

BOWEN'S BLOWN AWAY! - SUCCESSFUL MANAGEMENT OF BOWEN'S DISEASE BY TOPICAL 5% 5-FU AND CRYOTHERAPY

Dermatology

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ABSTRACT

BACKGROUND: Bowen disease (BD) is a rare, persistent, and progressive form of in situ Squamous Cell Carcinoma characterized by a solitary red, scaly or crusted plaque with potential for malignant change around 8%. Persistent growth usually occurs but partial regressions are not uncommon. Several modalities of treatment are available which show varying results. In our Case Report, we present a 74-year-old male who was diagnosed with Bowen's Disease clinico-pathologically and was treated with cyclical topical 5% 5-FU cream and Cryotherapy using Liquid Nitrogen.

CASE DESCRIPTION: A 74-year-old male came to our OPD with complaints of a single, persistent, asymptomatic psoriasiform plaque of size measuring 4x4 cm over his abdomen for 3 years. The plaque was progressively enlarging and showed resistance to topical therapies with salicylic acid, potent topical steroids, and emollients for the past 3 years. A clinical diagnosis of Bowen's Disease was made, and biopsy was done. Histopathological Examination revealed intra-epidermal dysplasia with characteristic 'wind-blown' appearance of keratinocytes in the epidermis. Atypical mitotic figures were seen. Dense lymphocytic infiltrate with pigment laden macrophages were seen at DEJ. Patient was started on topical 5% 5-Fluorouracil (5-FU) cream which he applied three nights a week along with Cryotherapy using Liquid Nitrogen (8 sessions of cryotherapy with two 5-10 secs Freeze-Thaw cycles were done at 3 weekly intervals). Biopsy taken at end of 6 months showed a normal epidermis with no evidence of in situ changes. Next evaluation will be after 3 months.

CONCLUSION: There are multiple treatment modalities available for BD with no option superior to other. 5% 5-FU is showing increasing effectiveness (up to 96.2%) especially when combined with other treatment options such as cryotherapy which on its own showed great clearance rates (greater than 90%) depending on the duration of freeze-thaw cycles. Main advantage of this combination is its ease of application, low cost and non-invasiveness.

KEYWORDS

Bowens, SCC, 5-FU, Cryotherapy

INTRODUCTION

Bowen's Disease (BD) is an intraepidermal or *in situ* Squamous Cell Carcinoma. It was first described by John T Bowen in 1912 after whom its' named^[1]. It typically affects individuals older than 60 years and rarely before 30 years affecting men and women equally. However, some studies have shown an increased preponderance towards women. Potential for malignant change is around 8%. Lesions are usually solitary but multiple lesions can occur in 10-20% of patients. It usually presents as a discrete slowly enlarging scaly erythematous to salmon red plaque which is well circumscribed and ill-defined. They may be few millimetres to several centimetres in diameter eventually becoming hyperkeratotic, crusted and fissured. Ulceration can occur and may be a sign of malignant transformation. Persistent growth usually occurs but partial regressions are not uncommon. Several modalities of treatment are available and show varying results.

In our Case Report, we present a 74-year-old male who was diagnosed with Bowen's Disease clinico-pathologically and treated with 5% 5-FU topically and Cryotherapy using Liquid Nitrogen.

CASE DESCRIPTION

A 74-year-old male came to our OPD with complaints of a single, persistent, asymptomatic psoriasiform plaque of size measuring 4x4 cm over his lower abdomen for 3 years [FIG 1]. Patient was getting treated elsewhere for discoid eczema / psoriasiform dermatitis. The plaque was progressively enlarging and not responding to topical therapies with salicylic acid, potent topical steroids, and emollients for the past 3 years. Based on the history and clinical examination, a provisional diagnosis of Bowen's Disease was made.

A biopsy was taken and sent for histopathological examination. HPE revealed intra-epidermal dysplasia with characteristic 'wind-blown' appearance of keratinocytes in the epidermis. Atypical mitotic figures

were also seen. Dense lymphocytic infiltrate with pigment laden macrophages were seen at DEJ.

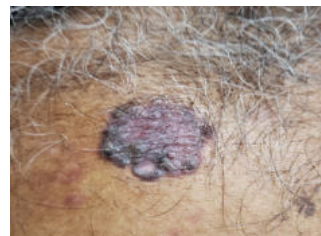


FIG. 1 – Scaly plaque over lower abdomen

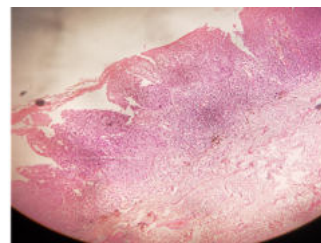


FIG. 2 – HPE showing wind-blown appearance of keratinocytes

Patient was started on cyclical topical 5% 5-Fluorouracil (5-FU) cream which he applied three nights a week along with Cryotherapy using Liquid Nitrogen. 8 sessions of cryotherapy with two 5-10 secs Freeze-Thaw cycles were done at 3 weekly intervals after which the lesion resolved [FIG 3]. Repeat biopsy taken at the end of 6 months showed a normal epidermis with no evidence of in situ changes [FIG 4]. Next evaluation will be done after 3 months.



FIG. 3 – Six months after therapy

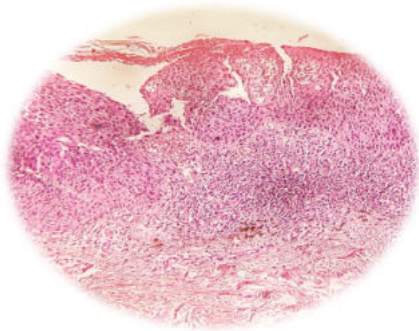


FIG. 4 – Six months after therapy showing normal epidermis

DISCUSSION

Several causative factors have been implicated in Bowen's Disease. Chronic UV exposure causing UVB induced p53 mutation is the most common cause with lesions occurring over sun exposed areas. Chronic arsenical exposure is also an important cause for lesions occurring over non sun-exposed sites. Human Papilloma Virus types 8, 16, 18, 39 and 51 are associated with genital BD while 15 and 16 are linked to BD of extremities^[2]. BD has also been described with increased incidence in patients who have previously taken psoralen with UVA (PUVA) therapy. Other causes of BD include genetic factors, trauma, chronic irritation, irradiation and immunosuppression.

Usually sun exposed areas are affected including head and neck, followed by limbs but can affect covered areas as well. Rare sites include nail bed, periungual region and glans penis where it is referred to as Erythroplasia of Queyrat. The risk of malignant invasion is 5-10% and hence an early diagnosis and treatment is essential. Several histopathologic variants include psoriasiform, atrophic, verrucous, hypertrophic, pigmented, and irregular type. The characteristic histopathological features of BD include the wind-blown pattern of epidermis with loss of cellular polarity and presence of nuclear atypia and mitotic figures which was seen in our patient.

Various treatment options are available for BD. Comparison of different options is difficult due to the various protocols available. Success of treatment depends on several factors like the site of lesion, size and thickness of lesion as well as the modality of treatment used. Treatment choice should be tailored on an individual basis considering the patient's age, site of lesion, willingness of the patient and the expertise and experience of the treating physician. Commonly available treatment options include topical therapies like 5-Fluorouracil and Imiquimod; surgical interventions like Excision and Curettage; destructive methods like Cryotherapy; and Photodynamic therapy.

Cryotherapy with Liquid Nitrogen is a commonly used procedure because of its easy availability and low cost. It is considered as treatment of choice especially for solitary and small lesions^[4]. Good results and low recurrence rates (0–0.8% at 5 years) are achieved when liquid nitrogen cryotherapy is used in a single 30-s freeze-thaw cycle. Different studies have showed clearance rates ranging from 50% to 100% by also using one to three 20s freeze-thaw cycles.^[13]

Curettage with cautery is another safe and effective method and showed cure rates ranging from 81% for curettage up to 93% to 98% with a follow up of 2.5 to 4 years^[15]

Excision including Mohs micrographic excision has advantage of securing histologically free excision margins and is commonly performed for solitary lesions.

Most commonly used topical preparation of 5-fluorouracil is 5% 5-FU in propylene glycol. Once or twice daily application with clearance rates ranging between 87% and 92% have been reported^[6]. Pulse therapies have also been tried with varying responses. Efficacy improves when combined with other modalities like iontophoresis, acitretin, topical imiquimod, cryotherapy and erbium:YAG laser. Erosions and ulcerations may occur if applied daily.

External beam radiotherapy, Grenz rays and radioactive skin patches have shown variable results as Radiotherapy for BD. However it should be avoided in lesions occurring in poor healing sites such as lower legs. Photodynamic therapy using topical photosensitizer precursors like 5-Aminolevulinic Acid (ALA) and Methyl Aminolevulinate (MAL) is being done. MAL-PDT is approved for the treatment of BD in 22 European countries. Argon, CO₂ and Nd:YAG lasers have also been tried.

Newer treatment options include 5% Imiquimod cream and 3% Diclofenac gels. Different regimens are being studied.

CONCLUSION

Bowen's Disease has about an 8% chance of malignant transformation. Hence, we should always have a high index of suspicion and treat it as early as possible. There are multiple treatment modalities available for BD with no option superior to other. 5% 5-FU is showing increasing effectiveness (up to 96.2%) especially when combined with other treatment options such as cryotherapy which on its own showed great clearance rates (greater than 90%) depending on the duration of freeze-thaw cycles. Main advantage of cyclical topical 5% 5-Fluorouracil combination with Cryotherapy is its ease of application, low cost and non-invasiveness ensuring a good patient compliance and follow-up. However, erosions and ulcerations may occur which can be managed easily.

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