

Metastatic Basal Cell Carcinoma Presenting as Unilateral Axillary Lymphadenopathy: Report of a Case and Review of the Literature

JOSHUA M. BERLIN, MD, MICHAEL R. WARNER, MD, AND PHILIP L. BAILIN, MD

Department of Dermatology, Cleveland Clinic Foundation, Cleveland, Ohio

BACKGROUND. Although basal cell carcinoma (BCC) is one of the most common forms of cancer worldwide, the incidence of metastatic basal cell carcinoma (MBCC) is exceedingly low. Of reported cases, it is estimated that up to 85% arise in the head and neck region.

OBJECTIVE. Case presentation of a BCC measuring 1.1 cm arising in a nonfacial site that presented with unilateral axillary lymphadenopathy.

METHODS. Case presentation with literature review.

J. M. BERLIN, MD, M. R. WARNER, MD, AND P. L. BAILIN, MD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

RESULTS. Risk factors which should lead to a higher index of suspicion among clinicians for identifying these patients include large tumor size, previous irradiation, local invasion, and recurrence. The lymph nodes, lungs, bones, and skin are among the most common sites in which metastases arise.

CONCLUSION. We report an unusual case of MBCC arising from a small, nonfacial primary BCC that presented with unilateral axillary lymphadenopathy.

BASAL CELL carcinoma (BCC) is one of the most prevalent forms of cancer worldwide. Despite the large number of primary BCCs diagnosed each year, the rate of metastatic BCC (MBCC) ranges from 0.0028 to 0.5%.¹ Since MBCC was first reported in 1894 by Beadles, there have been more than 240 cases reported in the literature.² Of these cases, 66–85% of MBCCs arise from primary lesions in the head and neck region.^{2,3} In 1951 Lattes and Kessler⁴ outlined criteria needed for proper diagnosis of MBCC. These criteria include the primary tumor must originate from the skin and not the mucosa, metastasis must occur at a site distant from the primary tumor without evidence of direct extension, and the primary and metastatic tumors must have similar histopathology.

In this article we describe the case of a patient with MBCC arising from a small, nonfacial primary BCC that presented with unilateral lymphadenopathy. We review the epidemiology, risk factors, TNM classification for BCC, and therapeutic modalities for patients with MBCC.

Case Report

A 59-year-old white woman was evaluated by the Department of Dermatology at the Cleveland Clinic Foundation, Cleveland, Ohio, in March 2000. She was referred by cardiothoracic surgery after MBCC was discovered in one of three left axillary lymph nodes during a biopsy to evaluate a 2-month history of painless lymphadenopathy. The patient was in good health without any ongoing medical problems. Her past dermatologic history was remarkable for a 1.1 cm superficial, solid and infiltrative BCC excised from her back in 1994. As the BCC was located on her back, the patient did not know when the tumor first appeared. There was no family history of skin cancer and no personal history to suggest basal cell nevus syndrome.

Physical examination revealed a 3 cm soft, flat, flesh-colored scar on her left mid-back near T5. Two pearly 5 mm papules were noted on her right chest wall and right shin whose morphologies were consistent with BCC. The remainder of the examination revealed no additional scars to suggest sites of prior excisions. The biopsy from the BCC previously excised from her back was reviewed and revealed a virtually identical histology to that seen in the left axillary lymph nodes (Figure 1).

A bone scan as well as chest, abdominal, and pelvic computed tomography (CT) scans were unremark-

Address correspondence and reprint requests to: Philip L. Bailin, MD, Department of Dermatology – A61, 9500 Euclid Ave., Cleveland, OH 44195, or e-mail: bailinp@ccf.org.

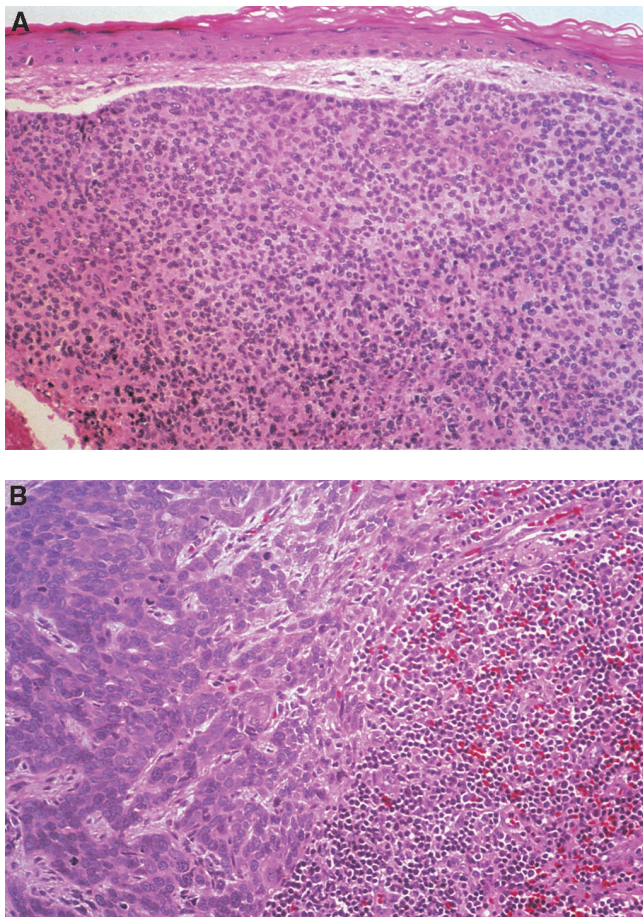


Figure 1. A) A superficial, solid, and infiltrative BCC is identified from the primary tumor located on the back. (Hematoxylin and eosin; original magnification 100 \times .) B) MBCC of the same histologic type as seen in the primary tumor is identified in the axillary lymph node. (Hematoxylin and eosin; original magnification 100 \times .)

able. The patient subsequently underwent Mohs micrographic surgery to the scar on her back which revealed no residual tumor at the scar margins or within the scar substance. The presumed BCCs on her chest and shin were excised with 5 mm margins. Pathologic examination confirmed multinodular BCCs which were of different histology than the metastatic axillary lymph node and showed no evidence of residual tumor at the margins. A left axillary node dissection revealed MBCC in 7 of 13 nodes, with extranodal extension identified. This procedure was followed by a second resection 2 months later showing no further evidence of MBCC. To date, the patient has been doing well and regular complete skin examinations have found only one additional multinodular BCC on her right thigh which was excised. There have been no other signs of recurrence or metastasis in the past 18 months of follow-up.

Discussion

Metastatic basal cell carcinoma remains a rare disease entity with an incidence of only 0.0028–0.5% of all BCCs. The best evidence-based information comes from two retrospective literature reviews representing more than 220 cases.^{5,6} The male:female ratio of MBCC is 2:1.⁶ Although the vast majority of reported cases occur in Caucasians, there have been case reports of MBCC affecting African American patients.⁷ The median age of onset for the primary tumor is 45 years, and the median interval between appearance of the primary tumor and metastasis is 9 years.⁶ Once metastasis is detected, there is a high mortality rate of 50% within 8 months.⁶ Two-thirds of MBCCs arise from primary tumors on the face, with the ear being the most common location.⁵ Higher rates of metastasis also occur from primary lesions on the scalp⁵ and genitalia.⁸

There have been many risk factors identified to help the clinician identify patients at risk of developing MBCC. In a retrospective study of 45 patients by Snow et al.,⁵ the size of the primary tumor was an important predictor of those patients who developed MBCC. The mean areas of the primary lesion of MBCC originating from facial and nonfacial sites were 62 and 217 cm², respectively. In a review of 41 publications of MBCC, Snow et al.⁵ found only one case of MBCC arising from a primary tumor less than 2 cm in diameter. In this case reported by Menz et al.,⁹ the patient had six BCCs on the arm and back that were all less than 1 cm in diameter. Although no local recurrences occurred, the patient developed metastatic BCC to the axillary lymph node 12 years later.

The depth of tumor involvement plays a role in patients with MBCC. In a review of 67 cases reported in the literature, 34% were tumors classified as T4 by the TNM classification system (Table 1).⁵ Case reports of distant metastasis from primary BCCs invading bone,¹⁰

Table 1. TNM Classification for Carcinoma of the Skin⁵

Primary tumor (T)
T0, no evidence of primary tumor
T1, tumor <2 cm in diameter
T2, tumor >2 cm but <5 cm
T3, tumor >5 cm
T4, tumor invades deep extradermal structures (ie, cartilage, skeletal muscle, or bone)
Regional lymph nodes (N)
N0, no regional lymph nodes
N1, regional lymph node metastasis
Distant metastasis (M)
M0, no distant metastasis
M1, distant metastasis

the parotid gland,¹ and sinuses⁵ have been described. A previous history of radiation therapy and tumor recurrence refractory to treatment have also been found to lead to an increased incidence of MBCC.^{1,5,11} Siegle and Wood¹² found that primary BCCs refractory to treatment account for at least 80% of cases of MBCC.

MBCC has been described with many histologic subtypes of BCC. There is no consensus as to whether any one histologic subtype of the primary tumor predisposes to MBCC. Nodular, micronodular, morpheaform, metatypical or basosquamous, and infiltrative histologies have all been reported.¹³ A retrospective review of 5270 morpheaform or invasive BCCs over a 50-year period did not reveal an increased rate of metastasis compared to other histologic subtypes.⁵

Primary BCC metastasizes through hematogenous and lymphatic routes.⁶ As was the case with our patient, metastasis to the lymph nodes has been estimated to occur in 70% of cases.¹⁴ The most common organs involved in hematogenous spread are lungs, bone, and skin.⁶

The paucity of cases of MBCC has limited the ability to perform prospective studies on the effectiveness of various treatment modalities. In general, treatment for localized metastasis, such as to the lymph nodes, is with surgical intervention.¹¹ The survival time in patients with disease confined to the lymph nodes is 3.6 years on average.¹⁰ With distant metastases, the average survival time decreases to 8 months.⁶ Treatment options for patients with distant metastases include some combination of surgery, radiation therapy, and chemotherapy. In an extensive review of the use of chemotherapy in patients with BCC, Pfeiffer et al.¹⁵ found cisplatin to be the most effective agent.

In conclusion, this case report of MBCC is unusual given the nonfacial site and small size of the primary tumor. It is important for the treating physician to be

aware of the entity of MBCC, especially in patients with T3 and T4 lesions, but it can rarely occur in T1 lesions. In these patients, close follow-up is recommended for at least 10 years.⁵ However, our patient emphasizes that persons with no obvious predisposing risk factors can develop MBCC.

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