

A Rare Presentation of Cutaneous Metastases in Advanced Lung Adenocarcinoma

Liyana Dhamirah Aminuddin, Sabrina Ab Wahab, Suhaili Shariffudin, Tarita Taib

Dermatology Unit, Department of Medicine, Faculty of Medicine, Universiti Teknologi MARA (UiTM), Selangor, Malaysia

Received

25th March 2020

Received in revised form

6th May 2020

Accepted

5th June 2020

Corresponding author:

Liyana Dhamirah Aminuddin,

Dermatology Unit,
Faculty of Medicine,
Universiti Teknologi MARA (UiTM)
Sungai Buloh Campus,
47000 Sungai Buloh, Selangor,
Malaysia

Tel: +603-61264800/ +60126480020

Fax: +603-61265164

Email: liyanadhamirah@uitm.edu.my

ABSTRACT

Patients with lung cancer may present with respiratory and systemic symptoms. However, cutaneous metastases from primary lung cancer is a rare phenomenon, especially in women, that signifies a poor prognosis. This paper reported a case regarding a 71-year-old woman who was first presented with a cutaneous nodule over the year. Her condition was further progressed to multiple lesions on the back and abdomen, dyspnoea, haemoptysis and weight loss. The results of the skin lesion biopsy exhibited metastatic lung adenocarcinoma with positive immunohistochemistry for thyroid transcription factor 1 (TTF1) and cytokeratin 7 (CK-7). Computed tomography (CT) scan was conducted, and it revealed a left upper lobe lung mass. The patient was subsequently scheduled for additional management, but she had succumbed to complications of pulmonary embolism before the necessary interventions could be provided. In this particular case presentation, the biopsy of cutaneous lesions obtained had revealed an undiagnosed primary malignancy.

KEYWORDS: cutaneous metastases, lung adenocarcinoma, skin metastases, lung malignancy

INTRODUCTION

Cutaneous metastases are generally an uncommon manifestation; however, its presentation is usually a sign of the dissemination of internal malignancy. Besides, other malignancies such as melanomas, haematolymphoid malignancies, germ cell tumours and sarcomas are also associated with metastasis to the skin. Multiple studies reported that the incidence of cutaneous metastasis in lung cancer patients was within a range of 1 to 12 % [1]. The common sites where lung cancers typically invade comprise of hilar nodes, liver, adrenal glands, bones and brain [2, 3] whereas malignant spread to the skin is deemed unusual. However, on the infrequent occasion that transmission through the skin does happen, the metastasis would be anticipated in the chest, abdomen, head and neck [4-6]. Previous studies also reported that lung cancer has a higher incidence of cutaneous metastasizing in men as compared to women [1].

CASE PRESENTATION

A 71-year-old Chinese woman first presented with a cutaneous nodule on the left lateral axilla was then progressed to multiple nodules on the upper back and lower abdomen within a year. Aside from that, she also recounted episodes of progressive dyspnoea, haemoptysis, associated constitutional symptoms and significant loss of body weight amounting to 10 kg in the span of that year itself. The patient had a past medical history of hypertension and malignancy. Besides, her family history revealed that both her mother and sister were diagnosed with ovarian cancer.

There were no significant abnormalities in her vital signs on clinical examination except for a low-grade temperature and the patient being tachypneic, measuring a respiratory rate of 28 breaths per minute. Meanwhile, physical examination of the chest detected bilateral diffuse crackles that were more evident on the right chest with no obvious lymphadenopathy.



Skin examination revealed multiple subcutaneous nodules on the right upper back, left axilla and lower abdomen, each approximately 10 to 15 mm in diameter. These subcutaneous nodules were purplish and erythematous in appearance with well-defined borders, being firm, fixed and non-discharging in nature (Figure 1). The results from other systemic examinations were normal. The results of laboratory tests reflected mild anaemia, leucocytosis, an elevated erythrocyte sedimentation rate (ESR) at 82 mm/hr and abnormal C-reactive protein (CRP) levelling at 12.6 mg/l. The results from other routine investigations were normal.

Chest X-ray depicted bilateral interstitial infiltrates (Figure 2a), whereas CT of the thorax confirmed the presence of a mass on the anterior segment of the left upper lobe of the lung (Figure 2b). Based on the CT scan results, further imaging of the abdominal and pelvic region proceeded accordingly for staging. The imaging results showed that the pleural, nodal and bony areas were positive for metastases, not ruling out the possibility of liver metastasis owing to the discovery of hypodense lesions on the said organ.

Samples were extracted from the subcutaneous nodules on the left axilla and lower abdomen. These samples were subsequently subjected to histopathological evaluation using the haematoxylin and eosin (HE) staining protocol. Microscopic assessment of the specimens pinpointed tumour infiltration within the dermis extending up to the subcutaneous fat layer (Figure 3a; Figure 3b). Morphologically, small, scattered clusters of tumour cells were arranged in a glandular pattern, illustrating

mild-to-moderate nuclear pleomorphism and round-to-oval vesicular nuclei with prominent nucleoli. Apart from that, a desmoplastic reaction was noted between the stromal component of the cells and the existing scanty fibroadipose tissue. The specimens showcased affinity for thyroid transcription factor 1 (TTF1) and cytokeratin 7 (CK7) markers and thus, being conclusive of underlying lung adenocarcinoma (Figure 3c; Figure 3d).

Following that, bronchoscopy, bronchoalveolar lavage (BAL) and biopsy were performed, and their respective results supported the diagnosis of lung adenocarcinoma. Based on the interpretation of the aforementioned outcomes, the patient was diagnosed with stage IV lung adenocarcinoma with cutaneous metastasis. However, she was unfortunately passed away after two weeks of hospitalization with the cause of death attributing to a massive pulmonary embolism.

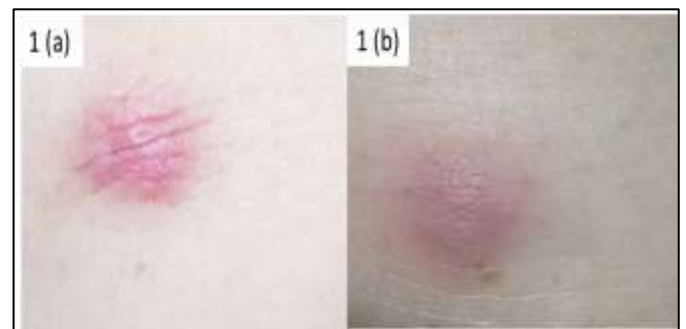


Figure 1: Purplish and erythematous subcutaneous nodules on the (a) left axilla and (b) lower abdomen

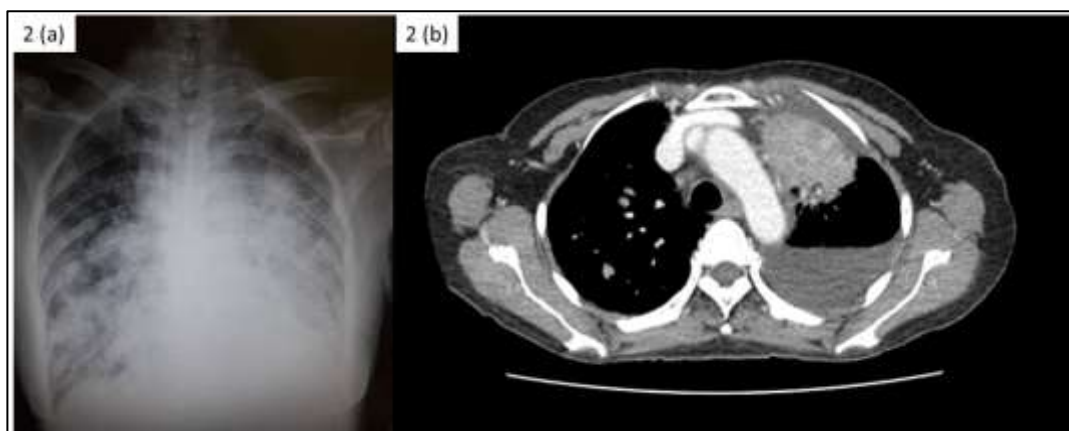


Figure 2: (a) Chest X-ray showed the bilateral interstitial infiltrates, which mainly concentrated over the lower and middle lobes; (b) CT of the thorax showed a heterogeneously enhancing mass with spiculated margin occupying the anterior segment of left upper lobe measuring 5.0 x 5.5 x 6.9 cm

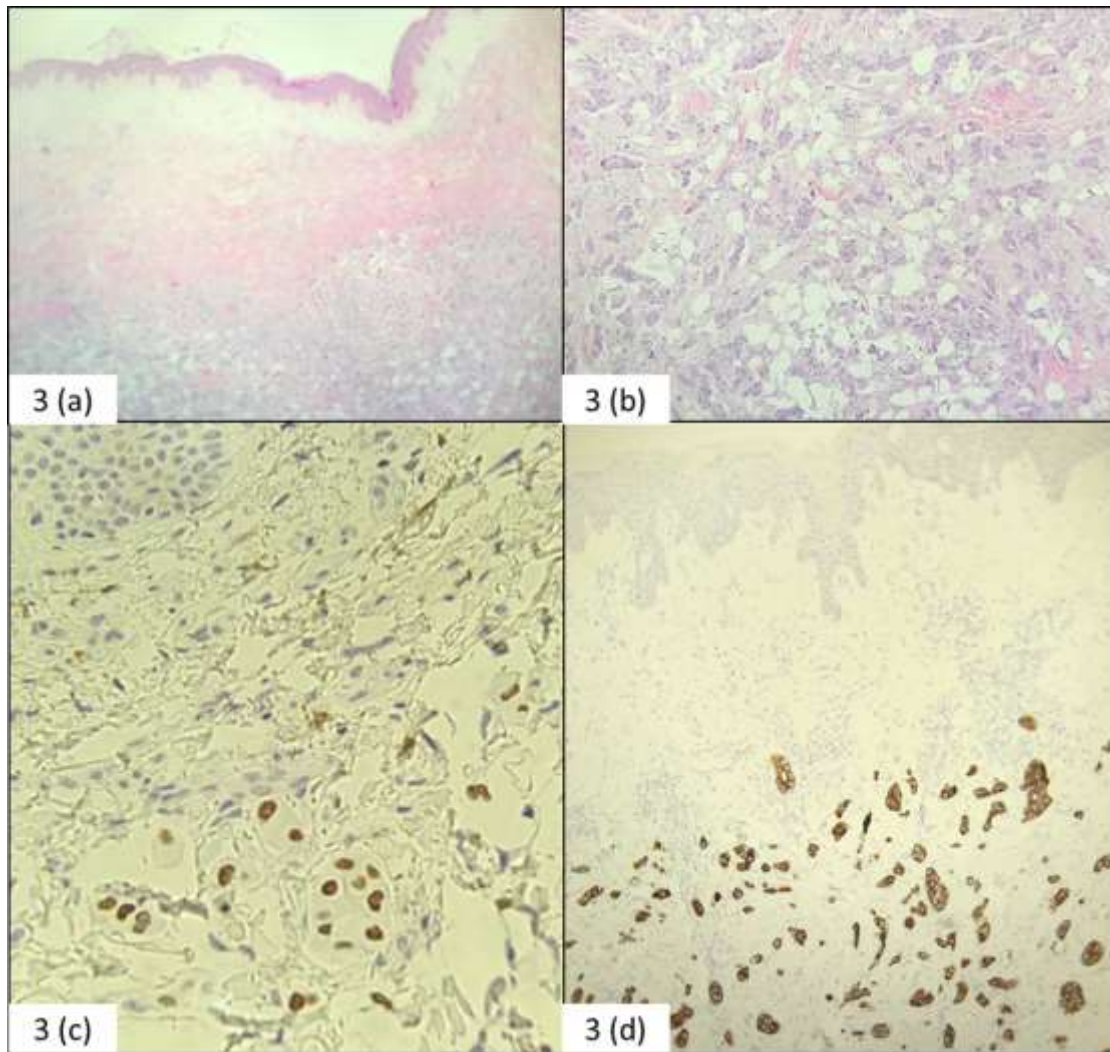


Figure 3: (a) The skin stained with HE stain at 40x magnification showed tumour infiltration in the dermis; (b) The skin stained with HE stain at 100x magnification showed tumour infiltration up to the subcutaneous fat layer in which they were arranged in small clusters, some were having ample cytoplasm while some displayed prominent nuclei; (c) The skin stained with immunohistochemistry (IHC) staining for TTF1 at 400x magnification showed tumour cells with positive focal nuclear staining; (d) The skin stained with IHC for CK7 at 40x magnification showed tumour cells with positive cytoplasmic staining

DISCUSSION

Cutaneous metastases may spread via venous, arterial or lymphatic systems before the identification of the primary tumour and usually, it is indicative of poor prognosis. Previous studies reported an average survival time between 3 to 5 months [7, 8], and such malignant metastases are often associated with disseminated diseases [9, 10]. Cutaneous metastases are usually manifested as a painless solitary nodular lesion, which is predominantly located at the head and neck areas and followed by the chest, lower limbs and upper limbs. Nonetheless, cases with multiple skin lesions were also reported, albeit rare. Also, they may manifest

as inflammatory lesions, epidermoid cysts, lipomas or basal cell carcinoma of the skin. Even though less common, they can be painful, itchy, exudative and ulcerated [12]. It was reported that tumours from the upper and right lobes were more frequently associated with skin metastases [11]. Besides, adenocarcinoma is the most frequent histology observed in such lesion. Thus, it is recommended to further investigate to exclude other distant metastatic diseases if cutaneous metastases are observed [12].

While cutaneous metastases are commonly known to be rare in women and usually manifested as a solitary nodule, our patient was presented with multiple

painful skin lesions all over her trunk. Excisional skin biopsy for histology, IHC and electron microscopy examinations is the gold standard for diagnosis confirmation. Hence, in the present case, the diagnosis was confirmed with the positive results from both the TTF1 and CK-7 IHC staining, which are used to detect immunohistochemical markers for lung adenocarcinoma diagnosis. Moreover, CT thorax and bronchoscopy were also performed to confirm the diagnosis as her symptoms pointing to lung malignancy. However, the prognosis was poor, as expected, and the patient inevitably succumbed to her ailment as a consequence.

The presentation of skin metastases aids the diagnosis in asymptomatic patients or patients with delayed symptoms. However, lung cancers with cutaneous metastases are generally having poor prognosis and are less likely to be cured despite aggressive chemotherapy and/or radiation therapy, which is possibly due to inadequate blood supply to the skin [11]. Therefore, they are usually offered palliative chemotherapy, with or without radiation. Radiation therapy is usually ordered for the patient with skin lesions that are associated with severe pain or bleeding [12].

CONCLUSION

Skin metastases are a rare manifestation of lung cancer in women and even more so if they are identified in multiple anatomical sites. In view of that, any cutaneous lesion accompanied by plausible signs of malignancy should warrant suspicion of skin metastasis or a paraneoplastic growth. To verify such differential diagnoses, histology and IHC techniques should be utilized to aid the diagnosis of the primary malignancy.

Conflict of Interest

Authors declare none.

Acknowledgement

We would like to dedicate our utmost appreciation to Dr Nur Amalina Abdul Mokhtar, the medical officer assigned to the patient, for disclosing detailed information on the case. We would also like to express

our gratitude to all clinicians involved in the care of the patient, as well as her family members for consenting to the publication of this case report.

REFERENCES

1. Rolz-Cruz G, Kim CC. Tumor invasion of the skin. *Dermatol Clin*. 2008; 26(1): 89-102.
2. Goljan EF. Rapid review pathology: with student consult online access. 4th ed. Elsevier Health Sciences, Philadelphia, US. 2013.
3. Mollet TW, Garcia CA, Koester G. Skin metastases from lung cancer. *Dermatol Online J*. 2009; 15(5): 5.
4. Dreizen S, Dhingra HM, Chiuten DF, Umsawasdi T, Valdivieso M. Cutaneous and subcutaneous metastases of lung cancer: clinical characteristics. *Postgrad Med*, 1986; 80(8): 111-16.
5. D'Aniello C, Brandi C, Grimaldi L. Cutaneous metastasis from small cell lung carcinoma. Case report. *SScand J Plast Reconstr Surg Hand Surg*. 2001; 35(1): 103-105.
6. Neel V, Sober A. Metastatic tumors to the skin. In: Holland-Frei Cancer Medicine. 6th ed. eds Kufe DW, Pollock RE, Weichselbaum RR, Bast RC, Gansler TS, Holland JF. Frei E. BC Decker Inc, Hamilton, ON. 2003.
7. Song Z, Lin B, Shao L, Zhang Y. Cutaneous metastasis as a initial presentation in advanced non-small cell lung cancer and its poor survival prognosis. *J Cancer Res Clin Oncol*. 2012; 138(10):1613-17. doi: 10.1007/s00432-012-1239-6.
8. Hyde L, Hyde CI. Clinical manifestations of lung cancer. *Chest*, 1974; 65(3): 299-306.
9. Garrido MJ, Ponce CG, Martínez JL, y Sevilla CM, Mena AC, Antón FM. Cutaneous metastases of lung cancer. *Clin Transl Oncol*. 2006;8(5):330-33.
10. Sweldens K, Degreef H, Sciot R, Van Damme B, Peeters C. Lung cancer with skin metastases. *Dermatology*, 1992; 185(4): 305-306.
11. Ambrogi V, Nofroni I, Tonini G, Mineo TC. Skin metastases in lung cancer: analysis of a 10-year experience. *Oncol Rep*. 2001;8(1):57-61.
12. Kamble R, Kumar L, Kochupillai V, Sharma A, Sandhoo MS, Mohanti BK. Cutaneous metastases of lung cancer. *Postgrad Med J*. 1995;71(842):741-3.