Current therapies for Bowen's disease

Bowen's disease is a squamous cell carcinoma *in situ*. GPs play an important role in identifying and treating patients with this condition and, where appropriate, referring patients to a specialist. Different therapeutic modalities are currently available to GPs to treat Bowen's disease.

GILBERTO MORENO
MD

ADRIAN LIM
FRACGP, FACD

STEPHEN SHUMACK
FACD

Dr Moreno is a Resident Medical Officer at The Royal North Shore Hospital of Sydney, St Leonards. Dr Lim is a Consultant Dermatologist at uRepublic, Sydney. Dr Shumack is a Consultant Dermatologist at The Royal North Shore Hospital of Sydney, St Leonards, NSW.

Bowen's disease is a common but under-recognised skin condition. Patients with Bowen's disease commonly present to GPs with concerns about the appearance and nature of their condition. The GP's role is to correctly diagnose the lesion, treat according to the practitioner's resources and experience, or to refer the patient to a specialist for definitive management or reassurance. This article emphasises the clinical features and treatment options that can be selected for Bowen's disease.

Definition

Bowen's disease is a squamous cell carcinoma (SCC) *in situ*. It is, therefore, by definition confined to the epidermis and has no metastatic potential; however, up to 5% of lesions may progress to become an invasive SCC. Different aetiological factors including chronic sun damage, arsenic exposure and human papillomavirus (HPV) infection have been associated with the development of Bowen's disease. In this article, Bowen's disease caused by chronic sun exposure will be discussed, because it is by far the most common form seen in Australia.

Epidemiology and demographics

The annual age-incidence for SCC and related keratinocytic tumours (e.g. Bowen's disease and keratoacanthoma) is estimated to be 387 per 100,000 in Australia.[1] This is largely dependent on the age and skin type of the patient, and history of chronic sun exposure. Older individuals born in Australia and with a fair complexion are at a much higher risk of developing a SCC.

An Australian analysis of 1001 biopsies of Bowen's disease showed a male to female ratio of 1:1.3.[2] A peak age of between 70 and 79 years was identified for both sexes. Interestingly, after the age of 60 years, however, female cases of Bowen's disease outnumbered male cases.

IN SUMMARY

- **Bowen's disease is a squamous cell carcinoma *in situ* that may become invasive in up to 5% of cases.**
- **In Australia, chronic sun exposure is by far the most common cause of Bowen's disease.**
- **The GP's role is to identify and treat Bowen's disease according to the practitioner's resources and experience, or refer the patient to a specialist for definitive management or reassurance.**
- **A number of therapies are accessible to the GP to treat Bowen's disease; however, the outcome is dependant on the practitioner's skill and the choice of therapy.**

Downloaded for personal use only. No other uses permitted without permission. © MedicineToday 2008.

Clinical presentation

Bowen's disease often presents as sharply demarcated, scaly, erythematous plaques (Figure). These lesions usually enlarge very slowly overtime. Bowen's disease can also present with less common clinical features such as in verrucous, pigmented or hyperkeratotic forms.

Anatomical distribution is primarily related to the cause (sun exposure). In general, Bowen's disease on sun-exposed areas will most likely be related to chronic sun damage, whereas lesions on the palms or the soles are more likely due to occupational-related arsenic exposure. Bowen's disease affecting the genital, anal or perianal area are more likely due to HPV infection.

Sites that are affected by sun-related Bowen's disease are usually distributed differently in males and females. This is because the areas affected by chronic sun exposure vary between the sexes. Face and neck is the most common site affected by Bowen's disease in both sexes. Scalp and ears are more commonly affected in men, whereas the cheeks tend to be more commonly involved in women.

The lower limb is a site that is also commonly affected by Bowen's disease. A sex-related difference is clear with more women having Bowen's disease below the knee. Bowen's disease in this area may need special consideration with regards to treatment because of a slower healing time. The back of the hands is another common site of involvement in which no sex-related difference has been identified.

The least common site affected by Bowen's disease is the torso, where the chest and back are more frequently involved compared with the abdomen. Gender, dress style, hair pattern and distribution, and sun protection practices of the patient need to be taken into account when considering the site distribution of sun-related Bowen's disease.

Differential diagnoses

Eczema, psoriasis, fungal infection, superficial basal cell carcinomas and invasive SCCs are all differential diagnoses of Bowen's disease.

Eczema and psoriasis tend to be symmetrical and generalised in appearance with multiple areas of involvement, and patients usually have a positive past and/or family history. Eczema is invariably itchy and is often accompanied by skin thickening from scratching. Psoriasis classically presents as indurated, red, scaly plaques with well-defined borders. Nail and scalp psoriatic changes will further assist with the diagnosis. Lesions caused by fungal infections typically have an active erythematous edge with central clearing.

Superficial BCCs can be difficult to distinguish from Bowen's disease, but the former may have a typical pearly appearance when stretched, rolled borders and surface telangiectasis. Invasive SCC is a more advanced progression of Bowen's disease and is usually more indurated, nodular and circumscribed.

Bowen's disease of unusual sites such as the digits, finger nails (periungal or subungal), mucous membranes and genitalia need to be further investigated to exclude chronic arsenicism and HPV infection. Diagnosis of Bowen's disease in these specific areas is difficult and may rely more on a histopathological confirmation rather than clinical inspection.

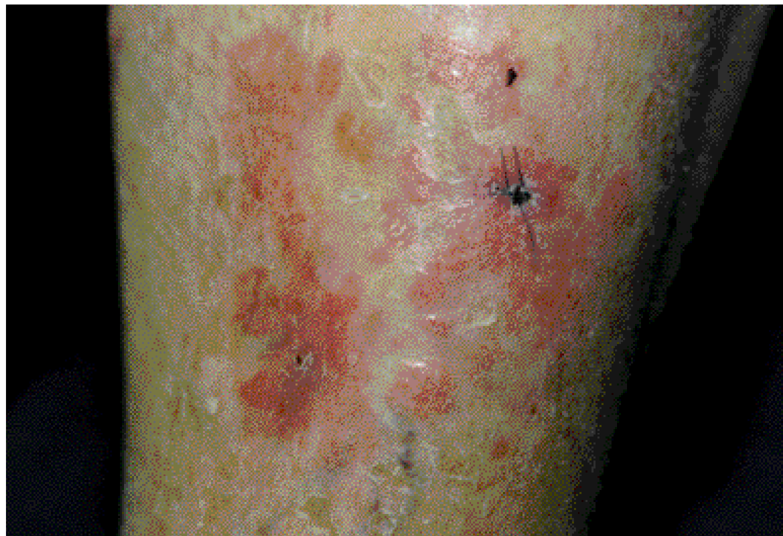


Figure. Bowen's disease of the lower limb.

Biopsy

When a clinical diagnosis cannot be established or suspicion of invasive disease arises, a biopsy should be undertaken. To obtain a tissue sample, shave or punch biopsies are needed. Dermal tissue needs to be included in the biopsy because it is important to rule out an invasive SCC, especially with large and/or multiple lesions of Bowen's disease. Multiple biopsies are often required for

Downloaded for personal use only. No other uses permitted without permission. © MedicineToday 2008.

continued

Summary of the therapies available for Bowen's disease

Cryotherapy
- Widespread accessibility, low cost and easy to use
- Preferred choice for single and small lesions
- In areas of poor healing or poor vascularity (e.g. the shins), this therapy should be used with caution
- A 30-second single freeze-thaw cycle is recommended to achieve low recurrence rates (0 to 0.8%)

Curettage and cautery
- Cost effective
- To decrease recurrence rate, it should be repeated up to three times
- Efficacy is related to the clinician's skill
- Short healing times and few complications when used in poorly vascularised areas

Surgery
- Indications for surgery are very specific – good choice in areas of small lesions and poor vascularisation
- Treatment of choice for perianal and anal Bowen's disease

Topical 5-fluorouracil
- High cure rate (87 to 92%) when used twice daily for eight weeks
- Common side effects include irritation of the skin, ulceration and superinfection

Radiotherapy
- Effective and beneficial for recurrent lesions, HPV-induced Bowen's disease or lesions on special anatomical areas
- Major complications can occur

Imiquimod
- A new therapy that is not TGA approved for Bowen's disease
- Cosmetic outcome is superior
- Clearance rates of 75 to 93%
- Effective for genital and perianal lesions
- Follow-up studies are required to assess long-term efficacy
- Expensive

PDT using methyl aminolevulinate
- A new therapy that is TGA approved for Bowen's disease
- Used on small or large lesions on poorly vascularised sites
- Clearance rates vary from 69 to 100%
- Cosmetic outcome is superior
- Follow-up studies are required to assess long-term efficacy
- Expensive

large lesions or where there is increased thickness within areas of the Bowen's disease.

Treatment

Different therapeutic modalities are available for the management of Bowen's disease. Evidence is currently more supportive of the newer therapies, whereas experience and cost-effectiveness support more traditional methods of treatment (see the box on this page for a summary of the therapies for Bowen's disease). Factors that should be taken into consideration when treating Bowen's disease include the size and number of lesions, availability of therapy, the clinician's expertise, the patient's preference and the site of involvement.

Cryotherapy

Cryotherapy refers to a method whereby complete destruction of the tumour is achieved with a cryogenic agent. Due to its widespread accessibility, low cost and ease of use, cryotherapy with liquid nitrogen is the preferred choice for single and small lesions of Bowen's disease. However, in areas of poor healing or poor vascularity (e.g. the shins), cryotherapy should only be used with great caution. Up to a 30-second single freeze-thaw cycle is recommended to achieve low recurrence rates (0 to 0.8%).

Repeated and longer freezing-thaw cycles are associated with delayed healing and increased complications such as ulcer development and infections.

Curettage and cautery

Curettage and cautery is a specialised method that consists of removing the lesion with a curette and following this with desiccation of the base with electrocautery. The procedure is repeated up to three times to decrease the recurrence rate. Curettage and cautery is often performed by experienced GPs with a special interest in skin conditions. However, the efficacy of this technique is related to the clinician's skill. A 93 to 98% cure rate has been reported with the correct use of this technique.

Curettage and cautery has been advocated as one of the most cost-effective therapies. When used in poorly vascularised areas, it also has the advantage of shorter healing times and fewer complications compared with other therapies.

Some specialists combine curettage with cryotherapy or CO_2 laser, instead of cautery, but no additional benefit has been proven with either option.

Surgery

Complete primary excision with histological confirmation of successful removal of the tumour is the goal of surgery. Although cosmetic outcome, patient preference and healing properties of the area involved with Bowen's disease play an important role when considering surgery, the indications for this therapy are very specific. Surgery is considered a good choice in areas with small lesions and poor vascularisation. It is also considered the treatment of choice when treating perianal and anal Bowen's disease secondary to HPV infection. Other sites affected by Bowen's disease can be treated effectively with less destructive methods.

Topical 5-fluorouracil

Topical 5-fluorouracil (Efudix), a cytotoxic agent, can also be used to treat Bowen's disease. This therapeutic option induces cell death in tumour cells and has a high cure rate (87 to 92%) when used twice daily for eight weeks. Treatment of patients with topical 5-fluorouracil requires

Downloaded for personal use only. No other uses permitted without permission. © MedicineToday 2008.

close supervision because common side effects (e.g. irritation of the skin, ulceration and superinfection) can develop quickly during treatment.

Radiotherapy

Radiotherapy has been described as a very effective therapy for Bowen's disease. Nevertheless major complications such as nonhealing and radiation damage to adjacent skin do not warrant its use for simple, small, solitary or multiple lesions that can be effectively treated by other methods. The role of radiotherapy is more beneficial for patients who have recurrent lesions or HPV-induced Bowen's disease or in those who have the condition in special anatomical areas such as the fingers.

New therapeutic options

New therapeutic options, such as imiquimod (Aldara) and photodynamic therapy have been developed over the past decade and are now available for the management of Bowen's disease. At present, imiquimod is not TGA-approved for the treatment of Bowen's disease so its use is on an 'off-label' basis. Imiquimod is a topical immune response modifier, which ultimately modulates an immune response against tumour cells. This tissue-sparing method has been used to treat Bowen's disease in comparative trials and other open-label studies with clearance rates of 75 to 93%. Imiquimod has also been reported as an effective therapy for genital and perianal lesions.

Photodynamic therapy using methyl aminolevulinate (Metvix) is TGA approved for the treatment of Bowen's disease. This therapy is based on the destruction of tumour cells absorbing a photosensitising agent (methyl aminolevulinate), which is later activated by a specific light source. This normal-tissue sparing method is of great advantage when used on small or large lesions on poorly vascularised sites. Clearance rates vary from 69 to 100%, but as with imiquimod, follow-up studies are required to assess the long-term efficacy of these methods.

Comparative studies show that both of these less destructive options are equally effective to the other therapies summarised above. Cosmetic outcome is also superior to the more traditional treatment modalities. Cost of therapy is a major issue with both of these new treatment options.

Conclusion

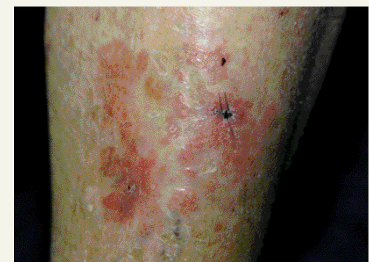
Bowen's disease is a relatively common and often overlooked condition that rarely progresses to an invasive SCC. Its diagnosis can be simple when it presents with typical clinical features; however, a biopsy may be required to help with the diagnosis or to document the presence of an invasive SCC. Multiple therapeutic options are available, but the choice is based on the size, number and location of lesions, accessibility of therapies and patient preference. Long-term follow-up (more than two years) is essential when assessing the efficacy of a given therapy. MT

References

1. Staples M, Elwood M, Burton RC, Williams JL, Marks R, Giles GG. Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985 Med J Aust 2006; 184: 6-10.
2. Kossard S, Rosen R. Cutaneous Bowen's disease. An analysis of 1001 cases according to age, sex and site. J Am Acad Dermatol 1992; 27: 406-410.

COMPETING INTERESTS: Dr Shumack and Dr Lim have previously received study grants and speaking honoraria from 3M, the previous owners of imiquimod. Dr Moreno: None.

Online CPD Journal Program



Bowen's disease is a form of glomerulonephritis – true or false?

Review your knowledge of this topic and earn CPD/PDP points by taking part in Medicine Today's Online CPD Journal Program.

Log on to **www.medicinetoday.com.au/cpd**

Downloaded for personal use only. No other uses permitted without permission. © MedicineToday 2008.