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Review Article

Management of cutaneous intra-epithelial squamous cell carcinoma (Bowen's disease)

Ahmed Nadeem Abbasi

Deptartment of Radiation Oncology, Faculty of Health Sciences, Aga Khan University, Karachi.

Abstract Bowen's disease is an intraepithelial squamous cell carcinoma. The disease commonly affects fair skin people. This review article focuses on the advances in the treatment of this disease including different medical and surgical modalities.

Key words
Skin cancer, Bowen's disease, radiotherapy, cryotherapy, photodynamic therapy, laser.

Background

Cutaneous intra-epithelial squamous cell carcinoma commonly known as Bowen's disease is more frequently seen in women and most of the patients present with these lesions between the ages of 60-70 years.[1,2] Women constitute about 2/3rd of all the patients presenting with this disease. Most of the lesions occur on the sun exposed areas of the body e.g. head and neck and lower leg.[1,3] In our oncology practice highest cure rates are achieved in cutaneous malignancies. These malignancies are more common in the West in fair skin people. In the Northern mountainous areas of Pakistan a wide range of skin conditions are prevalent, which include pre-malignant and malignant diseases as well. A clinical correlation of pathognomonic features is quite important as the primary modality of treatment varies from one disease to other. A spot diagnosis of cutaneous lesions, which is done during the first oncology consultation, is not sufficient. An accurate and thorough histopathological diagnosis is established before making any decisions regarding the management.

At the time of commissioning of modern radiation oncology facilities in Europe and North America a superficial X- ray therapy unit is allocated that is exclusively used for the treatment of Skin tumours.Low energy electrons delivered by Linear Accelerators serve the same purpose. In case of electron therapy a tissue equivalent bolus is used in order to build up dose to the skin surface.

Etiology

The exact etiology of Bowen's disease is not known. It has been suggested that occupational, environmental and medical exposure to arsenic can result in the development of intra-epithelial squamous cell carcinoma.[4] These patients are not at increased risk of developing internal malignancies.[5]

Address for correspondence
Dr. Ahmed Nadeem Abbasi,
Consultant Radiation Oncologist &
Assistant Professor,
Aga Khan University Hospital,
PO Box No; 3500
Stadium Road, Karachi 74800
Tel # 021 486 1880, Fax # 021 493 4294
E mail: nadeem.abbasi@aku.edu

Clinical features

Patients present with isolated scaly erythematous patch with irregular margins on the exposed parts of body. Histological examination of the lesion is important in order to identify whether it is benign or malignant. It also helps in differentiating lesions due to actinic keratosis, basal cell carcinoma, squamous cell carcinoma, seborrhic keratosis, psoriasis and eczema.[6,7] Clinical and histological similarities between various types of skin malignancies are quite common. A meticulous clinical examination complemented by a thorough histopathological assessment is recommended before making a conclusive diagnosis of skin lesions. One cannot label Bowen's disease as an innocent or benign condition .It has been reported in a cohort based population study of 1147 patients with skin cancers that there is a four-fold increased incidence of non-melanoma skin cancer in patients with intra-epithelial squamous cell carcinoma.[3]

Role of radiotherapy

The rationale of employing external beam radiation treatment was studied in various clinical studies. Two studies in patients with intra-epithelial squamous cell carcinoma treated with radiotherapy have shown cure rates of 100% with only 6% rate of local recurrences.[2,8]

A non-randomised study performed on patients with lesions on lower leg comparing external beam radiotherapy and cryotherapy,[8] has found poor healing in 20% of patients treated with radiotherapy and only 2% in patients treated with cryotherapy. Hence the high cure rate of radiotherapy is at the expense of impaired healing. Delayed or impaired wound healing can lead to major quality of life issues particularly in older patients. Lower limb lesions treated by external beam radiotherapy take a longer time to heal and close follow up is required after the completion of treatment.

Depending on the site, extent and depth of lesion a superficial X ray or electron energy is selected and an area around the visible lesion is included in the treatment field. This is regarded as a safe margin covering any potential microscopic extension of the carcinoma. Ninety kilovoltage superficial X-ray machine delivers 100% dose to the skin surface which drops down to 89% at a depth of 5 millimeters.

Another retrospective study involving 11 patients aged 75 or over, with a total of 16 lesions located on the lower leg found that most of the lesions healed and only 25% developed non-healing ulcers after a median follow-up of around 28 months. The authors concluded that care should be undertaken in attempting radiotherapy for cutaneous lesions situated at the lower extremity.[9]

5-Fluorouracil (Efudix®) cream

5-Fluorouracil (5-FU) in the strength of 5% in cream form is the only licensed preparation of topical 5-FU available in the market. It is applied once or twice a day for 3-4 weeks.[10] 5-FU is extensively used as a cytotoxic agent in the treatment of various visceral cancers, notably in head and neck and gastro-intestinal malignancies. In one study of 41 lesions measuring about 1.5-

6.2cm in diameter on head, neck and limbs in 39 patients showed that all patients were cured (clinically clear of disease) with one or two application of topical fluorouracil (1-3%concentration, applied twice daily for 4-12 weeks).[11]

Cryotherapy

Randomised studies involving patients treated with liquid nitrogen cryotherapy have reported cure rates of 97-100%, with local recurrence rate of 10-50% of patients.[2] Patients with larger or multiple lesions when treated with cryotherapy developed local discomfort (95%), blisters (35%) and ulcerations (25%). Therefore, its clinical use is limited.[12]

Surgical approach

Surgical excision is not appropriate for patients with lesions that are large or numerous or where healing is poor.[13] Curettage is another way of surgical removal of Bowen's lesions. Healing is better with curettage than cryotherapy and the overall recurrence rate is of the order of 20 %.[13] Curettage is regarded as a convenient option for small lesions as it is simple to perform.

Photodynamic therapy

It involves application of aminolaevulinic acid (ALA) to the lesions as ALA is taken up by the dysplastic cells in 3-6 hours. Then patient is exposed to red light as this promotes conversion of ALA to protoporphyrinIX (PPIX) by cellular enzymes[13,16] and causes cellular damage by production of oxygen free radicals. In a study comparing photodynamic therapy and cryotherapy, more lesions cleared with a single treatment with photodynamic therapy (75%) than with cryotherapy (50%). Post-treatment complications were less common with photodynamic therapy.[12]

Photodynamic therapy is a useful option in patients with larger lesions that are refractory to other forms of treatment. The Scottish Photodynamic Therapy Centre has carried out 3,442 treatments on 762 patients with superficial skin lesions, especially superficial basal cell carcinoma, Bowen's disease and actinic keratosis. In their experience, topical photodynamic therapy is generally well tolerated and is an effective treatment of Bowen's disease.[14]

Laser

Gordon *et al*. have achieved good local control and have claimed a cure rate of the order of 80% in patients who were treated with carbon dioxide laser vaporization for Bowen Disease lesions on digits.[15] Similar results are reported by Kerrar *et al*.[16]

Surveillance

Patients with small and slow progressing lesions in poor healing areas are managed by watchful waiting. In these patients, morbidity from poor healing due to active treatment might exceed that from the original disease and death from unrelated disease is more likely. A case of Bowen's disease showing a clinical tendency towards spontaneous regression is being reported by Nihei *et al*. from Japan. The patient, a healthy 86-year-old woman, had Bowen's disease presented as an erythematous lesion situated on her left forearm. Over a period of

two years the lesion had gradually enlarged. At the first examination, it was a well-demarcated, 4x3 cm, erythematous plaque, partially covered with crusting and erosions near the wrist. Diagnosis of Bowen's disease was confirmed by a biopsy. Since the patient refused surgery and also discontinued hyperthermic treatment with disposable chemical pocket warmers after a brief trial, it was decided to continue the observation of disease progression without any treatment. Two years after the initial visit, the lesion showed a clinical tendency towards spontaneous regression, with a fine erythematous plaque that showed the obscurely demarcated border of the lesion. After three years the patient exhibited a similar symptomatic improvement and a skin biopsy showed a few residual tumor cells.[17]

Summary of management options

At good healing sites a small lesion can be managed with curettage, cryotherapy and excision where as a larger lesion or multiple lesions require cryotherapy, photodynamic therapy[18] and fluorouracil. At poor healing sites such as lower leg and patients who have peripheral vascular disease or oedema or for patients who are obese, a small lesion can be managed with curettage but a larger and multiple lesions[19] need treatment with fluorouracil and photodynamic therapy. It represents early SCC confined to the epidermis. The vast majority of Bowen's disease lesions are asymptomatic. Each suspicious lesion should be treated before it progresses to invasive squamous cell carcinoma. Destructive modalities, such as cryosurgery using liquid nitrogen and electrodessication and curettage, usually performed by a dermatologist, are the mainstay of therapy.[20]

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