

**Case Report**
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## Metastatic Basal Cell Carcinoma

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**ABSTRACT**

Basal cell carcinoma (BCC) is the most common cancer worldwide with an estimated annual incidence of 2 million in the United States. Majority of the patients present with a suspicious skin lesion with surrounding soft tissue destruction, but distant metastasis is rare, reportedly in less than 0.05-0.1% of all cases. So far, around 350 cases have been reported with majority of metastases occurring in primary lesions of head and neck. Here, we present a patient with high-risk BCC lesion presenting with distant metastasis.

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**Introduction**

Basal cell carcinoma (BCC) is the most common cancer worldwide and with an estimated annual incidence of 2 million in the United States [1]. BCC is a slow growing tumor and follows an indolent course. BCC mostly presents as lesions in the sun exposed regions of the skin and is usually diagnosed based on clinicopathological findings. Definitive diagnosis is by skin biopsy and treatment is predominantly surgical removal by Mohs micrographic surgery. Mohs micrographic surgery is effective for complete tumor removal as it is characterized by histopathologic confirmation for tumor free margins recurrence or distant metastasis of BCC is rare. Metastasis from BCC is reported to be less than 0.05-0.1% of all cases and so far, around 350 cases are reported in literature [2]. Risk factors for metastasis for BCC are patients with high-risk skin lesions, previous history of radiation, history of immunosuppression and poor patient compliance. Distant metastasis via both lymphatic and hematogenous route have been reported. Most common sites of involvement include lymph nodes, followed by bone involvement. Other less frequently involved sites include pleura, abdominal viscera, pleura, and lung. Here, we aim to present a case of high-risk BCC lesion in an uncommon location, diagnosed to have metastatic BCC.

**Case**

A 63-year-old male presented with an enlarging skin lesion on his low back. The patient reported the lesion had been present for 10 years, mostly unchanged in size with occasional episodes of bleeding. He had previous history of hairy cell leukemia which was treated and in remission for over 10 years. Physical examination showed mass over patient's lower back measuring 18mm x 9mm, nonbleeding. The patient initially underwent radical resection of the back lesion. Subsequent Computed tomography (CT) of head/chest/abdomen/pelvis showed a 1.2 cm lymph node in the right inguinal region, no evidence of metastasis. Lymphoscintigram demonstrated radiotracer uptake activity within sentinel lymph nodes in the left lower quadrant near the skin lesion and radiotracer activity crossing the midline in the right lower quadrant. The

histopathology of back lesion showed infiltrative basal cell carcinoma with no perineural invasion. Sentinel node biopsy of the right groin was performed which showed one positive lymph node consistent with metastasis. Immuno-stains were positive for BerEP-4, BCL-2 and CAM5 and negative for CD10, confirming the diagnosis of metastatic BCC. PET scan showed no other metastatic lesions. Upon patient's discharge from the hospital, he was lost to follow up and did not receive further treatment.

**Discussion**

Basal cell carcinoma accounts for approximately 80% of nonmelanoma skin cancers. It is typically a slow growing tumor [1,2]. Metastatic basal cell carcinoma is a rare complication of basal cell carcinoma with high rates of morbidity and mortality if left untreated [2]. Majority of the metastases occur in primary lesions originating in the head and neck. The median survival time for patients with metastatic BCC is 8 months [4].

Key risk factors for recurrence of BCC and metastasis include location and size of the lesion. Head and neck lesions of any size are considered high-risk compared to lesions of the trunk which must be greater than 20mm to be considered high-risk. Other high-risk features for metastasis include poorly defined borders, recurrent BCC lesions, history of radiotherapy and immunosuppression. Pathological risk factors include aggressive growth pattern including micronodular, infiltrative, sclerosing and morpheaform patterns [5]. While our patient had a seemingly low risk 18.2 mm lesion on his back; however, pathology of the lesion was consistent with a high-risk feature. The significance of sentinel lymph node biopsy in detecting metastasis has not been studied for basal cell carcinoma extensively due to the extremely low rates of metastasis [6]. However, as with our patient, it may be useful in detecting metastatic disease in high-risk lesions.

Localized BCC is primarily treated with surgery with radiotherapy as a viable alternative. Therapeutic options for metastatic BCC remain limited. In recent years, the FDA has approved

hedgehog pathway inhibitors for metastatic BCC. Vismodegib was investigated in a single arm 2-cohort open label study (ERIVANCE) with an objective rate response of 33% in patients with metastatic disease at median duration of 7.6 months [7]. Sonidegib was also investigated with an objective response rate of 17 % [8]. Sonidegib showed similar or better results compared to ERIVANCE with a median response time of 2.6 to 2.8 months. Sonidegib is another Hedgehog pathway inhibitor that was approved for patients with locally advanced BCC who are not candidates for surgery and radiation therapy or in those with recurrence. Poor response rates and resistance to therapy are the major limiting factors to Hedgehog pathway inhibitors. In February 2021, the FDA approved cemiplimab, a programmed death receptor-1 (PD-1) blocking antibody for the treatment of locally advanced and metastatic BCC refractory to Hedgehog pathway inhibitors. Cemiplimab showed an objective response rate of 21% of patients with metastatic BCC. Other alternatives include chemotherapy with carboplatin and paclitaxel combination, or the use of itraconazole but these therapies have limited supporting data.

The prognosis of basal cell carcinoma of the skin is generally good due to the low rate of metastasis. Patient education about sun protection and frequent follow-ups are essential. A few studies suggest a 10-fold increase in the risk of developing another BCC within 5 years of the initial presentation in these patients. The rarity of the metastatic BCC remains the key limitation for ongoing clinical trials investigating Hedgehog pathway inhibitors and further research is needed.

### Conclusion

Metastatic basal cell carcinoma is a rare entity with significant morbidity and mortality. While most of the metastasizing tumors originate in the head and neck, our case demonstrates the importance of considering metastasis in primary tumors of other sites, especially in longstanding lesions.

**Conflict of Interest:** None for all authors

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