Metastasizing Basal Cell Carcinoma

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Basal cell carcinoma (BCC) is the most common malignancy worldwide and is characterized by invasive growth and local tissue destruction. Cure rates for BCC exceed 90% with most treatment modalities. Metastasizing BCC (MBCC) is a rare complication of BCC with high morbidity and mortality rates. We report the case of a 66-year-old man with a large ulcerative lesion on the left side of the flank that was histopathologically diagnosed as a BCC. Clinical and imaging evaluations revealed substantial local invasion with regional lymph node, lung, liver, bone marrow, and bone metastasis. The patient died 7 months after the diagnosis was made. Potentially metastasizing BCCs cannot be definitely identified; thus early intervention with adequate treatment of all BCCs is advised.

Case Report

A 66-year-old white man presented with a large ulcerative lesion on the left side of the flank of at least 1 year's duration (Figure). The patient reported that the lesion was a slow-growing, asymptomatic, pigmented nodule that rapidly had become ulcerated. His medical history was otherwise unremarkable. Clinical examination revealed a large, 11×6-cm, ulcerative lesion with raised edges on the left side of the flank. Histologic examination of a punch biopsy specimen revealed an infiltrative BCC. Microscopically, the neoplasm was deeply ulcerated with necrosis and overlying inflammatory exudate.

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A large ulcerative lesion with raised edges on the left side of the flank.
involving the subcutaneous adipose tissue. A prominent infiltrating pattern with nests of atypical basaloid cells that exhibited prominent peripheral palisading was observed. No squamous differentiation or glandular formation was seen. The patient reported no personal or family history of skin cancer and no additional clinical features that were suggestive of basal cell nevus syndrome. A complete blood cell count, liver function tests, and chest radiograph all were normal.

One month later the patient developed a firm, palpable, nodular mass in the left inguinal region. Fine-needle aspiration of surrounding lymph nodes showed medium-sized infiltrating neoplastic islands with peripheral palisading and stromal clefing between the epithelium and stroma. These histologic features confirmed the diagnosis of MBCC. Computed tomography of the chest revealed multiple bilateral pulmonary nodules, which were diagnosed as lung metastases. Multiple nodules of metastatic origin were discovered in the liver by ultrasonography. Technetium-99m bone scintiscanning showed multiple areas of metastatic involvement. A bone marrow biopsy showed fibrosis and invasion by islands of irregularly shaped aggregates, nests and cords of basaloid cells with peripheral palisading, and a variable intervening fibrotic stroma. The histologic pattern resembled the primary BCC tumor on the left side of the flank. A panel of immunohistochemical stains was performed. The neoplasm was positive for cytokeratin (AE1/AE3), and negative for S-100, chromogranin A, CK7, CK20, and synaptophysin. These findings supported the diagnosis of MBCC.

Because of the rapid progression of the disease and widespread bony and parenchymal metastases, the patient underwent chemotherapy with carboplatin and docetaxel. Six months following the diagnosis of MBCC, the patient died from metastatic disease.

**Comment**

Basal cell carcinoma is the most common human malignancy worldwide with a 30% lifetime risk for development. It is thought that tumor histogenesis originates from follicular germinative or pluripotent epithelial cells that bear a resemblance to basaloid undifferentiated keratinocytes. Despite the high incidence of BCC, metastasis rarely occurs. Criteria for the diagnosis of MBCC include tumor metastasis from a primary cutaneous BCC lesion to distant noncontiguous sites that display histopathologic features similar to primary BCC. The median age at primary tumor onset is 45 years. The period from onset of the primary tumor to metastasis can range from less than 1 to 45 years. Most MBCCs derive from a primary BCC in the head and neck region. A limited number of reports have suggested several potential risk factors for developing MBCC, including large primary tumors (ie, > 2 cm), location in the head and neck region, multiple tumor recurrences, prior radiation therapy, multiple primary tumors, large tumor depth, invasion of perineural space and blood vessels, fair skin, and male gender. Conversely, it is not clear if immunosuppression in affected patients is a risk factor for MBCC. To date, no consistent clinical, histopathological, or immunohistochemical features have been reported to distinguish aggressive and nonaggressive BCCs. Our patient presented with a large primary BCC that had been undetected for an unknown time, which confirmed the possibility that MBCC can arise from long-standing primary BCCs that are either large or recurrent following treatment. Dissemination to the regional lymph nodes or hematogenous spread usually is observed, as in our case. Common sites for metastasis are the lungs, bones, and skin. Although the lungs are a distant location, lung metastasis frequently is involved in cases of MBCC. In our patient, lung metastasis presented as multiple, small, disseminated nodules, consistent with hematogenous spread of tumor cells. Because MBCC is rare, this tumor may be unrecognized at initial presentation and erroneously diagnosed as another metastasizing neoplasm.

Immunohistochemistry can help to distinguish MBCC from other secondary tumors, particularly metastasis of Merkel cell carcinoma. It is difficult to determine the etiology, risk factors, and therapeutic options for metastasizing BCC; however, treatment can be guided by the location and extent of the neoplasm. Therapeutic options usually consist of surgery for local metastasis, and a combination of surgery, chemotherapy, and radiation therapy for distant metastasis. If complete surgical excision is not conceivable, chemotherapy is preferred, with cisplatin being the most effective agent. Radiation therapy may be administered postoperatively or concomitantly with chemotherapy. The course of the disease usually is aggressive. Metastasizing BCC carries a poor prognosis, with mean survival rates ranging from 8 months to 3.6 years. A lack of response to chemotherapy may be observed, as in our patient, who showed multiorgan metastasis. Although MBCC is rare, awareness among physicians is crucial, especially considering the increased prevalence of nonmelanoma skin cancers.

**Conclusion**

This case confirms that in rare instances BCC may become inoperable and potentially fatal. Because BCCs that may become aggressive and potentially metastatic cannot be confidently identified,
definitive diagnosis and adequate treatment of all BCCs is mandatory. The hedgehog signaling pathway represents a recently identified target for the control of advanced and metastasizing BCC.8

REFERENCES