bones and brain. Metastatic involvement of the thyroid gland is infrequent despite its rich vascular supply. Here, we report a case of thyroid metastasis of NSCLC as a primary which was treated by thyroidectomy which is not the conventional approach. A 71 year-old female with a solitary left lower lobe lung mass was diagnosed with invasive poorly-differentiated adenocarcinoma. She was treated with cisplatin and pemetrexed followed by video-assisted thoracoscopic left lower lobectomy. The resected mass showed poorly-differentiated adenocarcinoma and was staged as pT2bN0 (Stage IIA). On a surveillance Computed Tomography (CT) chest, a left thyroid nodule was noted with findings consistent with Hashimoto’s thyroiditis in a multinodular goiter. Fine-needle aspiration biopsy was consistent with metastasis from lung primary. This represented a solitary site of metastasis based on positron emission tomography (PET) Scan. Metastatic involvement of thyroid gland is infrequent despite its rich vascular supply. Given the long disease-free interval (DFI) of 1.5 years from initial diagnosis to documentation of isolated thyroid metastasis, she underwent total thyroidectomy followed by platinum-based adjuvant chemotherapy. Patient continues to be disease-free for more than 3 years as of her last follow up. A greater than 3-year disease-free survival to date in this case demonstrates that thyroidectomy can be a successful approach in the management of isolated metachronous thyroid metastasis from NSCLC in the well-selected patient.

Keywords: Hashimoto’s Thyroiditis; Metastasis; Lung carcinoma

Introduction

Metastatic involvement of the thyroid gland is infrequent despite its rich vascular supply [1,2]. Metastasis to the thyroid gland rarely occurs from lung tumors. Chemotherapy with platinum-based regimens remains the first-line treatment for the management of metastatic lung cancer [3]. Lung cancer is the leading cause of cancer deaths in both men and women in the most of the western world [4] and the most common cause of cancer-related deaths worldwide. Non-small cell lung cancer (NSCLC) accounts for about 75% of lung cancer cases [5]. However, a plateau in survival has been reached with median survival of about 10-12 months with cytotoxic therapy for advanced disease [6,7]. Here, we present a case where the patient presented with an isolated thyroid metastasis two years after resection of the primary lung tumor and was treated with thyroidectomy, an unconventional approach for the management of metastatic lung cancer given the isolated metachronous nature of the metastasis. A disease free survival of 40 months has been observed with this approach so far.

Case Presentation

A 71 year-old Caucasian female presented in 03/2008 with complaints of increasing shortness of breath, cough and hemoptysis.

Figure 1: Hematoxylin and Eosin stained image of adenocarcinoma of lung. Original magnification 40x
The patient was treated for pneumonia, without any resolution of symptoms. A core needle biopsy diagnosed the presence of an invasive poorly-differentiated adenocarcinoma in a solitary pulmonary nodule located in the left lower lobe of the lung. She received perioperative neoadjuvant chemotherapy with cisplatin and pemetrexed as part of a clinical trial and subsequently underwent videoscopic-assisted thoracoscopic (VATS) left lower lobectomy with lymph node dissection on 12/21/2008. All resected lymph nodes were negative. The resected 6.1 cm mass showed poorly-differentiated adenocarcinoma (Figure 1) with negative margins, no pleural or angiolymphatic invasion with final pathologic stage of pT2bN0 (stage IIA, AJCC 7th edition).

She received two additional cycles of chemotherapy followed by surveillance. Computed Tomography (CT) surveillance scan on 06/08/2009 showed bulky appearance of the thyroid gland with apparent increase in size of a left mid-lobe nodule to 1 cm at the junction of the isthmus. Thyroid function tests revealed elevated TSH (45.57uIU/ml, normal range 0.35-5.5) and low T4 level (T4 2.9ug/dl, normal range 4.5-10.9). Thyroid ultrasound showed diffuse multinodular thyroid gland, consistent with Hashimoto’s thyroiditis. The patient was started on levothyroxine following which her TSH decreased to 0.15 within the next 3 months. An interval thyroid ultrasound around this period in 01/2010 showed a decrease in the size of the thyroid nodule.

However, follow-up CT Scan in 06/2010 showed interval enlargement of the left thyroid lobe nodule. On further evaluation in 07/2010, ultrasound of the neck showed the dominant left thyroid nodule to measure 1.5x1.7x1cm. Biopsy of the left thyroid nodule was positive for CK7, TTF-1 and negative for CK20, thyroglobulin consistent with metastatic adenocarcinoma morphologically similar to her original lung primary. Restaging Positron-emission tomography (PET/CT) scan on 08/30/2010 showed prominent enhancement in the left lobe of the thyroid gland (Figure 2) but without evidence of local recurrence or any other distant site of metastasis. Given the patient’s overall good health, the long disease-free interval (DFI) from her initial primary lung cancer diagnosis (1.5 years) and the isolated focus of metastasis, the patient underwent a total thyroidectomy in 09/2010. Thyroidectomy specimen confirmed metastatic lung adenocarcinoma in a background of extensive Hashimoto’s thyroiditis (Figure 3). The patient subsequently received three cycles of chemotherapy with cisplatin and vinorelbine with ‘adjuvant’ intent. The patient continues to have no evidence of disease recurrence or metastasis as of her most current follow-up in 1/2014 with a disease free survival of 40 months. The patient continues to be on surveillance.

**Discussion**

More than 75% of the cases of NSCLC are diagnosed in advanced stages [8]. Patients with stage IV metastatic non-small cell lung cancer (NSCLC) are generally believed to have an incurable disease. The standard therapy for metastatic cancer is systemic therapy. Patients with solitary metastatic disease represent a distinct subset of patients among metastatic diseases and represent a subgroup with a better prognosis instead of other Stage IV patients. Factors favoring satisfactory outcome of isolated synchronous (disease free interval <6 months) / metachronous (disease-free interval >6 months) metastasis in NSCLC post-treatment include control of the primary site,
confirmed solitary metastatic disease, good performance status, metachronous lesions and longer disease-free interval (DFI) from the diagnosis of the primary tumor. Multiple studies in the past have analyzed the role of different therapeutic approaches in the management of isolated metastasis in NSCLC.

Case series in the past have shown that surgical resection of isolated synchronous or metachronous hematogenous metastasis positively affects patient’s survival [9-11]. This was evident in a literature review conducted by Karakiouzic et al. [12]. Another study conducted by Collaud et al in 2012 [13] suggested that patients with oligometastatic disease may benefit from resection of both the primary lung tumor and the metastatic sites. There have been several case series indicating an improvement in the long-term (5 years) survival rates of patients after surgical resection of solitary metastases of the brain, adrenal gland, liver and other sites [14-24]. Brain and adrenal glands are the two most common sites of oligometastases considered for local ablative therapy.

Surgical series in literature which have evaluated operative versus non-operative intervention in prolonging survival in solitary metastasis from NSCLC. Raz et al reported good outcome following surgical intervention for isolated adrenal metastasis with a survival benefit in well-selected patients compared to non-operative management. The 5-year overall survival was 34% among 17 patients out of a total of 37 patients who underwent adrenalectomy. On the other hand, there were no long term survivors among patients with isolated adrenal metastasis who did not undergo surgical resection (P=0.002) [25].

Multiple cases series suggest that disease-free interval is prognostic in managing patients with isolated metastasis surgically [24,26,27]. In a study conducted by Mercier et al. [24] on 23 patients, the 5-year survival reached 38% after resection of an isolated metachronous adrenal metastasis (17 patients), whereas all patients with synchronous metastasis (6 patients) with a DFI <6 months died within 2 years after the adrenalectomy. A recent systematic review was done on 114 patients on the outcomes of adrenalectomy for isolated synchronous (DFI of 0 months) vs. metachronous (DFI of 12 months) adrenal metastasis in NSCLC by Tanvetyanon et al [28]. Median overall survival (OS) was shorter for patients with synchronous than those with metachronous metastasis (12 months vs. 31 months) and the difference was statistically significant. It is not clear why patients with metachronous metastasis fare better. One possible explanation is that patients in the synchronous group experience early morbidity and mortality associated with thoracotomy as opposed to those with metachronous metastasis who have recovered from the procedure. Also, the intrinsic biology of the tumors in the two groups is different, with synchronous lesions representing more aggressive biology. Hence, we propose that surgical resection of metachronous isolated adrenal metastasis may be considered as the treatment of choice if the DFI is greater than 6 months and complete resection of the primary NSCLC has been achieved.

A mass in the thyroid gland should be treated as a metastatic lesion until proven otherwise in a patient with a history of carcinoma remotely, even if the primary tumor has been completely excised [29] and needless to say, the mass turned out to be a metastatic lesion in our case too!! In our patient, thyroid metastasis was documented when growth recurred in a nodule that had initially responded to thyroid hormone supplementation prescribed for Hashimoto’s thyroiditis with underlying multinodular goiter. While Hashimoto’s thyroiditis is associated with papillary thyroid carcinoma as has been shown in previous case reports [30,31], data showing its association with metastatic carcinoma is lacking and its occurrence in our case is most likely coincidental. Thyroid gland metastases from different primaries have been studied by Nahkjavani et al. [32] and aggressive surgical and medical therapies were effective in a small percentage of patients.

In our case, the enlarging thyroid mass was shown to be a metastasis from the lung cancer primary 1.5 years from initial diagnosis. Surgery as the primary approach of management was deemed to be feasible in our case because the patient presented with a solitary metachronous metastasis and several case series in the past have shown improved survival following solitary metastatectomy in similar presentation.

**Conclusion**

This is a rare case of an isolated metachronous thyroid metastasis from lung adenocarcinoma treated with thyroidectomy and adjuvant chemotherapy leading to a good outcome. Survival benefit has been demonstrated in NSCLC patients with solitary metastatic involvement of either the brain or adrenal gland who underwent surgical resection of both the primary and metastatic tumor. There are no such studies till date on thyroid metastasis given the rarity of isolated involvement and thus prospective studies are not feasible. A disease-free survival of 40 months after treatment of metastasis in this case suggests that thyroidectomy with curative intent may be regarded as the first line treatment in well-selected patients.

**References**


