

Scalp metastases as first presentation of pulmonary adenocarcinomas: a case report

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Abstract: Cutaneous metastasis from primary visceral malignancy is a relatively uncommon clinical entity, with a reported incidence ranging from 0.22% to 12% of all malignancies. Here we report a 64-year-old asymptomatic female patient with Peutz–Jeghers syndrome presenting with multiple scalp metastases as the initial manifestation secondary to lung adenocarcinoma. Subsequent lung computed tomography scan showed large masses involving the left upper lobe associated with extensive mediastinal lymphadenopathy. After treatment with an epidermal growth factor receptor inhibitor gefitinib, the size of the tumor in the lung reduced significantly and the condition of the patient also gradually improved. Our case demonstrated that scalp metastasis could be the first sign of an internal malignancy. Asymptomatic elderly patients presenting with multiple, painless, immobile cutaneous nodules should be considered for further investigations to rule out the underlying primary cause. Metastasis to the skin is often a preterminal event that heralds poor prognosis.

Keywords: cancer, metastasis, scalp, lung adenocarcinoma

Introduction

Cutaneous metastasis is one of the manifestations of the systemic spread of cancer. The tumor cells originate from either an internal malignancy or a primary skin cancer. Cutaneous metastasis from primary visceral malignancy is a relatively uncommon clinical entity, with a reported incidence ranging from 0.22% to 12% of all malignancies.^{1,2} Cutaneous metastasis can be observed at any stage of malignancy and is more likely in elderly individuals.³ Nodules or masses are the typical presentation of cutaneous metastasis.⁴ These metastases may be the first indication of the clinically silent visceral malignancies. Furthermore, it has been shown to reflect late-stage disease and has a poor prognosis.⁵ Therefore, further investigation of cutaneous metastasis is very important, not only for an accurate diagnosis, but also for proper treatment of the primary cancer.

Cutaneous involvement may occur because of direct extension of the cancer as a local metastasis or as a distant metastasis. The scalp is known to be a favored location for distant metastasis, with approximately 5% of cases involving this site.⁴ Previous studies have shown that most cutaneous metastasis were diagnosed in patients prior to the finding of visceral malignancy. The interval between primary and metastatic diagnosis is more than 5 years in about 7% of cases. Unfortunately, half of the patients with cutaneous metastasis die within the first 6 months after the diagnosis.²

Scalp metastasis as a first manifestation of lung cancer has been rarely reported before. Here, we report the case of an asymptomatic female patient with Peutz–Jeghers syndrome (P–JS), who presented with scalp metastasis as the first sign prior to the

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diagnosis of lung cancer and discuss the differential diagnosis as well as review of the literature.

Case report

A 64-year-old woman came to our dermatology clinic in June 2016 with a complaint of multiple, painless, slowly growing nodules in the scalp and the neck for the past 6 months. She denied having any skin infection or allergy in the past. She had a history of intestinal polyps for 10 years, for which she had undergone endoscopic polypectomy thrice. The biopsy report revealed it to be adenoma. The patient had no other significant medical history. She was a nonsmoker and a nonalcoholic. There was no history of similar disease in her family.

On physical examination, multiple red nodules and papules were seen in the scalp and the neck (Figure 1A and B). There was no bleeding or exudation. Hyperpigmented patches were seen on the lower lip (Figure 1C). On palpation, the size of the nodules was found to be approximately 1–2 cm in diameter, with a smooth surface. Nodules were immobile and hard. Other physical and dermatological examinations were unremarkable.

Laboratory results were as follows: serum carcinoembryonic antigen (CEA) 9.40 $\mu\text{g/L}$ (normal range, 0–5), carbohydrate antigen 153 more than 300.00 μmL (normal range, 0–25), carbohydrate antigen 199 (CA19-9) 48.97 μmL (normal range, 0–40), and neuron-specific enolase 19.95 ng/mL (normal range, 0–16.3). Other laboratory findings were within normal range. The positron emission tomography–computed tomography (PET–CT) test showed a large tissue mass measuring approximately 2.9 cm in diameter in the upper lobe of the left lung, with multiple miliary nodules scattered in the left and right lungs. The mediastinal and hilar lymph nodes were enlarged (Figure 1D). In addition, bones were destructed extensively with increased metabolism, suggesting bone metastasis (Figure 1E). Subsequent CT showed large masses involving the left upper lobe associated with extensive mediastinal lymphadenopathy. Multiple ring-enhanced lesions in the brain parenchyma were seen on Gd-enhanced brain magnetic resonance imaging (Figure 1F). The colonoscopy revealed multiple ileocecal polyps.

A biopsy of the scalp lesion with a diameter of 0.5 cm was obtained. Histological examination of biopsied tissues showed ill-circumscribed tumors in the middle and deep

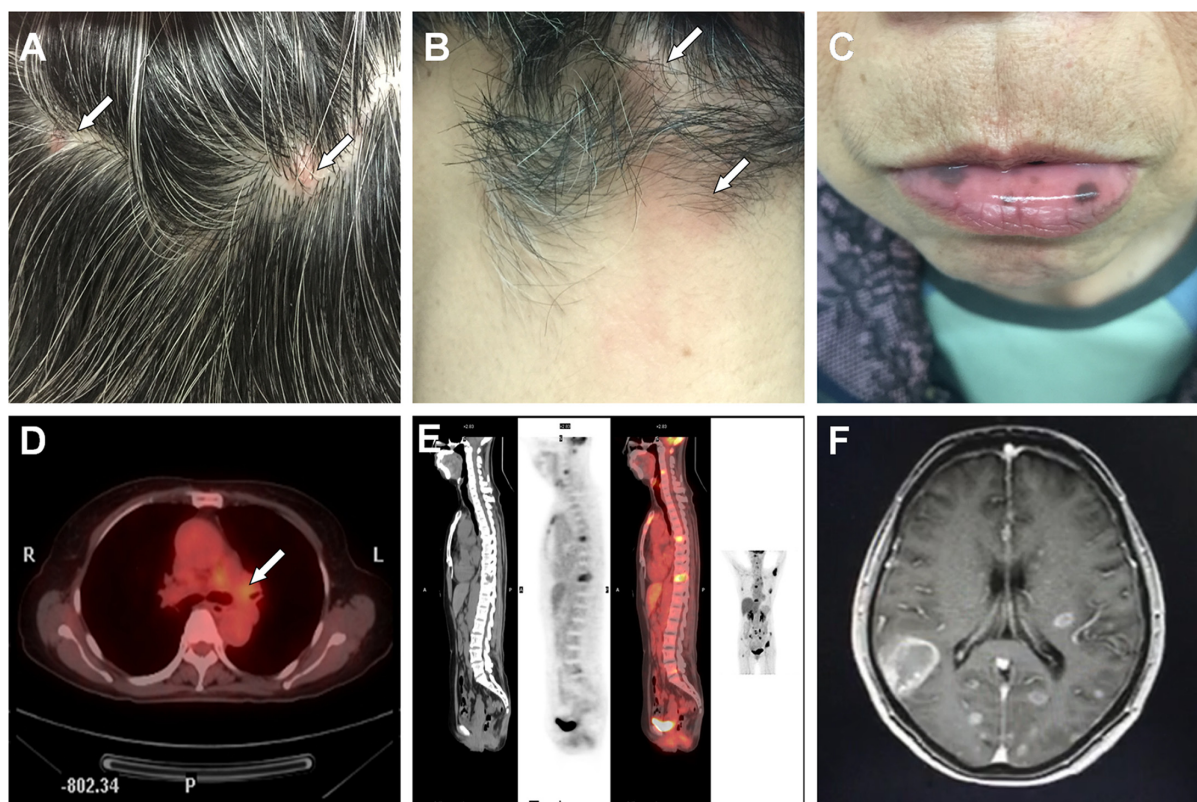


Figure 1 Imaging of scalp nodules, lung cancer, and its metastatic lesions.

Notes: (A, B) Multiple nodules in scalp and neck regions. (C) Brown spots in the labial mucosa. (D) A large tissue mass occupied the upper lobe of the left lung on PET–CT. (E) Multiple bones metastasis with increased metabolism on PET–CT. (F) Multiple ring-enhanced lesions in the brain parenchyma on Gd-enhanced MRI.

Abbreviation: PET–CT, positron emission tomography–computed tomography.

dermis. In addition, there was evidence of papillary adenocarcinomas showing a major component of a growth of glandular cells along central fibrovascular cores. Numerous papillary folds projecting into the cystic spaces and tubulopapillary structures were also seen (Figure 2A and B). Tumors consisted of an adenocarcinoma with back-to-back angulated acinar structures. The tumor cells ranged from cuboidal to columnar, with nuclear pseudostratification and atypical features (Figure 2C). Immunohistochemically, tumor cells were positive for CK7, GCDPF-15, TTF-1, CA19-9, and CEA and negative for P63, CK5/6, SMA, S-100, and CK20 (Figure 2D–H). A biopsy of the upper lobe of the left lung revealed adenocarcinoma. A biopsy of the intestinal polyp revealed a villous tubular adenoma, accompanied by a mild to moderate atypical hyperplasia of the glandular epithelium.

The patient was diagnosed as having lung adenocarcinoma (cT4 N3 M1c) with scalp metastasis coincident with P–JS. Detection of EGFR gene mutation in the blood showed the 19 exon deletion mutation. Then, the patient was advised to start molecular targeted therapy. She was treated with gefitinib 250 mg daily by oral administration, and the treatment was maintained. The size of the left lung mass decreased after a month's treatment, but no changes were seen in the nodules in the scalp and neck regions. The evidence of a decrease in the size of the mass in the upper lobe of the left lung was observed during a CT of the lung done

in June 2016, July 2016, September 2016, and November 2016, respectively (Figure 3).

Follow-up: No adverse event other than seborrheic dermatitis of the face is observed during the follow-up period. Six months later, the patient is still on treatment with gefitinib 250 mg daily, and her condition is still stable to date.

Consent for publication

Written informed consent for publication of clinical details and images was obtained from the patient.

Discussion

Cutaneous metastasis is closely related to lung cancer. The most frequent cause of cutaneous metastasis in men is lung carcinoma, while in women, it is the third cause. However, another study showed that the tendency of cutaneous metastases were breast carcinoma, melanoma, and gastric carcinoma.⁶ The tendency to metastasize to skin was seen to be greatest with large cell carcinoma and least with squamous cell carcinoma in one study.⁵ In contrast, another study showed that the tendency of the adenocarcinoma to metastasize to the skin was more and that of large cell carcinoma was the least.⁷ Lung adenocarcinoma, a type of non-small cell carcinoma, mostly occurs in women and nonsmokers, and easily metastasizes to the lymph nodes, bone, liver, brain, and the contralateral lung.⁸ The clinical features of our patient are

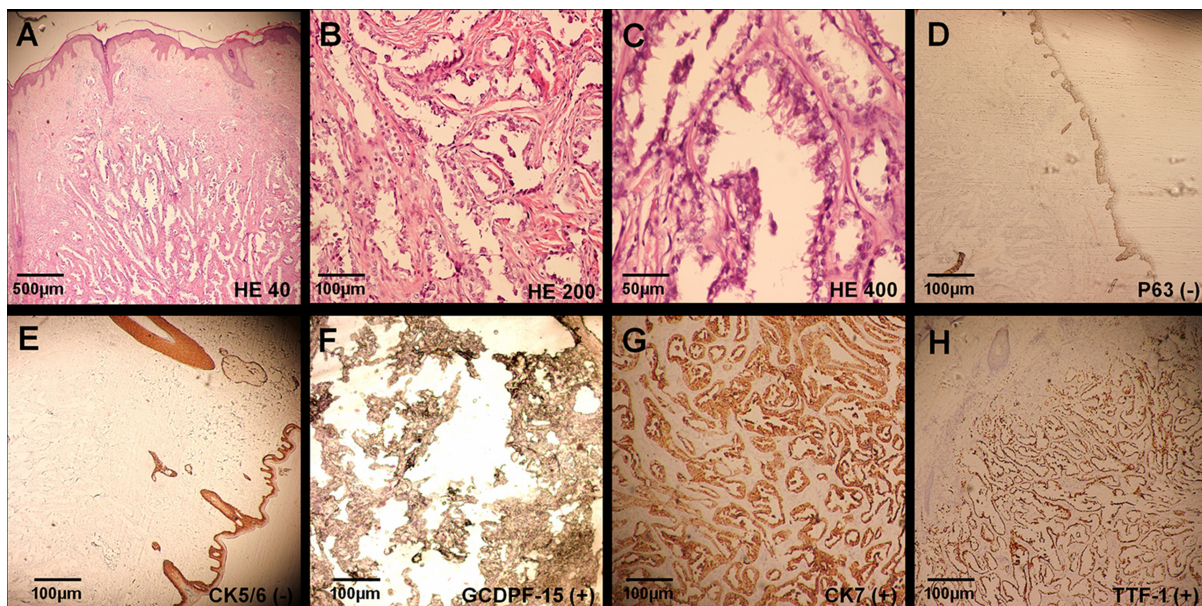


Figure 2 Histopathologic finding of scalp lesions.

Notes: (A, B) Hematoxylin and eosin staining showed circumscribed tumors in the middle and deep dermis, with tubulopapillary structures. Numerous papillary folds projecting into the cystic spaces were also seen. (C) High magnification showed round or oval nuclei, and some cells revealed atypia. Each of the numbers HE 40, HE 200, and HE 400 denotes the magnification of a microscope. (D–H) Immunohistochemical staining showed that nuclear negativity for P63 (D) and CK5/6 (E), and positivity for GCDPF-15 (F), CK7 (G), and TTF-1 (H).

Abbreviation: HE, hematoxylin and eosin.

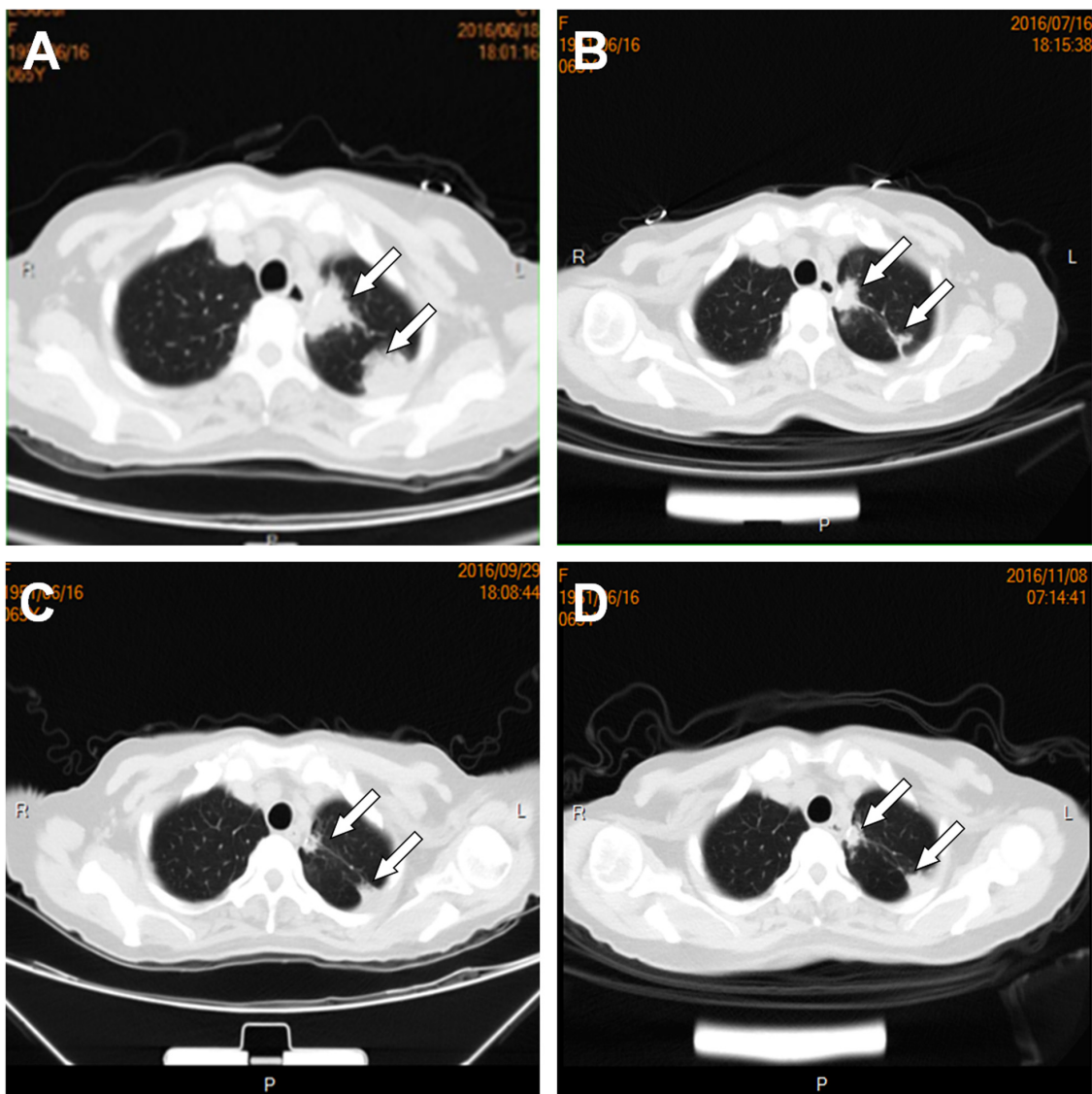


Figure 3 Imaging of lung cancer on CT.

Notes: (A) Large masses involving the left upper lobe associated with extensive mediastinal lymphadenopathy in June 2016. (B) After the first cycle of chemotherapy for 1 month, the large tissue masses in the lung decreased in size in July 2016. (C, D) The decreasing tissue masses in the lung on a followed-up CT in September 2016 and November 2016.

Abbreviation: CT, computed tomography.

consistent with the literature described earlier. The diagnosis of our patient was confirmed to be primary lung adenocarcinoma by pulmonary biopsy and PET-CT, and she already has a history of P-JS, as mentioned earlier. No patient had previously reported with cutaneous metastasis accompanied by P-JS, and the association between cutaneous metastasis and P-JS is unclear. We deduced that the concurrence of the two diseases was incidental.

The clinical presentation of cutaneous metastasis varies. Cutaneous metastasis from lung cancer most commonly occurs in the chest wall, abdomen, back, and upper extremities.^{9,10} Although solitary or multiple nodules are the most common manifestation, inflammatory and sclerodermoid morphology

can also be seen. Moreover, lesions can masquerade as herpes zoster, condyloma, epidermal inclusion cyst, and erythema annulare.¹ Lesions usually measure 1–5 cm in diameter. Palpation characteristics of lesions are varied. Nodules can be hard, painless, mobile, exudative, or ulcerated with deep extension into the subcutaneous tissue. In this case, the nodules were multiple, immobile, and hard, and the overlying skin was intact.

Diagnosis of cutaneous metastasis is confirmed by biopsy, which is still the golden diagnostic standard. In clinical practice, the diagnosis of the disease is conclusively proved by a history of visceral malignancy, metastatic skin lesion, and histopathological examination. The most common type

of cutaneous metastasis is adenocarcinoma. Histopathological examination reveals that cutaneous metastasis from lung cancer is often moderately to poorly differentiated adenocarcinomas. Immunohistochemical markers are important for a diagnosis of a primary cancer; for example, both TTF1 and CK7 positive suggested a source of lung cancer.⁹ However, a histological diagnosis of a primary cancer may be challenging, especially in patients with no previous history. Nevertheless, asymptomatic patients, especially those elderly individuals presenting with multiple, painless, and immobile cutaneous nodules, should be examined carefully as they may be signs of underlying malignancy.

Treatment of cutaneous metastasis emphasizes primary cancer, and the combinations of chemotherapy and radiation therapy are mostly applied in clinical practice. In general, only palliative chemotherapy (combinations of cisplatin and etoposide or cyclophosphamide, adriamycin, and vincristine) with or without radiotherapy is indicated for most patients. However, quite a few patients will receive only supportive palliative therapy.⁸ In addition, cutaneous metastasis has been shown to reflect advanced disease and is associated with a poor prognosis. The appearance of cutaneous metastasis in patients with lung cancer usually indicates a poor prognosis, with an average survival rate ranging from 2.9 to 6.0 months after the diagnosis.^{2,5,7}

Conclusion

In conclusion, scalp metastasis could be the first manifestation prior to an occult lung cancer. Given that the clinical characteristics of cutaneous metastases are not significantly specific, asymptomatic patients, especially those elderly individuals presenting with multiple or solitary, painless,

cutaneous nodules, should be examined and investigated carefully to rule out metastatic diseases as well as to detect primary internal malignancy.

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Disclosure

The authors report no conflicts of interest in this work.

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