


Photodynamic therapy for the treatment of cutaneous leishmaniasis: a case series from Pakistan

Karim Khan^{1,2}, Aakif Ullah Khan³, Banat Gul⁴, Arif Ullah², Moiz Khan⁵, Iftikhar Ahmad^{3*} 

European Journal of Medical Case Reports
Volume 5(7):203–208
<https://doi.org/10.24911/ejmcr/173-1606794043>



This is an open access article distributed in accordance with the Creative Commons Attribution (CC BY 4.0) license: <https://creativecommons.org/licenses/by/4.0/> which permits any use, Share — copy and redistribute the material in any medium or format, Adapt — remix, transform, and build upon the material for any purpose, as long as the authors and the original source are properly cited. © The Author(s) 2021

ABSTRACT

Background: Photodynamic therapy (PDT) offers an effective treatment in several dermatological disorders. Herein, PDT has been assessed for the treatment of cutaneous leishmaniasis (CL) in a series of six patients from Pakistan.

Cases Presentation: Six patients presenting with CL lesions at different face sites (i.e., cheek, nose, and lip) were treated with methylaminolevulinate-based PDT. The treatment was completed in three sessions, where a light dose of 75 J/cm² was delivered through a low power (300 mW) red laser (wavelength = 635 nm) in each session.

Results: The assessment of the disease at 10 months follow-up illustrated complete response in 5 patients, while partial response in 1 patient.

Conclusion: This case series study demonstrated that PDT may offer a viable treatment option to the CL patients.

Keywords: cutaneous leishmaniasis, PDT, dermatology, laser therapy, protozoan parasite.

Received: 01 December 2020

Accepted: 23 June 2021

Type of Article: CASE SERIES

Specialty: Infectious disease

Correspondence to: Iftikhar Ahmad

*Institute of Radiotherapy and Nuclear Medicine (IRNUM), University Campus, Peshawar, Pakistan.

Email: iahmadmp@gmail.com

Full list of author information is available at the end of the article.

Background

Cutaneous leishmaniasis (CL) is a common yet neglected contagious disease, caused by protozoan parasite of genus *Leishmania* which is transmitted by the bite of infected phlebotomine female sand fly [1]. Within the host macrophages, the parasites may colonize in the skin, mucous membranes, or internal organs causing cutaneous, mucocutaneous, and visceral leishmaniasis, respectively [2].

The disease affect patients' life with regards to symptoms (itching, soreness, pain, or burning sensations), emotions (reduced self-esteem, embarrassment or self-consciousness) and psychiatric problems (anxiety and depression), irrespective of the patients status, occupations, and educational levels [3]. The impact of CL on the quality of life, classified as no, low, moderate, high, and very high effect, has been assessed on the basis of six parameters including symptoms/ feelings, leisure, daily activities, work/school, relationships, exercise, and treatment; the results showed that the disease have high effect on quality of life of 18% patients [4]. CL is usually noted on exposed parts of the body, mainly arms, face, and legs [2]. Clinically, the manifestations of the disease are extremely diverse including both typical and atypical sites and unusual morphologies, most likely because of

the complex interaction between the infection (by the parasite) and immune response (by the host) [5].

The number of patients presenting with CL is rising in Pakistan, where the disease is epidemic like in many other parts of the world [6]. This alarming pattern of the disease is a major public health concern in the country, particularly in localities having influx of refugees and population bordering the neighboring Afghanistan. In 2019, numerous new cases of CL (around 35000) have been reported from the merged districts (previously called FAT: Federally Administrated Tribal Areas) of Pakistan. Despite the recent upsurge in the new cases of CL, the treatment and associated resources (e.g., expertise, facilities, medicine, etc.) and scarce in the country. To exemplify, meglumine antimoniate and sodium stibogluconate are typically used as the first line treatment for CL [7]; these drugs, however, are not even registered in the country. Consequently, effective management of the large number of CL patients in the country remains elusive.

The clinical use of photodynamic therapy (PDT) and its indications are expanding, particularly in dermatology. Specifically, PDT has been efficiently used for the treatment of skin pathologies like actinic keratosis, acne vulgaris, basal cell carcinoma, psoriasis, superficial

squamous cell carcinoma, verruca vulgaris and condy-
loma acuminatum [8]. Moreover, PDT has demonstrated
promising results in the treatment of CL patients [9].
Herein, we present the role of PDT in the treatment of CL
patients. In particular, treatment outcomes for six cases of
CL lesions at three different face sites (i.e., cheek, nose
and lip) are reported from Pakistan.

Cases Presentation

CL lesions on nose

Two patients presented with CL lesions on their nose.
Specifically, a 47-years-old man (Patient 1) presented with
a single highly disfiguring CL lesion (size ~ 5 cm) on the
nose. Another patient was a 09-years-boy (Patient 2) pre-
sented with multiple small CL lesions, the largest of size
~ 2 cm, as shown in Figure 1. The smear of Leishman-
Donovan (LD)-bodies from the lesions was positive, confir-
ming the diagnosis of CL. Real-time polymerase chain
reaction (PCR) studies revealed that the specific species
causing the disease was *Leishmania tropica*, which has
been reported as the most prevailing species in this region

(i.e., Pakistan and Afghanistan). Before presenting to our
clinic, both the patients had received pentavalent antimo-
niate; the disease, however, showed resistance to the said
treatment.

The patients were considered for PDT. The ethical
committee of the Swat Institute of Nuclear Medicine,
Oncology and Radiotherapy (SINOR), Pakistan assessed
and approved the protocol of the study. Written, informed
consent was signed by the patients/ their attendants. To
carry out PDT, the CL lesion and one centimeter margin
was cleaned and the necrotic tissue layer removed; this
significantly improves the uptake of the photosensitizer
in the lesion. The photosensitizer (i.e., methylaminole-
vulinatate; MAL 16%) was formulated in cream-base and
applied topically on the lesion under adhesive covering.
After waiting for an incubation period of 3 hours, the CL
lesions were washed with normal saline. The PDT was
carried out in three sessions, on day 1, day 15, and day
30, respectively. In each session of PDT, the light dose
~ 75 J/cm² was delivered by a red laser (wavelength ~
635 nm; Power 300 mW). White light photographs in high
resolution were recorded; the photograph before starting



Figure 1. Illustrative white light photos of the CL lesions on the nose: (A) a 47-year-old man (Patient 1) and (b) a 9-year-boy (Patient 2) at presentation and after three session of PDT. Complete response to PDT was seen for both patients, with excellent cosmetics.

PDT was considered as baseline for the assessment of the treatment response.

The response of PDT was evaluated in terms of clinical features of the CL lesions such as the size of both inner and outer border, the inflammatory signs (i.e., skin edema/hardening, etc.) and re-epithelialization [10]. The photographs at initial presentation were considered as baseline for the assessment of the treatment response. Both these patients showed complete response (CR) to PDT with excellent cosmetics.

CL lesions on check

Two patients presented with CL lesions on their checks. Specifically, a 68-years-old man (Patient 3) presented with a single disfiguring CL lesion (size ~ 3 cm) on the cheek. The second patient was a 10-years-boy (Patient 4) presented with single CL lesion of size ~ 4 cm, as shown in Figure 2. The (LD)-bodies smear from the lesions of both patients was positive, confirming the diagnosis of CL. Both patients showed resistance to the previously received meglumine antimoniate.

The patients were enrolled for PDT after written, informed consent was signed by the patients/ their attendants. The PDT protocol followed for these patients was same as that of the first two patients presented above. Briefly, the necrotic tissue layer of the lesion was removed, photosensitizer (i.e., MAL 16%) was topically applied, and light dose ~ 75 J/cm² was delivered after waiting for the incubation period of the photosensitizer. The PDT was carried out in three sessions, on day 1, day 15, and day 30. The first patient showed CR to PDT as the CL lesion disappeared completely without any scar/symptoms. The second patient showed partial response (PR) to PDT as significant reduction in the size and re-epithelialization were seen.

CL lesions on lip

Two patients presented with CL lesions on their lips. Specifically, a 27-years-old man (Patient 5) presented with a single dry, disfiguring CL lesion (size ~ 2 cm) on the lip. The second patient was a 26-years-girl (Patient 6) presented with single CL lesion of size ~ 2 cm, as shown in Figure 3. The diagnosis of CL was confirmed by PCR



Figure 2. Illustrative white light photos of the CL lesions on the check: (A) a 68-year-old man (Patient 3) and (b) a 10-year-boy (Patient 4) at presentation and after three session of PDT. Complete response to PDT was seen for patient 3 while partial response for patient 4.



Figure 3. Illustrative white light photos of the CL lesions on the lip: (A) a 27-year-old man (Patient 5) and (b) a 26-year-old woman (Patient 6) at presentation and after three sessions of PDT. Complete response to PDT was seen for both patients.

Table 1. Summary of patients' clinical, microscopic and molecular information.

| Patient | Gender | Age (yr) | Lesion duration (months) | Number of lesions | Lesion size | Dry/Wet | PCR | Molecular species |
|---------|--------|----------|--------------------------|-------------------|-------------|---------|-----|-------------------|
| 1 | M | 47 | 25 | S | 5 | D | +ve | T |
| 2 | M | 09 | 10 | M | 2 | D | +ve | T |
| 3 | M | 68 | 13 | S | 3 | D | +ve | T |
| 4 | M | 10 | 11 | S | 4 | D | +ve | T |
| 5 | M | 27 | 22 | S | 2 | D | +ve | T |
| 6 | F | 26 | 17 | M | 2 | D | +ve | T |

M: Male, F: Female, S: Single, M: Multiple, D: Dry, W: Wet, T: Tropica.

and positivity of (LD)-bodies smear from the lesions. The same treatment protocol was followed for these patients, as discussed above. Both patients showed CR to PDT as the CL lesions disappeared completely. A summary of the patients' clinical, microscopic, and molecular information is presented in Table 1.

Discussion

The primary purpose of this study was to evaluate the efficacy of PDT for the treatment of CL lesions in Pakistani

patients. Specifically, a total of six patients presenting with CL lesions at three different face sites (i.e., cheek, nose and lip) were treated with PDT; the patients follow up illustrated promising treatment outcomes, with good cosmetics.

The management of CL seems challenging and has not been standardized yet, probably because of the intrinsically diverse nature/ presentation of the disease. Besides the fact that multiple species of parasite cause the disease, the clinical manifestation, treatment response and

outcome remarkably vary with the geographic regions, globally [11]. Accordingly, multiple treatment modalities have been opted for the treatment of CL lesions, particularly in the developing countries like Pakistan; this case series of CL and treatment with PDT is also presented in this context.

The non-availability of the frequently used treatment for CL (i.e., meglumine antimoniate) has led to different management strategies for this disease in Pakistan. Previously, Low-Level Laser Therapy has been interrogated for the management of CL lesions ($n = 123$), classified in Grade I (papule; size ≤ 1 cm) to Grade V (ulceration with superadded infection; size > 4 cm); treatment outcomes showed CR and PR in 91 %, 9 % patients with early-stage disease (Grade I-II) and no response in patients with advance disease (i.e., Grade III-V), respectively [12]. Another interesting area for the treatment of CL in Pakistan is the anti-parasitic activities of medicinal plants. A total of 23 plants have been explored in this regard, with *Asteraceae* plants being the most extensively used family. Plant extracts in the form of pure compounds such as artemisinin, physalins and sitosterol proved their efficacy against CL parasites [13]. In the present study, the efficacy of PDT for the treatment of CL lesions in a series of six patients was assessed; the treatment outcomes were promising with good cosmetics.

For developing countries like Pakistan, PDT may offer an effective alternate to meglumine antimoniate in the treatment of CL [14]. In particular, PDT has the ability to fill the gap in the availability of the treatment based on meglumine antimoniate. Moreover, PDT allows for lower treatment costs and substantially reduced clinical visits, which are critically important in low socio-economic countries [15]. In addition, no or limited side effects, good cosmetics and higher treatment efficacy of PDT likely diminish the psychiatric problems associated with the disease. In summary, PDT offers a promising alternate for the treatment of CL patients in countries with low socio-economics and high burden of the disease.

Conclusion

In this study, six cases of CL and their management with PDT have been presented. Specifically, six patients presenting CL lesions at different face sites (i.e., cheek, nose and lip) were treated with three sessions of methylaminolevulinate-based PDT, which relieved the disease symptoms such as eradication of the lesion and re-epithelialization without any scar. This case series study demonstrates that PDT may offer a viable treatment option to the CL patients in countries with low socio-economics and high burden of the disease.

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent for publication

Written consent was obtained from the patient.

Ethical approval

The ethical committee of the Swat Institute of Nuclear Medicine, Oncology and Radiotherapy (SINOR), Pakistan assessed and approved the protocol of the study.

Author details

Karim Khan^{1,2}, Aakif Ullah Khan³, Banat Gul⁴, Arif Ullah², Moiz Khan⁵, Iftikhar Ahmad

1. Swat Institute of Nuclear Medicine, Oncology and Radiotherapy (SINOR), Swat, Pakistan
2. University of Malakand, Chakdara, Dir Lower, Khyber Pakhtunkhwa, Pakistan
3. Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan
4. Department of Basic Sciences, Military College of Engineering, National University of Science and Technology (NUST), Islamabad, Pakistan
5. Peshawar Medical College, Peshawar, Pakistan

References

1. Elmahallawy EK, Sampedro Martínez A, Rodriguez-Granger J, Hoyos-Mallecot Y, Agil A, Navarro Mari JM, et al. Diagnosis of leishmaniasis. *J Infect Dev Ctries*. 2014;8(8):961–71. <https://doi.org/10.3855/jidc.4310>
2. Burza S, Croft SL, Boelaert M. Leishmaniasis. *Lancet*. 2018;392(10151):951–70. [https://doi.org/10.1016/S0140-6736\(18\)31204-2](https://doi.org/10.1016/S0140-6736(18)31204-2)
3. Litt E, Baker MC, Molyneux D. Neglected tropical diseases and mental health: A perspective on comorbidity. *Trends Parasitol*. 2012;28(5):195–201. <https://doi.org/10.1016/j.pt.2012.03.001>
4. Vares B, Mohseni M, Heshmatkhan A, Farzadeh S, Dghk R, Rahnema Z, et al. Quality of life in patients with cutaneous leishmaniasis. *Arch Iran Med*. 2013;16(8):474–7.
5. Afghan AK, Kassi M, Kasi PM, Ayub A, Kakar N, Marri SM. Clinical manifestations and distribution of cutaneous leishmaniasis in Pakistan. *J Trop Med*. 2011;2011:359145. <https://doi.org/10.1155/2011/359145>
6. Ghatte MA, Taylor WR, Karamian M. The geographical distribution of cutaneous leishmaniasis causative agents in Iran and its neighboring countries, a review. *Front Public Heal*. 2020;8:11. <https://doi.org/10.3389/fpubh.2020.00011>
7. Yesilova Y, Surucu HA, Ardic N, Aksoy M, Yesilova A, Oghumu S, et al. Meglumine antimoniate is more effective than sodium stibogluconate in the treatment of cutaneous leishmaniasis. *J Dermatol Treat*. 2016;27(1):83–7. <https://doi.org/10.3109/09546634.2015.1054778>
8. Lee Y, Baron ED. Photodynamic therapy: Current evidence and applications in dermatology. *Semin Cutan Med Surg*. 2011;30(4):199–209. <https://doi.org/10.1016/j.sder.2011.08.001>
9. Khan K, Khan AU, Ghufuran, Khan A, Khan M, Ahmad I. Fractionated illumination improves the treatment outcomes of photodynamic therapy for high grade cutaneous leishmaniasis. *Photodiagnosis Photodyn Ther*. 2020;29:101622. <https://doi.org/10.1016/j.pdpdt.2019.101622>

10. Kip AE, Balasegaram M, Beijnen JH, Schellens JHM, Vries PJ De, Dorlo TPC. Systematic review of biomarkers to monitor therapeutic response in leishmaniasis. *Antimicrob Agents Chemother*. 2015;59(1):1–14. <https://doi.org/10.1128/AAC.04298-14>

11. Bhutto AM, Soomro RA, Nonaka S, Hashiguchi Y. Detection of new endemic areas of cutaneous leishmaniasis in Pakistan: a 6-year study. *Int J Dermatol*. 2003;42:543–8. <https://doi.org/10.1046/j.1365-4362.2003.01818.x>

12. Khan K, Khan AU, Ghufraan, Ullah A, Khan M, Ahmad I. Low-level laser therapy for the treatment of early stage cutaneous leishmaniasis: a pilot study. *Dermatol Ther*. 2020;33(6):e14232. <https://doi.org/10.1111/dth.14232>

13. Tariq A, Adnan M, Amber R, Pan K, Mussarat S, Shinwari ZK. Ethnomedicines and anti-parasitic activities of Pakistani medicinal plants against Plasmodia and Leishmania parasites. *Ann Clin Microbiol Antimicrob*. 2016;15:52. <https://doi.org/10.1186/s12941-016-0170-0>

14. Szeimies RM, Karrer S, Abels C, Landthaler M, Elmets CA. Photodynamic therapy in dermatology. *J Am Acad Dermatol*. 2000;42(3):389–413. [https://doi.org/10.1016/S0190-9622\(00\)90209-3](https://doi.org/10.1016/S0190-9622(00)90209-3)

15. Almeida OLS, Santos JB. Advances in the treatment of cutaneous leishmaniasis in the new world in the last ten years: a systematic literature review. *Ann Bras Dermatol*. 2011;86(3):497–506.

Summary of the case

| | | |
|---|------------------------------|--|
| 1 | Patient (gender, age) | The summary of gender and age for the six patients presented herein is given in Table 1. |
| 2 | Final diagnosis | Cutaneous Leishmaniasis |
| 3 | Symptoms | Disfiguring lesions on face |
| 4 | Medications | Photodynamic Therapy (PDT) |
| 5 | Clinical procedure | Photodynamic Therapy (PDT) |
| 6 | Specialty | Infectious disease |