Metastatic basal cell carcinoma to the lungs: Case report and review of literature

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ABSTRACT

Basal cell carcinoma is the most common form of skin cancer and it rarely metastasizes. The prevalence of metastatic basal cell carcinoma (MBCC) varies between 0.0028% and 0.55% of all cases. Over 250 MBCC have been reported in the literature. We present a case with large recurrent basal cell carcinoma of the face with radiological and histopathological findings indicating the presence of metastasis to the lungs.

Key words: Basal cell carcinoma, metastatic basal cell carcinoma, pulmonary metastasis

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INTRODUCTION

Basal cell carcinoma (BCC) is the most common low grade skin carcinoma, accounting for up to 80% of all carcinomas arising from the epidermis. Epidemiology suggests that BCC is more common among Caucasians and can develop anywhere on the body surface, especially on the exposed areas of the head and neck region, with high propensity for local recurrence. The prevalence of this form of cancer among the Caucasians has been attributed to the low amount of melanin in their skin which reflects directly on the sun protection factor. Despite the high incidence of BCC, metastatic BCC is extremely rare and is seen in 0.0028-0.55% with approximately 250 cases reported.[1,2] Most metastases occur in men. The BCCs from which they arise are commonly large, facial, locally invasive and destructive, ulcerated, long-standing, treatment-resistant and histologically aggressive. Lymphatic and hematogenous spread are equally prevalent, with lymph nodes, lungs and bone being the most common sites of metastases.[3]

This case in discussion has been chosen due the unusual metastasis of the basal cell carcinoma (BCC) to the lung and a probable metastasis to the brain and liver.

CASE REPORT

A 76 years old male patient was admitted in the emergency department with acute episodes of tonic-clonic convulsions. Clinically, a large ulceroproliferative growth measuring 5 × 6 cm [Figure 1] was seen involving his right lower eyelid, inferiorly from the infraorbital region to the nasolabial fold, medially to the right side of nose and cephalic border of ala of nose and laterally to the zygomatic region. No regional lymphnodes were palpable in the neck. Upon enquiry, it was found that the patient had undergone surgery for a small lesion adjacent to the nose on the same side. The lesion recurred a year later and he had left it untreated for the last seven years. After convulsion was stabilized, he was investigated for the same. Computed tomogram (CT scan) of the head showed a focal relatively hyperdense nodule 8 mm in diameter involving the left frontal lobe white matter with extensive perilesional edema [Figure 2], the grey-white matter differentiation was retained. The chest skiagram showed a large lobulated mass lesion in the left upper zone with surrounding ground glass haze with adjacent lung infiltrates. Sonogram of the abdomen showed multiple well defined rounded hypoechoic nodules measuring up to 1.2 cm in both the lobes. All these radiological features are suggestive of metastatic lesion to the brain, liver and lungs. The liver function test and other routine blood investigations which was done were within normal limits. Thoracic CT revealed a large solid lobulated margin mass lesion of size 7.8 × 5.3 × 5.3 cm involving the apical segment of the left upper lung lobe with minimal post-contrast enhancement (57 HU) [Figure 3a].

The adjacent lung field showed thickened interstitial network suggestive of lymphangitic carcinomatosa [Figure 3b]. Few enhancing (60 HU) precarinal and aortopulmonary nodes were noted measuring up to 7 mm in short axis diameter. Minimal bilateral pleural effusion was also noted. There were multiple non-enhancing hypodense lesions measuring up to 1 cm involving bilateral hepatic lobes [Figure 4]. The patient was subjected to CT guided fine needle aspiration cytology (FNAC) from the left lung lesion. Biopsy was taken from the facial lesion to confirm the diagnosis. Histopathological examination showed fragments of a neoplasm which were composed of nests and cords of basaloid and squamoid cells. These cells showed pleomorphism, anisokaryosis, hyperchromatic nucleus and average amount of cytoplasm. Nuclear palisading was also observed in these nests of neoplastic cells. Histopathology examination of the facial lesion confirmed BCC [Figure 5]. The FNAC from the lung lesion showed pleomorphic round to oval cells (basaloid cells) with nuclear palisading at foci, hyperchromatic nucleus, indistinct nucleoli, an anisokaryosis and average amount of cytoplasm consistent with a metastatic basal cell carcinoma (MBCC) [Figure 6]. In view of the cytological features of the lung metastasis consistent with BCC, the lesions in the liver and the brain were assumed to be metastasis of the similar lesion, though biopsies from the hepatic and brain lesions were not obtained. The patient was explained about the disease and prognosis. His decision for not obtaining any further treatment was respected. He was continued on supportive care and anti-epileptics.

DISCUSSION

BCC is the most frequent, slow growing and potentially locally aggressive skin neoplasm. Though they are commonly seen in the exposed area of the head and neck region, about ten per cent of all BCCs are located on the trunk and less than 1% of cases have been reported to occur in the unexposed areas of the genitalia. Although BCC is frequently regarded as a low grade malignancy, sometimes it is extremely aggressive, especially when giant lesions are involved.[4] MBCC is extremely rare, but when it occurs, it carries high morbidity and mortality rates. Many risk factors that appear to predispose patients to MBCC have been identified, including long duration, site (seen with primary tumor in the head and neck region especially mid face or ears which is seen in 85% of cases) and size of the tumor, number of lesions, depth of invasion, persistence of BCC for many years, recurrence despite optimal treatment, BCC refractory to conventional methods of treatment, infiltrative histological pattern, incomplete surgical resection and previous radiation therapy either in early adulthood or for localized cancer.[1,5,6] It has been seen that most primary metastatic lesions are more than 3 cm in diameter.[4] Amongst the various histological subtypes of BCCs, the superficial, infiltrative/morpheaform and micronodular subtypes have a high propensity for recurrence and metastasis.[6] However this is controversial and there is no evidence to support that a particular subtype predisposes to MBCC.[1] Primary BCC metastasises usually via lymphatics, although it also spreads hematogenously. Metastasis most commonly occurs in regional lymph nodes, lung and bone although cases involving the spinal cord, parotid gland, skin, bone marrow, spleen, liver, adrenal glands, brain, dura mater, esophagus, heart and kidney have been documented.[5,7]

The criteria for diagnosing metastasizing BCC are: primary tumor localized to the skin and not mucous membranes, metastases in the lymph nodes or viscera, site distant to the primary and

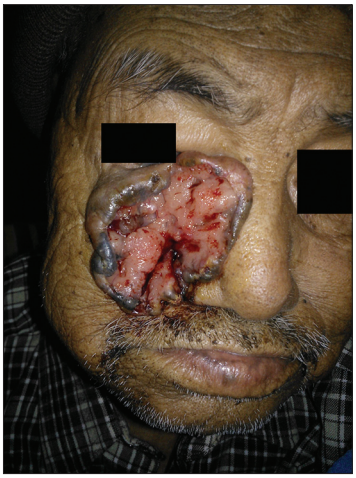

Figure 1: Ulceroproliferative lesion on the right side face

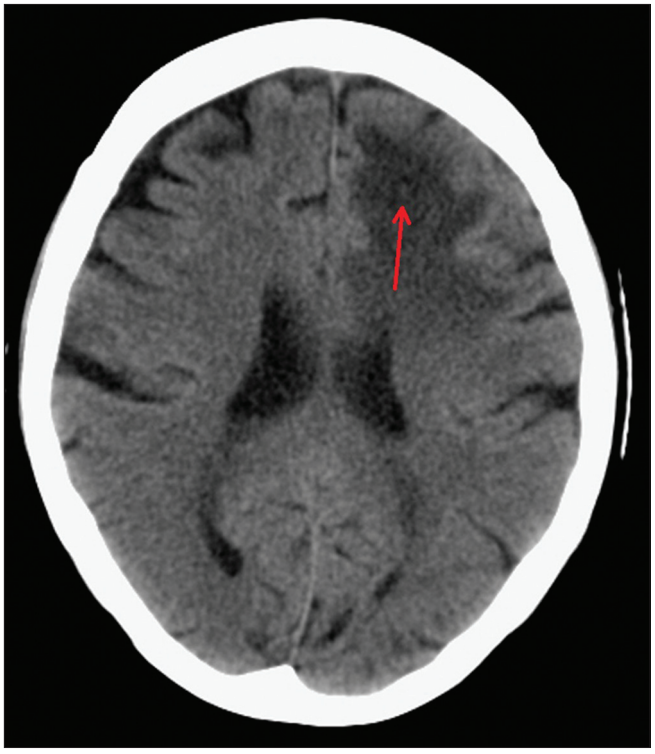

Figure 2: Computed tomogram brain showing a focal relatively hyperdense nodule (arrow) in the left frontal lobe white matter with extensive perilesional edema

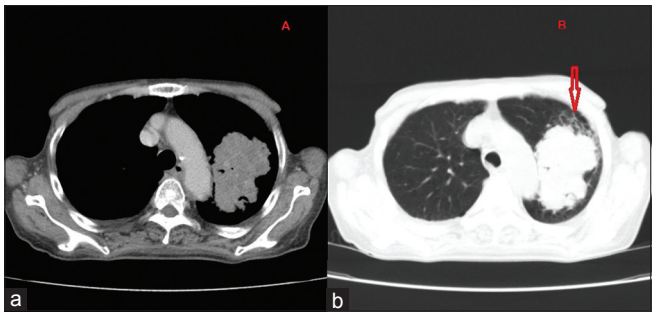

Figure 3: Thoracic computed tomogram showing a large solid lobulated margin mass lesion involving the apical segment of the left upper lung lobe with minimal post-contrast enhancement and features of lymphangitic carcinomatosa (red arrow in Figure 3b)

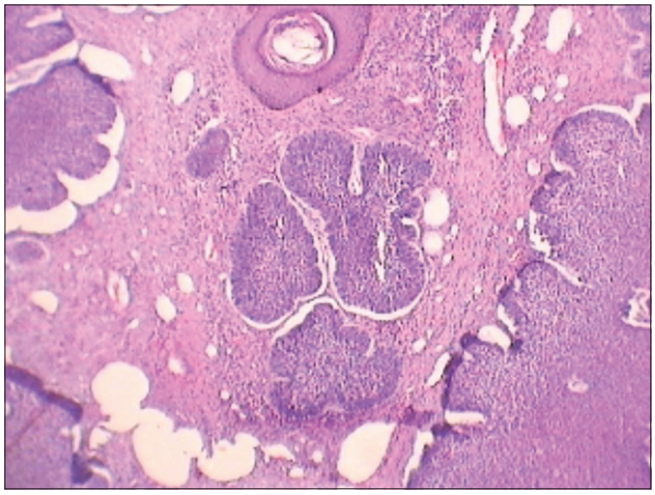

Figure 5: Histopathology of the facial lesion showing features of a basal cell carcinoma (H and E, ×10)

not related to simple extension and histologic features of both the primary tumor and the metastases typical of BCC, without signs of epidermoid differentiation.[1] The case presented here fulfills all the criteria for a metastatic BCC and the primary lesion in our case was significantly large. Currently no established guidelines for the treatment of metastatic disease are available, because all forms of treatment so far have shown dismal results in terms of morbidity and mortality. Therapy of metastatic BCC depends upon the location and extent of the tumor and generally consists of wide surgical excision alone for local metastasis or its combination with chemotherapy and radiation therapy for distant metastasis. It has long been thought that treatment of primary cancers with radiotherapy can contribute to their metastatic potential, although there is no evidence to support this. In fact, the incidence of MBCC in patients treated primarily by radiotherapy is estimated to be 1 in 25,000, which is much less than the incidence of MBCC in all patients with primary tumors.[2] One study reported excellent results on treatment with surgical excision with or without adjuvant radiation therapy; chemotherapy was not advocated by the authors.[8] However, presentation with widely disseminated disease would not allow this approach such as in our case. Chemotherapy

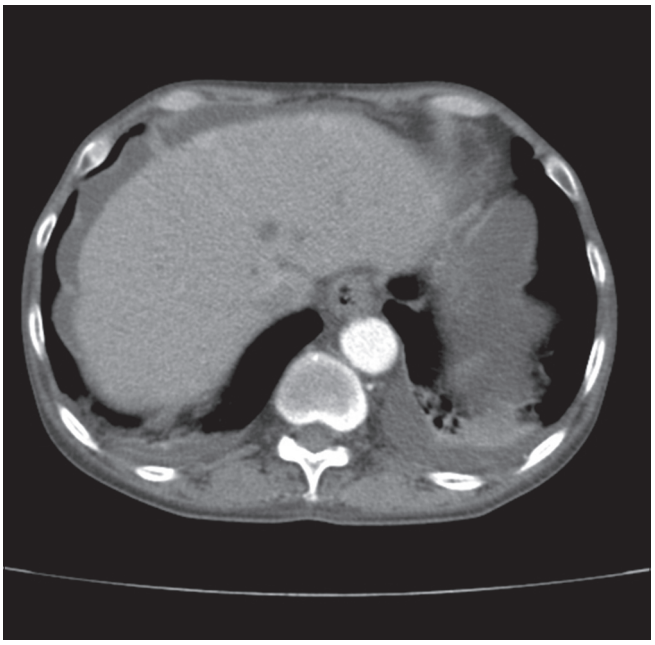

Figure 4: Computed tomogram showing multiple non-enhancing hypodense lesions involving bilateral hepatic lobes

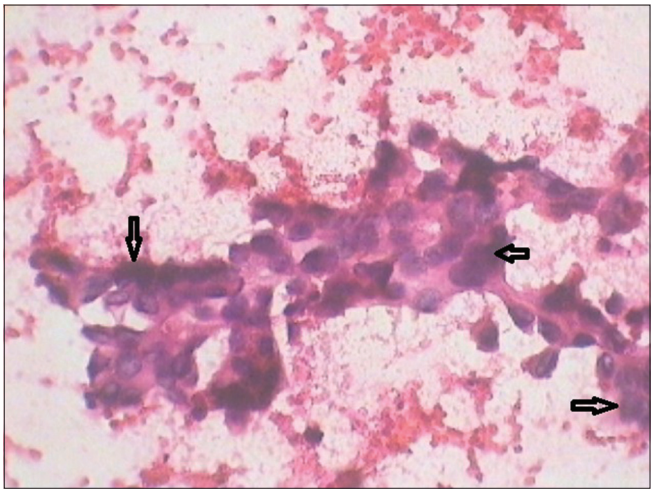

Figure 6: Fine-needle aspiration cytology from the lung lesion with features of a metastatic basal cell carcinoma (arrow showing basaloid cells with nuclear palisading at foci) (×40)

with a single agent or in combination has been used but has failed to show promising results, except in a few isolated reports which have shown significant positive response to cisplatin, cyclophosphamide and cis-diamine dichloroplatinum, vincristine, bleomycin either alone or in combination.[1,2,5] Trials with GDC-0449, a small-molecule inhibitor of smoothened homologue (SMO), have shown promising results. SMO is involved in activation of the hedgehog pathway that has been implicated in the development of BCC. In a phase 1 trial, oral GDC-0449 was used to treat 33 patients with locally advanced or MBCC. The overall response rate was found to be 50% and 60% for MBCC and locally advanced tumor respectively.[9] Vismodegib (GDC-0449), an oral administrable molecule has

been approved by the US Food and Drug Administration. It is the first systemic treatment for patients with locally advanced or MBCC that is not amenable to surgery and radiation. A meta-analysis shows a good overall outcome (30.3% and 42.9% objective response rate in MBCC and locally advanced disease), but the data available is too limited to determine overall survival.[10] The prognosis for these patients is poor with a mean survival time of only eight months from the time of diagnosis,[5,9] though there has been one reported case where a patient survived 25 years after diagnosis.[11]

CONCLUSION

Although MBCC is a rare entity, its occurrence should be borne in mind especially when dealing with a giant, recurrent, or long standing tumor in the head and neck region.

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