



Lung Cancer with Multiple Cutaneous Metastases – A Diagnostic Dilemma

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Abstract

Cutaneous metastases of the different visceral malignancies (0.7-9%) and especially of the lung cancer are rare and worsen the prognosis (1-12%). We report the case of a 55 year old gentleman who presented with a right upper lung lesion diagnosed as poorly differentiated squamous cell carcinoma and was treated with concurrent chemo radiation therapy followed by adjuvant chemotherapy. He developed recurrent multiple cutaneous lesions which were surgically excised after being identified on biopsy as metastatic lesions. He received salvage chemotherapy and died within 10 months of developing the cutaneous metastasis. This case highlights the poor prognosis of skin metastasis in a primary lung carcinoma and the fact that a comprehensive analysis and examination is essential for suspected cutaneous lesions, during which a pathological biopsy is of great importance in order to form the correct diagnosis for timely treatment inpatient with metastatic lung carcinoma.

Received: Apr 15, 2023

Accepted: May 09, 2023

Published Online: May 16, 2023

Journal: Case Reports of Oncology: Open Access

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

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Keywords: Cutaneous; Malignant; Chemotherapy; Radiation.

Introduction

Cutaneous metastasis refers to the growth of cancer cells in the skin originating from internal cancer [1]. Most cutaneous metastases occur in a body region near the primary tumor [2]. Lung cancer is one of the most common tumors globally; it is highly malignant and has a high rate of distant metastasis. In total, ~50% of these patients already have distant metastasis when diagnosed, with the most common metastatic sites being the lungs, liver, bone, brain, adrenal glands [3] and skin being an uncommon site. The percentage of patients with lung cancer who develop cutaneous metastases is rare and ranges from 1 to 12% [4]. And it worsens the prognosis. Its pathogenesis is by either lymphovascular invasion or hematogenous metastasis [5].

The histology of cutaneous metastasis most commonly reveals adenocarcinoma (2.95%), then squamous carcinoma (1.16%), 0.81% for small cell lung carcinomas followed by large-cell carcinoma [6]. Commonly, the skin metastases are seen over the chest, abdomen, followed by the scalp, head and neck, extremities, and back [7-9]. Clinical findings include a red-pink, ulcerated nodule and sometimes skin metastasis may be the first sign of the tumor [10,11]. Therefore, it is important for

both dermatologists and pathologists to be able recognize and diagnose these metastases. Median survival time after the diagnosis of a cutaneous metastasis is between 2.9 and 4.9 months [12]. Treatment modalities cannot usually change this progress. Our patient died 11 months after the diagnosis of his cutaneous metastasis.

Case presentation

A 55-year old man presented to the oncology OPD with chief complaints of on/off fever and cough with expectoration since two months. He underwent bronchoscopy that revealed a bulge at the opening of right upper lobe bronchus and mucosa of right lower lobe bronchus was oedematous. HRCT was suggestive of right upper lobe consolidation with brown glass opacity of size 3.9 x 2.9 cm with mediastinal lymphadenopathy. Histopathology of right lung lesion revealed poorly differentiated squamous cell carcinoma with CK 56, p 63 + and CK20, Napsin A, TTF-1, CDX2-negative. Patient was treated with chemo radiotherapy delivering a dose of 59.4 Gy/ 33 F at 1.8Gy/ F with concurrent two cycles followed by adjuvant 2 cycles of Inj. Cisplatin 90mg and Inj. Etoposide 90mg every 3 week. A follow up CECT chest was done after 6 weeks of RT that showed post RT changes with



no evidence of residual disease.

Five months post treatment, patient developed a hypertrophic lesion in palm of left hand. Biopsy of the lesion reported it as Bowen disease squamous cell insitu with: CK 56, S100, HMB 45 +: Ki 67 - markedly increased. Patient was treated with 3 sittings of cryotherapy under dermatology supervision but it didn't subside. Patient eventually underwent local excision and STSG of left ring finger for the non healing ulcer.

Three months later he developed a non healing ulcer over the right buttock 3x 3 cmin size with bilateral inguinal lymphnodes and also multiple lesions on palms and soles as well as non healing lesion over left ring finger which were progressive in nature. Biopsy from right gluteal region was suggestive of moderate to poorly differentiated squamous cell carcinoma. The case was discussed in detail with the pathologist to rule out arsenic toxicity due to multiple skin lesion & lung cancer.

On imaging, PET CT revealed post RT changes in right upper lobe lung with bilateral inguinal lymphadenopathy with FDG avidity (SUV 6.2) and an ulcerative lesion in the right gluteal region with a SUV of 11.07 and lesion in the left hand with FDG avidity (SUV 5.4). Fine needle aspiration cytology from the inguinal nodes were identified as metastatic carcinomatous deposits. He received EBRT to the right gluteal region and bilateral inguinal lymph nodes to a dose of 64Gy/ 32 F @ 2Gy/F over 6.2weeks.

4weeks post RT CECT chest & abdomen showed stable right upper lobe lung collapse consolidation with bronchial and tractional bronchiectasis. There was interval appearance of Sub pleural nodule in right lower lobe lung and near stable b/l inguinal nodes. With stable irregular non enhancing right gluteal thickening.

Within two months, he developed new pustular multiple small lesions over the penile and scrotal skin. Biopsy was suggestive of moderately differentiated squamous cell carcinoma. He was planned for salvage chemotherapy with single agent Inj. Docetaxel 75mg/m² Q3W and received 2 cycles after which he developed superadded infection, maggots and sepsis. He was managed conservatively with a palliative intent and succumbed after 5days.

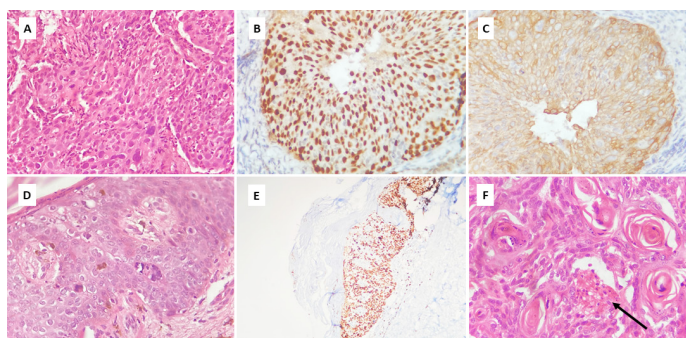


Figure 1: (A) Photomicrograph showing moderately differentiated squamous cell carcinoma of the lung, H&E, 400x. The tumour showed positivity with (B) p63 and (C) CK5/6, respectively, DAB chromogen, 400x. (D) Photomicrograph from skin of hand showing Bowen's disease, H&E, 400x. (E) The atypical squamous epithelial cells showed increased proliferative activity with Ki67 immunolabelling, which was involving the entire thickness of the epidermis, DAB chromogen, 100x. (F) Photomicrograph from scrotal biopsy showing moderately differentiated squamous cell carcinoma with perineural invasion (arrow), H&E, 400x.

Discussion

Cutaneous metastasis from lung carcinoma is rare and worsens the prognosis. There are two largest reported studies of cutaneous metastases secondary to lung cancer: A meta-analysis in 2003 showed the incidence of cutaneous metastases in lung cancer was 3.4% in 89 patients among 2,597 subjects [13]. A retrospective study in 2012 indicated that 2.8% of 2,130 patients with advanced non-small cell lung showed cutaneous metastases as an initial presentation [14].

Dreizen et al reported that adenocarcinoma has highest tendency for cutaneous metastasis followed by squamous cell carcinoma and others. Metastatic deposits from squamous cell carcinoma are mostly moderately differentiated or poorly differentiated. Metastases from lung cancer are macroscopically indistinguishable from metastases of other cancers. Usually they present as fast-growing solitary or multiple nodules with a diameter of 5 mm–10 cm and are firm, mobile, and covered with normal skin. Sometimes exudative or ulcerative lesions are also seen [15]. As seen in this case of rare unexpected skin metastasis of squamous cell carcinoma, the skin metastases lacked a pathognomonic physical appearance.

Metastases to skin may occur by a hematogenous route or via lymphatics. Carcinoma of the breast and carcinoma of the oral cavity spread via lymphatics, whereas the rest of the cancers including lung cancer spread mainly via a hematogenous route. Lymphatic dissemination may explain why skin metastases tend to be close to the primary site of the tumor [16]. However, in our case, the metastatic nodules were seen all over the body, suggesting lymphatic as well as hematogenous spread. They were also seen in gluteal region, with nodal metastases, as well as penile and scrotal lesions which are rare and have not been reported in literature.

Treatment modalities include surgery, chemotherapy and radiotherapy, and treatment varies based on prognosis and symptoms [17,18]. Cryosurgery is used to treat malignant lesions of the skin, inducing ice formation, extracellular osmolarity changes, and vasoconstriction that enhances cellular injury [19]. Moreover, cryosurgery is thought to have immunological effects also.

Although treatment of solitary skin metastasis includes surgery combined with either or both chemotherapy and radiation; multiple cutaneous lesions may be better treated with chemotherapy [20]. Patients with resectable skin lesions have better survival than those who have multiple, non-resectable sites and are not candidates for surgery [21]. But due to the aggressive nature of lung cancer with cutaneous metastasis, both chemotherapy and radiation therapy may be effective only as palliative treatment [22]. In reviewing the literature, some studies demonstrated the adequacy of surgery followed by chemotherapy in case of single lesion. In case of multiple cutaneous metastases, many authors suggest only chemotherapy, although the ideal scheme hasn't been discovered yet. We managed our patient with all three modalities – surgery, radiation therapy and chemotherapy.

Cutaneous metastases from lung cancer are rare; however the appearance of skin lesions, in patients with a positive oncological history, requires much attention. Accurate evaluation of the patient is paramount in choosing the adequate therapeutic algorithm.

Conclusion

Cutaneous metastases are relatively rare in clinical practice and their diagnosis requires a high index of suspicion because clinical findings can be subtle. Therefore, physicians should be vigilant about this entity. Atypical skin lesions of the cancer patients should be evaluated and timely biopsies should be done to diagnose metastases and consider further adjuvant and supportive treatments. Given the rarity of skin metastasis in lung carcinoma, this case report will definitely add a much-needed view point to treating oncologists towards managing similar cases in a way that is essential for better survival by a comprehensive analysis and multidisciplinary treatment approach including resection, chemotherapy, and radiotherapy.

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