Basal cell carcinoma with intravascular invasion: A case report and review of the literature

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Abstract

The significance of basal cell carcinoma (BCC) invading the intravascular space is unknown. We report a case of an infiltrative BCC on the scalp that showed evidence of both intravascular and perineural invasion. The tumor locally recurred in the bone marrow space 4.5 years following the initial procedure. Since recurrence and metastasis of BCC can be delayed for many years, we recommend long term follow-up for tumors showing aggressive features.

Keywords: basal cell carcinoma, intravascular, Mohs, perineural, bone marrow space

Introduction

Basal cell carcinoma (BCC) is the most common neoplasm in humans and generally carries a favorable prognosis. Despite the propensity for local tissue destruction, BCC metastasizes infrequently. Risk factors associated with metastasis include the size of the tumor, depth of penetration beyond subcutaneous tissue, and perineural involvement [1]. The significance of vascular invasion remains unknown with some studies suggesting that this is a high-risk feature and others dismissing any prognostic utility of this finding [2, 3]. We report a case of an infiltrative BCC on the scalp that showed evidence of both intravascular and perineural invasion (PNI) during Mohs surgery. The tumor was surgically excised with clear *en face* margins and adjuvant radiation therapy was subsequently administered to the tumor bed. The patient presented with locally recurrent BCC in the bone marrow space 4.5 years following the initial procedure.

Case Synopsis

A healthy 61-year-old man presented for Mohs excision of residual infiltrative BCC on the vertex of the scalp. A recent attempt at excision with frozen section margin control was aborted by the referring plastic surgeon owing to persistent positive margins. Examination prior to Mohs surgery showed a 5.0cm linear scar (**Figure 1**) and no palpable

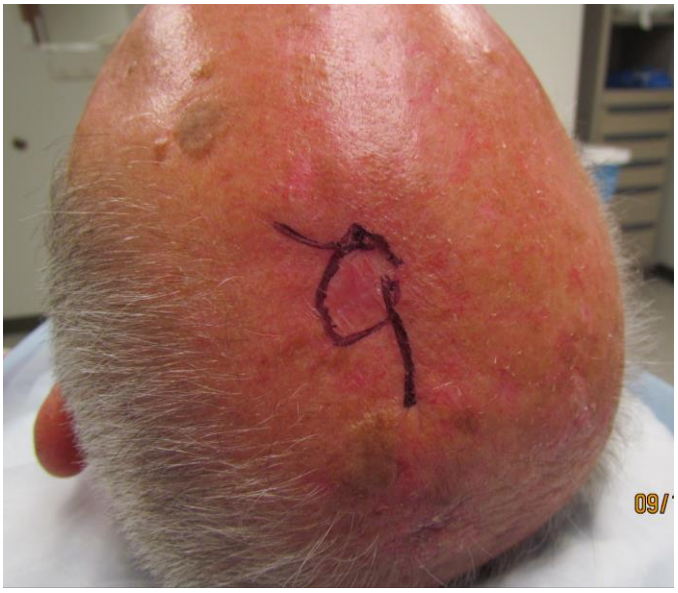

Figure 1. *Basal cell carcinoma on the vertex of the scalp within scar.*

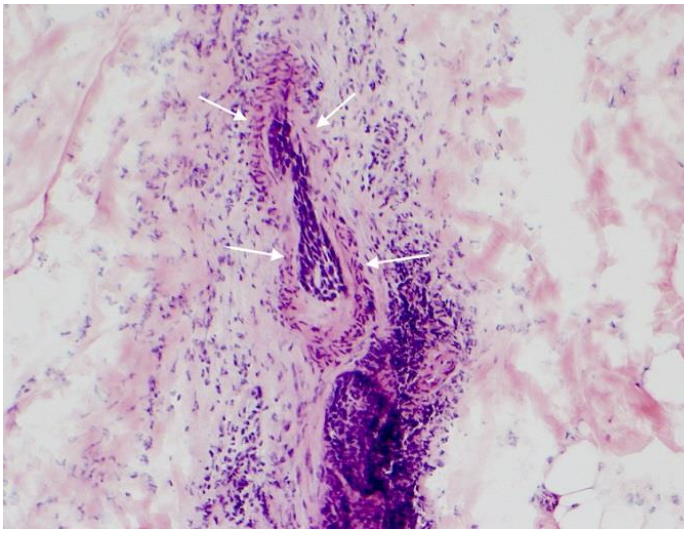

Figure 2. *Mohs frozen section showing subcutaneous tissue with basal cell carcinoma within vein annotated with arrows. H&E, 10×.*

lymphadenopathy was appreciated in the head and neck. An infiltrative BCC with both intravascular (**Figures 2, 3**) and perineural invasion (**Figure 4**) was noted on horizontal frozen sections. The tumor was noted in the galea. The tumor was cleared with four Mohs stages, resulting in an 8.2×6.2 cm defect focally devoid of periosteum (**Figure 5**). The Mohs defect was repaired with placement of a bilayer matrix dressing followed by delayed full thickness skin graft. After complete skin graft healing, the patient underwent post-operative radiation with 50 Gray divided over 25 treatments owing to the presence of perineural and intravascular invasion. One year following the procedure, a PET CT scan performed did not show any evidence of metastatic disease. The patient presented with skin breakdown in the skin graft 4.5 years following the initial procedure. Repeat biopsy showed recurrent BCC invading the bone marrow space. This case highlights the importance of long term follow up of BCC cases presenting with high risk features, since locoregional recurrence and metastasis can be delayed for many years.

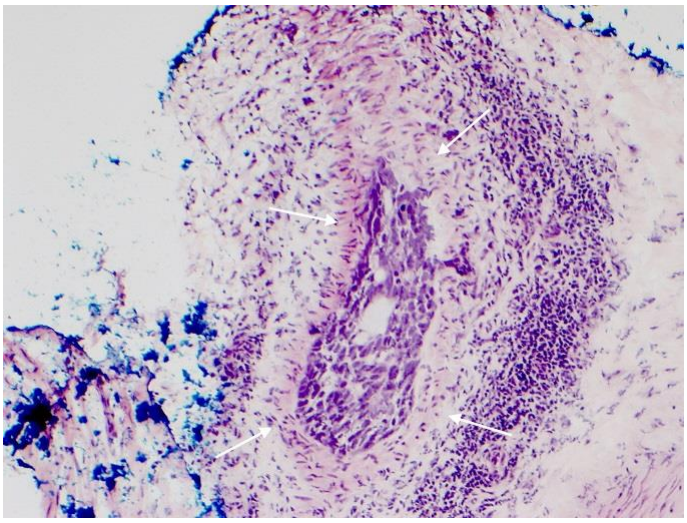

Figure 3. *Higher power view of Mohs frozen section showing subcutaneous tissue at deep inked margin with basal cell carcinoma within vein annotated with arrows. H&E, 20×.*

Case Discussion

Basal cell carcinoma with intravascular invasion (IVBCC) is exceedingly rare and the clinical significance of this histological finding remains unknown. In the setting of squamous cell carcinoma, lymphovascular invasion is generally regarded as a high risk histopathological feature associated with recurrent tumors and has been found to predict nodal metastasis [4]. Given the stromal dependency of BCC, the ability of basal cells to survive intravascularly and seed elsewhere has been questioned. In early studies, attempts at grafting and transplantation of BCC into nude mice succeeded only when stroma was transplanted along with epithelial components [2, 3]. Domarus and Stevens reviewed 170 cases of metastatic basal cell

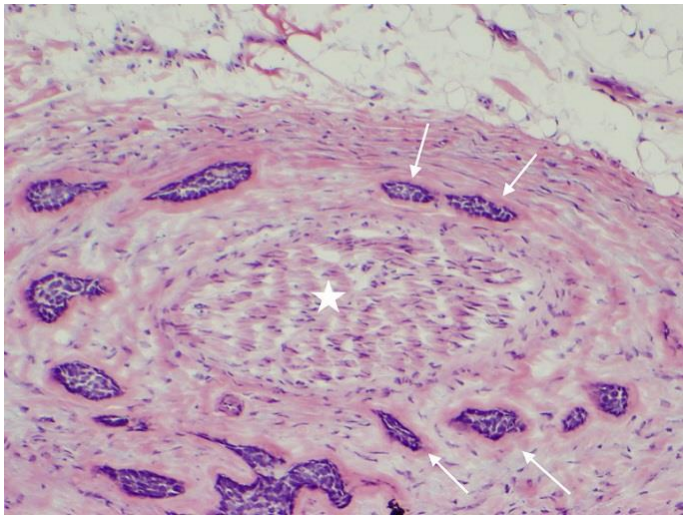

Figure 4. *Mohs frozen section showing large caliber nerve annotated with star; diameter >0.1mm with perineural invasion of basal cell carcinoma just into the epineurium at arrows. H&E, 10×.*

carcinoma (MBCC) and found that hematogenous and lymphogenic metastasis occurred with equal frequency. Hematogenous spread occurs most frequently to the lung and pleura followed by the bone [3]. Two theories have been proposed to support the occurrence of MBCC. Tumor emboli, composed of epithelial and stromal cells, may seed these distant sites. Alternatively, metastatic deposits of epithelial cells may induce stromal proliferation within the surrounding tissue [2].

Basal cell carcinoma with intravascular invasion is likely an underreported phenomenon and the incidence remains unknown. There are 8 other cases of IVBCC reported in the literature and these are summarized in Tables 1, 2. In 3 cases, intravascular invasion was associated with tumors that eventually gave rise to metastatic disease. The majority of patients with IVBCC are $\geq$50 years of age; however, there was one report detailing a 27-year-old man with a long-standing, ulcerative BCC on the left cheek that resulted in metastasis to the submandibular nodes and lung [3]. The average size of tumors showing intravascular invasion was 1.2cm^2. Intravascular invasion was most commonly associated with infiltrative and undifferentiated histology. Perineural invasion was associated with IVBCC in less than half of cases. Three patients developed metastasis in a time frame ranging from 2 to 13 years after initial presentation. Metastases were reported in the regional lymph nodes in all cases with concomitant lung metastasis in two cases.

In the 6 cases of IVBCC occurring without evidence of end organ metastasis, the follow up period was short ranging from 4 months to 4.5 years. Interestingly, only 2 patients in this series received adjuvant radiation to the primary tumor bed following complete excision of IVBCC and metastasis was not reported in either case. Similarly, recurrence and metastasis were not reported in the 4 patients with IVBCC who were treated with surgery alone.

Review of the literature suggests that many cases of IVBCC are not associated with end organ metastasis; however, it is prudent to remember that metastasis of BCC occurs a median of 9 years following initial presentation [3]. The follow-up period was short or not given in many cases reviewed, possibly leading to false perception that these cases did not lead to metastasis. Alternatively, the association between MBCC and IVBCC may be inflated falsely since MBCC is an exceedingly rare phenomenon and is often reported.

Conclusion

Herein, we report a case of BCC with intravascular and perineural invasion that was associated with local recurrence within the bone marrow space but not associated with metastasis. The aggressive tumor recurred 4.5 years after initial treatment despite clear *en face* margins and adjuvant radiation therapy. Currently, there is no consensus on management of IVBCC. This case suggests that intravascular tumor may be a risk factor for local recurrence. However, whether intravascular invasion is an independent risk factor for a poor outcome remains unknown since this tumor was also associated with PNI of large caliber nerves. Radiation could be considered on a case-by-case basis in patients with IVBCC and may be warranted when other high-risk features are present. Patients with IVBCC and PNI should be followed clinically for years after initial presentation since local recurrence and metastasis of BCC are often delayed.

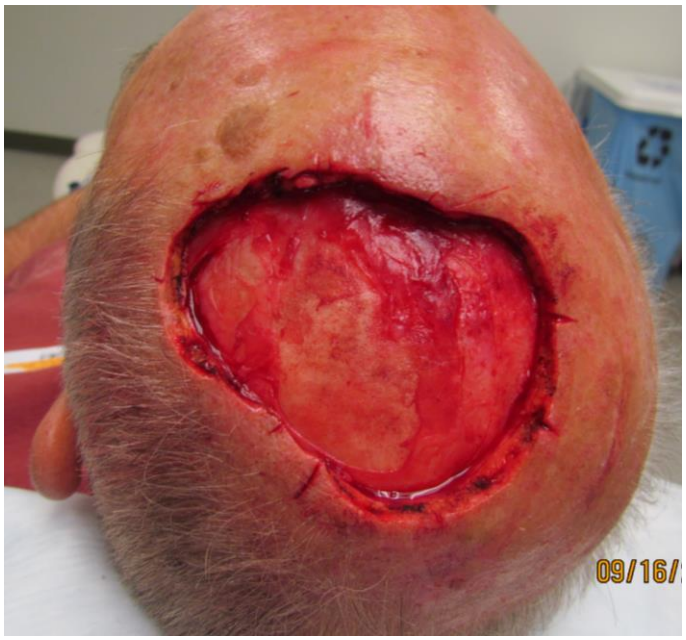

Figure 5. *Post Mohs defect on vertex of scalp.*

Table 1. *Case reports in the literature describing non-metastatic intravascular basal cell carcinoma and associated characteristics.*

Case report	Location	Age/ sex	Size (cm)	Follow up	PNI	Adjuvant therapy	Site of metastasis	Histology of tumor
Current case	Scalp	61/M	5cm scar	4 years, Local recurrence 4.5 year after initial encounter	Yes	Radiation to the primary tumor bed (50Gy in 25 fractions) after Mohs	No metastasis	Infiltrative
Slutsky, J (2010) [5]	Right anterior parietal scalp	60/M	1.5×1.1	1 year, no recurrence	No	No	No metastasis	Not given
Machan et al. (2012) [6]	Upper chest	51/M	0.9×0.4	Unknown	No	No	No	Infiltrating, micronodular
Lonie et al. (2016) [7]	Right nasal tip	81/F	0.8× 0.8	4 months, no recurrence	No	Radiation (50Gy in 20 fractions), to the primary tumor bed following excision with tumor noted in vessels at the margin	No metastasis	Sclerosing
Milam et al. (2016) [8]	Left nasal side wall	75/M	2.0×1.1	Unknown	No	No	No metastasis	Nodular and morpheic
Shea et al. (2016) [9]	Right posterior helix	96/F	1.6×1.0	Unknown	No	No	No metastasis	Irregular basaloid cells

Abbreviations: (PNI- perineural invasion, GY- Gray, MBCC- metastatic basal cell carcinoma).

Table 2. *Case reports in the literature describing metastatic intravascular basal cell carcinoma and associated characteristics.*

Case report	Location	Age/ sex	Size (cm)	Follow up	PNI	Adjuvant therapy	Site of metastasis	Histology of tumor
Domarus and Stevens, (1984) [3]	Left chin	54/ M	Not given	16 years	Yes	Initial tumor treated with radiation, 4 subsequent recurrences treated with radiation and surgery; vascular invasion noted in fourth recurrence	13 years after initial tumor treatment, found in sub-mandibular nodes	Undifferentiated, adenoid cystic foci, keratotic foci

Table 2, continued. *Case reports in the literature describing metastatic intravascular basal cell carcinoma and associated characteristics.*

Domarus and Stevens (1984) [3]	Left cheek	27/ M	Not given	4 years with death	Yes	Radiation performed to the site of metastasis in the submandibular node	2 years after initial tumor treatment, found in sub-mandibular nodes, lungs	Undifferentiated, infiltrative, keratotic foci
Robinson and Dahiya (2003) [2]	Right posterior shoulder	55/ M	3.2×3.8 (scar from previous 2 excisions)	13 years with death	No	Radiation to site of metastasis in axilla	5 years after Mohs, palpable axillary nodes + for MBCC. Lung mets 8 years after axillary dissection	Infiltrative

Abbreviations: (PNI- perineural invasion, GY- Gray, MBCC- metastatic basal cell carcinoma).

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