Successful treatment of facial cutaneous leishmaniasis with photodynamic therapy

Sir,

Leishmaniasis is a widespread protozoan zoonosis transmitted by sandflies that can cause a wide range of manifestations. Cutaneous leishmaniasis is the most common form, usually presenting as a papule on exposed skin that enlarges and finally ulcerates. Therapies for cutaneous leishmaniasis are limited and the systemic treatments available are hampered by toxicity and parasite resistance. As an alternative, photodynamic therapy has been reported to be a safe and effective treatment for cutaneous leishmaniasis.[1,2]

An otherwise healthy woman in her 60s, presented to the dermatology department with a solitary, asymptomatic, violaceous papule on her left cheek that enlarged slowly in the past four months [Figure 1a]. Travel history was significant for a trip to Peru, mainly the urban areas, one year prior to the current complaint. Dermoscopic examination showed a symmetric mildly pigmented lesion, with some comedo-like openings, white interfollicular structures and a few focused telangiectatic vessels [Figure 1b]. Reflectance confocal microscopy (Vivascope® 3000, Mavig, Germany) revealed dilated follicular openings in the epidermis, marked adnexal structures and dense material in the superficial dermis with inflammatory cells and prominent horizontal vessels. With the suspected diagnosis of cutaneous leishmaniasis, a punch biopsy was performed. Histopathologic examination showed dilatation of the follicular infundibulum associated with a mixed inflammatory infiltrate in the dermis. Non-necrotizing granulomas and intracytoplasmic structures compatible with amastigotes were also observed, confirming the diagnosis of cutaneous leishmaniasis [Figures 1d–f]. After discussing treatment options with the patient, local therapy was chosen due to the potential side effects of systemic alternatives. The patient was treated with three courses of photodynamic therapy three weeks apart. Carbon dioxide (CO_2) fractional laser was used as a drug delivery technique to improve the absorption of the photosensitizer (wavelength 10.600 nm, energy density 31.8 J/cm^2, coverage 8%, power 30W, beam size 500 µm). This method increases the therapeutic efficacy of photodynamic therapy, shortening the incubation time and contributing to a reduction in the number of photodynamic therapy sessions.[3] Subsequently, topical 7.8% 5-aminolevulinic acid was applied and occluded for two hours. The lesion was then irradiated using a red light-emitting diode lamp (BF-RhodoLED®, 635 nm, 37 J/cm^2). After the third session, the lesion showed a complete clinical response with excellent cosmetic results [Figure 1c]. Photodynamic therapy was well tolerated and the patient only experienced mild erythema and a transient burning sensation as side effects. To confirm the treatment response, reflectance confocal microscopy was performed which demonstrated a regular honeycomb pattern with unremarkable dermal features two months later. The patient has not presented with a relapse of the lesion during six months of follow-up.

Although cutaneous leishmaniasis is usually a self-limited infection, treatment is advised to avoid ulceration, scarring or disease progression. Cutaneous leishmaniasis may constitute a therapeutic challenge since evidence for optimal treatment is ambiguous.[2] Systemic drugs have potential adverse effects and the risks and benefits of the available therapies should be discussed with every patient. In recent years, photodynamic therapy has been introduced as a safe and effective alternative therapy for cutaneous leishmaniasis, with mild side effects and excellent cosmetic outcomes.[1] It has been reported as a successful treatment for cutaneous leishmaniasis in at least 75 cases, most of which are due to *L. donovani, L. major* and *L. tropica,* and some with complex cutaneous leishmaniasis involving the face [Table 1]. Asilian *et al*.[1] compared photodynamic therapy versus topical paromomycin and placebo, showing a complete response in 93.5% versus 41.3% and 13.3% of lesions respectively.[1] Photodynamic therapy protocols for treating cutaneous leishmaniasis have not yet been standardized. In most reported cases; topical aminolevulinic acid or methyl aminolevulinate were applied as photosensitizers, followed by incubation and red light irradiation, with three to eight weekly sessions. Enk *et al*.[4] assessed the use of daylight-activated photodynamic therapy in 31 patients with cutaneous leishmaniasis and reported an overall cure rate of 89%. This modality requires

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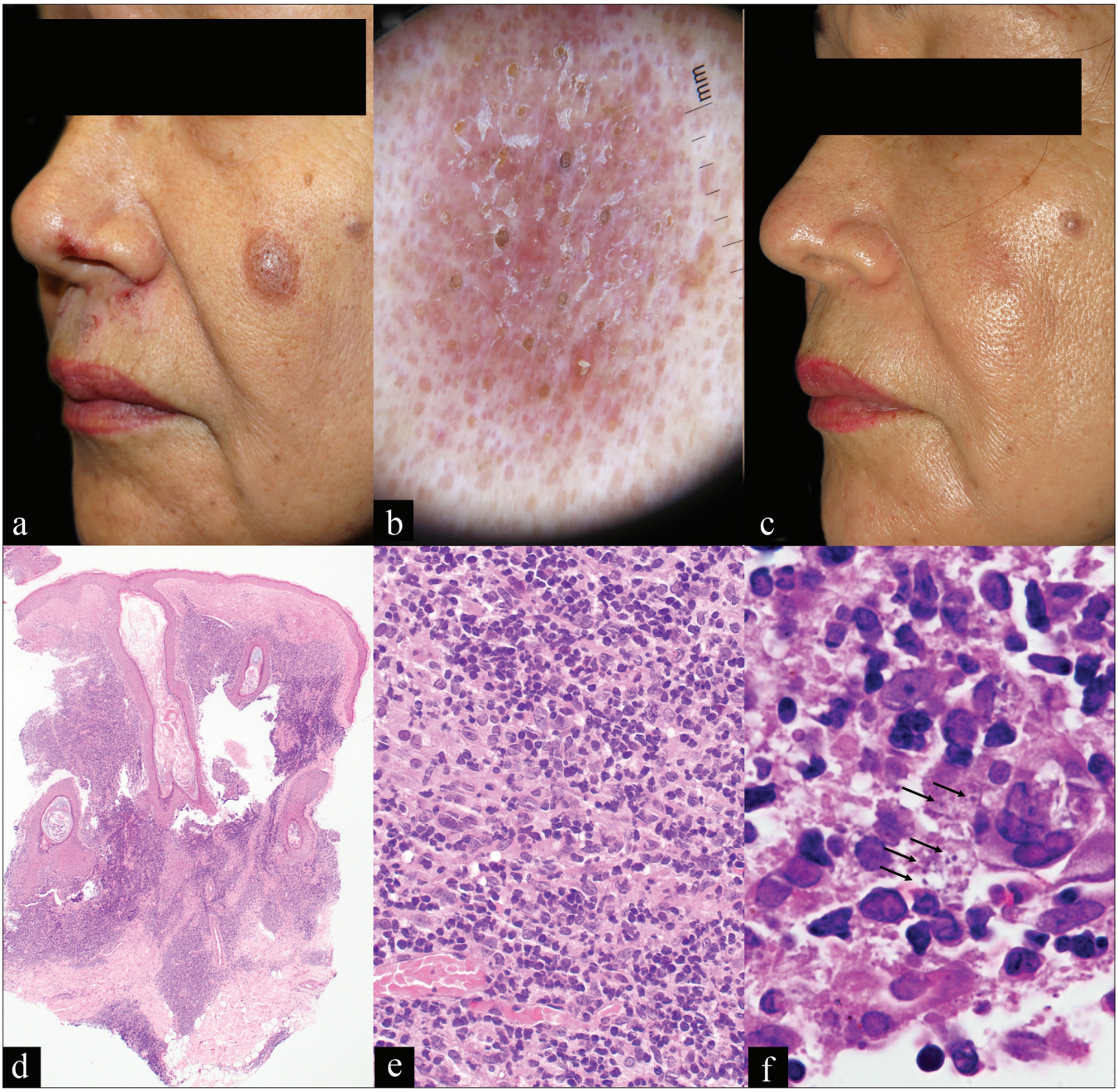

Figure 1: (a) The initial clinical presentation showed a violaceous plaque on the left cheek. (b) Dermoscopy revealed superficial scales, orange comedo-like openings and white interfollicular structures over an erythematous background (DL100, 3Gen, California, ×10). (c) Clinical resolution after 3 sessions of photodynamic therapy. (d, e) The flattened epidermis marked dilation of the follicular infundibulum and a mixed dermal inflammatory infiltrate consisting primarily of lymphocytes, plasma cells and histiocytes (Hematoxylin and eosin, ×20) (Hematoxylin and eosin, ×40). (f) Scattered intracytoplasmic structures (arrows), consistent with leishmania amastigotes (Hematoxylin and eosin, ×100)

almost no equipment and could be performed in rural areas and technologically underdeveloped countries.[4] Although the response to treatment should be assessed by clinical criteria, testing for parasites is often performed.[2] Despite the limitation of in-depth evaluation, reflectance confocal microscopy can help rule out common tumours of the face as it can show findings more suggestive of cutaneous leishmaniasis such as dilated linear and comma-shaped vessels, follicular plugging and the presence of multinucleated giant cells in the superficial dermis.[5] Reflectance confocal microscopy, along with dermoscopy, could be a useful, non-invasive tool, not only to support the diagnosis of cutaneous leishmaniasis but also to monitor healing, avoiding unnecessary biopsies or additional photodynamic therapy sessions.

Photodynamic therapy is an effective and well-tolerated therapeutic option for the treatment of simple cutaneous leishmaniasis. The use of fractional CO_2 laser as a drug-delivery method could shorten the number of photodynamic therapy sessions needed. Further studies are needed to establish

Table 1: Studies and case reports describing cutaneous leishmaniasis treated with photodynamic therapy

Author & year	No. (Lesions)	Sex/Age	Lesion location	Leishmania species	Therapy regimen	Dose (Sessions)	Outcome (weeks to achieve)	Adverse effects	Follow-up
Gardlo *et al.* 2003	1 (10)	M/34	Left arm and leg	*L. donovani*	Five lesions:PDT with topical MAL and red light, 630 nm	75 J/cm^2 (28)	Complete response in all 5 lesions treated with PDT (16)	Erythema, burning sensation during irradiation and residual hyperpigmentation	16 months with no clinical recurrence.
Enk *et al.* 2003	11 (32)	NA	NA	*L. major*	PDT with topical 5-ALA and red light, 570–670 nm	100 J/cm^2 (1–3)	Complete response in 96.9% of lesions (1–3)	Transient burning sensation	ND
Gardlo *et al.* 2004	1 (1)	M/19	Left shoulder	ND	PDT with topical MAL and red light, 630 nm	ND (5)	Complete response (5)	Burning, pain and suppuration in the irradiation zone. Residual hypopigmentation.	12 weeks with no clinical recurrence.
Asilian *et al.* 2006[1]	20 (ND)	NA	NA	*L. major*	PDT with topical 5-ALA and red light, 633 nm	100 J/cm^2 (4)	Complete response in 93.5% of lesions. Partial response in 6.5% (4)	Mild pruritus, burning, erythema, oedema and pain	ND
Ghaffarifar *et al.* 2006	5 (7)	NA	NA	*L. major*	PDT with topical 5-ALA and red light, 570–670 nm	100 J/cm^2 (4)	Complete response (4)	Local inflammation and residual hyperpigmentation.	4 months with no clinical recurrence.
Sohl *et al.* 2007	1 (1)	M/56	Left cheek	*L. tropica*	PDT with topical MAL and red light, 635 nm	100 J/cm^2 (3)	Complete response (6)	ND	ND
Pizinger *et al.* 2009	1 (9)	M/39	Forearms, neck, and thigh	ND	Five lesions: PDT with topical 5-ALA and red light, 580–680 nm	75 J/cm^2 (6)	Complete response of the 5 lesions treated with PDT	Minimal pigmentation and central scarring	12 months with no clinical recurrence.
Song *et al.* 2011	1 (3)	M/ND	Left flank, left ear and left cheek	ND	Low dose pentavalent antimony (5 mg/kg/d), PDT withmethylene blue and red light, 580–680 nm	20 J/cm^2 (4)	After the second PDT session, the lesion no longer comprised an open wound (2)	ND	ND
Evangelou *et al.* 2011	1 (1)	M/69	Left cheek	ND	PDT with intralesional 20% 5-ALA, 630 nm	100 J/cm^2 (3)	Complete response (3)	Local burning and erythema during irradiation	24 months with no clinical recurrence.
Enk *et al.* 2015[4]	27 (64)	NA	NA	*L. major* and *L. tropica*	SFP and daylight-activated PDT with topical MAL. Exposure to daylight during 2.5 hours.	ND (<8)	Complete response in 89%	Mild pain was reported with a mean score of 0.6/10	ND
Fink *et al.* 2016	1 (3)	F/18	Face, forearm and back of the hand	*L. tropica*	PDT with 5-ALA and red light, 630 nm	37 J/cm^2 (5)	Complete response (5)	Local burning and erythema during irradiation	9 weeks with no clinical recurrence.

(Contd...)

Table 1: *(Continued)*

Author & year	No. (Lesions)	Sex/Age	Lesion location	Leishmania species	Therapy regimen	Dose (Sessions)	Outcome (weeks to achieve)	Adverse effects	Follow-up
Sainz-Gaspar *et al.* 2018	1 (2)	M/10	Left lower eyelid and left forearm	ND	Meglumine antimoniate + PDT with MAL and red light, 630 nm	37 J/cm^2 (7)	Complete resolution (7)	Slight to moderate pain during irradiation and residual hypopigmented superficial scarring	3 months with no clinical recurrence
Slape *et al.* 2018	1 (1)	M/29	Nose dorsum	*L. tropica*	PDT with MAL and red light, 630 nm	ND (7)	Complete resolution (7)	ND	Patient was lost to follow up
Broby Johansen *et al.* 2019	1 (1)	M/15	Right lower leg	*L. major*	PDT with 5-ALA and red light	37 J/cm^2 (24)	Complete resolution (12)	ND	ND
Costin *et al.* 2020	1 (1)	M/31	Forehead	ND	Meglumine antimoniate + PDT with MAL and red light, 630 nm	37 J/cm^2 (8)	Complete resolution (16)	Local stinging and erythema during irradiation	12 months with no clinical recurrence
Goldin *et al.* 2020	1 (1)	F/82	Left ear	*L. tropica*	PDT with 5-ALA and red light, 633 nm	75 J/cm^2 (3)	Recurrence 2 months after the second session. Complete resolution after the third session (18)	ND	22 months with no clinical recurrence
Current case	1 (1)	F/65	Left cheek	ND	Pre-treatment with fractional CO_2 laser, PDT with 5-ALA and red light, 635 nm	37 J/cm^2 (3)	Complete resolution (9)	Mild erythema and burning sensation. Residual hypopigmented superficial scarring	6 months with no clinical or RCM-assessed recurrence

No: number, M: Male, F: Female, PDT: photodynamic therapy, 5-ALA: 5-Aminolevulinic acid, MAL: Methyl aminolevulinate, ND: Not described, NA: Not applicable, SFP: Solar photoprotector, RCM: reflectance confocal microscopy

the optimal photodynamic therapy protocol for treating cutaneous leishmaniasis and evaluate its use in cosmetically relevant regions. Reflectance confocal microscopy is a promising complementary tool in the diagnosis and follow-up of patients with cutaneous leishmaniasis.

Declaration of patients consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

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