Basaloid squamous cell carcinoma of the skin

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Background: Basaloid squamous cell carcinoma (BSCC), an aggressive tumor of the aerodigestive tract, was described over 20 years ago, and its defining histologic parameters remain largely unchanged. While rare reports have noted cutaneous metastatic deposition, primary tumors have not been previously described.

Objective: Although most cutaneous malignancies with basaloid features comprise variants of basal cell carcinomas, a subset exhibit histologic attributes suggestive of more aggressive tumors. We evaluated 3 such tumors submitted to our dermatopathology service over a 6-month period.

Methods: Immunohistochemical stains useful in differentiating the lineage of cutaneous malignancies with basaloid-appearing tumor cells were employed. Human papillomavirus (HPV) detection and typing were performed by using polymerase chain reaction and sequencing.

Results: The tumor cells expressed high molecular weight cytokeratin (34βE12) and cytokeratin 5/6 but not Ber-EP4 or bcl-2. This pattern of immunohistochemical staining and the histologic attributes of the neoplasms are inconsistent with those expected in better defined cutaneous basaloid malignancies but are characteristic of BSCC. Two of the tumors arose in the inguinal crease of middle-aged men, and two patients were known to be immunosuppressed. HPV genotype 33 was detected in the tumor tissue from both inguinal lesions.

Limitations: The number of cases available for evaluation is small and any prognostic implications therefore tenuous.

Conclusions: The differential diagnosis of cutaneous malignancies exhibiting basaloid cells should include BSCC, a tumor with an unusual pattern of immunohistochemical staining and a potentially poor prognosis.
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In 1986 Wain et al[1] reported 10 patients with aggressive and unusual mucosal malignancies from the tongue, hypopharynx, and larynx. Six presented with cervical lymph node involvement and 4 patients of this subset also demonstrated distant metastases. Of the remaining 4 patients, two later experienced metastatic spread. Four of the cohort died within 4 years of diagnosis. The authors termed these tumors "basaloid squamous carcinoma" and established the major histologic criteria for their diagnosis. The tumor aggregates demonstrated a solid and lobular growth pattern of basaloid-appearing cells usually closely apposed to the surface mucosa. The cells were small and crowded with minimal cytoplasm and possessing dark hyperchromatic nuclei without readily visible nucleoli (nucleoli were subsequently noted ultrastructurally). Small cystic spaces with periodic acid—Schiff stain and/or alcian blue—positive

Abbreviations used:

ACC:	adenoid cystic carcinoma
BSCC:	basaloid squamous cell carcinoma
CK:	cytokeratin
HPV:	human papillomavirus
ISH:	in situ hybridization
NSE:	neuron-specific enolase

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mucinous material were also noted. Additional findings included hyalinosis and coagulative necrosis of the tumor nodules. Of note was the association in the accompanying mucosa of dysplasia, squamous cell carcinoma in situ, or frankly invasive squamous cell carcinoma. Subsequently, numerous papers have been published on this tumor, with the name "basaloid squamous cell carcinoma" having become the accepted appellation.[1-14] Although the existence of this malignancy has been reported in the skin as metastatic deposits and as primary tumors from the anus, penis, vulva, and external auditory canal, it has not been noted in other cutaneous sites.[3,9,11,15-18]

CAPSULE SUMMARY

- Basaloid squamous cell carcinoma (BSCC) has been described in the aerodigestive tract, but not as a primary cutaneous neoplasm.
- Three patients with tumors exhibiting features of a BSCC are reported. Each expressed cytokeratin 5/6 and cytokeratin 34βE12, but not Ber-EP4 or bcl-2, a pattern at variance with that of basal cell carcinoma. Two tumors arose in the inguinal crease of middle-aged men.
- BSCCs of the aerodigestive tract and skin are associated with poor clinical outcomes.

CASE REPORT

A 59-year-old white woman was referred to the Vanderbilt University Dermatology Clinic for evaluation before kidney transplant surgery. In 1995 she had been diagnosed with antineutrophilic cytoplasmic antibody—positive small vessel vasculitis, which eventuated in necrotizing and crescentic glomerulonephritis. End-stage renal disease ensued despite the administration of prednisone, cyclophosphamide (Cytoxan), cyclosporine, azathioprine, and rituximab. In May 2005 a biopsy was performed on a nodule, of indeterminate duration, on her left forearm. A pathologic diagnosis of "cutaneous malignancy with adnexal differentiation" was rendered, and in May 2006 she underwent a definitive excision of the site with lymph node dissection. No metastatic disease was detected. The pathology report at that time described a cutaneous malignancy with basaloid features suggestive of a sweat gland carcinoma. Subsequently, she has had a basal cell carcinoma on her left leg and a squamous cell carcinoma on her right thigh, both of which have been excised with clear margins and without further sequelae. To date, she continues to demonstrate no evidence of recurrent or residual disease from the excision on her left forearm.

The outside pathology blocks from the 2006 excision were obtained and additional sections performed. Within the dermis were large aggregates of basaloid cells with surrounding fibroplasia and stromal mucin deposition (Fig 1, *A* and *B*). Peripheral palisading and stromal retraction were not appreciated. The cells displayed marked anaplasia and pleomorphism with readily visible mitotic figures and dyskeratotic cells (Fig 1, *C* and *D*). Contiguity with the epidermis was not visible as the specimen displayed broad epidermal ulceration. Areas of intact epidermis demonstrated cytologic atypia consistent with that of an actinic keratosis. Evidence of vascular and neural involvement was not appreciated, but rare squamous pearls were noted (Fig 1, *E*). The tumor cells were strongly positive for high molecular weight cytokeratin (34βE12) (Fig 1, *F*), cytokeratin 5/6, and $p16^{INK\ 4a}$. Staining for low molecular weight cytokeratin (CAM 5.2) demonstrated faint and focal uptake within the tumor aggregates. A vimentin stain was positive in some tumor lobules but not in others. Epithelial membrane antigen, leukocyte common antigen, thyroid transcription factor 1, neuron-specific enolase (NSE), S-100, MART-1, cytokeratin 20, synaptophysin, chromogranin, CD99, CD57, bcl-2, and Ber-EP4 stains were negative. In situ hybridization (ISH) for high- and low-risk HPV types was also unremarkable.

Subsequently, the 2009 archives of the Vanderbilt University Dermatopathology Division were searched for tumors with similar features believed to represent poorly differentiated basal cell carcinomas. Two additional cases were found.

Patient 2 was a 78-year-old man taking long-term methotrexate for rheumatoid arthritis with a history of numerous squamous cell carcinomas. A lesion in his right inguinal crease had been present for several years but had recently increased in size (Fig 2, *A*). An excision of the tumor was performed without complications. Regional adenopathy was not noted. Histologically, the tumor displayed an ulcerated epidermis and intradermal aggregates of basophilic cells with a high nuclear to cytoplasmic ratio, marked atypia, coagulative necrosis (Fig 2, *B*) and squamous eddy formation (Fig 2, *C*). Epidermal keratinocytes adjacent to the tumor nodules exhibited squamous atypia.

Patient 3 was a 50-year-old man with a 2-year history of a gradually enlarging mass in the left inguinal crease (Fig 3, *A*), with steadily worsening edema of his left lower extremity. He had been