

Introduction

Skin cancer develops primarily on areas of sun-exposed skin. These include the scalp, face, lips, ears, neck, chest, arms and hands, and on the legs in women. It can also appear on areas that rarely see the light of day — the palms, beneath the fingernails or toenails, and the genital area, especially in individuals with darker skin tones.

[Picture Credit: Bowen's Disease]

Skin cancer affects people of all skin tones, including those with darker complexions. When melanoma occurs in people with dark skin tones, it is more likely to occur in areas not normally exposed to the sun.



Bowen's Disease

Bowen's disease is a very early form of squamous cell skin cancer. It is also called squamous cell carcinoma *in situ*. Bowen's disease is often referred to as 'pre-invasive'. This means that there are cancer cells present but they are only in the outermost layer of skin, the epidermis. Sometimes it can spread along the skin surface.

[Picture Credit: Bowen's Disease]

If left untreated, there is a chance that Bowen's disease can spread into the deeper layers of the skin. This means it has become an invasive cancer and can then spread into the lymphatic system. It takes a long time for Bowen's disease to develop into an invasive cancer. The risk, however, of developing into a fully blown skin cancer remains until



Bowen's disease is treated.

Wozniak-Rito, A.M. & Rednicka, L. 2018.

“Bowen's disease, named after John Templeton Bowen, also known as squamous cell carcinoma in situ is a type of non-melanocytic intraepidermal malignancy. It is estimated that in general population around 3% to 5% of Bowen's disease transform into invasive squamous cell cancer. Dermoscopy aims in the identification of the Bowen's disease. The most typical dermoscopic features of Bowen's disease include glomerular vessels and scaly surface. Although dermoscopy of Bowen's disease has been well established other skin lesions may present similar or identical structures in dermoscopic images leading to differential diagnosis dilemmas. Histopathological confirmation should be obtained prior the treatment of suspected cases of Bowen's disease in order to avoid a misdiagnosis.”

Incidence of Squamous Cell Carcinoma (SCC) in South Africa

The outdated National Cancer Registry (2017), known for under reporting, does not provide any information regarding the incidence of Bowens/ Disease in South Africa.

Scalvenzi, M., Villani, A., Mazzella, C., Fabbrocini, G. & Costa, C. 2019.

“Bowen's disease (BD), also known as squamous cell carcinoma in situ, is a type of non-melanocytic intraepidermal malignancy characterised by a slowly enlarging erythematous to pink, scaly patch or plaque with irregular and well-demarcated borders. These lesions are usually persistent and progressive; it has been estimated that in general population around 3% to 5% of Bowen's disease transform into invasive squamous cell carcinoma. This report describes our experience with cutaneous BD and assesses the differences found about age, sex and anatomical site. Bowen's disease was seen more frequently in male patients rather than in female patients in contrast to what confirmed in literature - this difference is probably because being head-neck an exposed region, patients are more easily induced to autoexam and to consult the dermatologist.”

Signs and Symptoms of Bowen's Disease

Bowen's disease can occur anywhere on the body but is usually found on the lower legs. To begin with, it often looks like a red, scaly patch, or sometimes like raised spots or warts. The affected skin may become itchy, sore and may bleed. As Bowen's disease can look like other skin conditions such as eczema or psoriasis, it is important to get any skin problems checked by a doctor, preferably a dematologist.

[Picture Credit: Bowen's Disease 2]



Diagnosis of Bowen's Disease

Diagnosis of Bowen's Disease is done by means of a shave or punch biopsy for histological diagnosis. Where possible, it is suggested that a hair follicle should be included in the biopsy material.

The following conditions should be considered as possibilities in differential diagnosis:

- Actinic Keratosis

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- Basal Cell Carcinoma
- Lichen Simplex Chronicus
- Paget Disease (mammary)
- Psoriasis (plaque)
- Squamous Cell Carcinoma
- Tinea Corporis

Ferreira, J.CB., de Paula, H.M., Caixeta, G.N. & Mendonca, E.F. 2020.

“Bowenoid papulosis (BPap) is an uncommon skin disorder linked to human papillomavirus (HPV) infection and characterized clinically by the presence of scattered papules or small plaques, multiple and pigmented, that involve the stratified squamous epithelium. Bowen disease (BD) is recognized as the main differential diagnosis of BPap. An 80-year old white woman was referred for the evaluation of multiple, brown verrucous papules measuring 3 to 4 mm in diameter on the right maxillary gingiva. Histopathological analysis revealed disturbed epithelial maturation with papillary stratified squamous epithelium, koilocytic dysplasia, parakeratosis, acanthosis, basal double-layer, loss of cellular polarity, nuclear hyperchromatism and pleomorphism, scattered mitosoid bodies, and a high degree of cytologic atypia. An immunohistochemical investigation for p53 and Ki67 showed staining of the basal and suprabasal layer, while p16 was strongly expressed in the nuclei of epithelial cells and Bcl-2 was positive only in mitosoid bodies and the lymphocytic inflammatory infiltrate. In situ DNA hybridization was negative for HPV. Oral BPap is an uncommon lesion in which the diagnostic process includes clinical, histopathological, and molecular correlations due to the similarity to aggressive behavior lesions such as BD.”

Li, M.X., Wang, Q., Li, X.L., Zhao, C.K., Zhu, R.Z., Chen, J., Li, L., Guo, L.H. & Xu, H.X. 2020.

Objectives: To compare the imaging findings of Bowen's disease (BD) between ultrasound biomicroscopy (UBM) and conventional high-frequency ultrasound (HFUS).

Methods: A total of 29 pathologically proven BD lesions in 28 patients were retrospectively enrolled in the study, and all were after surgery. All the lesions were imaged with both UBM and HFUS. The imaging features on HFUS and UBM were analyzed and compared. The diagnostic results of ultrasound for BD were referenced with pathology results.

Results: All the 29 (100%) BD lesions appeared hypoechogenicity, solid component, and superficial hyperechoic layer (ie, keratinization) on both UBM and HFUS. The typical imaging feature of BD lesions, that was, infiltration depth confined to the epidermis, was visualized in 25 (86.2%, 25/29) lesions on UBM whereas 15 (51.7%, 15/29) on HFUS (P = .002). A "wave sign," which corresponds to the surface keratinization of BD lesion, was visualized in 17 (58.6%, 17/29) of BD lesions on UBM whereas 6 (20.7%, 6/29) on HFUS (P = .001). UBM and HFUS correctly diagnosed 25 (86.2%, 25/29) and 15 (51.7%, 15/29) BD lesions, respectively (P = .002).

Conclusions: Bowen's disease has some typical imaging features on US. The "wave sign" of the superficial hyperechoic layer and the clear borderline between the tumor in epidermis and the slightly hyperechoic dermis layer are better depicted by UBM in comparison with HFUS, which leads to a more accurate diagnosis of BD. UBM has potential to be used as a diagnostic tool for characterization of BD on account of its high resolution.

Risk Factors of Bowen's Disease

Risk factors for Bowen's Disease include:

Sun damage – UV exposure in sunlight (especially with fair skin) is a strong risk factor

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Other irradiation damage - radiotherapy, photochemotherapy

Carcinogens - particularly arsenic. Exposure to inorganic arsenic is less common than it used to be in the past.

Viral infection - There is a strong association with human papillomavirus (HPV), HPV-16 particularly in genital and perianal lesions. Some other HPV types have also been implicated.

Immunosuppression - following organ transplants, or Aids. Malignant and premalignant skin tumours are more common in patients who have received organ transplants.

Chronic skin injury or dermatoses - it may arise (rarely) in pre-existing skin lesions such as seborrhoeic keratoses

Staging of Skin Cancer

Doctors use a staging system that is common to all cancers. It is called the TNM system:

- The T indicates the size and depth of the tumour
- The N shows whether the cancer has spread to the lymph nodes
- The M shows whether the cancer has spread to another part of the body (metastasis)

Treatment of Bowen's Disease

There are a number of treatment options and one's dermatologist should take into consideration where the patch is on one's body, as well as its size, thickness and the number of patches one has before deciding on the most appropriate treatment.

He/she will also consider how well the skin is likely to heal afterwards – for example, skin on the lower legs tends to be tight, fragile and slower to heal.

Treatment options may include:

- Cryotherapy – Liquid nitrogen is sprayed onto the affected skin to freeze it. The procedure may be painful and the skin may remain a bit uncomfortable for a few days.
- Application of skin creams – This is applied to the affected skin regularly as prescribed.
- Curettage and cautery – The affected area of skin is scraped away under local anaesthetic.
- Photodynamic therapy – A light-sensitive cream is applied to the affected skin, and a laser is directed onto the skin four to six hours later, to destroy the abnormal cells.

Wu, M-F., Lv, T. & Wang, H.W. 2020.

“Bowen's disease, also named squamous cell carcinoma in situ, is usually treated by surgical excision. However, surgery is not suitable to patients with large area of lesions, multiple lesions or in cosmetically important areas where a scar will be visible. Photodynamic therapy (PDT) has advantages of efficacy, safety, and does not generally induce scar or damage to joint function. It could also be used repeatedly. Therefore, PDT might be recommended to treat multiple Bowen's disease. This report shared a case of a patient having suffered from multiple Bowen's disease successfully treated by PDT. PDT not only avoided scars and joint dysfunction, but also raised quality of the patient's daily life.”

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Zhong, S., Zhang, R., Mei, X. & Wang, Li. 2020.

Background: This is a systematic review and meta-analysis on the effectiveness of Photodynamic Therapy (PDT) in Bowen's Disease (BD), with further summary of the data from all randomized controlled trials (RCTs).

Methods: Relevant data were extracted after conducting a literature search via PubMed, Embase, Scopus, the Cochrane Library, CNKI, and Wanfang databases, from inception until 31 July 2019. Meta-analyses of the data were performed using RevMan V.5.3. A total of 392 published RCTs related to the efficacy of PDT in BD treatment were identified. The papers were screened for duplicates and excluded based on title and abstract. Subsequently, 85 full-text articles were thoroughly reviewed and finally, data from 446 patients with 1147 skin lesions across 12 eligible studies were collated.

Results: Our findings revealed significant differences between the efficacies of PDT and other treatments, where a higher lesion reduction rate was observed after the first treatment session following PDT ($P < 0.00001$, $Z = 4.98$). PDT was found to be more effective than 5-fluorouracil ($P < 0.00001$, $Z = 4.42$) and cryotherapy ($P = 0.008$, $Z = 2.67$). However, there were no significant differences in recurrence rates following treatments with PDT, cryotherapy, and 5-fluorouracil.

Conclusions: This systematic review and meta-analysis confirms and collates data from all RCTs pertaining to the efficacy of PDT for BD treatment. Our study has reiterated that PDT is more effective than 5-fluorouracil and cryotherapy for the treatment of BD.

Min-Feng, Wu, Ting, Ly. & Hong-Wei, Wang. 2020.

“Bowen's disease, also named squamous cell carcinoma in situ, is usually treated by surgical excision. However, surgery is not suitable to patients with large area of lesions, multiple lesions or in cosmetically important areas where a scar will be visible. Photodynamic therapy (PDT) has advantages of efficacy, safety, and does not generally induce scar or damage to joint function. It could also be used repeatedly. Therefore, PDT might be recommended to treat multiple Bowen's disease. This report shared a case of a patient having suffered from multiple Bowen's disease successfully treated by PDT. PDT not only avoided scars and joint dysfunction, but also raised quality of the patient's daily life.”

Aguilar-Bernier, M., Rodríguez-Barón, D., Rivas-Ruiz, F., Segura-Palacios, J.M. & de Troya Martín, M. 2019.

BACKGROUND: Photodynamic treatment with methyl aminolevulinate (MAL-PDT) is considered an effective and highly recommended treatment for Bowen's disease. However, its long-term efficacy remains to be established, as significant differences have been reported in this respect.

OBJECTIVE: The aim of the present study was to describe the results of a retrospective analysis of patients with Bowen's disease treated with MAL-PDT during the period 2006-17 at the Costa del Sol Hospital (Marbella, Spain).

MATERIAL AND METHODS: This study is based on a retrospective descriptive analysis of the clinical records of patients treated with MAL-PDT from June 2006 to September 2017. The analysis was based on calculating the mean and standard deviation values for the quantitative variables, and frequency distributions for the qualitative ones. The survival curves were plotted by the Kaplan-Meier method, and the log-rank test was used to assess differences in survival between groups. A cox regression analysis was performed to clarify the significant prognostic factors.

RESULTS: A total of 537 tumours with histologically confirmed Bowen's disease were treated with MAL-PDT. Recurrence-free survival at one year was 88%, and at 5 years, 71%. Tumour size $>300 \text{ mm}^2$ ($\geq 21 \text{ mm}$ in diameter $P = 0.019$), its location in the upper extremities ($P = 0.029$) and patient's age <70 years ($P = 0.028$) were all associated with an increased risk of recurrence.

LIMITATIONS: Given the retrospective design of our study, the possible existence of information bias cannot be ruled out.

CONCLUSIONS: Although it is an appropriate treatment option for patients with Bowen's disease, MAL-PDT presents a risk of recurrence of almost 30% at 5 years. Larger lesions (>300 mm² ; ≥21 mm in diameter) are more likely to recur than smaller ones. Therefore, appropriate selection is needed of the tumour to be treated, and prolonged follow-up should be provided.

- Surgery – The abnormal skin is cut out and stitches may be needed afterwards.

Lee, D.W., Ahn, H.H., Kye, Y.C. & Seo, S.H. 2018.

“There are only a few anecdotal case reports about Bowen's disease (BD) treated with ingenol mebutate (IM) gel but no clinical study has been published yet. The aim of this study was to evaluate the effectiveness of IM gel in the treatment of BD and to observe the therapeutic efficacy of IM alone or IM with ablative fractional laser pretreatment. Nineteen patients with BD or squamous cell carcinoma in situ confirmed by skin biopsy were enrolled. IM was applied with 0.015% gel on facial lesions for 3 days consecutively and 0.05% gel on other sites for 2 days consecutively, with a 5-mm application margin around the visible lesion. Nine patients applied IM gel immediately following fractional CO₂ laser treatment. Two patients were lost to follow up and a total of 17 patients were enrolled. Nine patients (9/17, 52.9%) had a clinically complete response at 2 months after treatment. Among the patients treated with the fractional CO₂ laser before applying IM gel, eight (8/9, 88.9%) showed a complete response and one (1/9, 11.1%) showed partial response. Among the patients treated with IM gel alone, only one patient (1/8, 12.5%) showed a complete response, four (4/8, 50%) showed a partial response and three (3/8, 37.5%) did not respond to therapy. IM gel alone seems to have limited value for treatment of BD; however, a combination therapy with the ablative fractional laser can increase its therapeutic effectiveness.”

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The **South African National Clinical Trials Register** provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Bowen's Disease

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Bowen's Disease 2

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<http://www.derm101.com/dpc/october-2012-volume-2-no-4/the-centennial-of-bowens-disease-a-critical-review-on-the-occasion-of-the100th-anniversary-of-its-original-description/>

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