

Extensive Basal Cell Carcinoma With Probable Bone Metastasis

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GOAL

To understand metastasis of basal cell carcinoma (BCC) to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss criteria for diagnosing metastatic BCC.
2. Describe clinical and radiographic findings of BCC metastatic to bone.
3. Identify treatment recommendations for metastatic BCC.

CME Test on page 52.

This article has been peer reviewed and approved by Ranon Ephraim Mann, MD, Assistant Professor, Department of Medicine (Dermatology), Montefiore Medical Center Medical Arts Pavilion. Review date: June 2007.

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Metastasis of basal cell carcinoma (BCC) rarely occurs. Few cases have been reported in the literature; those cases reported generally resulted

from chronic, extensive, recurrent lesions on the head or neck. Metastases may involve lymph nodes, the lungs, and bone, as well as abdominal viscera. Once distant metastasis takes place, survival usually is short and palliative treatment is sought. With regard to bone metastases, several case reports have demonstrated similar clinical features indicative of osseous involvement. We present a case report of a patient with an extensive BCC with histologic documentation and probable bone metastasis of BCC. Clinical and radiographic features of this case were consistent with previously reported patients. However, confirmatory postmortem biopsy of the bone specimen was refused by the patient's family.

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Basal cell carcinoma (BCC) is the most common of all malignant neoplasms; approximately 1 million new cases occur annually in the United States, with increasing incidence.¹ Although BCC is locally invasive, the occurrence of BCC metastasis is exceedingly rare, with an average rate of approximately 0.03%,² typically involving a large, long-standing, locally destructive, recalcitrant tumor of the head or neck.³ BCC metastasis is rare because of the early recognition of the disease, current treatment, and the noninvasive character of the tumor. In the event of metastatic spread, the most commonly involved sites (in descending order of frequency) include regional lymph nodes, the lungs, and bone, but also may involve the pleura and abdominal viscera.⁴ Criteria used to establish the diagnosis of metastatic BCC were put forth in 1951 by Lattes and Kessler⁵ and include: (1) the neoplasm must originate

from skin, not mucous membranes; (2) direct invasion of the neoplasm to the presumed metastatic site must be ruled out; and (3) primary and metastatic lesions must show identical histologic features consistent with BCC.

Bone is involved in approximately 20% to 30% of metastatic BCCs.^{3,6} In addition to the above guidelines, other objective findings in BCC metastatic to bone have been reported in the literature, such as increased skeletal uptake on bone scintigraphy, elevated serum levels of alkaline phosphatase, and radiographic imaging studies that demonstrate lytic bone lesions.⁷ We report a case of BCC with probable extensive metastases to the axial skeleton above the pelvis. Results of a physical examination, as well as x-ray and bone scintigraphy findings, were consistent with extensive skeletal involvement by metastatic tumor. Histologic confirmation of bone metastasis was not possible due to the patient's family's refusal of a postmortem biopsy of the bone specimen.

Case Report

A 56-year-old white male veteran presented to a Midwestern United States veterans affairs medical center with 2 prominent skin lesions of unknown duration. The patient stated that the lesions began as small boils on his upper back and right arm many years ago and subsequently enlarged. He had not been seen by a physician for many years. Results of a physical examination revealed the patient was a cachectic man in no apparent distress; he had no fever and his vital signs were within reference range. His skin examination revealed an extensive, ulcerated, weeping lesion with rolled borders on his upper back extending to the posterior neck, and another similar lesion on his right arm. The lesion on his back measured 26×15 cm, and



Figure 1. Extensive, ulcerated, weeping lesion of basal cell carcinoma with rolled borders on the upper back extending to the posterior neck, measuring 26×15 cm (A). Ulcerated weeping lesion with elevated borders on the right arm, measuring 12×6 cm (B).

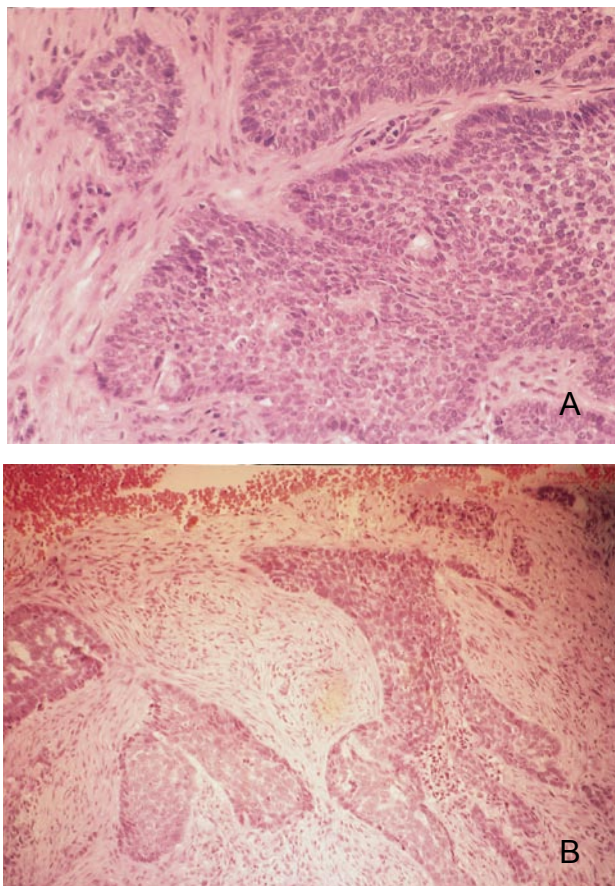


Figure 2. A biopsy of upper back lesion demonstrates basaloid cells interspersed in a fibrous stroma (H&E, original magnification $\times 50$)(A). A biopsy of right arm lesion also demonstrates basaloid cells interspersed in a fibrous stroma (H&E, original magnification $\times 25$)(B).

the lesion on his arm measured 12×6 cm (Figure 1). No mucous membrane involvement was noted. Biopsies of skin specimens were obtained from both lesions for histologic diagnosis, which confirmed the presence of BCC (Figure 2). Because of the lesions' proximity to bone, bone radiographs were performed on the patient's chest, bilateral shoulders, and right arm, revealing punched-out lytic bone lesions in the ribs, left clavicle, scapulae, and right humerus (Figure 3A). Next, a bone scintigraphy scan was performed to survey the extent of disease, revealing a "superscan," with increased bony uptake in most of the axial skeleton above the pelvis along with other discreet areas of increased uptake in the upper extremities (Figure 3B). Additional laboratory data were not available. The patient was admitted to the medical center for improvement of his nutritional status and for the management of his skin lesions. On the seventh day of hospitalization, the patient unexpectedly died, and his family refused an autopsy.

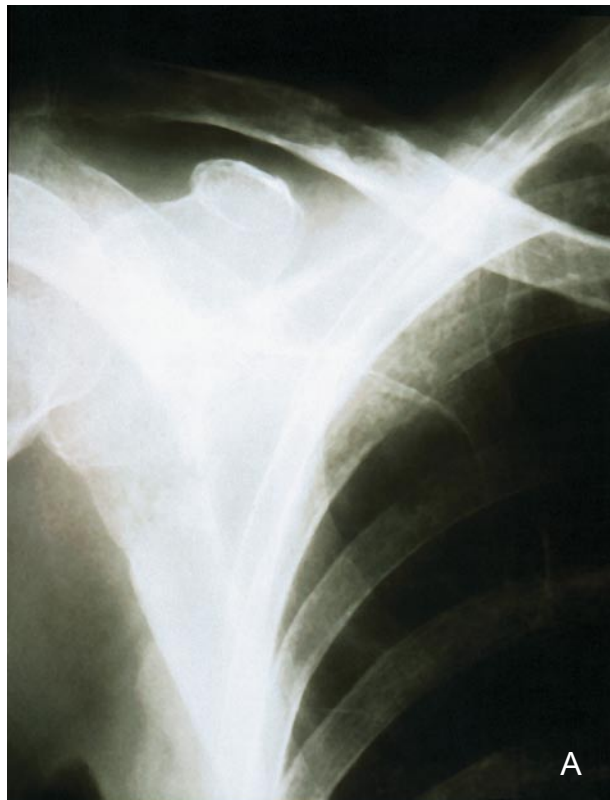


Figure 3. Bone radiograph of the clavicle demonstrates a lytic bone lesion (A). A bone scintigraphy scan demonstrates extensive diffuse increased bony uptake in the axial skeleton above the pelvis (B).

Characteristics of Several Cases of BCC With Biopsy-Proven Bone Metastasis*

Reference	Age at Onset of Primary BCC, y	Age at Discovery of Bone Metastasis, y	Location of Primary BCC	Bone Scintigraphy Findings	XR and CT Scan Findings
1	45	55	Nose, cheek	Increased bony uptake in right hemipelvis	XR: Destructive lesion on right iliac wing
4	62	69	Frontoparietal temporal area	Increased bony uptake in T8 vertebra and left ninth rib	XR: Osteolytic changes in T8 vertebra
7	58	65	Scalp	Increased bony uptake in multiple skeletal areas	XR: Osteolytic and osteoblastic metastases to thoracic and lumbar spine, pelvis
9	53	59	Nose	NA	CT: Extensive bony involvement
10	NA	45	Ear	Increased bony uptake in skull, scapulae, thoracic and lumbar spine, ribs, pelvis, right femur	CT: Lytic destruction in T7 and T8 vertebrae, ribs, iliac crests
11	31	51	Neck	Multiple metastatic bone lesions	XR: Widespread osteolysis of vertebrae, ribs, clavicles, femurs, pelvis
12	41	54	Temple area	NA	XR, CT: Lytic lesions of C2 and C3 vertebrae
13	50	60	Anterior chest wall	NA	XR: Lumbar vertebrae involvement
14	47	53	Scapular area	NA	XR: Right pelvis involvement
15	55	65	Upper back	Widespread increased skeletal uptake	XR: Generalized osteoblastic and osteolytic lesions

TABLE CONTINUED ON PAGE 64

Table. (continued)

Reference	Age at Onset of Primary BCC, y	Age at Discovery of Bone Metastasis, y	Location of Primary BCC	Bone Scintigraphy Findings	XR and CT Scan Findings
16	45	51	Ear	NA	XR: Spine and pelvis involvement
16	26	32	Nasolabial fold	NA	XR: Spine and pelvis involvement
16	69	69	Chest	NA	CXR: Bone involvement
16	76	78	Eyelid	NA	CXR: Bone involvement
16	32	33	Cheek	NA	CXR: Bone involvement
17	42	51	Cheek	Increased bony uptake in thoracic and lumbar vertebrae, humerus, pubic bone	XR: Lytic lesions of thoracic and lumbar vertebrae, humerus, pubic bone
18	53	68	Cheeks, chin, nose	NA	XR: Osteolytic and osteoblastic lesions in lumbar vertebrae, pelvis
19	40	47	Scapula	NA	XR: Lytic lesion of femur
Present case [†]	Unknown	56	Upper back/posterior neck, right arm	Increased diffuse bony uptake in axial skeleton and extremities	XR: Lytic lesions in clavicle, ribs, humerus, scapulae

*BCC indicates basal cell carcinoma; XR, x-ray; CT, computed tomography; NA, not available; CXR, chest x-ray.

[†]Bone metastasis not confirmed histologically.

Comment

The first case of BCC metastatic to a submandibular lymph node was reported by Beadles⁸ in 1894. Few cases have been described in the literature since then, and rates of metastasis have been reported to be from 0.0028% to 0.4%, depending on the study protocol used.⁹ Although histologic confirmation of bone involvement is lacking, in the absence of other

detectable malignancies, our objective clinical and radiographic findings point toward bone metastasis in our patient. A review of several case reports of BCC metastatic to bone demonstrates clinical and radiographic similarities with those of our patient (Table).

In contrast to nonmetastatic BCC, the age of onset of metastatic lesions is approximately 45 to 59 years, with an interval of approximately 9 to

11 years between primary tumor onset and spread.¹ However, cases of metastasis have been reported after latency periods of up to 23,²⁰ 26,²¹ and even 45³ years following diagnosis of primary lesions. Men are more often affected, and tumors generally are large, long-standing, and refractory to treatment.³ No significantly different histologic characteristics in metastatic tumors were identified by Wermuth and Fajardo²²; however, other authors have concluded that metatypical BCC, or BCC with foci of squamous differentiation, demonstrates more aggressive behavior and increased potential to metastasize.^{9-11,16,19} Factors noted to be associated with an increased incidence of metastasis include long duration of a large primary lesion on the head or neck,²³ recalcitrance to treatment,¹ immunodeficiency combined with stromal independence of the tumor,²⁴ inadequate excision followed by immediate wound closure,²⁵ and lesion depth.²⁶ Farmer and Helwig¹⁶ noted a paucity of inflammatory cells in the vicinity of recurrent tumors, implicating the possibility of a defective cellular immune response as a contributing factor. Our patient's evolving history, however, was unclear due to his inability to provide an accurate account.

Total excision of primary tumors following recommended treatment guidelines does not tend to halt metastatic spread,⁴ and prior to discovery of metastases, lesions generally tend to recur locally following excision and/or radiation therapy.^{1,4,9} Approximately equal rates of hematogenous and lymphatic spread are observed, and the lung is the most likely distant organ to be involved, followed by bone, liver, and pleura.³ Cases of bone metastasis may present with symptoms of spinal cord compression⁶ or anemia,¹⁵ as well as bone pain¹⁷ and pathologic fractures,^{7,15} and tend to involve the lumbar spine more frequently than the thoracic and cervical regions.¹⁰ Our patient did not complain of any such symptoms indicative of osseous lesions, even with extensive bony involvement.

von Domarus and Stevens³ noted a slightly better survival rate among patients with lymphatic metastases versus those patients whose tumors disseminated hematogenously. Patients with metastatic BCC have a 5-year survival rate of approximately 10%; patients with distant spread typically survive only 10 to 14 months.¹ Prognosis is especially poor with metastases to the lungs, bone, or liver,^{12,16} and palliative treatment generally is used in these cases.

Aggressive treatment should be pursued if BCC metastasis has been detected. Unfortunately, once distant metastasis occurs, cure is not possible and

survival generally is short.¹² Excision of the primary lesion with free margins is the initial objective, but it may not always be possible due to the size or extent of the tumor. Therapeutic options for bone metastases include chemotherapy with agents such as cyclophosphamide, etoposide, fluorouracil, methotrexate, cisplatin, bleomycin, and doxorubicin.¹¹ Radiation therapy is an effective palliative treatment, but its use has not demonstrated increased survival benefit.¹² Laminectomy has been used for vertebral involvement.^{10,12} Because of the rare nature of metastatic BCC, appropriate treatment protocols have not been formulated, and combination therapy with the above modalities generally is employed. Nevertheless, therapeutic response to treatment usually is poor. Because of our patient's untimely death, no treatment options were sought.

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