

[CASE REPORT]

Multiple Pulmonary Metastases of Cutaneous Squamous Cell Carcinoma

Hisako Kushima, Hiroshi Ishii, Rikako Shima, Yoshiaki Kinoshita,
Kentaro Watanabe and Masaki Fujita

Abstract:

We herein report a rare case of diffuse pulmonary metastasis occurring approximately one year after surgical excision of cutaneous squamous cell carcinoma that had been thought to be stage I with a free margin of healthy tissue. In addition, this case had chest imaging findings unusual for a skin cancer patient, showing a miliary pattern on computed tomography (CT). Distant metastases may develop even if early-stage cutaneous squamous cell carcinoma is completely resected. When observing a miliary shadow on chest CT, metastatic lung tumor from skin cancer should be considered as a differential diagnosis.

Key words: cutaneous squamous cell carcinoma, pulmonary metastasis, miliary shadow

(Intern Med 58: 833-835, 2019)

(DOI: 10.2169/internalmedicine.1889-18)

Introduction

No detailed report has described whether or not the recurrence or survival rate in patients with cutaneous squamous cell carcinoma (cSCC) is improved by preoperative imaging examinations. At present, preoperative imaging is considered useful when there are risk factors for lymph node metastasis or when metastasis is suspected by a physical examination.

In addition, there is no clear evidence that regular imaging tests for screening of distant metastases can prolong the survival in postoperative cSCC patients. Strict clinical observation by a physical examination may in fact be more useful for identifying early lymph node metastasis.

We herein report a case of diffuse pulmonary metastasis in a postoperative patient with early stage cSCC.

Case Report

A 45-year-old man was admitted to our hospital due to an abnormal shadow on chest imaging. He had smoked from the age of 20 to 35 and had a history of alcoholic hepatitis. He had never been found to have abnormal findings on a chest roentgenogram in a previous medical checkup. A skin lesion on his nose had arisen on otherwise normal skin one

year earlier. A biopsy of the skin revealed sheets of large polygonal malignant cells containing keratin in individual cells without keratin pearls, which was classified as moderately or poorly differentiated cSCC (Fig. 1). No distant metastases were observed on chest X-ray, enhanced computed tomography (CT) of the face, or ultrasound of the parotid or cervical regions.

The clinical stage was determined to be stage I, and the patient underwent surgical excision with a 10-mm margin of healthy tissue. The excision margin was negative for SCC, and there was neither lymphatic vessel invasion nor vascular invasion. He was carefully followed by a dermatologist once a month, and neither local recurrence nor swelling of the regional lymph nodes were observed at approximately one year after resection.

However, severe pain occurred in his right hip, so positron emission tomography (PET)/CT of the whole body was performed. Although the hip lesions were suspected of being myositis ossifications, the accumulation of 18-fluorodeoxyglucose (FDG) in the cervical lymph nodes was noted. In addition, diffuse granular shadows without the accumulation of FDG were found in the lungs without laterality, with innumerable, small (1-4 mm) pulmonary nodules scattered throughout the lungs (Fig. 2).

The patient was not febrile and had no skin or respiratory

symptoms. The serum levels of tumor markers, such as carcinoembryonic antigen, SCC, and cytokeratin 19 fragment, were not elevated. No abnormal findings were found in his head or neck organs, including the pharynx and larynx. The tuberculosis-specific interferon-gamma release assay test was negative. As a transbronchial lung biopsy did not provide significant findings, a surgical lung biopsy was performed. The cell morphology of the lung tissue obtained from the tenth segment of the left lower lobe was quite similar to that of the nose cSCC (Fig. 3). Both the skin and lung tissues showed atypical epithelium with a large and clear nucleolus proliferating in sheet form without cancer pearls. Immunohistochemically, the carcinoma cells were negative for 34be-

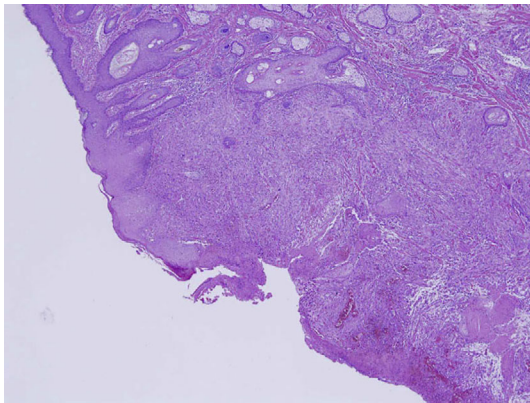


Figure 1. The biopsy specimen of the skin shows sheets of large polygonal malignant cells containing keratin in individual cells without keratin pearls, which was classified as moderately or poorly differentiated cutaneous squamous cell carcinoma.

taE12, CK5/6, p40, and calretinin but were focally positive for D2-40. Furthermore, blood vessel invasion was detected by Elastica van Gieson staining. These findings were consis-

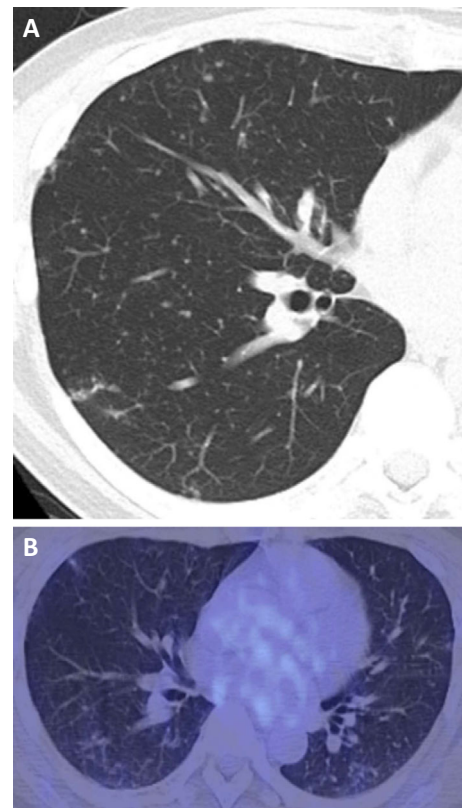


Figure 2. Computed tomography of the chest shows innumerable small (1-4 mm) pulmonary nodules throughout the lungs (A) without the accumulation of FDG (B).

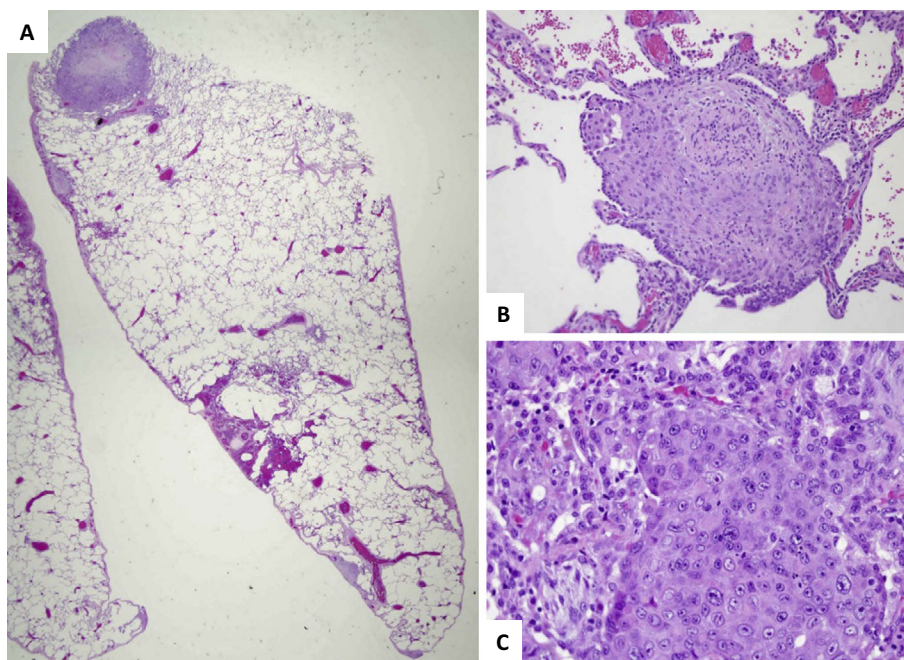


Figure 3. A surgical lung biopsy specimen obtained from the left lower lobe (Hematoxylin and Eosin staining) shows a nodule in the peripheral area (A, B). This nodule had findings quite similar to those of the cutaneous squamous cell carcinoma on the patient's nose (C: high magnification).

tent with pulmonary metastasis of cSCC but not with lung SCC.

Discussion

This was a rare case of diffuse pulmonary metastasis of cSCC occurring approximately one year after surgical excision that had been thought to be stage I with a free margin of healthy tissue. Reportedly, less than 4% of cSCC cases are at risk of metastasis (1). Motley et al. reported that the risk of regional lymph node metastasis was higher in the following cases: recurrence; pathological findings of infiltration into the deep region, invasion around the nerve or differentiation; primary tumor ≥ 2 cm; anatomical site at the ears, lips, limbs, or mucous membranes; and an immunosuppressed state. (2). In the present case, complete resection including normal tissues with a 10-mm margin was performed considering the risks of recurrence and metastasis due to the pathological findings of moderate or poor differentiation, although there were no preoperative findings of regional lymph nodes metastasis. Therefore, based on the previous findings, it was deemed quite unlikely for the present case to develop metastasis to the lungs and cervical lymph nodes at approximately one year after surgery (3, 4).

Local recurrence and metastasis of cSCC appear within 5 years after treatment in 95% of cases (2). Therefore, at least five years' follow-up to check for recurrence and metastasis is considered appropriate, especially for patients in the high-risk group. However, no report has clarified whether or not regular radiological examinations help prolong the survival and achieve an early detection of recurrence or metastasis in the postoperative follow-up observation.

Ross et al. reported that 139 (24%) of 585 cases of cSCC arising from the anal/genital region metastasized to sentinel lymph nodes. In contrast, 17 (21%) of 82 cases of cSCC arising from non-anal regions metastasized to sentinel lymph nodes (5). No high-level evidence has been obtained regarding the clinical significance, including any survival improvement, of sentinel lymph nodes biopsies for cSCC. However, cSCC is thought to metastasize to other organs via the lymphatic pathway. In the present case, the accumulation of FDG was observed in the cervical lymph nodes on PET/CT, and the pathological findings of the lung lesions showed both lymphatic (D2-40-positive) and vascular invasion. Based on these findings, we inferred that the cSCC had migrated to the lung at least partly via the cervical lymph nodes and had spread hematogeneously throughout the lung (6). One factor associated with the development of metastasis in this case was thought to be the pathological findings of moderate to poor differentiation. Therefore, even if there are no physical or radiological findings in the regional

lymph nodes other organs, in addition to a follow-up with careful observation of physical and radiological examinations, dermatologists should be aware that there is a possibility of the existence of distant metastases. A sentinel lymph node biopsy might be a useful examination for the early detection and prevention of distant metastasis in high-risk cases (5).

The present case was also unusual, in terms of the chest image findings presenting with a miliary pattern in skin cancer patients. Randomly-distributed small nodules, known as miliary shadow, on chest CT in patients with metastatic lung tumor are usually found in cases of thyroid carcinoma, renal cell carcinoma, breast carcinoma, malignant melanoma, pancreatic neoplasms, and osteosarcoma, through hematogenous and lymphogenous pathways. No comprehensive report has described the chest imaging findings when cSCC metastasizes to the lung. This is therefore a valuable case report showing that cSCC can present with a miliary pattern on chest imaging when it metastasizes to the lung.

In conclusion, dermatologists should be aware of the possibility of distant metastases, including multiple pulmonary metastases, even if cSCC has been completely resected. In addition, radiologists and pulmonologists should consider the possibility of metastatic lung tumor from skin cancer when they find randomly distributed small nodules (miliary shadow) on chest CT.

The authors state that they have no Conflict of Interest (COI).

References

1. Chollet A, Hohl D, Perrier P. Risk of cutaneous squamous cell carcinomas: the role of clinical and pathological reports. *Rev Med Suisse* **8**: 743-746, 2012 (in French, Abstract in English).
2. Motley R, Kersey P, Lawrence C. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. *Br J Dermatol* **146**: 18-25, 2002.
3. Cancer council Australia/Australian cancer network 2008: Surgical treatment. Clinical practice guide, Basal cell carcinoma, squamous cell carcinoma (and related lesions)-a guide to clinical management in Australia. Cancer Council Australia, Sydney, 2008: 51-54.
4. NCCN: Clinical practice guideline in oncology. Basal cell and squamous cell skin cancers. V.2. 2013, SCC-1-MS-25.
5. Ross AS, Schmulls CD. Sentinel lymph node biopsy in cutaneous squamous cell carcinoma: a systematic review of the English literature. *Dermatol Surg* **32**: 1309-1321, 2006.
6. Barzilai G, Greenberg E, Cohen-Kerem R, Doweck I. Pattern of regional metastases from cutaneous squamous cell carcinoma of the head and neck. *Otolaryngol Head Neck Surg* **132**: 852-856, 2005.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).