Case report

Second primary lung carcinoma in patients with first primary breast carcinoma: two case reports and review of the literature

Shi-Ping Luh¹*, Ching-Chung Chiang² and Mao-Te Chuang¹

Addresses: ¹Department of Surgery, Chia-Yi St Martin De Porres Hospital and Institute of Biomedical Engineering, National Chiao-Tung University, No. 565, Sec 2, Da-Ya Rd, Chia-Yi City, Taiwan
²Chia-Yi Christian Hospital and Institute of Biomedical Science, National Chung-Cheng University, No. 539, Chung-Shiao Rd, Chia-Yi City, Taiwan

Email: SPL* - luh572001@yahoo.com.tw; CCC - gschiang@yahoo.com.tw; MTC - chuang.maote@msa.hinet.net
*Corresponding author

Received: 27 May 2009 Accepted: 19 June 2009 Published: 24 July 2009

Cases Journal 2009, 2:7993 doi: 10.4076/1757-1626-2-7993

This article is available from: http://casesjournal.com/casesjournal/article/view/7993

© 2009 Luh et al; licensee Cases Network Ltd.
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Introduction: Patients undergoing complete treatments of breast carcinoma can be found with pulmonary nodules during the follow up period. Either metastasis from breast carcinoma or second primary bronchogenic carcinoma should be considered as a possible diagnosis.

Case presentations: Two female patients with ages of 66 and 64, underwent modified radical mastectomy for breast carcinoma 5 and 2 years ago, were found with single pulmonary nodule, 1.0 cm and 0.8 cm from the left lower and right upper lobe. There was no other site of metastasis being noted after systemic survey.

Wedge resections through video assisted thoracic surgery were performed and one of them underwent lobectomy and mediastinal lymph node dissection after the primary lung carcinoma being proved pathologically (thyroid transcription factor 1 and cytokeratin 7 positive). The dissected lymph node in this patient is negative for malignancy. They underwent low dose chemotherapy postoperatively because of increased risk of tumor occurrence for these patients. Patients with smoking or irradiation history usually favor the diagnosis of second primary lung carcinoma. However, these two treated breast carcinoma cases, which didn’t have smoking or irradiation history, developed second primary lung carcinomas. It is relatively rare reported before.

Conclusions: Pulmonary nodules in patients with prior breast carcinomas were usually regarded as metastatic lesions. However, the possibility of second primary still cannot be excluded, especially to the solitary type. Video assisted thoracic surgery can provide early and accurate diagnosis as well as effective treatment.

Introduction

Pulmonary nodules that appear in a patient with prior malignancy may be a metastasis or a second primary lung cancer [1]. Lung cancer is so prevalent in the world that the possibility of a second primary lesion in the above situation, especially a solitary nodular type, is much higher than before. Many factors, such as the type of prior malignancies, the choice of treatment strategies especially.
the field and dose of irradiation, the smoking history and
the radiographic characteristics will influence the possi-
bility of diagnosis [2]. Herein two treated breast carcinoma
cases without prior smoking or irradiation history,
developed second primary lung carcinomas, which were
relatively rarely presented before.

Case presentations

Case report 1
A 66-year-old non-smoking Taiwanese woman had
received modified radical mastectomy (MRM) for her
left breast carcinoma 5 years ago. No axillary lymph
nodal metastasis (0/11) was noted. The estrogen and
progesterone receptors are negative, and Her2/neu shows
over-expression (2+) on the resected specimen. She
underwent postoperative adjuvant chemotherapy with
6 courses of intravenous epirubicin and fluorouracil, oral
UFUR control for 24 months and Nolvadex for 5 years.
No local irradiation was administered before. The clinical
course was smooth postoperatively, until a pulmonary
nodule was accidentally found on the Chest X-ray several
days ago. Chest computed tomography (CT) revealed a
1 cm mild enhancing nodule in posterior segment of
left lower lobe of lung with spiculated margin (Figure 1).
The serum carcino-embryonic antigen (CEA) level was
within normal range (0.5 ng/ml). Pulmonary primary
carcinoma or metastasis is highly suspected and thus she
underwent tumor wedge resection through video-assisted
thoracoscopic surgery (VATS) (Figure 2). The pathologi-
cal report revealed a TTF1 and CK7 positive primary
lung adenocarcinoma. Thus she underwent left
lower lobectomy and mediastinal lymph nodes dissec-
tion. No residual tumor or lymph nodes metastasis was
noted on histopathological examination. She underwent
oral UFUR control postoperatively and her condition is
stable without evidence of tumor recurrence or
metastasis.

Case report 2
A 64 year old non-smoking Taiwanese woman received
MRM for her right breast carcinoma 2 years ago. No
axillary lymph nodal metastasis (0/21) was noted. The
estrogen and progesterone receptors are negative, and
Her2/neu shows over-expression (3+) on the resected
specimen. She underwent oral chemotherapy with UFUR
and hormone therapy with Nolvadex postoperatively.
However, a tiny pulmonary nodule was noted accidentally
on the chest X-ray after two years of follow up. Chest CT
revealed a 0.8cm nodule with smooth margin over the
right upper lobe of lung (Figure 3). She underwent VATS
wide excision under the impression of pulmonary metas-
tasis from breast carcinoma (Figure 4). However, the
pathological report revealed a TTF1 (+) and CK7 (+)
bronchoalveolar carcinoma with mucinous variant and the
safety margins were over 2 cm. After discussion with
her families, she was undergoing postoperative intravenous

Figure 1. Chest X-ray and CT in Case 1 revealed a 1 cm nodular shadow over the supra-diaphragmatic area of the left lung.
NC (navelbine/cisplatin) regimen for four courses. She was stable on the 4 months of follow up period.

**Discussion**

Breast irradiation will increase the risk of second primary lung carcinoma, and a multiplicative effect was observed in smokers. For both smokers and nonsmokers, this effect only existed in the ipsilateral lung [3,4]. Modern techniques, however, significantly decrease the radiation dose to the lungs, which may decrease the risk of lung cancer [5]. Galper S et al (2002) reviewed about 1800 stage I or II breast carcinoma patients who underwent surgery followed by adjuvant radiotherapy [6]. Second non-breast malignancies occur in a substantial minority (8%) of patients treated with conservative surgery and radiotherapy, and the absolute excess risk compared with the general population is very small (1%) and this excess risk is only evident after 5 years. Obedian E et al (2000) also found that lumpectomy followed by modern irradiation technique will not increase the risk of second malignancies compared with mastectomy [7]. Fowble B et al (2001) found that in breast carcinoma patients undergoing lumpectomy and irradiation treatment, contralateral breast cancer will occur more likely in young patients, and the non-breast cancer second malignancy will more commonly occur in older ones [8]. The correlation between cigarette smoking and bronchogenic carcinoma still exists, but never so strong as before. In recent years, more and more non-smokers suffered from lung cancers, especially the adenocarcinoma. However, these above rules are contradictory to our two patients with prior breast carcinoma and second primary lung carcinoma. Both of them were old aged non-smokers, and never received irradiation before.

*Figure 2. Video-assisted thoracoscopic surgery in Case 1. (A) the nodule revealing visceral pleural retraction sign. (B) and (C) This nodule was resected by Endo-GIA stapling and division. (D) The thoracoscopic wound (three ports design).*
Prior tumor type and number of nodules will influence the possibility of diagnosis in patients with pulmonary nodules at the follow up period. Solitary pulmonary nodule (SPN) is more likely to be a second primary lung carcinoma than multiple nodules. SPN in patients with carcinomas of the head and neck, bladder, breast, cervix, bile ducts, esophagus, ovary, prostate, or stomach, were more likely to be a primary bronchogenic carcinoma than a metastatic lesion. SPN in patients with carcinomas of the colon, salivary glands, adrenal gland, thyroid, thymus, kidney or uterus had fairly even odds in the above two possibilities. However, SPN will be more likely a metastatic lesion than a primary tumor in patients with melanoma, sarcoma, or testicular carcinoma [1,9,10].

Solitary pulmonary nodule (SPN) occurs in about 1 per 500 chest radiographs. The most important goal of its diagnosis is to differentiate benign from malignant lesions. Computed tomography (CT) should be considered for all patients with SPNs, because it can provide more information for subsequent management strategies [11]. Nodule morphology might provide valuable information to judge the type of lesion. Smooth margins would be more indicative of a benign lesion or metastasis, whereas irregular margins might be suggestive of a new lung cancer [12]. The existence of regional lymph nodes, the number of nodules and their relationships with adjacent structure can also give information to discern these two possibilities. Further imaging evaluation, such as positron-emitted tomography (PET), is generally not recommended because of its limited specificity for the diagnosis of SPN [13].

Tissue diagnosis is usually required except that the possibility of malignancy is very low. Needle biopsy through the guidance of CT or sonography can be considered but with lower specificity and result in significant complications, such as pneumothorax and hemothorax [14]. Total excision of the SPN through video-assisted thoracic surgery or thoracotomy is usually indicated for specific diagnosis and definite therapy [15,16]. Many localization techniques, such as hooks, coils, and radiotracer markers can be used to facilitate the subsequent resection procedures [17]. However, in our experience most of the peripheral nodule, even though sub-centimeter in size, can be located by imaging and confirmed by finger palpation.

The distinction of a primary lung carcinoma from a metastatic lesion is important, because the treatment and prognosis differ for patients with these malignancies. In histological sections, the existence of acini, lepidic growth, nuclear pseudoinclusions, and scar favor the diagnosis of primary lung adenocarcinoma; on the contrary, comedonecrosis, solid nests, trabecular architecture, and cribriform growth can be identified in metastatic breast carcinoma [18]. Such a distinction can also be achieved by detection of special markers on the histological specimens, such as Thyroid transcription factor-1 (TTF-1) or mammaglobin 1 [19,20]. TTF-1, which was used in our presented cases, is a protein that regulates transcription of genes, and thus it is used as a marker to determine if a tumor arises from the lung or thyroid [19]. TTF1 is usually positive in pulmonary adenocarcinoma or small cell carcinoma. However, rarely...
does it be positive in the squamous or large cell carcinoma of lung. TTF1 will also express in tumors other than lung and thyroid, such as ovarian or endometrial carcinoma [21,22]. PE-10, a monoclonal antibody against components of human surfactant proteins, and cytokeratin (CK) 7 and 20, are also fairly specific markers for the diagnosis of primary lung tumors [23]. The survival of patients with second primary lung cancer depends on the timing of diagnosis and the staging during resection [24], and thus early detection of pulmonary nodule by image follow up and surgical intervention at early stage are very important for these patients.

Conclusions
Pulmonary nodules in patients with prior breast carcinomas were usually regarded as metastatic lesions. However, the possibility of second primary lesions still cannot be excluded, especially to the solitary type. VATS can provide early and accurate diagnosis as well as effective treatment.

Abbreviations
CT, computed tomography; SPN, solitary pulmonary nodule; VATS, video-assisted thoracoscopic surgery; CK, cytokeratin; PET, positron emitted tomography.

Consent
Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.
Authors’ contributions
SPL performed the surgery, cared for the patient and wrote the manuscript. CCC assisted SPL in performing the surgery and writing the manuscript. MTC assisted SPL in writing the manuscript.

References
1. Mery CM, Pappas AN, Bueno R, Mentzer SJ, Lukanic JM, Sugarbaker DJ, Jaklitsch MT: Relationship between a history of antecedent cancer and the probability of malignancy for a solitary pulmonary nodule. Chest 2004, 125:2175-2181.
2. Swensen SJ, Silverstein MD, Itslrup DM, Schleck CD, Edell ES: The probability of malignancy in solitary pulmonary nodules. Application to small radiologically indeterminate nodules. Arch Intern Med 1997, 157:849-855.
3. Neugut AI, Murray T, Santos J, Amols H, Hayes MK, Flannery JT, Robinson E: Increased risk of lung cancer after breast cancer radiation therapy in cigarette smokers. Cancer 1994, 73:1615-1620.
4. Kaufman EL, Jacobson JS, Hershman DL, Desai M, Neugut AI: Effect of breast cancer radiotherapy and cigarette smoking on risk of second primary lung cancer. J Clin Oncol 2008, 26:392-398.
5. Inskip PD, Stovall M, Flannery JT: Lung cancer risk and radiation dose among women treated for breast cancer. J Natl Cancer Inst 1994, 86:983-988.
6. Galper S, Gelman R, Recht A, Silver B, Kohli A, Wong JS, Van Buren T, Baldini EH, Harris JR: Second nonbreast malignancies after conservative surgery and radiation therapy for early-stage breast cancer. Int J Radiat Oncol Biol Phys 2002, 52:406-414.
7. Obiedian E, Fischer DB, Haffty BG: Second malignancies after treatment of early-stage breast cancer: lumpectomy and radiation therapy versus mastectomy. J Clin Oncol 2000, 18:2406-2412.
8. Fowlke B, Hanlon A, Freedman G, Nicolau N, Anderson P: Second cancers after conservative surgery and radiation for stages I-II breast cancer: identifying a subset of women at increased risk. Int J Radiat Oncol Biol Phys 2001, 51:679-690.
9. Quint LE, Park CH, Iannettoni MD: Solitary pulmonary nodules in patients with extrapulmonary neoplasms. Radiology 2000, 217:257-261.
10. Massard G, Ducrocq X, Beaufigeau M, Elia S, Kessler R, Herve J, Vilholm J: Lung cancer following previous extrapulmonary malignancy. Eur J Cardiothorac Surg 2000, 18:524-528.
11. Miller DL: Management of the subcentimeter pulmonary nodule. Semin Thorac Cardiovasc Surg 2002, 14:281-285.
12. Cahan WG, Shah JP, Castro EB: Benign solitary lung lesions in patients with cancer. Ann Surg 1978, 187:241-244.
13. Ost D, Fein A: Management strategies for the solitary pulmonaty nodule. Curr Opin Pulm Med 2004, 10:272-278.
14. Mitamura S, Landreneau RJ, Mack MJ, Fetterman LS, Gammie J, Bartley S, Sutherland SR, Bowers CM, Keenan RJ, Ferson PF et al.: Diagnosing the indeterminate pulmonary nodule: percutaneous biopsy versus thoracoscopy. Surgery 1995, 118:676-684.
15. Rona O, Papalia E, Ruffini E, Filosso PL, Oliaro A, Maggi G, Casadio C: The role of surgery in the management of solitary pulmonary nodule in breast cancer patients. Eur J Surg Oncol 2007, 33:546-550.
16. Luh SP, Liu HP: Video-assisted thoracic surgery – the past, present status and the future. J Zhejiang Univ Sci B 2006, 7:118-128.
17. Daniel TM: A proposed diagnostic approach to the patient with the subcentimeter pulmonary nodule: techniques that facilitate video-assisted thoracic surgery excision. Semin Thorac Cardiovasc Surg 2005, 17:115-122.
18. Herbst J, Jenders R, McKenna R, Marchevsky A: Evidence-based criteria to help distinguish metastatic breast cancer from primary lung adenocarcinoma on thoracic frozen section. Am J Clin Pathol 2009, 131:122-128.
19. Agrios George N: Plant Pathology. 4th edition. New York: Academic Press; 1997.
20. Okazaki T, Usami N, Mitudomi T, Yatabe Y, Matsuo K, Yokoi K: Stepwise examination for differential diagnosis of primary lung cancer and breast cancer relapse presenting as a solitary pulmonary nodule in patients after mastectomy. J Surg Oncol 2008, 98:510-514.
21. Kubba LA, McClellough WG, Liu J, Malpica A, Euscher ED, Silva EG, Deavers MT: Thyroid transcription factor I expression in ovarian epithelial neoplasms. Mod Pathol 2008, 21:485-490.
22. Siami K, McClelgough WG, Ordneze NG, Euscher ED, Malpica A, Sniege N, Silva EG, Deavers MT: Thyroid transcription factor I expression in endometrial and endocervical adenocarcinomas. Am J Surg Pathol 2007, 31:1759-1763.
23. Chhieng DC, Cangigrella JF, Zakowski MF, Goswani S, Cohen JM, Yee HT: Use of thyroid transcription factor I, PE-10, and cytokeratins 7 and 20 in discriminating between primary lung carcinomas and metastatic lesions in fine-needle aspiration biopsy specimens. Cancer 2001, 93:330-336.
24. Kerendi F, Gal A, Corvera JS, Halkos ME, Miller JJ: Characteristics of second primary lung malignancy in patients with known breast cancer. South Med J 2009, 102:269-274.

Do you have a case to share?
Submit your case report today
- Rapid peer review
- Fast publication
- PubMed indexing
- Inclusion in Databases

Any patient, any case, can teach us something

www.casesnetwork.com