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CASE REPORTS

Photodynamic Therapy for Actinic Cheilitis

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Abstract. Actinic cheilitis is a subtype of actinic keratosis that mainly affects the lower lip and has a higher risk of malignant transformation. Its location on the labial mucosa influences the therapeutic approach. Vermilionectomy requires local or general anesthetic and is associated with a risk of an unsightly scar, and the treatment with 5-fluorouracil or imiquimod lasts for several weeks and the inflammatory reaction can be very intense. A number of authors have used photodynamic therapy as an alternative to the usual treatments. We present 3 patients with histologically confirmed actinic cheilitis treated using photodynamic therapy with methyl aminolevulinic acid as the photosensitizer and red light at 630 nm. The clinical response was good, with no recurrences after 3 to 6 months of follow-up. Our experience supports the use of photodynamic therapy as a good alternative for the treatment of actinic cheilitis.

Key words: actinic cheilitis, treatment, photodynamic therapy.

TRATAMIENTO DE QUEILITIS ACTÍNICAS CON TERAPIA FOTODINÁMICA

Resumen. La queilitis actínica es un subtipo de queratosis actínica que afecta fundamentalmente al labio inferior y tiene un riesgo incrementado de transformación carcinomatosa. La localización en la mucosa labial condiciona las distintas posibilidades terapéuticas. La bermellectomía obliga a realizar anestesia local o general y se asocia con un riesgo de cicatriz inestética; el tratamiento con 5-fluorouracilo o imiquimod se prolonga a lo largo de varias semanas y la reacción inflamatoria puede ser muy intensa. Varios autores han empleado la terapia fotodinámica como una alternativa a los tratamientos habituales. Presentamos a tres pacientes con queilitis actínica confirmada histológicamente que fueron tratados con terapia fotodinámica utilizando ácido metilaminolevulínico como fotosensibilizante y luz roja de 630 nm. La respuesta clínica fue buena, con ausencia de recidiva al cabo de 3 a 6 meses de seguimiento. Nuestra experiencia avala el empleo de la terapia fotodinámica como una buena alternativa terapéutica para la queilitis actínica.

Palabras clave: queilitis actínica, tratamiento, terapia fotodinámica.

Introduction

Actinic cheilitis is a subtype of actinic keratosis that mainly affects the lower lip and is caused by chronic exposure to sunlight. Like actinic keratosis, it is considered a premalignant lesion. Several factors aggravate this condition. The percentage of transformation into squamous cell carcinoma was as high as 16.9% in some series.[1] Furthermore, squamous cell carcinoma of the lip metastasizes up to 4 times more frequently than that of the skin, with percentages that range between 17% and 25%.[2]

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The location of actinic cheilitis on the lower lip influences the therapeutic approach. Many of the treatments applied have disadvantages, such as a prolonged treatment and recovery period, unsightly results, or even limited efficacy. Among the ablation therapies are cryotherapy and electrocoagulation. Both are appropriate techniques for localized actinic cheilitis, but with more extensive lesions, they usually lead to hypopigmented scars and prolonged recovery times (approximately 3 weeks). Topical chemotherapy (5-fluorouracil) and immunomodulators (imiquimod) can be used in more extensive actinic cheilitis; however, treatment and recovery time take several weeks, and the low level of patient compliance due to the intense inflammatory reaction seems to lead to failure rates as high as 60%.[3] Vermilionectomy requires local or general anesthesia and is associated with a risk of unsightly scarring.

Photodynamic therapy (PDT) is an accepted treatment for actinic keratosis, Bowen disease, and superficial basal

Figure 1. Actinic cheilitis on the lower lip of patient 1.

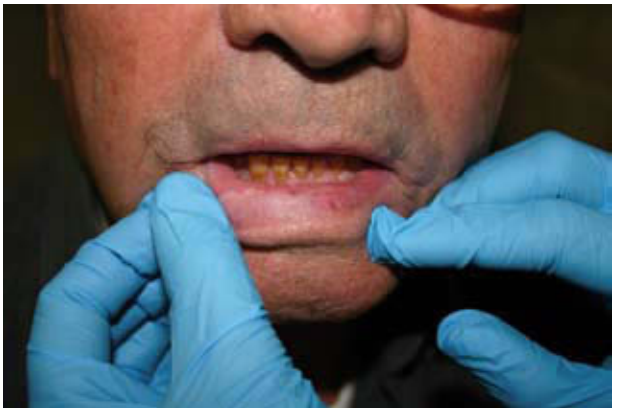

Figure 2. Complete remission after 5 months of treatment with photodynamic therapy.

cell carcinomas. In 1996, Stender and Wulf[4] published the first cases of patients with actinic cheilitis treated with PDT. We present 3 patients who underwent this treatment.

Case Descriptions

Patient 1 was a 70-year-old man with arterial hypertension, diabetes mellitus, and dyslipidemia, attended for a crusty bleeding lesion located on the lower lip which had been progressing for 1 month (Figure 1). Histological study showed atypical cells in the epithelium, without underlying infiltrates. The lesion was treated using PDT by applying methyl aminolevulinic acid (MAA) under occlusion for 3 hours, followed by exposure to red light at 630 nm (Omnilux) in a single session at a dose of 50 J/cm^2, with an excellent outcome after 5 months (Figure 2). The session was well-tolerated without requiring regional nerve block or local anesthesia.

Patient 2 was 56-year-old man with nothing of interest in his clinical history, attended for a crusty lesion on the lower lip that had been progressing for 1 year. Histological study confirmed this as ulcerated actinic cheilitis. He was a smoker who consumed 1.5 packs/day and his work (in construction) involved extensive exposure to sunlight. No treatment other than emollients had been applied. The lesion was treated using PDT by applying MAA under occlusion for 3 hours, followed by exposure to red light at 630 nm (Omnilux) in 2 sessions separated by 1 month; the first at a dose of 60 J/cm^2 and the second at 80 J/cm^2. The sessions were well-tolerated without requiring regional nerve block or local anesthesia. The response was good with no recurrence after 6 months.

Patient 3 was a 63-year-old man with no clinical history of interest, nonsmoker, with erythema and diffuse desquamation of the lower lip in progression for several months. Histological study confirmed the lesion as actinic cheilitis. It was treated by applying MAA under occlusion for 3 hours, followed by exposure to red light at 630 nm (Omnilux) in 3 sessions at a dose of 60 J/cm^2, with a 1-month interval between them. Tolerance was acceptable, although the sessions had to be interrupted occasionally, but without requiring infiltration anesthesia or regional nerve block. The response was good 3 months after the final session.

Discussion

Topical PDT was described by Kennedy et al[5] as a therapeutic alternative for nonmelanoma skin cancer in 1990. Currently, it is routinely used to treat actinic keratosis and superficial basal cell carcinomas. Several studies have documented a response rate of 70% to 90% when using PDT to treat actinic keratosis, with good esthetic results and a high level of patient satisfaction.[6] Photodynamic therapy has been proposed as an alternative treatment for actinic cheilitis as it is a noninvasive technique that involves no risk of bleeding, extensive areas can be treated at the same time, and it provides excellent esthetic results without leaving residual scars.

A search of the literature found 6 studies in which PDT was used to treat actinic cheilitis[4,7-11] (Table). A total of 51 patients have been treated with this technique. The response was complete in 36 patients (70.5%) and partial in 10 (19.6%), having an efficacy that, depending on the series, ranged between 70% and 90%, and was similar to that established for actinic keratosis.

The basic procedure was similar in all cases, but there are certain differences. The photosensitizing agent used was 5-aminolevulinic acid (ALA)[4,7,8,11] in 33 patients, whereas MAL was used in 18.[9,10] The photosensitizing agent was maintained for 3 hours in all cases when MAL was used,[7,10] whereas when ALA was used the period ranged between 2 and 3 hours.[4,8,9,11] The greatest

Table. Clinical Data for Patients With Actinic Cheilitis Treated Using Photodynamic Therapy

	No./Age/Sex (M/F))	*Photosensitizer*	*Occlusion Time*	*Radiation Source*	*Dose Applied*	*No. Sessions*	*Response*	*Follow-up Time*
Sotiriou et al 2008[8]	10/60-71/10 M	5-ALA 20%	3 h	Waldmann PDT 1200/570-670 nm	40 J/cm^2	2	9 CR	3 mo
Kodama et al 2007[9]	1/67/F	5-ALA 20%	2 h	Excimer laser 630 nm	30 J/cm^2	5 (150 J/cm^2)	PR	NR
Berking et al 2007[7]	15/36-88/9 M; 6 F	MAA	3 h	Aktilite 630 nm	37 J/cm^2	2	7 CR, 7 PR, 1 NR	3 mo
Hauschild 2005[10]	3/58-81/1 M; 2 F	MAA	3 h	Aktilite 630 nm	20 J/cm^2	2	3 CR	13 mo
Alexiades 2004[11]	19/42-86/NR	5-ALA 20%	2 -3 h	PDL 595 nm	7-7.5 J/cm^2	3	13 CR, 2 PR, 1 NR	12 mo
Stender 1996[4]	3/59-74/2M; 1F	5-ALA 20%	3 h	Noncoherent light	55 J/cm^2	3	3 CR	6 -12 mo
Castaño 2008	3/56-70/3M	MAA	3 h	Omnilux 630 nm	50-80 J/cm^2	1-3	3 CR	6 mo

Abbreviations: ALA, aminolevulinic acid; F, female; M, male; MAA, methyl aminolevulinic acid; NR, not reported; CR, complete remission; PR, partial remission.

differences involved the light source. A Waldman PDT 1200 lamp was used at 570/670 nm in 10 patients,[8] an excimer laser at 630 nm in 1 patient,[7] an Aktilite lamp at 630 nm in 18 patients,[9,10] a PDL at 595 nm in 19 patients,[11] and noncoherent light in the first 3 patients.[4] As might be expected from such different light sources, the doses applied were also very different. There were even great variations when the same light source was used, as in the case of the Aktilite lamp: Berking et al[7] treated 15 patients with a dose of 37 J/cm^2, whereas Hauschild et al[10] applied 20 J/cm^2 in their 3 patients. Each patient essentially underwent between 2 and 3 sessions,[4,8-11] except in the case of the patient treated with an excimer laser,[7] who underwent 5 sessions.

Despite these differences, the efficacy of PDT and tolerance was similar in all cases. In general, the treatment was well tolerated. The patients reported mild to moderate pain during the session. Only one of the studies included, as part of the protocol, prior local anesthesia with mepivacaine 1%, and oral analgesia using 1 g paracetamol 1 hour before the session.[9] Infiltration anesthesia was not needed in the remaining published cases, and only in 1 patient, due to poor tolerance in the first session, was metamizole magnesium administered before the subsequent sessions.[10] All the patients described a burning sensation during the session and erythema was observed up to 1 week after the session. Swelling and blistering sometimes occurred. The maximum follow-up time was 13 months.

Our experience confirms the results reported in the literature. Our patients were treated with an Omnilux lamp, whose use has not been reported by any other author, and thus we lack a reference to which we can make an appropriate comparison. Although the wavelength used was 630 nm, like the Aktilite lamp, the manufacturers of the Omnilux lamp recommend a dose of 70 J/cm^2 as standard. While consensus on treatment protocol is lacking, we begin treatment with a conservative dose and decide to maintain or increase the dose depending on the response, though always staying within the range recommended for this lamp. The number of sessions ranged from 1 to 3, depending on the degree of response observed in each patient. Tolerance was good without the need for local or regional infiltration anesthetic or oral analgesia before the procedure. Complete remission was obtained at the conclusion of treatment, without observed recurrence after a follow-up time that ranged from 3 to 6 months.

However, a critical assessment of the cases described shows that it is difficult to draw uniform and definitive conclusions. The photosensitizer and the occlusion time varied between studies. At least 4 different light sources were used at different radiation doses, even when using the same light source, and with variations in the number of sessions. Most cases were clinically assessed, whereas histological assessment after treatment was only reported in 2 publications.[7,9] Thus, we consider that PDT is an effective and safe therapeutic option in actinic

cheilitis,[12] and one that provides excellent esthetic results. Nevertheless, the optimal dose and number of sessions required remains unknown, and a longer follow-up time is needed to determine recurrence rates.

Conflicts of Interest
The authors declare no conflicts of interest.

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