Basal cell carcinoma in situ of the skin revisited: case reports of the superficial type and fibroepithelioma type of this in situ cutaneous neoplasm

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Abstract

Cutaneous basal cell carcinoma in situ is a recently proposed subtype of this skin cancer. It is characterized by either restriction of the tumor cells within the epidermis or the presence of tumor cells contiguous with the overlying epidermis that extend into the underlying dermis, or both. Importantly, cancer invasion—demonstrated by non-contiguous aggregates of basaloid tumor cells in the dermis—is not a feature of in situ basal cell carcinoma of the skin. A 63-year-old woman with cutaneous basal cell carcinoma in situ—superficial type that presented as an erythematous scaly plaque on her abdomen and a 61-year-old man with a cutaneous basal cell carcinoma in situ—fibroepithelioma type that presented as a flesh-colored smooth exophytic nodule on his back are reported. The characteristics of in situ basal cell carcinoma of the skin in these individuals are summarized. In conclusion, similar to other cutaneous malignant neoplasms—such as squamous cell carcinoma, malignant melanoma, and Merkel cell carcinoma—basal cell carcinoma of the skin can also present as an in situ cancer.

Keywords: basal, carcinoma, cell, cancer, cutaneous, fibroepithelioma, in situ, neoplasm, superficial

Introduction

Squamous cell carcinoma, malignant melanoma, and Merkel cell carcinoma are invasive cutaneous tumors [1-17]. In contrast, in situ variants of these malignancies are characterized by neoplasms in which tumor cells are restricted to the epidermis [3,7,8,18-31]. Cutaneous basal cell carcinoma in situ is a recently proposed variant of basal cell carcinoma of the skin [32]. Two patients with this in situ variant of cutaneous basal cell carcinoma are described and the clinical and pathologic features of this neoplasm are summarized.

Case Synopsis

Case 1

A 63-year-old woman presented with a lesion on her trunk that she had recently noticed. The red area on her body was painless and did not itch; however, it had increased in size. She had no prior history of skin cancer.

A complete evaluation of her skin was performed. Cutaneous examination showed an asymptomatic 5cm×3cm scaly erythematous plaque on her left her left lower abdomen (**Figure 1**). A shave biopsy of part of the lesion was performed.

Microscopic examination showed orthokeratosis and acanthosis of the epidermis (**Figure 2**). On the left side of the tissue specimen, atypical keratinocytes appeared in a parallel arrangement along the basal layer of the epidermis (**Figure 2A, C**). On the right side of the biopsy specimen, there was contiguous extension of the epidermal rete ridges—with atypical basal cells in the lower layers of the epidermis—into the papillary dermis (**Figure 2B, D**).

Correlation of the clinical morphology and pathologic findings established a diagnosis of basal

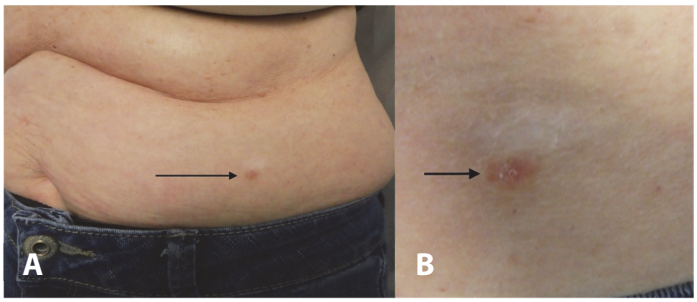

Figure 1. *Clinical presentation of a basal cell carcinoma in situ on the left lower abdomen of a 63-year-old woman.* ***A)*** *Distant and* ***B)*** *closer views of the woman's left lower abdomen demonstrate the tumor (pointed to by the black arrow) presenting as a 5cm×3cm scaly erythematous plaque. Correlation of the morphologic presentation and pathology findings established the diagnosis of a basal cell carcinoma in situ (superficial type).*

cell carcinoma in situ—superficial type. The residual tumor was excised. There has been no recurrence after four years of follow-up.

Case 2

A 61-year-old man presented for evaluation of a new skin lesion that had appeared on his back. His medical history was significant for diabetes, gastroesophageal reflux disease, hyperlipidemia, hypertension, gout, and lower back pain. His daily medication included allopurinol, aspir-low, atenolol, atorvastatin calcium, fenofibrate, glimepiride, lisinopril, metformin, omeprazole, triamterene-hydrochlorothiazide, and vitamin D.

His history of skin conditions included acrochordon on the neck and axilla (that were removed by snip excision), tinea corporis (which had been successfully treated with topical ketoconazole 2% cream), numerous sebaceous hyperplasia papules on the face (many of which had been removed using

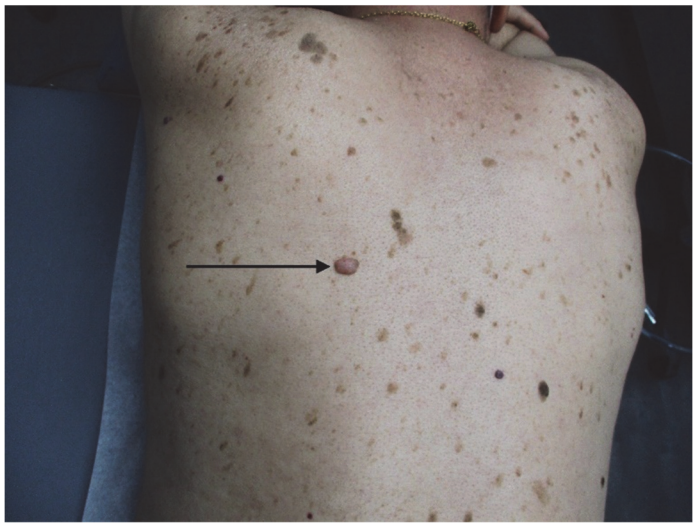

Figure 3. *Clinical presentation of a basal cell carcinoma in situ on the left midback of a 61-year-old man. The man's left midback demonstrates the tumor (pointed to by the black arrow) that appears as a 3cm×2cm exophytic nodule. Correlation of the morphologic presentation and pathology findings established the diagnosis of a basal cell carcinoma in situ (fibroepithelial type).*

hyfrecation), and multiple seborrheic keratoses on the back (some of which had been removed by cryotherapy using liquid nitrogen). He had no prior actinic keratoses or skin cancer. His new skin lesion was neither tender nor pruritic but it was raised on a stalk and he noticed that it rubbed against his clothing.

A complete evaluation of his skin was performed. Cutaneous examination of his back showed numerous brown plaques consistent with seborrheic keratoses. An asymptomatic 3cm×2cm smooth, flesh-colored exophytic nodule was also on his left mid back (**Figure 3**). A shave excision of the lesion was performed.

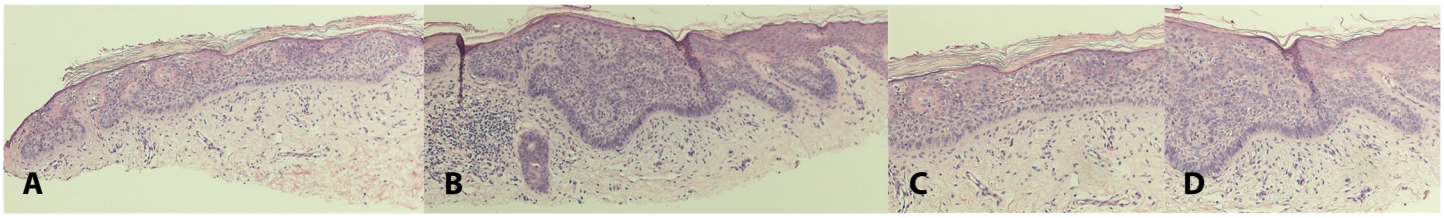

Figure 2. *Microscopic examination of a basal cell carcinoma in situ on the left lower abdomen of a 63-year-old woman.* ***A, B)*** *Low, and* ***C, D)*** *higher magnification views of A,* ***C)*** *the left side, and the right side of the tissue specimen from the shave biopsy of the woman's left lower abdomen tumor.* ***A, C)*** *The left side of the specimen shows orthokeratosis, acanthosis and atypical basal cells in the lower layers of the epidermis.* ***B, D)*** *The right side of the specimen also shows orthokeratosis and acanthosis and atypical keratinocytes in the basal layers of the epidermis; in addition, there is contiguous extension of the epidermis into the underlying papillary dermis. However, there is no invasion of tumor cells that are not attached to the overlying epidermis into the dermis. These are the features of an in situ basal cell carcinoma-superficial type. H&E,* ***A)*** *10×;* ***B)*** *10×;* ***C)*** *20×; and* ***D)*** *20×.*

Microscopic examination showed a thin irregular epidermis with sparse and focal orthokeratosis (**Figure 4**). Narrow strands of basaloid cells, that are attached to the overlying epidermis, extend into the underlying dermis; however, there is no invasion of basaloid cells that are non-contiguous with the epidermis into the dermis. The basaloid tumor cells were admixed with abundant loose fibrous stroma which contains a few leukocytes.

Correlation of the clinical morphology and pathologic findings established a diagnosis of basal cell carcinoma in situ—fibroepithelioma type. The shave excision performed during the biopsy completely removed the tumor. There has been no recurrence after two years of follow-up.

Case Discussion

The designation of a tumor as a carcinoma implies that it is an invasive cancer. Invasive cancer is defined by the National Cancer Institute as a "cancer that has spread beyond the layer of tissue in which it developed and is growing into surrounding, healthy tissues [33]. A cutaneous carcinoma is an invasive tumor in which neoplastic cells, that are not contiguous with the overlying epidermis, are present in the underlying dermis.

In contrast, a cutaneous in situ carcinoma is not an invasive tumor. An in situ carcinoma of the skin may show extension of tumor cells that are contiguous with the epidermis into the dermis. However, isolated aggregates of neoplastic cells are not present in the dermis of a cutaneous in situ carcinoma [34-36].

Table 1. *In situ and invasive cutaneous carcinomas.*

Cutaneous neoplasm	In situ carcinoma[a]	Invasive carcinoma[b]
Basal cell carcinoma	[32],CR	[5,6,37-48]
Malignant melanoma	[23-27]	[5,9-11]
Merkel cell carcinoma	[28-31]	[12-17]
Squamous cell carcinoma	[3,7,8,18-22]	[1-8]

[a]References for in situ carcinoma.
[b]References for invasive carcinoma.
CR, current report.

Squamous cell carcinoma and malignant melanoma are cutaneous malignancies that usually develop from in situ neoplasms (**Table 1**), [1-32,37-48]. Merkel cell carcinoma also has an in situ precursor that less commonly has been observed (**Table 1**), [1-32,37-48]. Recently, a case series of three men with proposed cutaneous basal cell carcinoma in situ has been described [32].

The basal cell carcinoma in situ of the skin that were reported had a distinctive clinical morphology and pathologic presentation. They appeared as scaly erythematous plaques on the abdomen or back; microscopic examination showed superficial extension of basaloid tumor cells—that were contiguous with the overlying epidermis—into the papillary dermis [32]. This tumor has generally been referred to as a superficial basal cell carcinoma [5,6,37-43].

The concurrent presence of an in situ cancer and an invasive neoplasm has been observed not only for squamous cell carcinoma and malignant melanoma, but also for basal cell carcinoma. In the latter setting, it is referred to as a basal cell carcinoma with mixed

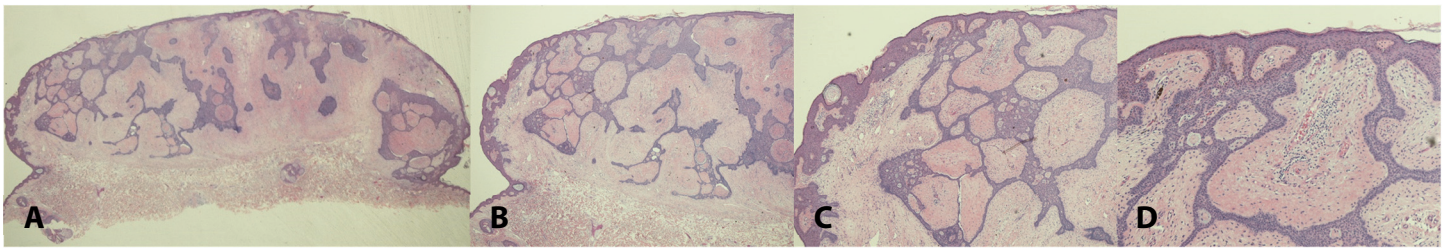

Figure 4. *Microscopic examination of a basal cell carcinoma in situ on the left midback of a 61-year-old man.* ***A)*** *Low , and* ***B-D)*** *higher magnification views of the tissue specimen from the shave excision that completely removed the tumor on the man's left midback. There is sparse and focal orthokeratosis and contiguous strands of epithelium, containing basaloid cells, extending from the epidermis into the underlying dermis. However, there is no invasion of tumor cells that are not attached to the overlying epidermis into the dermis. Admixed with the strands of basaloid tumor cells is abundant loose fibrous dermal stroma and rare leukocytes. These are the features of an in situ basal cell carcinoma—fibroepithelial type. H&E,* ***A)*** *2×;* ***B)*** *4×;* ***C)*** *10×; and* ***D)*** *20×.*

histology which demonstrates a tumor characterized by combined basal cell carcinoma subtypes. The in situ carcinoma (traditionally referred to as a superficial basal cell carcinoma) occurs with either a non-aggressive pathologic subtype of basal cell carcinoma (such as a nodular basal cell carcinoma) or an aggressive pathologic subtype of basal cell carcinoma (such as an infiltrating or micronodular or morpheaform or sclerosing basal cell carcinoma), or both [49-52].

Clinicopathologic correlation is suggested for establishing the diagnosis of a basal cell carcinoma in situ. If a cutaneous neoplasm is a basal cell carcinoma with mixed histology and a very superficial biopsy specimen—that only extends into the papillary dermis—is obtained using the shave technique, only the in situ subtype portion of the basal cell carcinoma may be present for microscopic evaluation and the deeper—potentially aggressive—subtype may not be diagnosed. Therefore, when a skin cancer is clinically suspected, the clinician should consider the morphology and location of the lesion when determining whether to use a shave technique, or a punch tool, or a scalpel excision to perform the biopsy [49-54].

The basal cell carcinoma in situ on the left lower abdomen of the woman in this case series is similar in appearance, location, and pathologic findings to those previously described [32]. However, the basal cell carcinoma in situ on the left midback of the man in this paper expands the clinical and pathology presentation of this in situ tumor. Currently, his neoplasm has been referred to as a fibroepithelioma of Pincus [44].

Fibroepithelioma of Pinkus was described in 1953. It clinically presents as a nodular lesion often on the back. Microscopic examination shows strands of basaloid tumor cells—that are contiguous with the overlying epithelium—that extend from the epidermis into the dermis [44-48].

Similar to superficial basal cell carcinoma, the fibroepithelioma of Pinkus variant of basal cell carcinoma is categorized as a non-aggressive basal cell carcinoma since it also has an indolent growth pattern. However, by referring to these tumors as carcinomas, both of these neoplasms are currently considered to be invasive tumors. However, to the best of my knowledge, neither superficial basal cell carcinoma nor fibroepithelioma of Pinkus—when presenting as a neoplasm without mixed histology—has been reported to demonstrate pathologic features of invasion.

Hence, fibroepithelioma of Pinkus is not an invasive carcinoma. Similar to what is commonly referred to as a superficial basal cell carcinoma, fibroepithelioma of Pincus also may be considered a cutaneous basal cell carcinoma in situ. Therefore, there are two variants of basal cell carcinoma in situ of the skin: superficial type and fibroepithelioma type.

Appropriately incorporating the diagnosis of cutaneous basal cell carcinoma in situ has the potential to be clinically relevant to the management of the patient. Several investigators have commented on the over-treatment of basal cell carcinoma in elderly patients. Particularly, in patients with limited life expectancy, either a less aggressive treatment (such as topical agents or superficially destructively modalities) or watchful waiting and active surveillance could be considered for these individuals with an in situ basal cell carcinoma [55-60].

In addition, the surgical management of superficial basal cell carcinoma—particularly Mohs micrographic surgery—is not uniformly successful and may be associated with significant morbidity. In a retrospective study of patients who underwent Mohs micrographic surgery at a single center during a three-year period, the investigators discovered that patients with superficial basal cell carcinoma were not only 9.03 times more likely to need two or more stages, but also 6.5 times more likely to develop a complication, including tumor recurrence [61]. However, if the skin cancer that these patients had was diagnosed as an in situ basal cell carcinoma, less aggressive superficially destructive modalities or topical agents may have been used without the individuals requiring prolonged surgery or developing subsequent complications or both.

Basal cell carcinoma, including those currently classified as superficial, have been observed to occur

with an acute eruptive onset of several tumors or the chronic development of multiple tumors or both. Specifically, these neoplasms have been noted in patients with a cancer-related genodermatosis (such as basal cell nevus syndrome, Bazex syndrome, epidermolysis bullosa simples-Dowling Meara subtype, myotonic dystrophy type I, oculocutaneous albinism, Rombo syndrome, and xeroderma pigmentosum), [62-65], a prior bone marrow transplant [66], a drug (lenalidomide)-related susceptibility [67], or an acquired immunosuppression (such as immunodeficiency from either human immunodeficiency virus infection [68] or agents to prevent rejection following a solid-organ transplant [69]). For most of these individuals, carcinoma-appropriate surgical management of their numerous skin cancers is not a feasible alternative. However, if their neoplasms are diagnosed as cutaneous basal cell carcinomas in situ, non-surgical interventions—simultaneously directed toward multiple tumors—can be considered as a reasonable treatment option.

Conclusion

Cutaneous in situ carcinomas—including those associated with squamous cell carcinoma, malignant melanoma, and Merkel cell carcinoma—are characterized by restriction of the neoplastic cells within the epidermis. Presence of the in situ cancer beneath the epithelium may occur only when tumor cells contiguous with the overlying epidermis extend into the underlying dermis. Invasion of the carcinoma, demonstrated by non-contiguous aggregates of cancer cells in the dermis, is not a feature of an in situ skin cancer. Two patients proposed as exhibiting in situ basal cell carcinoma of the skin are described. The woman had the superficial type of cutaneous basal cell carcinoma in situ and the man had the fibroepithelioma type of cutaneous basal cell carcinoma in situ. Cutaneous basal cell carcinoma in situ can concurrently occur in the same lesion as an invasive basal cell carcinoma. Therefore, the diagnosis of basal cell carcinoma in situ may require not only correlation of the clinical presentation and pathology findings, but also adequate sampling of the lesion during biopsy to ensure that a basal cell carcinoma with mixed histology is excluded. It can be anticipated that more appropriately classifying a skin cancer as a cutaneous basal cell carcinoma in situ will influence the clinical management of the patient; specifically, for individuals with a limited life expectancy, watchful waiting and active surveillance would be appropriate. For patients who develop eruptive and/or multiple tumors, a less aggressive—yet effective—therapy could be used to simultaneous treat the numerous skin cancers. In summary, similar to other malignant neoplasms of the skin, cutaneous basal cell carcinoma can present similarly as an in situ cancer.

Potential conflicts of interest

The author declares no conflicts of interest. Although he was a consultant for ParaPRO, this activity has no influence as a potential conflict of interest with regard to the manuscript.

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