

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

Shipra Gandhi¹, Neha Gupta^{2*}, Saraswati Pokharel³ and Grace K. Dy⁴

¹Department of Internal Medicine, University at Buffalo, NY, USA

²Department of Internal Medicine, Banner Medical Group, AZ, USA

³Department of Pathology, Roswell Park Cancer Institute, NY, USA

⁴Department of Oncology, Roswell Park Cancer Institute, NY, USA

*Corresponding author: Neha Gupta, Internal Medicine Department, Banner Medical Group, 14502 W Meeker Blvd, Sun City West, AZ 85375, USA, Tel: +623-524-8814; E-mail: neha.gupta@bannerhealth.com

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Abstract

Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer deaths in the Western population. Chemotherapy with platinum-based regimens is the first-line management for the 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 the 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.

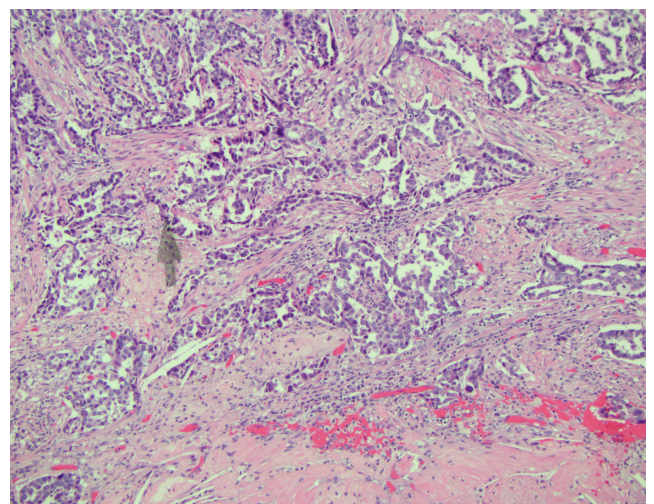


Figure 1: Hematoxylin and Eosin stained image of adenocarcinoma of lung. Original magnification 40x

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).



Figure 2: PET/CT shows prominent FDG-avidity in the left thyroid lobe

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.

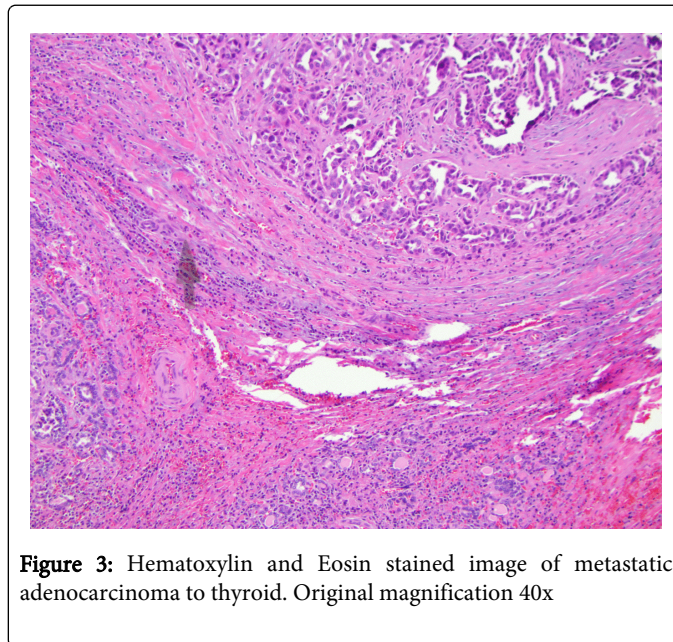


Figure 3: Hematoxylin and Eosin stained image of metastatic adenocarcinoma to thyroid. Original magnification 40x

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 Nakhjavani 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

1. Dionigi G, Uccella S, Gandolfo M, Lai A, Bertocchi V, et al. (2008) Solitary intrathyroidal metastasis of renal clear cell carcinoma in a toxic substernal multinodular goiter. *Thyroid Res* 1: 6.
2. Lam KY, Lo CY (1998) Metastatic tumors of the thyroid gland: a study of 79 cases in Chinese patients. *Arch Pathol Lab Med* 122: 37-41.
3. Bunn PA Jr, Kelly K (1998) New chemotherapeutic agents prolong survival and improve quality of life in non-small cell lung cancer: a review of the literature and future directions. *Clin Cancer Res* 4: 1087-1100.
4. Greenlee RT, Murray T, Bolden S, Wingo PA (2000) Cancer statistics, 2000. *CA Cancer J Clin* 50: 7-33.
5. Hoffman PC, Mauer AM, Vokes EE (2000) Lung cancer. *Lancet* 355: 479-485.
6. Kelly K, Crowley J, Bunn PA Jr, Presant CA, Grevstad PK, et al. (2001) Randomized phase III trial of paclitaxel plus carboplatin versus vinorelbine plus cisplatin in the treatment of patients with advanced non-small-cell lung cancer: a Southwest Oncology Group trial. *J Clin Oncol* 19: 3210-3218.
7. Schiller JH, Harrington D, Belani CP, Langer C, Sandler A, et al. (2002) Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med* 346: 92-98.
8. Jemal A, Siegel R, Ward E, Murray T, Xu J, et al. (2007) Cancer statistics, 2007. *CA Cancer J Clin* 57: 43-66.
9. Sonett JR, Suntharalingam M, Edelman MJ, Patel AB, Gamliel Z, et al. (2004) Pulmonary resection after curative intent radiotherapy (>59 Gy) and concurrent chemotherapy in non-small-cell lung cancer. *Ann Thorac Surg* 78: 1200-1205.
10. Hu C, Chang EL, Hassenbusch SJ 3rd, Allen PK, Woo SY, et al. (2006) Nonsmall cell lung cancer presenting with synchronous solitary brain metastasis. *Cancer* 106: 1998-2004.
11. Yamanaka R (2009) Medical management of brain metastases from lung cancer (Review). *Oncol Rep* 22: 1269-1276.

12. Karagkiouzis G, Kouloxouzis G, Tomos P, Spartalis ED, Konstantinou F, et al. (2012) Solitary metastasectomy in non-small cell lung cancer. *J BUON* 17: 712-718.
13. Collaud S, Stahel R, Inci I, Hillinger S, Schneiter D, et al. (2012) Survival of patients treated surgically for synchronous single-organ metastatic NSCLC and advanced pathologic TN stage. *Lung cancer* 78: 234-238.
14. Schuchert MJ, Luketich JD (2003) Solitary sites of metastatic disease in non-small cell lung cancer. *Curr Treat Options Oncol* 4: 65-79.
15. Girard N, Cottin V, Tronc F, Etienne-Mastroianni B, Thivolet-Bejui F, et al. (2006) Chemotherapy is the cornerstone of the combined surgical treatment of lung cancer with synchronous brain metastases. *Lung Cancer* 53: 51-58.
16. Getman V, Devyatko E, Dunkler D, Eckersberger F, End A, et al. (2004) Prognosis of patients with non-small cell lung cancer with isolated brain metastases undergoing combined surgical treatment. *Eur J Cardiothorac Surg* 25: 1107-1113.
17. Billing PS, Miller DL, Allen MS, Deschamps C, Trastek VF, et al. (2001) Surgical treatment of primary lung cancer with synchronous brain metastases. *J Thorac Cardiovasc Surg* 122: 548-553.
18. Gaspar LE (2004) Brain metastases in lung cancer. *Expert Rev Anticancer Ther* 4: 259-270.
19. Modi A, Vohra HA, Weeden DF (2009) Does surgery for primary non-small cell lung cancer and cerebral metastasis have any impact on survival? *Interact Cardiovasc Thorac Surg* 8: 467-473.
20. Yoshinaga Y, Enatsu S, Iwasaki A, Shirakusa T (2006) [Surgical treatment for primary non-small cell lung cancer with synchronous brain metastases]. *Kyobu Geka* 59: 41-45.
21. Granone P, Margaritora S, D'Andrilli A, Cesario A, Kawamukai K, et al. (2001) Non-small cell lung cancer with single brain metastasis: the role of surgical treatment. *Eur J Cardiothorac Surg* 20: 361-366.
22. Bonnette P, Puyo P, Gabriel C, Giudicelli R, Regnard JF, et al. (2001) Surgical management of non-small cell lung cancer with synchronous brain metastases. *Chest* 119: 1469-1475.
23. Porte H, Siat J, Guibert B, Lepimpec-Barthes F, Jancovici R, et al. (2001) Resection of adrenal metastases from non-small cell lung cancer: a multicenter study. *Ann Thorac Surg* 71: 981-985.
24. Mercier O, Fadel E, de Perrot M, Mussot S, Stella F, et al. (2005) Surgical treatment of solitary adrenal metastasis from non-small cell lung cancer. *J Thorac Cardiovasc Surg* 130: 136-140.
25. Raz DJ, Lanuti M, Gaissert HC, Wright CD, Mathisen DJ, et al. (2011) Outcomes of patients with isolated adrenal metastasis from non-small cell lung carcinoma. *Ann Thorac Surg* 92: 1788-1792.
26. Kim SH, Brennan MF, Russo P, Burt ME, Coit DG (1998) The role of surgery in the treatment of clinically isolated adrenal metastasis. *Cancer* 82: 389-394.
27. Pfannschmidt J, Schlolaut B, Muley T, Hoffmann H, Dienemann H (2005) Adrenalectomy for solitary adrenal metastases from non-small cell lung cancer. *Lung Cancer* 49: 203-207.
28. Tanvetyanon T, Robinson LA, Schell MJ, Strong VE, Kapoor R, et al. (2008) Outcomes of adrenalectomy for isolated synchronous versus metachronous adrenal metastases in non-small-cell lung cancer: a systematic review and pooled analysis. *J Clin Oncol* 26: 1142-1147.
29. McCabe DP, Farrar WB, Petkov TM, Finkelmeier W, O'Dwyer P, et al. (1985) Clinical and pathologic correlations in disease metastatic to the thyroid gland. *Am J Surg* 150: 519-523.
30. Lee JH, Kim Y, Choi JW, Kim YS (2013) The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysis. *Eur J Endocrinol* 168: 343-349.
31. Zhang L, Li H, Ji QH, Zhu YX, Wang ZY, et al. (2012) The clinical features of papillary thyroid cancer in Hashimoto's thyroiditis patients from an area with a high prevalence of Hashimoto's disease. *BMC Cancer* 12: 610.
32. Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA (1997) Metastasis to the thyroid gland. A report of 43 cases. *Cancer* 79: 574-578.