

# Treatment of cutaneous leishmaniasis with photodynamic therapy: The first case report from Khyber Pakhthunkhwa (KPK), Swat Pakistan

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**Abstract** Cutaneous Leishmaniasis (CL), the most common subtype of leishmaniasis, is a vector borne disease transmitted by sand fly. Herein, we report a case of CL being treated for the first time with photodynamic therapy (PDT) in KPK, Pakistan. A 55-year-old female patient presented with a single chronic disfiguring ulcerated lesion on the chin. The patient had received pentavalent antimoniate for the last 2 years, with no satisfactory outcome. We treated the patient with methylaminolevulinate based PDT and observed complete response after three sessions of the PDT treatment, each with a light energy dose of 75 J/cm<sup>2</sup>. The patient has remained disease-free for over 2 years. This study demonstrates the promising role of PDT in the treatment of CL.

## Key words

Cutaneous leishmaniasis, photodynamic therapy, pentavalent antimoniate, photosensitizer, methylaminolevulinate.

## Introduction

Leishmaniasis; the sixth most important disease affecting the public health worldwide, is a vector borne disease, transmitted among mammalian hosts by female sand fly,<sup>1</sup> primarily affecting the skin. Many animal species can carry leishmania parasite including rodents, dogs and foxes.<sup>2</sup> Rarely leishmaniasis can be passed from person to person through blood transfusion, infected needles and syringes or congenitally from mother to baby. The disease can be diagnosed by performing blood test for antibodies against parasite or by urine tests, Polymerase chain reaction (PCR) test can identify parasite based on its genetic fingerprint.<sup>3</sup> The best test to

identify the parasite is documenting its presence through a microscope (smear test).

There are several types of leishmaniasis. For instance, cutaneous leishmaniasis (CL), a relatively benign skin condition, is characterized by sore(s) on the skin, which usually develop in a few weeks after the bite of the sand fly.<sup>4</sup> The sores may heal spontaneously within 12-24 months if the immunity of the patient is strong enough. World Health Organization (WHO) estimates 1-1.5 million new cases of CL every year.<sup>5</sup> In Pakistan, the incidence of CL is increasing, most likely due to poverty, inadequate medical facilities, negligible planning for vector control, armed conflicts and mass migration of human and cattle. Mucocutaneous leishmaniasis (MCL) is a less common form, either carried by direct bite of sand fly on mucus membranes or extension to mucosal membranes from the skin lesion. It can

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**Figure 1** Sample white light photos summarizing the progress of PDT treatment of the CL lesion. Single chronic disfiguring ulcerated lesion on the chin (A), express significant improvement after first (B) and second (C) session of PDT. Complete response with excellent cosmetic results was observed after third session of PDT (D).

lead to partial or complete destruction of mucous membranes in the nose, throat or mouth. Visceral leishmaniasis (VL) is the systemic form of the disease the incubation period of which may range from days to years after the bite of infected sand fly, and it affects the internal organs usually the spleen, liver, and bone marrow. Patients may present with episodes of fever, weight loss, anemia, and enlargement of the spleen and liver.<sup>4</sup>

The conventional treatment of CL is directed towards the eradication of amastigotes and reduction of the size of the lesions to promote healing. At present meglumine antimoniate and sodium stibogluconate are the first line drugs worldwide.<sup>6,7</sup> Photodynamic therapy (PDT) is a rapidly evolving therapeutic option for CL. The FDA approved indications of PDT include actinic keratosis, basal cell carcinoma, and

superficial squamous cell carcinoma, while inflammatory skin diseases, such as psoriasis, acne vulgaris, and sarcoidosis are the off label uses of PDT. Moreover, PDT have a crucial role in the treatment of infectious skin diseases, including verruca vulgaris, condyloma acuminatum and CL.<sup>8,9</sup>

Herein, we present the first case of CL treated with PDT from Pakistan. A 55 year old female patient presented with a CL lesion on the chin, which did not responded to pentavalent antimonials. The patient showed complete response to PDT and has remained disease-free for over 2.5 years after a regular follow up.

### Case report

A 55 year old female patient presented with the complaint of a single chronic disfiguring

**Table 1** Summary of clinical features of the patient with CL, lesion characteristics and PDT.

Clinical Features		Lesion Characteristics		PDT Treatment	
Age	55 years	Site	Chin	Photosensitizer	MAL*
Gender	Female	Size	4cm diameter	Laser wavelength	635 nm
Previous Treatment	Pentavalent antimoniate	Ulceration	Present	Light dose	75 J/cm <sup>2</sup>
Treatment outcome	No response	Disfigurement	Present	No. of sessions	03

\*MAL: Methylaminolevulinate

ulcerated lesion on the chin, shown in **Figure 1A**. The lesion had been diagnosed as cutaneous leishmaniasis (CL). The patient had received treatment (i.e., pentavalent antimoniate) for the last 2 years, with no satisfactory outcome. Clinical assessment showed that the patient had developed resistance to pentavalent antimoniate. The patient was planned for photodynamic therapy (PDT). Written and informed consent was obtained from the patient.

To perform PDT, the lesion and the adjacent skin were cleaned and scrubbed to remove the necrotic layer and exudates dried up. The photosensitizer, methylaminolevulinate (MAL), was applied locally on the lesion under adhesive covering, followed by an incubation period of 3 hours for absorption of the photosensitizer. After incubation period, the cream was removed and the lesion was washed with normal saline. The lesion was irradiated with red laser light (wavelength 635nm); a light energy dose of 75 J/cm<sup>2</sup> was delivered, as per the institutional protocol. The patient received three sessions of PDT; the first two sessions were repeated at two weeks interval, while the third session was given at one month interval. The clinical features of the patient, lesion characteristics and PDT protocol used have been summarized in **Table 1**.

The response of the PDT was evaluated through clinical examination, and evaluation of inflammation was assessed by erythema and swelling and size of lesion. Figure 1b-d shows the progressive improvement of the patient. Currently, the patient is on regular follow up and remained disease free after over two years.

Besides the complete response, excellent cosmetic outcome with no recurrence throughout the observation time and no complication was observed.

### Discussion

The incidence/ prevalence of leishmaniasis is alarming in Pakistan,<sup>1</sup> presumably due to low socio-economic conditions and lack of awareness and education. The situation is even exacerbating by the limited advancement at the therapeutic end, as there is no significant improvement in the treatment of CL for more than 90 years worldwide.<sup>5</sup> The leishmania species has been reported to have developed resistance to the drugs being administered<sup>10,11</sup> in some cases, the resistance is as high as 65%. Moreover, the prevailing treatment paradigm of the CL has been reported to cause higher rate of side effects, which include renal, hepatic and cardiac toxicity, myalgia, joint stiffness, malaise, anorexia and bradycardia with ECG changes, prolongation of the QT interval and T-wave inversion.<sup>12</sup> Apart from potential systemic toxicities, these medicines have limited success of complete response rates and a healing period of over 4 months<sup>13</sup>. In addition, the current treatment protocol necessitates time investment for daily clinical visits (for the subcutaneous injections) and patient discomfort. Hence better treatment options must be explored and practiced for the eradication of this highly prevalent disease.

Photodynamic therapy (PDT) may offer an improved alternate treatment for leishmaniasis,

potentially countering the shortcomings of the prevailing treatment options,<sup>9</sup> as it offers lower treatment expense, a limited profile of side effects and good treatment efficacy. Specifically, leishmaniasis has been shown to exhibit complete response in about 95% and partial response in about 5% of the patients with just 3-4 treatment sessions of PDT.<sup>16</sup> Moreover, it has markedly reduced the healing time to less than three months. In addition, the PDT treatment has no known side effects except for mild burning sensation and pain during the application of laser light only; however, these are well-tolerated and manageable.

In this study, we have successfully treated a case of cutaneous leishmaniasis, which did not respond to the prolonged treatment (i.e., two years) of pentavalent antimoniate. PDT not only reduced the treatment time significantly (i.e., from over 02 years to 1.5 months), but also proved efficacious. Moreover, the patient ease and satisfaction for PDT was markedly high, as the treatment offered excellent cosmetic outcome without any considerable side effects. Due to the encouraging results from the treatment of this case, we have planned (and initiated) a regional project for the treatment of leishmaniasis with PDT (a manuscript based on the initial results is in the preparation phase).

## Conclusion

Photodynamic therapy is safe and effective treatment option for cutaneous leishmaniasis with excellent cosmetic results.

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