The Cutaneous Manifestations of Metastatic Lung Cancer: Case Report and Review

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Abstract
Cutaneous metastasis comprises a tiny minority of skin tumors, estimated at 2%, and its timely diagnosis is extremely important to the clinical course of patients. Cutaneous metastasis of all primary systemic cancers usually indicates a poor prognosis with only a few months of survival time. Lung cancer remains the leading cause of cancer-related death among men and women in the United States. This article highlights an atypical presentation of lung metastasis to the skin and provides an overview of other uncommon and common cutaneous effects of lung cancer in general.

Introduction
Although uncommon in clinical practice, cutaneous metastasis is important to keep on a clinical provider’s list of differential diagnoses. Lung cancer continues to earn listings as the “most common cause of cancer-related deaths in both men and women,” “cancer most likely to metastasize in general,” and, affecting dermatologists particularly, “most common tumor to metastasize to the skin in males,” particularly in men over 40.1–3 The data reinforce the importance of having a low threshold for biopsy, especially if patient history directs.

Case Presentation
An 83-year-old male presented to our dermatology clinic with a complaint of a rash on his lower abdomen for approximately two months. The patient’s rash was asymptomatic. He had cataract surgery planned, which was put on hold due to this rash, which he attributed to a reaction from EKG leads placed in the area of the rash upon his pre-op clearance studies. He was sent to the ER for a suspected cellulitis-type infection, and subsequently we were consulted. His past medical history was notable for intestinal resection for colon cancer resulting in the use of an ostomy bag for more than 18 years. He also had a history of lung cancer for which he underwent partial lobectomy of the right lower lobe along with radiation two years prior for a T2aN0M0 lung tumor non-small-cell type (adenocarcinoma). He had regular follow-ups with all of his subspecialists and primary care providers, and review of systems was negative.

On exam, his left lower abdomen was significant for an intact ostomy bag, with superior and bilateral lower abdominal quadrants demonstrating large, indurated, erythematous and violaceous blanchable plaques oriented horizontally, not extending below his pannus fold. The left aspect of the rash had a “peau d’orange,” palpable nodularity (Figure 1).

Two 4.0 mm punch biopsies were performed at initial consultation, with an initial differential diagnosis inclusive of infection; panniculitis; erysipelas and/or carcinoma en cuirasse-like presentation of underlying carcinoma; atypical angiosarcoma; and interstitial granulomatous dermatitis.
Pathology revealed findings consistent with metastatic carcinoma, lymphangitic-type spread (Figure 2, H&E). The immunostain pattern of CK-7 positive (Figure 3), TTF-1 positive (Figure 4), and CK-20 negative (Figure 5) favored primary lung carcinoma.

The patient was then referred to hematology/oncology. On close review of past records and considering findings on new imaging demonstrating two new masses at an area adjacent to his previous partial lobectomy, this was thought to be a recurrence of a previous diagnosis of non-small-cell cancer. He was quickly started on a chemotherapy regimen of gemcitabine and followed regularly in dermatology clinic to track his metastatic lesions. Although initially given an ominous prognosis, the patient is doing very well. His abdominal lesions are fading, which correlate to his overall response to treatment (Figure 6, almost one year after initial biopsy).

Discussion
Although usually detected in a patient with known and widespread disease, on occasion cutaneous metastasis may be the presenting sign of clinically silent lung cancer. Early detection of cutaneous metastasis, then, affects how fast a patient may be diagnosed and placed on appropriate therapy by hematology/oncology. Further, depending on the morphologic presentation, cutaneous metastasis may not only help with diagnosis of otherwise asymptomatic disease, as with the case presented in this article, but may also serve as a marker in monitoring response to chemotherapy.

Reviewing statistics involving cancers most likely to metastasize to the skin may be confusing. The proportion of patients with metastatic disease with cutaneous involvement depends upon the particular malignancy. When looking at the percentage of all patients with metastatic disease who have developed metastasis particularly to the skin, melanoma dominates. Differences also occur when factoring in age and sex of patients. When approached broadly, one retrospective study of 4,020 patients showed that breast, melanoma, and lung, in that order, top the list for most common cancers to spread to the skin. For older men who present with skin metastases, lung cancer is the most common primary, at about 24%, followed by colorectal cancer, melanoma, and carcinoma of the oral cavity. In women, lung cancer ranks fourth after primary breast cancer, colon cancer, and melanoma. Overall, if a patient has lung cancer, their chance of cutaneous metastasis varies, ranging 1% to 12%. Although the skin is not the first organ it usually spreads to, when it does it does so quickly, with mean time of less than six months.

Clinical Presentation
In most cases, skin metastases present after the diagnosis of a known primary. Occasionally, these lesions may be the inciting event that eventually leads to diagnosis of underlying disease. In one study, 11 out of 21 patients with metastatic lung cancer had their metastatic skin lesions present as the first sign of extranodal disease.

Skin metastasis from lung cancer does not have a typical presentation. Anatomically, the chest, abdomen, and head and neck are common sites. Morphologically, lesions are usually nodular, painless, and may be either single or multiple. The scalp, head and neck are the most common sites, along with anterior chest and abdomen. Several atypical presentations of metastatic lung cancer have been described including spread to both upper and lower limbs, gingiva, genitalia, and incision sites. Although nodules are the most common presentation, different patterns have been reported including zosteriform, ulcerative, fungating, and erysipeloid-like presentations.

Diagnosis
Diagnosis is made on biopsy. Patterns on H&E are generally either nodules of tumor cells within the dermis or cords of atypical tumor cells mixed within a fibrotic stroma.

The most common type of lung cancers reported to metastasize to the skin are adenocarcinoma and large-cell carcinoma, followed by squamous-cell. A couple of studies from Japan have demonstrated that large-cell carcinoma has the highest incidence of metastasis to the skin. On histology, metastatic adenocarcinoma of the lung may display glandular, well-differentiated structures with mucin, in which case GI, ovarian, breast and kidney metastases must be ruled out. CK 20 paranuclear dot positivity helps differentiate from Merkel-cell carcinoma. Other types of lung cancer that rarely metastasize to the skin include mesothelioma and bronchial carcinoid, which usually show more of a trabecular pattern and sometimes present with carcinoid syndrome.

Immunohistochemistry (IHC) has evolved into a reliable tool in diagnosis. An IHC battery of an unknown cutaneous metastasis helps narrow down the differential diagnosis. Although not originally studied in the skin, useful markers include CK 7 and CK 20 and anti-thyroid transcription factor (TTF). CK 7 is very sensitive and is positive in virtually all cases of primary lung adenocarcinoma; however, it has lower specificity since it is also positive in may other types of lung carcinoma (70% of large-cell neuroendocrine, 40% of large-cell, and 23% of squamous-cell). Anti-TTF is a sensitive and specific marker that identifies pulmonary origin of an adenocarcinoma, bronchoalveolar carcinoma, and small-cell carcinoma if a thyroid origin is excluded.

Overall, IHC panels are not substitutes for the big-picture approach to diagnosis, incorporating a thorough review of systems and history, exam, and screening tools such as appropriate bloodwork and radiologic studies. Communication of the above to pathology and consulting specialists may prove to be invaluable.

Treatment and Prognosis
Treatment approach for any cutaneous metastasis is multidisciplinary. If the cutaneous metastases are localized and discrete, surgery alone or combined with chemotherapy and/or radiation may be possible for functional or even cosmetic reasons. Some studies have shown that treatment of localized disease with surgery or combination modalities may increase survival. If disease is more disseminated, chemotherapy remains the best option. Sometimes during chemotherapy, cutaneous lesions may be thought of as a marker for response to therapy. Patients without cutaneous metastasis tend to live longer than those who present with them. Mean survival is short, usually five to six months after diagnosis of cutaneous metastasis. Living past a year, as with our patient, is unusual but has been reported.

Conclusion
Although uncommon, cutaneous metastasis may occasionally be the presenting sign of an internal
malignancy. Since lung cancer is so prevalent, it is an important differential diagnosis of any unexplained, fresh lesion in someone with risk factors. These lesions are usually on the trunk, head and neck, but could present practically anywhere and with many morphologies, like the erysipeloid and peau d’orange presentation in this case. Despite an ominous prognosis, early recognition and timely diagnosis usually confers a better survival time, as with our patient. Biopsy is essential, with immunohistochemical panels proving to be helpful and guiding tools. Likely these panels will become more sophisticated and expand their utility in terms of determining prognosis and targets for therapy.

References