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E-CASE RESEARCH

Treatment of Bowen Disease With Photodynamic Therapy and the Advantages of Sequential Topical Imiquimod☆

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KEYWORDS
Bowen disease;
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Treatment

Abstract Photodynamic therapy (PDT) has been shown to be useful and effective in the treatment of actinic keratosis, Bowen disease, and basal cell carcinoma. We present a series of 13 Bowen disease lesions treated using PDT. Complete responses were achieved in 11 (84%) of the lesions after 3 months of treatment; at 18 months, complete responses were seen in 9 (70%) of the lesions. Patients who presented a partial response or recurrence were treated with topical 5% imiquimod and achieved complete responses. The lesions that presented partial response or recurrence were the largest lesions, between 3 and 5 cm in diameter. PDT in monotherapy or combined sequentially with imiquimod is an excellent and well-tolerated therapeutic option for Bowen disease. The treatment has few adverse effects and shows satisfactory results, particularly in multiple large lesions in areas of difficult surgical reconstruction or in elderly patients with a high surgical risk.

PALABRAS CLAVE
Enfermedad de Bowen;
Terapia fotodinámica;
Imiquimod tópico;
Tratamiento

Tratamiento de la enfermedad de Bowen con terapia fotodinámica y ventajas de la aplicación secuencial de imiquimod tópico

Resumen La terapia fotodinámica (TFD) ha demostrado ser un tratamiento útil y eficaz en queratosis actínicas, enfermedad de Bowen (EB) y carcinoma basocelular. Presentamos una serie de 13 lesiones de EB tratados con TFD. A los 3 meses del tratamiento 11/13 (84%) lesiones presentaron respuesta completa. A los 18 meses la respuesta completa fue de 9/13 (70%) lesiones. Los pacientes que presentaron respuesta parcial o recidiva fueron tratados con imiquimod tópico al 5%, con la consiguiente respuesta completa. Las lesiones con respuesta parcial o recidiva fueron las de mayor tamaño: entre 3 y 5 cm de diámetro. La TFD en monoterapia o combinada

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secuencialmente con imiquimod es una excelente opción terapéutica para la EB, bien tolerada, con mínimos efectos secundarios y unos resultados satisfactorios, y sobre todo indicada en lesiones de gran tamaño, múltiples, en áreas de difícil reconstrucción quirúrgica o en pacientes ancianos con riesgo quirúrgico elevado.

Introduction

Bowen disease (BD) is a squamous cell carcinoma (SCC) in situ. It typically affects elderly patients and usually manifests as a slow-growing solitary erythematous, scaling plaque that can reach a considerable size. Lesions are mainly located on the head, the neck, or the extremities.

Several treatment options exist, including surgery, electrocoagulation, cryotherapy, 5-fluorouacil, 5% imiquimod, laser therapy, radiation therapy, and photodynamic therapy (PDT).[1]

PDT is approved for the treatment of actinic keratosis, superficial and nodular basal cell carcinoma (BCC), and BD. It is a simple technique, suitable for outpatient use, and has proven to be both useful and effective in BD.

Topical 5% imiquimod has also been used in the treatment of BD. It has been combined with PDT to treat diverse forms of non-melanoma skin cancer, including BD, and the combination appears to have a synergic effect.

We present a series of 13 BD lesions treated with PDT or with PDT and topical imiquimod at our department.

Case Descriptions

Table 1 summarizes the characteristics of the 13 lesions treated with PDT at our department. The lesions corresponded to 10 patients (7 women and 3 men) and they were all biopsied to confirm diagnosis and in some cases to investigate suspected cases of partial clearance or recurrence.

Eleven lesions were treated with methyl aminolevulinate (MAL) 160 mg/g cream and 2 were treated with a 5-aminolevulinic acid (ALA) 78 mg/g nanoemulsion-based gel. The same PDT protocol was used in all cases. Following curettage of the area, the photosensitizing agent was applied to the lesion, which was covered with an occlusive dressing for 3 hours before illumination. The lesions were irradiated with red light (PDT 1200 L, Waldmann) at a wavelength of between 580 and 760 nm (dose, 75 J/cm^2; fluence, 69-75 mw/cm^2). All the patients were treated with 3 sessions, each separated by a week. The lesions were photographed before and after treatment. Patients with recurrent lesions or lesions that only partially cleared were treated with 5% imiquimod applied 5 times a week for 6 weeks.

The mean age of the patients was 85.4 years. The most common locations were the lower limbs (38%), the head (31%), the trunk (24%), and the upper limbs (7%).

Most patients had a history of prolonged sun exposure and 1 patient, a radiologist, had been chronically exposed to ionizing radiation at work. Seven (70%) of the 10 patients had a history of nonmelanoma skin cancer. One patient also had a systemic lymphoma being treated with chemotherapy (Fig. 1). Most of the lesions were large (mean diameter, > 3.5 cm).

Treatment response was evaluated at 3 and 18 months. At the 3-month evaluation, 11 of the 13 lesions (84.6%) had cleared completely, while the other 2 (15.4%) showed partial clearance. At the 18-month follow-up, 2 recurrences (18.1%) were detected among the 11 lesions that had initially cleared. The 2 recurrent lesions and the 2 that had responded only partially to PDT were treated with imiquimod. They all cleared completely (Fig. 2) and had not recurred at the time of writing. The 4 lesions were all large (5 cm, 4.5 cm, 4 cm, and 3 cm); 2 were located on the face, 1 on the leg, and another on the chest.

The most common adverse effect during PDT was pain, which was rated with a mean score of 5.2 on a visual analog scale of 1 to 10. None of the treatments had to be interrupted due to pain. Some patients were administered local anesthesia. Transient swelling and redness were also observed after illumination.

Sequelae consisted of hyperpigmentation or hypopigmentation of the treated area. The cosmetic results were very good (Fig. 3) and the patients were all very satisfied with the outcome.

Mean follow-up was 3 years (range, 18 months-7.5 years).

Discussion

We have reported on a series of patients with BD treated with PDT or with PDT and 5% imiquimod in the case of partial response or recurrence.

BD is an intradermal SCC. The risk of progression to invasive SCC has been estimated at between 3% and 8%, but it may be higher in the case of genital involvement (erythroplasia of Queyrat).[2,3]

PDT was approved for the treatment of BD in 2006. According to European guidelines, its use is supported by a level of evidence I and a strength-of-recommendation grade A. It is classified as a good or very good option for the treatment of large lesions, multiple lesions (which may need to be treated simultaneously), lesions in areas where surgical reconstruction is complicated, lesions in elderly patients with a high surgical risk, and lesions in immunosuppressed patients with altered wound healing.[4]

Several studies have shown that PDT is more effective and has fewer adverse effects than other nonsurgical alternatives.[5] Complete clearance rates of 86% to 93% were reported at 3 months following 1 or 2 cycles (separated by a