Acantholytic and Pagetoid Variant of Bowen’s Disease with Microinvasion on the Scalp of a Young Female Patient: A Case Report

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Abstract
Bowen’s disease (BD) is a non-melanoma skin cancer with several histological subtypes. Herein we describe a case of a 35-year-old woman with a 4-cm diameter crusted plaque on the parietal scalp region. She had the lesion for 2 years. It had previously been histologically diagnosed as pemphigus vulgaris and only treated with a topical cream. The lesion progressively became thicker and larger. A new biopsy showed atypical cell proliferation through the whole thickness of the epidermis and follicular epithelium, with dermal microinvasion along with acantholysis and clear cell formation. The patient underwent total lesion excision (1 cm margin) with the diagnosis of both acantholytic and pagetoid subtypes of BD and dermal microinvasion. We describe a rare case of a young female patient with both subtypes of BD present in one lesion on an area not exposed to the sunlight. The lesion was initially misdiagnosed as pemphigus vulgaris.

Keywords ● Bowen’s disease ● Pemphigus ● Keratin-7 ● Skin neoplasms ● Acantholysis

Introduction
Bowen’s disease (BD) is a variant of squamous cell carcinoma (SCC) in situ with full-thickness epidermal dysplasia; often seen in elderly people.1 It appears as a well-demarcated, scaly, crusted, erythematous plaque with an irregular border on sun-exposed regions of skin. The size of the lesion varies from a few millimeters to several centimeters.2 The most common sites are the head, neck, and lower extremity, but it can also occur in the nail bed, palmar, anogenital, oral mucosa, and conjunctiva.2,3 Several histological subtypes such as psoriasiform, atrophic, epidermolytic, acantholytic, and pagetoid variants have been reported.4 Pagetoid BD is a rare histologic variant that presents atypical pagetoid cells with abundant pale cytoplasm. The differential diagnosis includes extramammary Paget's disease (EMPD) or pagetoid melanoma in situ.5 The acantholytic variant of BD, due to the lack of cohesion between keratinocytes resulting in the formation of intra-epidermal clefts, has also been described.2

Herein we describe a rare case of BD in a young female patient with both pagetoid and acantholytic features on the covered area of the scalp. The patient was initially misdiagnosed with pemphigus vulgaris (PV) due to acantholysis. The histologic and immunohistochemical findings supported the diagnosis of...
the acantholytic and pagetoid subtypes of BD.

**Case Report**

A 35-year-old woman with a crusted erythematous lesion on her scalp referred to Razi hospital affiliated to Tehran University of Medical Sciences (Tehran, Iran) in September 2016. She had the lesion for 2 years and a previous biopsy indicated PV. In addition, the direct immunofluorescence (DIF) study had been negative. Regrettably, her past medical information was not available and the last biopsy sample could not be reviewed. She had been treated with an over-the-counter topical cream.

Her medical history and general physical examination were unremarkable. She also did not smoke nor consumed alcohol. There was no history of other dermatologic or autoimmune disorders among her family members. Physical examination revealed a 4-cm diameter lesion that appeared as scaly, erythematous, crusted plaque, and alopecia, which was confined to the parietal scalp region (figure 1). Since the lesion did not respond to the topical treatment and enlarged, a second biopsy with differential diagnosis of pemphigus vulgaris, pemphigus foliaceus, erosive pustular dermatosis, and cicatricial pemphigoid was conducted. The histological examination revealed atypical cell proliferation through the whole thickness of the epidermis and follicular epithelium, with dermal microinvasion along with acantholysis and clear cell formation (with pagetoid features). The tumor cells showed high nuclear pleomorphism, hyperchromatic nuclei, increased number of mitotic figures, and negative DIF (figures 2, 3). The neoplastic cells were positive for cytokeratin 7 (CK7) and negative for carcinoembryonic antigen (CEA), cytokeratin 20 (CK20), and S100 protein. The patient underwent total lesion excision (1 cm margin) with the diagnosis of acantholytic and pagetoid subtypes of BD and dermal microinvasion. A subsequent histological study confirmed the initial diagnosis and a negative resection margin. A follow-up in September 2018 showed no recurrence of the lesion. Written informed consent was obtained from the patient for the publication of her case report.

![Figure 1: A 4-cm diameter lesion that appeared scaly, erythematous, crusted plaque, and alopecia confined to the parietal scalp region.](image1)

![Figure 2: Histological examination showed atypical cell proliferation with high nuclear pleomorphism, hyperchromatic nuclei, and increased number of mitotic figures that involved the entire epidermis (a); H&E 400×. Atypical cell proliferation that involved the entire epidermis with acantholysis and dyskeratotic cell (b); H&E 100×.](image2)
Discussion

BD is a form of non-melanocytic intraepidermal malignancy. It occurs in the seventh decade of life and predominantly affects women. The risk factors of the disease include radiotherapy, arsenic exposure, ultraviolet exposure, immunosuppression, chronic dermatosis, and exposure to the human papillomavirus type 16. The present case report is of interest since the lesion was on an area of the skin that was not exposed to the sunlight and there were no risk factors present. In most patients, the period between the onset of symptoms and diagnosis is 5-6 years. In our case, however, the diagnosis was confirmed after just 2 years.

The acantholytic variant of BD is characterized by epidermal proliferation and pseudo-glandular structures due to the loss of intercellular cohesion. In our case, acantholytic cells appeared extremely bizarre, large, and multinucleated. Acantholytic SCC most commonly occurs on the head and neck of older men whereas in our case the patient was a young woman (35 years old) and the lesion appeared on an area not exposed to the sunlight. Note that in accordance with religious beliefs, Iranian women cover their head and neck, and thus not exposed to the sunlight. The etiology of acantholysis is desmosomal defects. A previous study reported that desmoglein-3 and E-cadherin levels were reduced in acantholytic BD and SCC. Although acantholysis in pemphigus and Hailey-Hailey disease is well-known, they are part of the differential diagnosis of acantholytic BD and SCC. Our patient had also been diagnosed with PV. It has been reported that in extragenital lesions, the risk of BD progressing to an invasive SCC is 3-5%. The presence of an ulcer is most likely a sign of invasive SCC. The metastasis rate of acantholytic SCC has been estimated at 3-10% and its mortality rate at 3-19%. Therefore, acantholytic SCC has been categorized as an SCC with intermediate risk.

Prognosis of acantholytic BD is dependent on the characteristics of the patient and the size, location, penetration, differentiation of tumor, and previous treatment of the disease. Of all the histological variants, only 5% of BD was associated with pagetoid BD. Histologic criteria for the diagnosis of pagetoid BD include the presence of atypical cells in the full thickness of the epidermis, the presence of dyskeratotic cells, detection of transmission between atypical cells and keratinocytes; no destruction of the basal layer by the formation of atypical nests, and the lack of atypical cells in the stratum corneum. Unlike typical BD, pagetoid BD commonly occurs in the extremities followed by the head, neck, and trunk area. Lesions with a pagetoid spread of neoplastic cells include malignant melanoma, extra-mammary Paget’s disease (EMPD), and mycosis fungoides. Various markers to differentiate EMPD from SCC are CEA, gross cystic disease fluid protein-15 (GCDFP-15), epithelial membrane antigen (EMA), BerEp4, proliferating cell nuclear antigen (PCNA), cytokeratin 10 (CK10), and other cytokeratins. Recent studies have indicated that p63 might be a useful marker for the diagnosis of BD. Antibodies against CEA are known to express EMPD. In the present study, we ruled out EMPD with CEA negative, melanoma with S100 negative, and Merkel cell carcinoma with CK20.
negative. However, we had some limitations in selecting the IHC markers. CK7 is expressed in the secretory cells of EMPD, but usually absent in BD, which makes it a sensitive marker for EMPD. However, some researchers have reported that CK7 is sometimes expressed in pagetoid BD and invasive SCC, particularly in poorly differentiated tumors.13

Conclusion

The acantholytic and pagetoid subtypes of BD are uncommon variants of BD. We have described a rare case of a young female patient with both subtypes of BD on skin area not exposed to the sunlight. Both acantholysis and pagetoid features can be present in BD and should not be misdiagnosed as PV or EMPD. Although CK7 can be expressed by pagetoid BD, it is not always indicative of Paget's disease. Early diagnosis of BD could prevent the progression of the disease.

Conflict of Interest: None declared.

References


