B. Duarte,* N. Cunha, A. Lencastre, J. Cabete

Servico de Dermatología, Hospital de Santo António dos Capuchos, Centro Hospitalario de Lisboa Central, Lisboa, Portugal

*Corresponding author.
E-mail address: brunoduarte@campus.ul.pt (B. Duarte).

25 December 2018 27 January 2019

https://doi.org/10.1016/j.adengl.2020.10.023

Actinic Cheilitis Treated With Daylight Photodynamic Therapy☆

Terapia fotodinámica con luz de día en el tratamiento de la queilitis actínica

To the Editor,

Actinic cheilitis is a chronic premalignant disease that generally affects the lower lip and that is considered equivalent to actinic keratoses of the skin.[1–3] Several treatments have been proposed for actinic cheilitis, but none of these are considered definitive. Daylight photodynamic therapy (PDT) is a widely used treatment for actinic keratoses and has shown efficacy similar to that of conventional PDT, with no or minimal pain.[4,5] The objective of our study was to describe the efficacy and safety of daylight PDT in the treatment of actinic cheilitis according to our experience. Between May and October 2018, 6 patients were treated. After gentle curettage, a roll of cotton wool was placed in the internal labial mucosa to expose the lower lip and sufficient quantity of methyl aminolevulinate cream was applied. Then exposure to ambient sunlight for 2 hours without occlusion was recommended. The rest of the skin was protected with factor 50+ sunscreen. After 2 hours of exposure, the treated area was washed and factor 50+ sunscreen was applied to the lip. Another session was performed 2 weeks later and the patients were examined after 2 months (Figs. 1 and 2). Patients were assessed with a clinical scale (affected area and complete/partial/no response) and a visual analogue scale (VAS) for pain. The characteristics of the study population and the outcomes of treatment are summarized in Table 1. Four of the patients (67%) showed complete response and 2 had a partial response with a mean reduction in the affected area of 58.3%. The mean score on the VAS was 0.5 out of 10.

Actinic cheilitis is a premalignant disease with a rate of transformation to squamous cell carcinoma (SCC) of 16.9% and a relative risk of 2.5 for developing this entity.[1,2] Furthermore, labial SCC has a 4-fold higher tendency for developing lymph node metastases compared with SCC on the skin.[6,7] Chronic exposure to ultraviolet radiation is the main risk factor implicated in the onset of actinic cheilitis, along with smoking and alcohol abuse.[3] Several different treatments have been used for actinic cheilitis, such as ablative methods (cryotherapy, CO_2 laser treatment), partial surgical resection, or vermilionectomy, and topical treatments such as imiquimod or 5-fluoracyl.[3,8] On the other hand, actinic keratoses are the skin equivalent of actinic cheilitis[3] and several different treatments similar to those listed above have been tried, although daylight PDT has also been used. This technique consists of a photosensitizing substance (MAL/5-ALA) that is activated by exposure to ambient sunlight (visible light) without the need for prior occlusion or exposure to red light from a lamp as is the case for conventional PDT.[4] Daylight PDT has been associated with efficacy rates similar to conventional PDT (clearance rate of 70% to 93% at 3 months after a single session[4,5]) with much better tolerance as there is no or minimal pain.[4] Conventional PDT has also been used in actinic cheilitis (15 previous studies)[3] with a mean clinical response of 60.25% and histological clearance of 47.4%.[3] Intense pain during treatment was the main side effect, requiring the administration of oral analgesics or local anesthetic.[3] Daylight PDT for actinic cheilitis has been used less frequently, and is only mentioned in 2 studies in the literature,[8,9] and in a description of 2 cases.[10] Fai et al.[8] treated 10 patients with actinic cheilitis with daylight PDT using aminolevulinate cream, obtaining total remission of the affected area in 70% of patients after 3 months; this was maintained in 50% of patients at 6 to 12 months of final follow-up. All patients showed partial remission that was maintained until the end of follow-up. In another study, 11 patients were treated, obtaining a cure rate of 91%,[9] and 2 isolated case reports with complete clearance after treatment.[10] No adverse effects were reported in any cases. Our results are very similar to those described previously in the literature. All patients experienced a reduction in the affected area after treatment, with complete resolution in 67% of patients. These results exceeded those obtained with other medical treatments such as 5-FU (clinical clearance in 30% to 40% of patients)[3] and were similar to imiquimod 5% cream[3] (40% to 100%). No side effects were detected other than mild discomfort, with the results obtained with the VAS for pain of 0 or 1 (range 0-10). Despite the limited number of patients, given the results obtained and those presented in previous studies, we consider that daylight PDT is a good alternative for treatment of actinic cheilitis. This technique obtains response rates similar to those of conventional PDT, without the associated pain. There is also no need for a PDT lamp, so it can be performed in any center.

☆ Please cite this article as: Martín-Carrasco P, Sendín-Martín M, Domínguez-Cruz JJ, Bernabeu-Wittel J. Terapia fotodinámica con luz de día en el tratamiento de la queilitis actínica. Actas Dermosifiliogr. 2020;111:883–885.

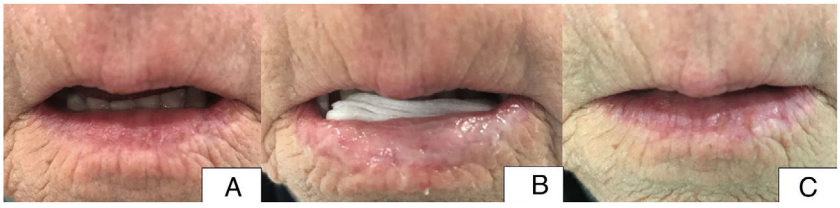

Figure 1 Patient 3. A, Initial state of the patient before treatment, with involvement of 75% of the surface of the lower lip (central region and adjacent lateral areas). B, Image of patient with methyl aminolevulinate cream applied and gauze on the posterior face of the lower lip. C, Image of the patient after 8 weeks of treatment. Complete resolution of the lesions.

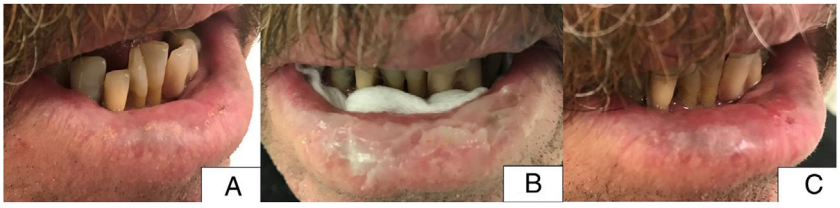

Figure 2 Patient 4. A, Initial situation of the patient before treatment with involvement of 75% of the surface of the lower lip (right lateral and central region). B, Image of patient with methyl aminolevulinate cream applied and gauze on the posterior face of the lower lip. C, Image of the patient after 8 weeks of treatment. Complete resolution of the lesions.

Table 1 Clinical Characteristics of the Patients and Outcomes of Treatment.

Patient	Age	Sex	% Initial Involvement	% Affected After PDT	Resolution	VAS
1	72	M	100	50	Partial	0
2	88	M	50	0	Complete	0
3	61	F	75	0	Complete	1
4	66	M	75	0	Complete	0
5	79	M	75	25	Partial	1
6	81	M	50	0	Complete	1

Funding

This study did not receive any funding.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Jadotte YT, Schwartz RA. Solar cheilosis: an ominous precursor: part I. Diagnostic insights. J Am Acad Dermatol. 2012;66:173–84.
2. Baker SR. Risk factors in multiple carcinomas of the lip. Otolaryngol Head Neck Surg. 1979;88:248–51.
3. Abyaneh MAY, Falto-Aizpurua L, Griffith RD, Nouri K. Photodynamic therapy for actinic cheilitis: a systematic review. Dermatol Surg. 2015;41:189–98.
4. Morton CA, Braathen LR. Daylight photodynamic therapy for actinic keratoses. Am J Clin Dermatol. 2018;19:647–56.
5. Rubel DM, Spelman L, Murrell DF, See JA, Hewitt D, Foley P, et al. Daylight PDT with methyl aminolevulinate cream as a convenient, similarly effective, nearly painless alternative to conventional PDT in actinic keratosis treatment: a randomized controlled trial. Br J Dermatol. 2014;171:1164–71.
6. Markopoulos A, Albanidou-Farmaki E, Kayavis I. Actinic cheilitis: clinical and pathologic characteristics in 65 cases. Oral Dis. 2004;10:212–6.
7. Nicolau SG. Chronic actinic cheilitis of the lower lip and the possibilities of its evolution toward precancerous and cancerous states. Rev Med Chir Soc Med Nat Iasi. 1968;72:9–14.
8. Fai D, Romanello E, Brumana MB, Fai C, Vena GA, Cassano N, et al. Daylight photodynamic therapy with methylaminolevulinate for the treatment of actinic cheilitis. Dermatol Ther. 2015;28:355–68.
9. Levi A, Hodak E, Enk CD, Snast I, Slodownik D, Lapidoth M. Daylight photodynamic therapy for the treatment of actinic cheilitis. Photodermatol Photoimmunol Photomed. 2019;35, http://dx.doi.org/10.1111/phpp.12415. Available from: https://pubmed.ncbi.nlm.nih.gov/30066408

10. Levi A, Wulf HC, Enk CD. Two cases of actinic cheilitis responsive to daylight activated photodynamic therapy (DA-PDT). Photodermatol Photoimmunol Photomed. 2013;29:268–71.

P. Martín-Carrasco,* M. Sendín-Martín,
J.J. Domínguez-Cruz, J. Bernabeu-Wittel

Servicio de Dermatología, Hospital Viamed Santa Ángela de la Cruz, Sevilla, Spain

*Corresponding author.
E-mail address: doctormartincarrasco@gmail.com
(P. Martín-Carrasco).

https://doi.org/10.1016/j.adengl.2020.10.015

Secondary erythromelalgia – case report☆

Eritromelalgia secundaria: informe de caso

To the editor,

A 56-year-old caucasian female presented to our dermatology department with episodes of erythematoviolaceous dyschromia along the outer side of the left foot. The dermatosis had started 1 year before and the patient was having 2-3 episodes per month, each one lasting from hours to a maximum of 2 days, with variable intervals between the crises. The condition was accompanied by a nonspecific local discomfort, although the patient denied manifest pain. Each episode evolved towards total resolution, with no sequelae. At this point, the functional impact caused by the dermatosis was negligible. Previous medical history was unremarkable and there were no new drugs administered. The patient had noticed the complaints were favored by the pending position of the left lower limb and contact with hot water and relieved with ibuprofen and by raising the limb. Physical examination revealed only 2 erythematoviolaceous plaques on the outer side of the left foot, with relatively well defined borders (Fig. 1). An incisional skin biopsy obtained from one of the lesions showed nonspecific findings: a capilar proliferation in the dermis, with some ectatic vessels, and a a discrete lymphocytic inflammatory infiltrate. In the following months, thrombocytosis (800×10^9/L) and a borderline erythrocitosis (15,4 g/dL) were detected in routine analyses and the patient was referred to hematology consultation. Concomitantly there was a clinical worsening of the dermatosis, with an increase in the frequency and severity of the episodes, including nocturnal, now inducing local pain, warmth and sensation of burning. The dimensions of the left foot plaque increased and the dermatosis progressed, involving both hands (Fig. 2) and feet, this time markedly limiting the functional capacity of the patient. At this point the patient underwent laboratory studies searching for autoimmunity, which were negative. Meanwhile the investigation performed in the context of hematology, with bone marrow examination findings compatible with a myeloproliferative neoplasm, allowed the diagnosis of polycythemia vera with positive JAK-2 mutation. Conjugating the clinical and histopathological data available with the polycythemia vera detected, the diagnosis of erythromelalgia secondary to the myeloproliferative disorder was established. In collaboration with hematology, the patient was started on hydroxyurea 500 mg/day and acetylsalicylic acid 100 mg/day and advised to avoid the precipitating factors and comply with resting periods with raised lower limbs. This approach lead to an evident symptomatic improvement: after 6 months the patient had no more episodes of erythematoviolaceous plaques although reported occasional warmth and discomfort on the left foot. Platelet count and hemoglobin normalized.

Erythromelalgia is a rare clinical syndrome characterized by episodes of erythema, increased temperature and burning pain, primarily involving the extremities,[1,2] with lower limbs being more commonly affected.[3] Physical exercise, dependency of the affected limbs and heat exposure are potential triggers, while cold, rest and elevation relieve symptoms.[1–4] The classification of this condition varies among authors, but essentially there are primary forms, which can be further divided into familial or sporadic of early (juvenile) or late (adult) onset, and secondary forms.[5] Multiple diseases are associated with this clinical picture, such as myeloproliferative neoplasms, arterial hypertension, venous insufficiency, diabetes mellitus, systemic lupus erythematosus, rheumatoid arthritis, lichen sclerosus, gout, spinal diseases and multiple sclerosis.[2,4,6] Associated diseases may precede erythromelalgia, coincide with the beginning of the disease or occur during its evolution.[7,8] Ethiopathogenesis of erythromelalgia is not known. Vascular abnormalities, small-fiber neuropathy and arteriovenous shunting are thought to be involved, contributing to the erythema and pain, but is unclear which one is the inciting event or primary abnormality.[1,4,5] Histology is usually non-specific and some biopsy specimens don't show any pathological findings but capillary proliferation, swelling of endotelial cells, perivascular edema and a sparse lymphocytic infiltrate are common.[2] There are no established diagnostic criteria, no clinical guidelines of management or large randomised controlled trials of treatment.[3,9] Erythema, burning pain and hyperalgesia are features of many conditions. Posttraumatic reflex dystrophies, including causalgia, reflex sympathetic dystrophy and shoulder-hand syndrome, can closely mimic erythromelalgia. Peripheral neuropathies, peripheral vascular disorders, Fabry disease and bacterial cellulitis should also be included in the differential diagnosis.[6,10] In the absence of a confirmatory diagnostic test, diagnosis is based on a careful history and supported by physical examination during the episodes and, once a diagnosis is established, potential secondary causes must be excluded.[5] There is no universally effective treatment for erythromelalgia and the

☆ Please cite this article as: Gil F, Luís P, Duarte M, Martins C. Eritromelalgia secundaria: informe de caso. Actas Dermosifiliogr. 2020;111:885–886.