Locally Destructive Metastatic Basal Cell Carcinoma

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PRACTICE **POINTS**

- Risk factors associated with metastatic spread of basal cell carcinoma (BCC) include larger tumor size, greater depth of invasion, long duration of disease, failure to respond to conventional treatment, and prior radiation treatment in the affected area.
- The median interval between onset of BCC and metastasis has been shown to be approximately 9 years.
- Vismodegib can be an effective oral therapy for patients with metastatic BCC, locally advanced BCC, recurrence following surgery, or those who are not candidates for surgery or radiation.

To the Editor:

A 60-year-old woman with a history of lymphoma presented to the emergency department for evaluation of intermittent diarrhea and vomiting of 2 weeks' duration. On presentation, a rather large dressing covering the entire right half of the face was noted. Removal of the bandage revealed a necrotic, extensively destructive, right-sided facial lesion with a fully exposed ocular globe (Figure 1). The patient lived alone and was accompanied by a neighbor, who disclosed that the lesion had been neglected and enlarged over the last 15 years. Moreover, the neighbor reported that the patient had recently experienced several episodes of vertigo and frequent falls.

On admission to the hospital, dermatology was consulted and initial workup included computed tomography (CT) scan of the head and maxillofacial region, which showed a destructive process involving the right frontotemporal bone, maxillofacial region, sphenoid, and skull base with exposure of intracranial contents (Figure 2). An aggressive wound care regimen was instituted. Biopsy of the wound margin revealed nodular and focally infiltrative basal cell carcinoma (BCC)(Figure 3). Culture of the necrotic bone grew *Rhizopus*, a causative organism of mucormycosis, and the patient was treated with posaconazole. A CT scan of the chest and abdomen showed multiple bilateral pulmonary nodules and necrotic lymph nodes in the left hilum and left axilla. The patient refused bronchoscopy to further evaluate the pulmonary nodules. Ultrasound-guided biopsy of the left axillary lymph node revealed metastatic disease (Figure 4).

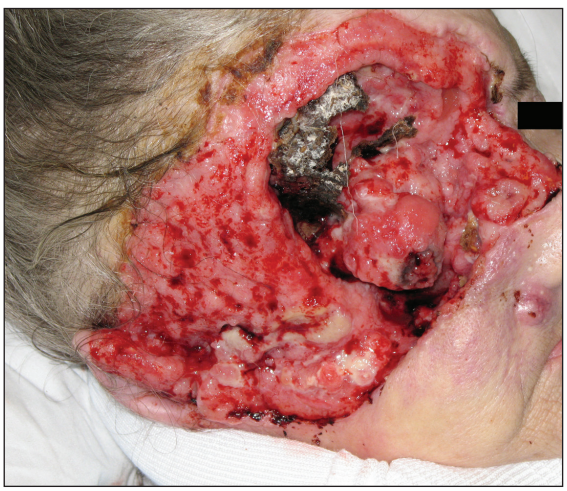

FIGURE 1. Necrotic ulceration of the right side of the face with extensive destruction and a fully exposed ocular globe.

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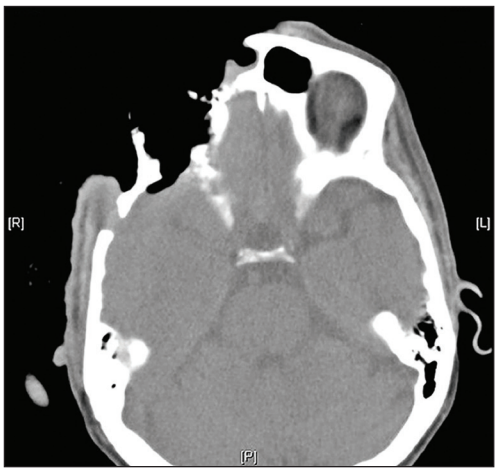

FIGURE 2. Computed tomography of the maxillofacial region showed a destructive process involving the right frontotemporal bone, maxillofacial region, sphenoid, and skull base.

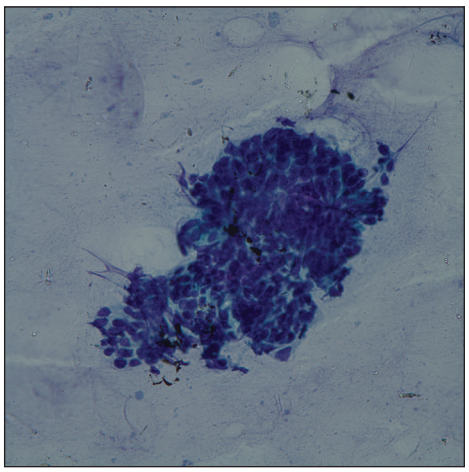

FIGURE 4. Ultrasound-guided biopsy of the left axillary lymph node revealed metastatic basal cell carcinoma.

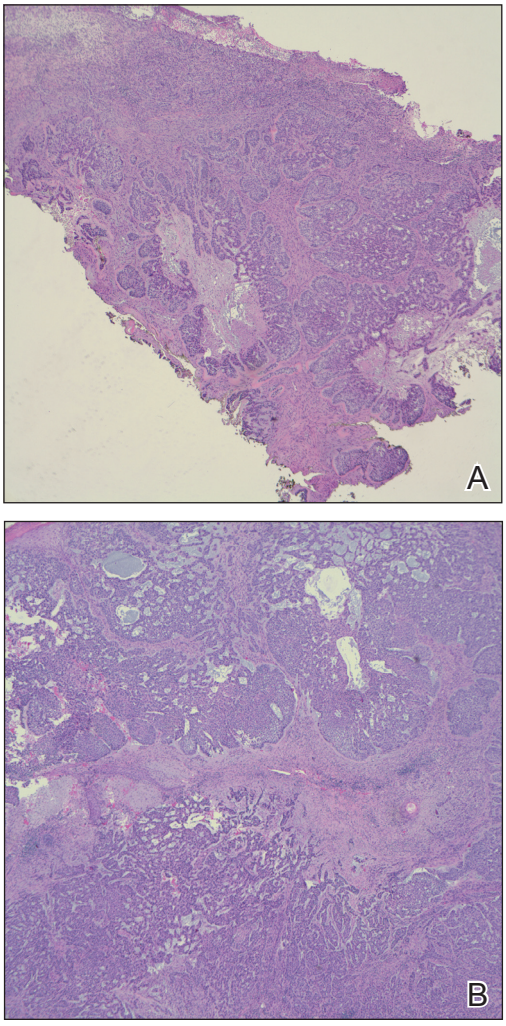

FIGURE 3. A and B, Biopsy of the wound margin revealed nodular and focally infiltrative basal cell carcinoma (H&E, original magnifications ×4 and ×10).

Several days into her hospitalization, the patient developed radicular pain in both arms and weakness in all 4 extremities. A CT scan of the neck revealed a pathologic fracture of the C7 vertebrae. Several medical and surgical services as well as psychiatry were consulted. Given the extensive nature of the disease involvement with limited treatment options, the patient sought to forego further interventions and was discharged to hospice care.

Basal cell carcinomas rarely metastasize, with a reported incidence of 0.0028% to 0.5%.[1] The likelihood of metastasis is most closely related to tumor size and depth of invasion. Tumors greater than 3 cm in diameter have a 2% incidence of metastatic spread and/or death. The incidence of metastatic spread and/or death is estimated to be 25% for tumors with a diameter of 5 cm and 50% for tumors with a diameter of 10 cm or greater.[2] Other risk factors for metastatic spread include long duration of disease, failure to respond to conventional treatment, and prior radiation treatment in the affected area.[1] In one review, the median interval between onset of BCC and metastasis was 9 years.[3] In our case, 15 years of neglect most likely led to the aggressiveness of the tumor. Although the workup in our patient was limited per her request, there was no evidence that her lymphoma had recurred or that she was in any other way immunocompromised. Unfortunately, in this patient's case, the local destructiveness of the carcinoma with subsequent bony invasion and necrosis was complicated with secondary *Rhizopus* infection. A PubMed search of articles indexed for MEDLINE using the terms *basal cell carcinoma* and *mucormycosis* revealed no other reported cases of BCC associated with mucormycosis; therefore, our case represents a rare presentation of this association. Rhinocerebral mucormycosis is the most common manifestation of mucormycosis and more commonly occurs in diabetics with ketoacidosis and in severely debilitated or immunosuppressed individuals.[4] The extensive bony

destruction, especially of the nasal region, of our patient's tumor likely led to secondary infection with *Rhizopus*.

Approximately 85% of all metastatic BCCs originate in the head and neck region, with lymph nodes being the first site of metastasis and involved in approximately half of all cases.[1,4] Metastases to the lungs, bone, liver, and other viscera can occur with advanced disease. Metastasis generally portends a poor prognosis, with survival rarely exceeding 1.5 years. Until recently, therapeutic options for metastatic disease were limited, with marginal response to chemotherapy with methotrexate, fluorouracil, bleomycin, and cisplatin.[4] Vismodegib, a novel smoothened receptor inhibitor that blocks the sonic hedgehog pathway implicated in BCC carcinogenesis, offers a new promising treatment for management and control of advanced disease.[5]

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