

## Subungual and Ocular Metastases from Small Cell Carcinoma of the Lung

*Nirav J. Mehta, MD*

*Rajal N. Mehta, MD*

*Ketan Jani, MD*

*Anupama Nehra, MD*

**A**lthough malignant neoplasms that develop in the lungs commonly metastasize to other areas of the body, they usually do not metastasize to the skin. In this report, a patient with a subungual metastasis, as well as ocular metastases, from a small cell lung carcinoma is described. Owing to the specific site in which the subungual lesion developed and its morphologic nature, it is unique among skin metastases resulting from internal malignant tumors.

### CASE PRESENTATION

A 61-year-old nonsmoking white woman with a history of small cell lung carcinoma with metastases to the brain was referred to our hospital for further evaluation after she began treatment for her condition.

### Previous Clinical Course

The patient's initial symptoms, 2 months previously, were left-hand numbness and weakness. She was subsequently taken to the emergency department of another hospital. Computed axial tomography and magnetic resonance imaging scans of her brain were taken at that hospital and showed 2 metastatic lesions in the right parietal cortex, each measuring 2 × 3 cm. Subsequent imaging studies showed approximately 5 lesions in the upper lobes of both of her lungs. She underwent neurosurgery and radiotherapy for removal of the brain lesions. Specimens of the brain lesions were examined, and the evaluation revealed small cell carcinoma, the histopathologic nature of which was identical to the lung lesions. The patient was started on chemotherapy with cisplatin and etoposide.

### Continued Clinical Course

By the time the patient had presented to our hospital, she had received 4 cycles of cisplatin and etoposide. However, new brain metastases developed, and the lung carcinomas had spread to her right iris. Owing to

the ocular metastases, she developed photophobia and blurred vision.

The results of a laboratory evaluation performed at our hospital showed that the patient had a leukocyte count of  $1.5 \times 10^3/\text{mm}^3$ , a hemoglobin level of 8 g/dL, a hematocrit of 26%, a platelet count of  $186 \times 10^3/\text{mm}^3$ , and normal results on a routine clinical chemistry analysis, with exception of a lactate dehydrogenase level of 660 U/L. As she received more courses of chemotherapy, she frequently developed absolute neutropenia, requiring reverse isolation. No paraneoplastic manifestation was observed.

Two months after the patient's initial presentation to our hospital, an area of black discoloration beneath her right thumbnail was noticed. No ulceration, surrounding edema, or discharge was observed, and the lesion was painless. There was no hyperpigmentation of periungual tissue, and no other skin lesions were noted.

The subungual lesion increased rapidly in size over the course of several days and eroded the thumbnail. Radiographs of her right hand showed only periarticular demineralization. A specimen of the lesion was taken via an incisional biopsy procedure, and a histopathologic evaluation of the tissue revealed metastatic small cell carcinoma (**Figure 1**). The lesion was surgically removed.

Meanwhile, the primary cancer had spread to the patient's spine, vertebrae, and proximal femur, and further courses of chemotherapy failed. The patient died approximately 4 months after the diagnosis of the subungual metastasis.

---

*Dr. Nirav Mehta is a Chief Resident and Dr. Rajal Mehta is a Senior Resident, Department of Internal Medicine, The Long Island College Hospital, Brooklyn, NY. Dr. Jani is a Fellow, Division of Pulmonary and Critical Care Medicine, State University of New York Health Science Center at Brooklyn, Brooklyn, NY. Dr. Nehra is a Chief Resident, Department of Internal Medicine, The Long Island College Hospital, Brooklyn, NY.*

## DISCUSSION

### Cutaneous Metastases

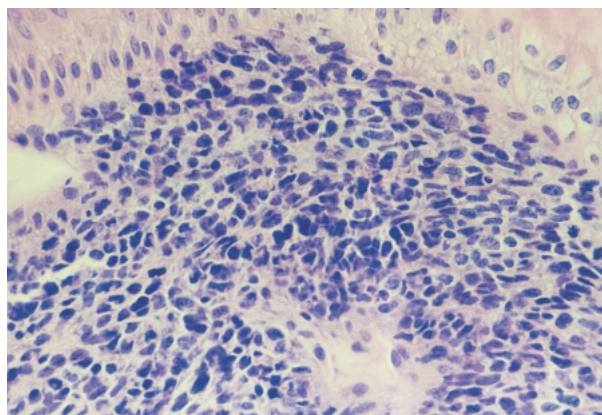
Although it is generally believed that cutaneous metastases from internal malignant neoplasms rarely develop, their exact incidence is unknown. Such metastases have been found in 0.2% to 9% of the subjects in some autopsy studies.<sup>1</sup> In 5 large-scale autopsy studies in particular, the incidence of skin metastases from internal malignant tumors was approximately 2% (146 cases in 7196 necropsies).<sup>2</sup>

Cutaneous metastasis may occur by way of a subcutaneous neoplasm directly invading the skin; by way of contiguous extension of the tumor cells through lymphatics, lymphatic emboli, or hemic emboli; or by accidental implantation of the tumor cells. Although any area of the skin may be affected, a cutaneous metastasis usually develops near the primary tumor. Moreover, it is unusual for any internal malignant tumor to metastasize to the skin of the hands or feet, and metastases to the subungual area are even more rare. A subungual lesion in a patient with a history of cancer, should alert the clinician to the possibility of a metastatic lesion. The differential diagnosis of a subungual lesion should include a subungual hematoma, a primary subungual melanoma, paronychia, a pyogenic granuloma, a glomus tumor, a keratoacanthoma, a primary squamous cell carcinoma, a primary epithelioma, a metastasis from an internal neoplasm, and a chronic fungal infection.

Physical characteristics alone may not be enough to distinguish benign and malignant subungual neoplasms; in either case, tenderness, discharge, ulceration, or inflammation may be present—features that can also cause them to be confused with infectious lesions.<sup>3</sup> Moreover, a cutaneous metastasis from a renal cell carcinoma may clinically resemble a Kaposi's sarcoma and pyogenic granuloma.

Nonetheless, when a subungual lesion is present, dark pigmentation of the surrounding subungual space (Hutchison's sign) should lead to the consideration of a malignant melanoma. A neuroblastoma may appear as multiple, firm, nontender, mobile, bluish, subcutaneous nodules, described by the term *blueberry muffin*.<sup>1</sup> Metastatic lesions from thyroid or renal cell carcinomas may be pulsatile.<sup>1</sup>

Any discharge from a subungual lesion should be cultured for pathogenic organisms, and a radiograph of the digit should be obtained to rule out bony involvement. Once an infection and primary bone lesion have been ruled out, an incisional biopsy procedure should be performed to obtain a tissue specimen from the nail bed. The specimen should be evaluated histo-



**Figure 1.** Micrograph of a tissue specimen of the case patient's subungual lesion showing small cell disease (hematoxylin-eosin, original magnification  $\times 200$ ).

logically and microbiologically. In some cases, radiotherapy, chemotherapy, wide local excision, or amputation of the finger has been used to treat cancerous lesions of the subungual area.<sup>3-6</sup>

Certain internal malignant tumors show a particular tendency for cutaneous metastasis. In one series of female patients with cutaneous metastases, breast cancer was found to be the primary malignancy in 67% of the patients. In another series of male patients with cutaneous metastases, the most commonly occurring primary malignant neoplasms, in order of decreasing prevalence, were bronchogenic carcinomas, adenocarcinomas of the gastrointestinal tract, malignant melanomas, and squamous cell carcinomas of the oral cavity.<sup>7</sup>

Among malignant neoplasms of the lungs, in particular, adenocarcinomas show the greatest tendency to metastasize to cutaneous sites, whereas large cell carcinomas show the least tendency. Small cell and squamous cell carcinomas of the lungs are intermediate in their tendency to metastasize.<sup>8</sup> In a series of 1084 patients with lung cancers, 34 (3.1%) developed cutaneous metastases.<sup>9</sup> The most common sites of skin metastases resulting from malignant neoplasms in the lungs are the chest, abdomen, back, upper extremities, face, and scalp.<sup>8</sup> A literature review showed no reports of subungual spread from a small cell carcinoma of the lung and only 1 case of subungual spread from a malignant tumor of the lung, in general.<sup>10</sup> (The tumor was an epidermoid carcinoma of the right main bronchus.)

In general, the prognosis of a patient with a cutaneous metastasis from an internal malignant neoplasm is extremely poor, and for some patients, a skin

metastasis may be the first indication of cancer. This is likely to be the case for patients with lung and renal cancers and, rarely, with breast cancers.<sup>7</sup> The appearance of a skin metastasis indicates advanced and aggressive disease. The occurrence of such a metastasis is generally a preterminal event, particularly when the primary lesion is in the lung. It has been suggested that the emergence of skin metastases in a patient with a lung carcinoma signifies that the primary tumor has reached a size of 1 to 2 cm in diameter.<sup>11,12</sup> In most studies, life spans after the appearance of a skin metastasis range between 3 and 5 months.<sup>1</sup>

### **Ocular Metastases**

Metastases to the eye result from fewer than 1% of internal malignant neoplasms. In approximately 25% to 30% of cases of internal malignant tumors resulting in eye metastases, the eye lesions are bilateral.<sup>13</sup> The most common site of ocular metastases is the posterior portion of the choroids, followed by the orbit, iris, and ciliary body.<sup>14</sup> Breast and lung tumors are the most common primary neoplasms leading to eye metastases. Patients with anterior uveal metastases may experience blurred vision, a visible mass, red eye, and photophobia. Clinically, it is very important to differentiate between a metastatic lesion and a primary malignant melanoma of the eye. Metastatic lesions are typically more flat and multifocal and often bilateral. Metastatic lesions typically grow much more rapidly. Also, rupture through Bruch's membrane is very unusual for metastatic lesions.

Occurrences of metastatic lesions in the eye are preterminal events when the primary tumor is a carcinoma of the lung.<sup>15</sup> A survival time ranging between 5.2 to 6.3 months has been reported in relation to primary lung tumors with metastases to the eye.<sup>16,17</sup>

### **CONCLUSION**

Metastases developing in unusual sites, such as the nailbed and iris, represent unique and interesting phenomena. Special care must be taken to delineate their histologic nature, their pathophysiology, the pattern of the disease to which they relate, and the type of treatment needed. The appearance of a skin lesion or an eye complaint by a patient with a history of cancer must be viewed with great suspicion, and a biopsy specimen of the cutaneous lesion must be obtained and carefully evaluated. **HP**

### **REFERENCES**

1. Safai B. Management of skin cancer. In: DeVita VT, Hellman S, Rosenberg SA, editors. *Cancer: principles and practice of oncology*. 5th ed. Philadelphia: Lippincott-Raven; 1997.
2. Rosen T. Cutaneous metastasis. *Med Clin North Am* 1980;64:885-900.
3. Cohen PR, Buzdar AU. Metastatic breast carcinoma mimicking an acute paronychia of the great toe: case report and review of subungual metastases. *Am J Clin Oncol* 1993;16:86-91.
4. Vine JE, Cohen PR. Renal cell carcinoma metastatic to the thumb: a case report and review of subungual metastases from all primary sites. *Clin Exper Dermatol* 1996; 21:377-80.
5. Barnett LS, Morris JM. Metastases of renal-cell carcinoma simultaneously to a finger and a toe. *J Bone Joint Surg Am* 1969;51:772-4.
6. Abangan DL, Solomon D, Kauffman CL. Suspicious violaceous subungual nodule. Metastatic renal cell carcinoma (RCC). *Arch Dermatol* 1994;130:915, 917-8.
7. Brownstein MH, Helwig EB. Metastatic tumors of the skin. *Cancer* 1972;29:1298-307.
8. Dreizen S, Dhingra HM, Chiuten DF, et al. Cutaneous and subcutaneous metastases of lung cancer. Clinical characteristics. *Postgrad Med* 1986;80:111-6.
9. Terashima T, Kanazawa M. Lung cancer with skin metastasis. *Chest* 1994;106:1448-50.
10. Camiel MR, Aron BS, Alexander LL, et al. Metastases to palm, sole, nailbed, nose, face and scalp from unsuspected carcinoma of the lung. *Cancer* 1969;23:214-20.
11. Ulmann JE, Phillips JL. Treatment of metastatic cancer. In: DeVita VT, Hellman S, Rosenberg SA, editors. *Cancer: principles and practice of oncology*. 5th ed. Philadelphia: Lippincott-Raven; 1997.
12. Folkman J. Tumor invasion and metastases. In: Holland JF, Frei E III, editors. *Cancer medicine*. 2nd ed. Philadelphia: Lea & Febiger; 1982.
13. Rubin P, Green J. Solitary metastases to other sites. In: *Solitary metastases*. Springfield (IL): Thomas; 1968.
14. Brady LW, O'Neill EA, Farber SH. Unusual sites of metastases. *Seminars Oncol* 1977;4:59-64.
15. Volpe NJ, Albert DM. Metastases to the uvea. In: Albert DM, Jakobiec FA, editors. *Principle and practice of ophthalmology: clinical practice*. Vol. 5. Philadelphia: WB Saunders Company; 1994.
16. Stephens RE, Shields JA. Diagnosis and management of cancer metastatic to the uvea: a study of 70 cases. *Ophthalmology* 1979;86:1336-49.
17. Freedman MI, Folk JC. Metastatic tumors to the eye and orbit. Patient survival and clinical characteristics. *Arch Ophthalmol* 1987;105:1215-9.

Copyright 2001 by Turner White Communications Inc., Wayne, PA. All rights reserved.