



PHENOMENAL OUTCOME IN METASTATIC BASAL CELL CARCINOMA: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT Introduction: Being the most common malignant tumors of the skin worldwide, basal cell carcinoma (BCC) has a low mortality rate. It rarely spreads to distant organs; documented cases of metastatic BCC are limited. Here, we describe the clinical course of an old female having BCC in right forearm with lung metastasis. At first, the patient underwent wide local surgery of the primary lesion. After that, she developed symptomatic right lung metastasis and received palliative radiation to lung followed by intravenous combination chemotherapy with cisplatin and cyclophosphamide. Post-treatment follow-up scan revealed patient had complete resolution of disease. Till then, the patient is on close follow up from 36-months from diagnosis and is disease free. This case report shows the significance of combined modality treatment in achieving complete response in metastatic BCC.

KEYWORDS : Basal cell carcinoma, chemotherapy, metastasis, radiotherapy, wide local excision

Introduction

Basal cell carcinomas (BCC) are the most common malignant tumors of the skin worldwide. [1] Major risk factors for BCC are sun exposure, immune suppression, male sex and increased age i.e., >40 years; while old burn scar, genetic factors or benign tumor like lesion, such as verruca vulgaris can also progress to BCC. [2-5] Despite a high incidence rate and intense locally aggressive nature, BCC has low mortality. [1] It also has extremely low metastatic rates with a frequency of 0.5%. [6] Metastatic basal cell carcinoma (MBCC) was first described by Beadles in 1894. (7) Due to the rarity of MBCC, at initial presentation this can be mistaken to have originated from other metastasis-prone tumors. Till date, less than 500 cases of metastatic BCC have been documented in literature. In this case report, we describe the clinical course of an old female having BCC with lung metastasis.

Case Summary

An 82-year-old female, without any past illness, presented to Surgery Department with ulcerative lesion over right forearm for 8-months duration. She underwent wide local excision of that ulcer with visible free margin. Histopathology of resected specimen revealed basal cell carcinoma [figure 1, A & B], with immunohistochemistry (IHC) positivity for Ber-EP4 9; tumor free resected margins in histopathology report concluded as R0 resection. Then she was referred to our department for further treatment. Local examination revealed healed, healthy scar mark of 4.0 × 1.5 cm in right forearm; without any sign of discharge [figure 2]. Routine systemic examination revealed decreased air entry on right side of chest with no other significant findings. On detailed enquiry, she gave history of dry cough & right sided chest pain for one week. Contrast enhanced computed tomography (CECT) of chest showed soft tissue attenuating lesion in right lower lobe of lung, along with few enlarged lymph nodes in mediastinum, suggestive of distant metastasis.

In view of symptomatic metastatic disease, patient was given palliative external beam radiation therapy (EBRT) 30Gy/10Fr/2-weeks to right chest and mediastinum. This was followed by 6-cycles of 3-weekly intravenous chemotherapy with injection cisplatin 100 mg and cyclophosphamide 1000 mg. Post treatment, local examination showed no evidence of disease. The patient underwent whole body positron emission tomography (PET) scan which revealed no evidence of metabolic active lesion in anywhere of the body suggestive of no residual disease [figure 3]. The patient is on close follow up from 36-months from diagnosis and is disease free.

Figure 1: Photomicrographs; Haematoxylin-eosin (H&E) stain,

original magnification ×20 A) showing nest of malignant cells separated by cleft like spaces; B) showing peripheral palisading, sign of basal cell carcinoma.

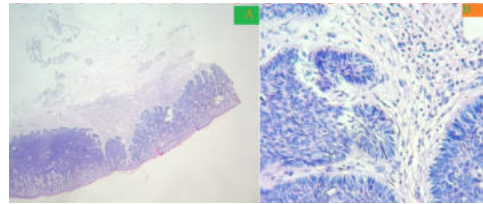


Figure 2: Post-operative clinical photograph showing healthy healed scar mark in right forearm



Figure 2: Post-operative clinical photograph showing healthy healed scar mark in right forearm

Discussion

BCC is the most prevalent non-melanomatous skin cancer globally and very common among Caucasians. [7] BCC was considered to be metastatic only when both primary and metastatic lesions have histological confirmation without any component of squamous cell carcinoma and metastatic lesion is not due to a direct continuation of primary lesion. [8] Despite criteria defined early in 1951, cases of metastatic BCC are very few; however, prognosis is poor when distant spread occurs in BCC. [1,7]

Treatment options for BCC include local (superficial) techniques, surgical intervention, radiation therapy, and systemic therapies. [9] Curettage and electrodesiccation are standard local ablation therapy

combined with surgical scrapping for low-risk superficial tumor. [10] Local superficial therapy in BCC includes topical therapy with imiquimod or 5-fluorouracil, photodynamic therapy (PDT) and cryotherapy. [11] These are considered in superficial BCC lesions without any risk factors, although cure rates are low. [9]

Among different surgical techniques, standard excision and Moh's micrographic surgery are generally employed. [10] Standard surgical excision is followed by immediate defect closure with post-operative margin assessment. [12] Moh's micrographic surgery along with peripheral and deep en face margin assessment is preferred over standard excision due to lowest recurrence rates and maximal tissue preservation. [10] 5-year recurrence rate has been reported as 1% and 4% for primary and recurrent BCC respectively in case of Moh's micrographic surgery; while it is 6% & 11-17% in standard excision. [10]

Although surgery is mainstay of treatment but radiation therapy can be considered as primary choice depending upon a few factors. [13] Post-operative radiation is employed in patients having risk factors like locally advanced T3/4 primary lesion, positive or doubtful margin status, nodal involvement and perineural invasion. [13,14] Radiation therapy is also a good option in case of recurrence after surgery and for palliation of advanced disease. [9,13]

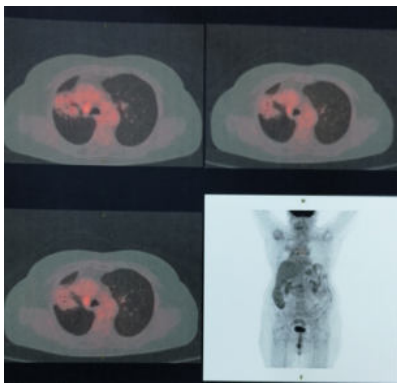


Figure 3: Post-treatment whole body 18-FDG PET CT scan showing no evidence of disease, suggestive of complete response to therapy

The lower frequency of distant spread in BCC primarily depends upon size of primary lesion and certain other risk factors. The incidence of metastasis in BCC increased from 2% to 50% for increase in primary lesion size from 3 cm to larger than 10 cm in diameter. [15] Other risk factors for distant spread include primary tumor in the head and neck region, male gender with old age, long-standing tumor, treatment-resistant and histologically aggressive BCC refractory to conventional methods of treatment, incomplete surgical resection and previous radiation therapy [15,16] Metastasis from BCC of extremities, as seen in our case, is comparatively more infrequent. Among the various histological subtypes of BCCs, all had been reported to metastasize; however, infiltrative histological pattern has a higher propensity for distant spread. [16,17] Distant organs involvement from primary BCC in decreasing order are regional lymph nodes, lungs, bones; with rare sites of involvement being spinal cord, parotid gland, skin, spleen & liver, adrenal glands, brain, esophagus, heart, and kidney [15] Mean interval between primary tumor diagnosis and appearance of distal lesion are 7-9 years. [7]

As stated before, prognosis for metastatic BCC generally remains poor. Average survival time differs largely depending upon metastatic site involved and factors mentioned earlier; with documented survival of 8 months in the presence of distant metastasis to 3.5 years for patients with disease confined to lymph nodes. [15, 18]

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. [18] The main aim of the surgery is complete excision of the tumor with clear margins. The recurrence rate following surgical excision varies between 5% for complete excision and 30% for excisions with positive margins. [17] Several chemotherapeutic agents including 5-FU, cisplatin, vincristine, etoposide, bleomycin, cyclophosphamide, methotrexate, and

doxorubicin have been used alone or in combination. [18,19] Recent studies are ongoing on targeted therapies in locally advanced or metastatic basal cell carcinoma, like hedgehog pathway inhibitor Vismodegib; with long follow-up data revealed overall response rate of around 50%. [20]

Our patient underwent wide local surgical excision for primary lesion. She further received palliative EBRT to chest followed by salvage chemotherapy to control metastatic disease. Surprisingly, post treatment scan revealed no evidence of disease anywhere in the body.

Conclusion

This case shows the rare occurrence of distant metastasis in a BCC lesion other than head and neck region. Primary lesion was successfully managed by wide local excision, while distant lung metastasis within a few months denotes the aggressiveness of BCC. Old age and long-standing primary lesion favors the occurrence of metastasis; while female gender and small lesion (<4 cm in longest diameter) conclude against it. However, complete resolution of all lesion from body demarcates the importance of combined modality approach in such patients. It is important to diagnose and treat all basal cell carcinomas at the earliest because of the fact that a BCC neglected for long time is potentially at risk of metastases. There is lack of consensus on chemotherapy protocol for widespread disease which demands in depth study for the same. Our patient is on regular follow up without any complaint for last 36-months. Long term survival in metastatic BCC is rare which happened in our case.

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