BOWEN'S DISEASE: A VERY UNUSUAL LOCATION

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Summary

Bowen's disease is a cutaneous squamous cell carcinoma in situ, a rare precancerous disease most frequently manifested by an erythematous, scaly crusted plaque on sun-exposed areas. We report on the case of an 83-year-old female, with an asymptomatic, erythematous scaly plaque, within an uncommon topographic setting, a peculiar localization that prompted a series of inquiries into multiple potential differential diagnoses. We also review the main treatment options, among which surgical extension, cryotherapy, topical agents, or photodynamic therapy are of paramount importance.

Keywords: *Bowen's disease, cutaneous squamous cell carcinoma, precancerous lesions.*

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Introduction

Bowen's disease or cutaneous squamous cell carcinoma in situ (cSCC) is a slowly progressive precancerous disease, named after Professor John Templeton Bowen, who reported in 1912 two atypical cases featuring numerous erythematous plaques across sun-protected areas, describing them as "chronic atypical epithelial proliferation". It is most frequently found in the elderly, with the average age of diagnosis ranking in the sixth decade. The ratio between men and women leans slightly towards men (1.2:1). [1]

Bowen's disease tends to affect various body areas, with a preference for sun-exposed surfaces (head, neck, hands) – 72% of cases occurring at these levels. Other body parts can be affected too, including the nail bed, oral mucosa, and conjunctivae. [2]

It is often connected with old age, ultraviolet radiation (UV), arsenic ingestion, ionizing radiation, immunosuppression (either due diseases: chronic lymphocytic leukemia or drugs: ciclosporin, azathioprine), and viral infections (HPV or Merkel cell polyomavirus).[2, 3] Ultraviolet radiation is the most predisposing factor for this disease. It induces damage to the nucleic acids (DNA) of skin cells, leading to a mutated form of the p53 gene, triggering unregulated growth of the skin cells.[3]UV radiation additionally inhibits the immune response, preventing recovery from damage.[3]

Due to the potential for malignant transformation, the treatment of choice is surgical extension with a five-mm surgical margin. For areas where tissue preservation is important, Mohs surgery is recommended. [1] Other treatment methods include destructive procedures, such as electrodesiccation, curettage or cryotherapy, but these have their limitations. An alternative to surgery is the application of topical

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agents, such as 5-fluorouracil or Imiquimod. Light-based procedures (laser therapy, photodynamic therapy) or radiotherapy can also be performed. [4]

Case report

We report on an 83-year-old female patient, who presented to our dermatology clinic with asymptomatic, erythematous scaly plaque with a rare topographical location, namely the popliteal fossa. The plaque was round-oval, with a diameter of 4.5/3 cm, with well-demarcated borders. Yellow scales and crusts were present on its surface, with an ulcerated area on the side (Fig. 1). According to the patient, the lesions had appeared for the first time as a small round papule and evolved progressively over about two years.

The patient's medical history included rheumatoid polyarthritis for 35 years (in treatment with methotrexate and tocilizumab), hypertension (in treatment with indapamide, spironolactone, simvastatin), and osteoporosis.

After we removed the sutures from the three biopsies we had performed, the crust from the ulceration fell off, leaving behind a moist granular surface, an erythematous base and yellow scales (Fig. 2).

The presumptive diagnosis according to the clinical aspect was Bowen's disease, but we had to eliminate other possible diagnoses, such as pagetoid basal cell epithelioma, actinic keratosis, extramammary Paget's disease, nummular eczema or psoriasis vulgaris. To eliminate these possibilities, we did a dermoscopic evaluation and we performed 3 punch biopsies for histopathological examination.

Dermoscopic evaluation displayed dotted and glomerular vessels, yellowish surface scales, and red-yellowish background color.

Histopathological examination revealed hyperkeratosis with parakeratosis through the entire thickness of the epidermis along with marked acanthosis, papillomatosis, and architectural disorganization: keratinocytes with multiple cytonuclear atypia, large hyperchromatic nuclei, and numerous mitosis. The superficial dermis shows a moderate inflammatory infiltrate (Fig. 3).

Following the corroboration of the clinical, dermoscopic, and histopathological data, the diagnosis of certainty of Bowen's disease was

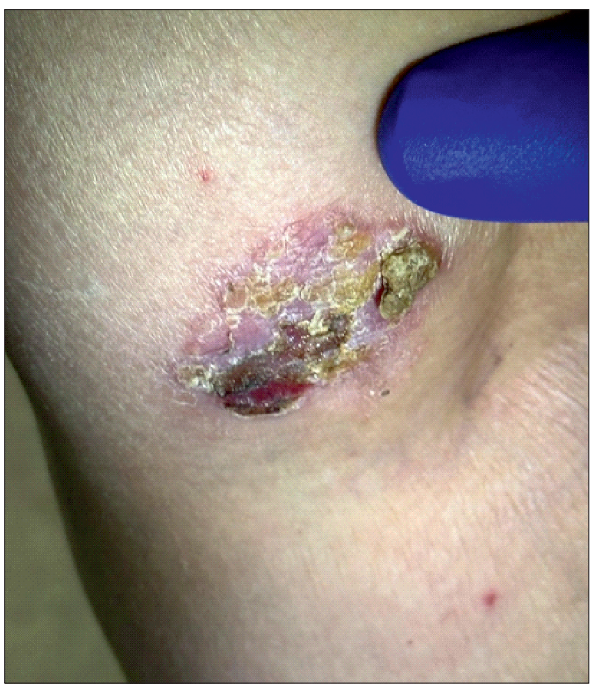

Fig. 1 – Erythematous scaly plaque situated on the popliteal fossa (image from our clinic)

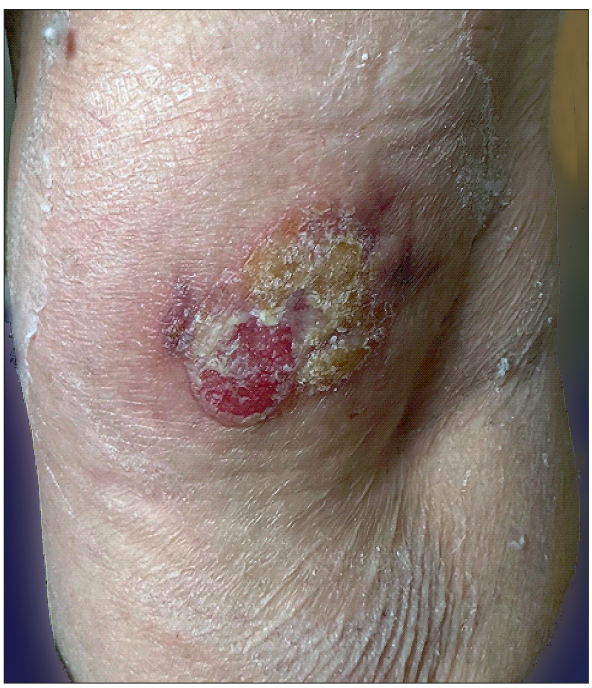

Fig. 2 - Erythematous scaly plaque with an ulceration on the side, after sutures removal (image from our clinic)

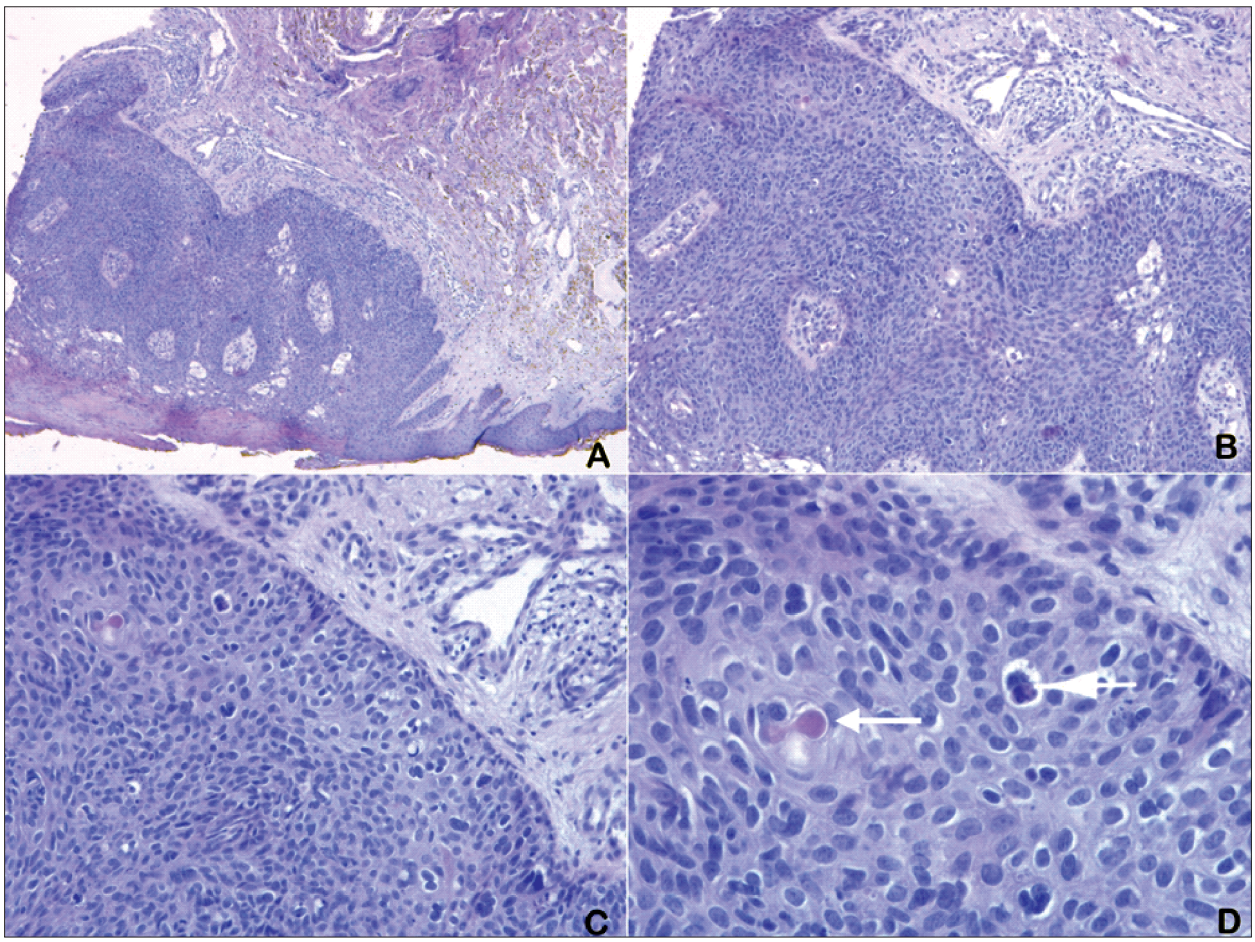

Fig. 3 – Bowen's disease/ CSC in situ – A. architectural disorganization and cytonuclear atypia, H&E, 10X. B. architectural disorganization and cytonuclear atypia, H&E, 20X. C. architectural disorganization and cytonuclear atypia, H&E, 30X. D. architectural disorganization and cytonuclear atypia, atypical mitoses (right arrow), cellular acantholysis (left arrow), H&E, 40X (image from our clinic).

established. In this case, we recommended surgical excision in the plastic surgery service due to extension, location, age, and genuine potential of medical complications.

Discussion

Bowen's disease is a type of precancerous disease, especially found among the elderly, with an occurrence rate more inclined towards men (1.2:1). [1] The localization of the lesion is especially on the areas chronically exposed to the sun: head, neck, and arms, with 72% of the cases manifesting at these levels. Cases have also been described at the level of the oral mucosa, anogenital area, and nail bed. [1] In our case, the particularity of the case is topographical localization, a very rare presence at the level of the popliteal fossa.

Bowen's disease is characterized by the appearance of an erythematous, scaly, crusted plaque that typically exhibits slow growth, gradually enlarging over the years. [5] Most often it is solitary, asymptomatic, with well-defined borders, ranging from a few millimeters to several centimeters in diameter. The contour of the lesion can be annular or polycyclic. The scale typically appears yellow or white and can be easily removed without causing bleeding, revealing a moist, erythematous surface.[2] The

lesions might exhibit fissures, have a verrucous texture, or rarely, display pigmentation. [1] The occurrence of ulceration is indicative of potential invasive disease development. The risk of Bowen's disease progressing to invasive squamous carcinoma is approximately 3%-5%, and one-third of those that become invasive SCC may metastasize. [3, 6]

Initial skin changes might be subtle and can overlap with clinical features observed in various conditions, such as tinea corporis, actinic keratosis, extramammary Paget's disease, nummular eczema or psoriasis vulgaris, which leads to delaying the correct diagnosis of Bowen's disease. [2]

To establish the correct diagnosis, the clinical features, the dermoscopic appearance, and the histopathological examination must be corroborated. Dermoscopic features that may be suggestive for Bowen's disease are glomerular vessels, pigmented false network, smooth distribution of brown and grey pigment, spots of hypopigmentation, irregular distribution of dots and globules, and squamous surface (scaly areas). [2, 7] In order to achieve a certain diagnosis of Bowen's disease, a shave or punch biopsy should be taken. Sampling multiple areas of larger lesions can be beneficial to rule out any signs of invasion resembling cutaneous squamous cell carcinoma. Histopathological examination shows keratinocytic dysplasia throughout the entire thickness of the epidermis, without any impact on the dermis. [5] There is also present hyperkeratosis with parakeratosis accompanied by acanthosis with elongated and thickened papillary ridges. [1] The keratinocytes display pleomorphism, characterized by hyperchromatic nuclei and numerous mitoses. [5] The dermis contains a moderate inflammatory infiltrate.

Due to the potential for malignant transformation, the treatment of choice is surgical extension with a five-mm surgical margin. For areas where tissue preservation is important, Mohs surgery is recommended. [1] Other treatment methods include destructive procedures, such as electrodesiccation, curettage or cryotherapy, but these have their limitations. Cryotherapy can be useful in patients with multiple lesions, a single freeze-thaw cycle of 30 seconds being sufficient to achieve complete clearance of the lesion in most cases. [4]

An alternative to surgery is the application of topical agents, such as 5-fluorouracil or Imiquimod. 5-fluorouracil is an antineoplastic agent whose mechanism of action consists of inhibition of thymidylate synthetase, thus it interferes with DNA synthesis. [8] Can be used for large lesions (>3 cm in diameter) and applied twice daily for a duration of two to eight weeks, depending on the location and individual response. [4] Regarding Imiquimod, a topical immune response modifier, treatment protocols differ, with daily application for a duration of 6 to 16 weeks. [9] The treatment duration is notably longer compared to topical fluorouracil, and it often elicits a pronounced inflammatory reaction. These factors can determine low compliance, leading to a low healing rate. The main adverse effect of topical agents consists of the presence of local erosions and ulcerations, which can last up to several weeks. [4]

Light-based procedures (laser therapy, photodynamic therapy) can be an option for patients with Bowen's disease. Photodynamic therapy (PDT) is a two-step treatment that harnesses light energy alongside a drug known as a photosensitizer, to eradicate cancerous and precancerous cells following light activation. [10] Photosensitizers are triggered by a particular wavelength of light energy, typically emitted by a laser. These photosensitizers remain non-toxic until they are activated by light. However, upon activation by light, the photosensitizer transforms into a toxic compound, specifically targeting the intended tissue. [10] The most frequently used photosensitizing agents are topical 5-aminolevulinic acid (ALA) or methyl aminolevulinate (MAL). Photodynamic therapy can be used on patients with multiple lesions, large lesions (>3 cm in diameter), and slow-healing sites. [4] The adverse reactions are rare and may include local erythema, hypo or hyperpigmentation, pruritus, and local phototoxic effects, such as burning or stinging sensations. Radiotherapy can also be done, especially for lesions > 3 cm in diameter. [2]

The evolution of the disease is chronic, with a 3%-5% risk of malignant transformation (invasive squamous carcinoma), ulceration and

infiltration being potential signs of invasiveness. [3] In this case, our patient presented the lesion for approximately 2 years, with progressive evolution during all this time, from a papule of several mm to a plaque of 4.5/3 cm. Given the clinical presentation involving crusts and ulceration, along with considerations of the lesion's evolution, location, and the patient's age, we considered that the appropriate treatment was surgical excision in the plastic surgery service.

Since most treatments carry a risk of recurrence, it is recommended to schedule follow-up appointments at 6-12 months. Under certain conditions, such as history of previous recurrence, high-risk location of the lesion, the presence of multiple lesions or immunosuppression, patients are called to the doctor in a shorter time for follow-up. [6]

Conclusion

Even if it is a rare condition, it should not be overlooked by dermatologists, especially when it appears in unexpected places. Considering the fact that the lesion is initially asymptomatic and can pose differential diagnosis problems, it is important to be diagnosed early for the most appropriate treatment.

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Conflict of interest
NONE DECLARED

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