

ALK-Rearranged Lung Adenocarcinoma Initially Presenting with Cutaneous Metastases: A Case Report

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Abstract

Only 1% - 12% of patients with lung cancer develop cutaneous metastases. While adenocarcinoma is incredibly common, it is rare for a cutaneous manifestation of the disease to be the initial presenting complaint. Skin manifestations can be difficult to identify and can appear to be deceptively benign, leading to delays in diagnosis and treatment. ALK+ lung cancer specifically has an increased frequency of distant lymph node involvement and lymphangitic carcinomatosis relative to typical EGFR+ lung cancer. Herein we report a case of ALK-rearranged lung adenocarcinoma that initially presented as cutaneous skin metastases to the neck. Such skin lesions should be identified early, and considered as a potential manifestation of an internal malignancy. Given the poor prognosis associated with cutaneous metastases, further diagnostic tests, such as imaging or biopsy, should be done with urgency.

Keywords

ALK-Rearranged, Lung Adenocarcinoma, Cutaneous Metastases, Case Report

1. Introduction

Lung cancer is the leading cause of cancer incidence and mortality worldwide, with approximately 2 million diagnoses and 1.8 million deaths [1]. Lung cancer is categorized into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC accounts for approximately 85% of all lung cancers, and includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma [2]. Adenocarcinoma is the most common histological subtype in both men and

women. Higher rates of adenocarcinoma are seen in women compared to squamous and small cell lung cancer [2] [3]. Although ALK has been recognized as an oncogene in lymphoma for many years, its association with NSCLC was first reported in 2007 [4]. ALK rearrangements are typically found in 3% - 7% of NSCLC, the majority being adenocarcinomas. 90% of those diagnosed with ALK+ NSCLC already have metastatic disease, reflecting the aggressiveness of these tumors [4]. The most frequent sites of metastasis of lung carcinomas are bone (34.3%), lung (32.1%), brain (28.4%), adrenals (16.7%), and liver (13.4%) [5]. The percentage of patients with lung cancer that develop cutaneous metastases ranges from 1% - 12% [6]. While adenocarcinoma is incredibly common, it is rare for a cutaneous manifestation of the disease to be the initial presenting complaint. In a retrospective study of 7316 cancer patients, cutaneous metastases were the initial presenting sign of an internal malignancy in only 0.8% of patients [7]. Here we present a rare case of ALK-rearranged lung adenocarcinoma that initially presented as cutaneous skin metastases to the neck.

2. Patient Case

A 60-year-old female with a history of smoking presented to the emergency room for right neck pain caused by a large ulcerating skin lesion (**Figure 1**). The lesion was painful, itchy, and had been progressively growing over the past eight months. She presented months prior to an outside hospital with a small neck lesion and an associated dry cough. She was subsequently seen multiple times by her family doctor, and her symptoms were still persistent despite treatment of the lesion with oral and topical steroids, antibiotics, and antifungal therapy. Her neck was not biopsied until two months later, resulting in undifferentiated carcinoma. At that time, she was referred to hematology/oncology and infectious disease, but she never followed up. One month later, the patient presented to the emergency room with shortness of breath secondary to a pulmonary embolism, and was found to have a pericardial effusion, for which cytology was consistent with poorly differentiated adenocarcinoma with ALK rearrangement. Following



Figure 1. Cutaneous metastases of the neck.

this hospital admission, an excisional right axillary lymph node biopsy was performed showing metastatic adenocarcinoma consistent with lung origin, with an EML4-ALK fusion, PD-L1 + and negative for BRAF, EGFR, ERBB2, KRAS, MET, RET, and ROS1. The patient was diagnosed with Stage IV ALK-rearranged adenocarcinoma of the right lung with lymphangitic carcinomatosis, leptomeningeal CNS involvement, right neck dermal involvement, and widespread lymph node masses (**Figure 2** & **Figure 3**). She was started on Alectinib and initially had good response with a decline in CEA from 117 ng/mL to 58 ng/mL. However, four months later her CEA had risen again to 174 ng/mL, and she had recurrent admissions for dyspnea and hypoxia. Given concern for treatment failure, the patient was switched to Lorlatinib, but her CEA remained persistently elevated on this therapy. Her course was complicated by multiple admissions for large pericardial and pleural effusions that lead to respiratory decompensation. Given the patient's continued disease progression, clinical decompensation, and overall poor prognosis, she was transitioned to comfort care, after which she had an



Figure 2. CT soft tissue neck with metastatic spread highlighted.

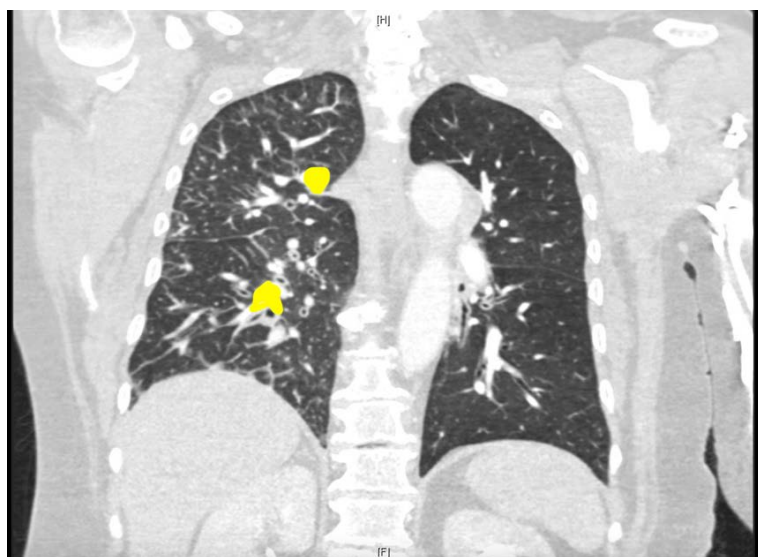


Figure 3. CT chest with right lung adenocarcinoma highlighted.

aspiration event resulting in hypoxic arrest.

3. Discussion

In women, the most common types of cancer to metastasize to the skin are breast cancer, colorectal cancer, and melanoma [8]. Cutaneous metastases are rare in lung cancer, presenting in only 1% - 12% of patients. Only 2.8% of advanced NSCLC patients show cutaneous metastases at initial presentation [6] [9]. The survival time of patients with metastases to the skin is significantly shorter than other metastasis, usually at less than 1 year [9]. Cutaneous metastases of lung cancer often indicates poor prognosis. The difference in overall survival in NSCLC patients with cutaneous metastases compared to those with non-cutaneous metastases is 3.9 months vs. 10 months respectively [9]. Our patient initially presented with painful cutaneous lesions of the neck, minimal respiratory symptoms, and no weight loss. Her neck lesion was initially treated as an infection, but later gradually grew in size. It wasn't until later that a malignancy was considered. Furthermore, it is important to note that our patient had ALK+ NSCLC, whose metastatic pattern differs from that of typical pulmonary adenocarcinoma. ALK + lung cancer has an increased frequency of distant lymph node involvement and lymphangitic carcinomatosis compared to typical EGFR+ lung cancer [10]. Our patient's extensive cutaneous metastases certainly demonstrated this increased tropism for the lymphatics, and therefore could serve as a clue in predicting future disease course. Overall, it is crucial to identify skin lesions early and consider them as a potential manifestation of an internal malignancy. Since they are usually associated with advanced disease, it is important to consider further diagnostic tests, such as imaging or biopsy, with urgency.

4. Conclusion

Cutaneous metastasis in lung cancer is rare, but is a poor prognostic factor with shorter survival. In our case, it is important to consider an internal malignancy if an atypical skin lesion is identified, especially in patients with a smoking history or a family history of cancer. Skin manifestations can be difficult to identify and can appear to be deceptively benign, leading to delayed diagnosis and treatment. ALK + lung cancer specifically has increased distal lymph node involvement and higher rates of extensive metastatic disease. Therefore, timely biopsy of suspicious lesions and further diagnostic imaging should be performed to aid in prognosis and management.

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Informed Consent

Informed patient consent was obtained for publication of this case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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