Intraepidermal macrophages as mimics of pagetoid lesions

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Introduction

Pagetoid spread (PS) refers to the discrete intraepidermal proliferation of cells occurring singly or in nests at all levels of the epidermis. It is a finding most commonly seen in association with neoplasms, the majority of which are malignant. The most common neoplasms demonstrating this finding are superficial spreading melanoma, mammary and extramammary Paget's disease, and squamous cell carcinoma in situ [1, 2]. However, PS may also be seen occasionally in association with a number of other neoplasms, such as epidermotropic carcinomas (particularly breast and Merkel cell), cutaneous T-cell lymphomas (pagetoid reticulosis), sebaceous carcinoma, eccrine porocarcinoma, granular cell tumor and middle ear adenoma [3-10]. Several other non-neoplastic entities such as clear cells of Toker, clear cell papulosis, pagetoid dyskeratosis and clonal seborrheic keratosis may show pagetoid spread of cells [11-14].

Although many of these disorders are rare, the histological similarity between benign and malignant processes demonstrating PS creates the potential for significant diagnostic error. As such, it is critical to recognize benign mimics of the neoplasms in which PS of cells occurs. In this case report, we describe epidermally located macrophages spreading in a pagetoid fashion, and present the features that allows separation from more serious disorders.

Case Report

We report an 87 year old male who initially presented with clinical concern of squamous cell carcinoma and an irregular, raised, dark gray skin lesion on the right forehead. A shave biopsy was performed and interpreted histologically as hypertrophic actinic keratosis. The deep portion of the lesion was not present in the specimen and underlying invasive squamous cell carcinoma could not be ruled out. Re-excision of the biopsy site was recommended to exclude this possibility.

The biopsy site was subsequently re-excised and submitted for histological analysis. Dermal scar with focal robust giant cell reaction was present in the dermis; no invasive squamous cell carcinoma was identified. The epidermis overlying the central portion of the dermal scar was ulcerated. In the epidermis adjacent to the ulcer were nests and single large, pale cells with round nuclei and prominent nucleoli (Figure 1). In the clinical setting of a previously biopsied squamoproliferative lesion, the possibility of pagetoid squamous cell carcinoma was considered; however, pan-keratin immunostaining was negative (Figure 2A). Although unlikely given the histology of the initial biopsy, the clinical description of an irregular pigmented lesion suggests that the pagetoid cells might be melanocytic, but immunostains for S100 (data not shown) and HMB-45 (Figure 2B) were negative. Histological similarity to the macrophages present in the underlying dermal scar suggested that the epidermal

cells exhibiting pagetoid spread were macrophages as well. This was confirmed by positive CD68 staining (Figure 2C) and negative CD1a staining (data not shown).

Discussion

Here we describe pagetoid spread of macrophages in the epidermis, which is a novel potential histological mimic of other entities capable of pagetoid spread and represents a potential diagnostic pitfall. In the clinical context of re-excision for residual tumor with the potential for pagetoid spread, such as melanoma or squamous cell carcinoma, intraepidermal macrophages may be mistaken for residual tumor. Pagetoid macrophages can be identified by the close relationship, both in cytological appearance and spatial association, between the macrophage in the epidermis and underlying dermal scar. In situations where there are no apparent dermal macrophages or the histology is unconvincing, confirmation of identity can be obtained immunohistochemically.

The source of the intraepidermal macrophages in this case is likely from the underlying dermal inflammatory infiltrate, although the process that localized these macrophages in the epidermis is unclear. The suprabasally located macrophages could be in tips of dermal papillae included in the plane of section with intervening papillary dermis not included, giving the impression of pagetoid spread; however, this does not explain macrophages higher in the epidermis and additional sections show no such connections with the underlying dermis (Figure 1, 2A-C). Intraepidermal macrophages have been described in blistering skin lesions [15], although there is no evidence of such processes occuring in this case. Other possible explanations include macrophages being incorporated during repithelialization after biopsy, response to inflammation in the adjacent ulcer, or transdermal elimination.

References

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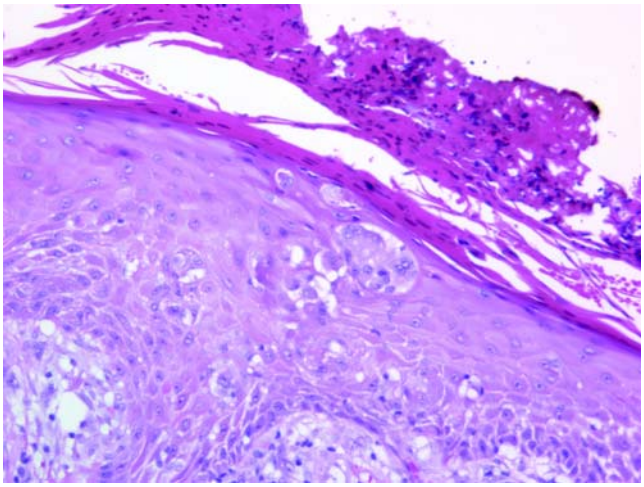

Figure 1. Representative micrograph of cells exhibiting pagetoid spread adjacent to previous biopsy site (H&E, 200x).

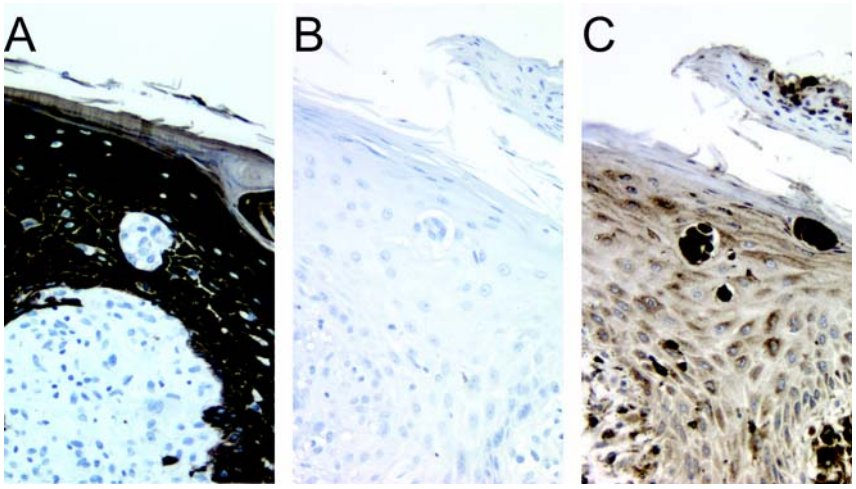

Figure 2. Cells exhibiting pagetoid spread are pan-keratin negative (A), HMB-45 negative (B) and CD68 positive (C). These cells are also S100 and CD1a negative (data not shown. 200x).