



## The use of Cryotherapy and Albendazole as a Beneficial Cutaneous Larva Migrans Therapy: A Case Report

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author FY designed the study, author RBY performed the statistical analysis, author BF wrote the protocol and author EDND wrote the first draft of the manuscript. Authors FY and BF managed the analyses of the study. Authors FY and HK managed the literature searches. All authors read and approved the final manuscript.*

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Case study

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### **ABSTRACT**

**Aims:** To describe the effect of combination albendazole and cryotherapy as a spesific CLM therapy.

**Presentation of case:** A 21-year-old man reported a winding reddish patches that felt itchy and hot since 1 month ago. Erythema papules and hyperpigmented patches and hyperpigmented macules in the serpiginous form were found at right brachial, right genu, and right cruris regions. The patient was given albendazole therapy 1x400 mg for 3 days orally and mixed cream (albendazole 400 mg, mupirocin, and clobetasol propionate) for 7 days showed only minimal clinical cure. For optimal results, we combine albendazole therapy with cryotherapy with liquid nitrogen. Combination therapy resulted in satisfactory improvement and no recurrences after therapy.

**Discussion:** The first-line therapy for the treatment of CLM cases is ivermectin 0.15-0.2 mg / kg / day and second-line albendazole 400 mg given for 3 consecutive days. Alternative therapy such as

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cryotherapy in an unsuccessful case with oral therapy and also to prevent recurrency.

**Conclusion:** Administration of albendazole combination therapy with cryotherapy using liquid nitrogen as management of CLM therapy is effective in unsuccessful case to oral therapy.

*Keywords: Albendazole; cryotherapy; cutaneous larva migrans.*

## 1. INTRODUCTION

Cutaneous larva migrans (CLM) or creeping eruption is a worm infection of the skin that is often caused by *Ancylostoma braziliense* and *Ancylostoma caninum* [1]. More cases of CLM have been reported in tropical and sub-tropic countries or in tourists who have visited the region. Based on data from the Center for Disease Control and Prevention (CDC), the prevalence of CLM is estimated at around 575 to 740 million people in the world [2]. Research conducted by Heukelbach et al (2008) in Brazil states that the prevalence of CLM is more common in children aged less than 5 years and adults over 20 years of age 14.9% and 0.7% [3,4]. Cutaneous larva migrans is an endemic disease in Central America, South America, Southeast Asia and Africa with a total prevalence of 8.2% of the total. Population [5]. The exact prevalence rate in Indonesia has never been reported before, but the number of CLM cases in RSUP Haji Adam Malik Medan in 2008-2012 was reported as 30% -50% of cases where more cases were found in plantation and coastal areas [6].

Risk factors that can cause CLM are environmental temperature and humidity, age, history of habit of not using footwear, direct contact with the ground, having a dog or cat as a pet and socioeconomic factors [7]. The inflammatory process in CLM is generally chronic and progressive, characterized by lesions. The typical skin is serpiginous in the form of raised reddish color, 2-3 mm in size then forms a tunnel (burrow) accompanied by itching to pain due to intradermal larvae migration [8]. In rare and severe cases, the clinical picture of CLM can be serpiginous or generalized bullae [9,10].

Albendazole and ivermectin are effective against all stages of worms, but the efficacy and success rate of single-dose albendazole therapy are lower (46-100%) than single-dose ivermectin (81-100%) so that albendazole administration must be repeated for 3 days [11]. Topical therapies that can be used include tiabendazole ointment with a concentration of 10-15% or ivermectin and albendazole in topical dosage form for 5-7 days.

In some cases that do not improve with systemic and topical treatments, a combination of frozen surgical therapy (cryotherapy) using carbon dioxide or liquid nitrogen can be considered, however, this is often difficult to do because of the presence of larvae or worm positions is not known with certainty [10]. The purpose of this study is to describe the use of albendazole combination therapy with cryosurgery in CLM cases so that it can add insight, especially as a dermatologist in the management of CLM that does not improve with systemic or topical therapy.

## 2. PRESENTATION OF CASE

A 21-year-old man came to the Dermatology and Venereology Polyclinic of Dr. Moewardi Surakarta with winding reddish spots that feel itchy and hot. The patient complained about 1 month ago that the lesion and spots was reddish then it widened and twisted on the left leg after the patient worked to clean the practicum space. The skin lesions feel itchy, hot and sometimes the patient feels like an animal is moving around, especially when resting. The patient had checked himself into the Puskesmas and received oral medicine and ointment, but the patient did not know the name of the medicine. One week later the skin lesions did not improve, so the patient went to a general practitioner and received oral worm medication in the form of Combantrin® (pyrantel pamoate) 1x250 mg/day and concocted ointment (the patient did not know the contents of the concocted medicine) for 3 days. The patient felt that the complaint has improved and the itching sensation is reduced.

Two weeks later, the patient said that he had a similar complaint on his right leg and it felt increasingly itchy, especially in the knee and right arm. The patient went to Dermatovenerology Clinic, Dr. Moewardi Hospital, Surakarta, and received oral albendazole 1 x 400 mg for 3 days and topical drugs (consisting of a mixture of 400 mg albendazole and 0.05% 15 grams of clobetasol propionate ointment) which were applied occlusively for 7 days. Complaints were felt to have improved but reappeared 1 week later.

From the physical examination, we found erythema papules and hyperpigmented patches and hyperpigmented macules in the serpiginous shape in the right brachial region. In the right genu and cruris regions, we found hyperpigmented patches and macules appear in the serpiginous shape (Fig. 1).

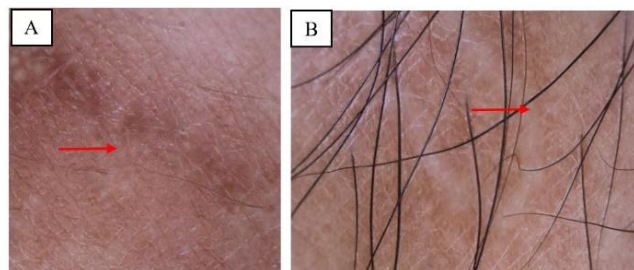
We performed a dermoscopic examination and the result was a serpiginous image consisting of hyperpigmented macules arranged segmentally in the area of the lesion (Fig. 2). Based on the results of anamnesis, physical examination of the morphology of skin lesions, and dermoscopy, we diagnosed the patient with cutaneous larva migrans.

The patient received therapy of oral albendazole 1 x 400 mg for 3 days and a mixed cream containing 400 mg albendazole, 0.05% clobetasol propionate ointment, 15 grams which were applied occlusively for 7 days. We also gave the patient cryotherapy using liquid nitrogen to the lesion in the knee and left leg area where there were still complaints of itching and spreading. The area around the lesion was smeared with Vaseline albumin before spraying liquid nitrogen and cryotherapy was applied twice within 2 weeks, then gentamicin ointment was applied twice a day for erosional areas after spraying (Fig. 3). Patients were advised to return to control 1 week after undergoing therapy and then evaluated for clinical improvement.



**Fig. 1. Clinical manifestations of CLM**

(A) Region brachii right showed erythematous papules (blue arrows) followed by hyperpigmented macules and hyperpigmented patches (red arrows). (B-C) The right genu region showed hyperpigmented patches (green arrow). (D) The left cruris region showed hyperpigmented macules in the serpiginous shape (yellow arrows) and hyperpigmented patches (red arrows)



**Fig. 2. Dermoscopy examination**

(A-B) Region brachii right and genu dextra appear brownish hyperpigmented macules forming serpiginous grooves with distinctive segmental structure (red arrow)



**Fig. 3. Cryotherapy in the hyperpigmented papules at right genus region**



**Fig. 4. A follow-up photo of the patient 2 weeks after the first cryosurgery**

(A) Right brachii region showed hyperpigmented macules in the form of serpiginous grooves (red arrow), (B) Right genus region showed erythema patches and hypertrophic scars (yellow arrows), (C) Left cruris region showed hyperpigmented macules (green arrows) and patches of erythema and hyperpigmentation with hyperpigmented scars (orange arrows)



**Fig. 5. A follow-up photo of the patient 1 month weeks after the second cryosurgery**

(A) Right brachii region showed hyperpigmented macules in the form of repaired serpiginous grooves (red arrow) (B) Right genus region showed erythema patches (repair) and minimal hypertrophic scars (yellow arrows) (C) Region cruris left showed hyperpigmented macules which had undergone improvement (green arrow) and patches of erythema and hyperpigmentation with repaired hyperpigmented scars (orange arrow)

Patients experienced clinical improvement in the form of reduced hyperpigmented areas accompanied by minimal hypertrophic scars after receiving the second cryotherapy, complaints of itching or radiating also improved (Figs. 4 and 5).

### 3. DISCUSSION

The CLM infection begins through direct contact of the intact skin with soil contaminated with feces from dogs or cats, where the feces contain hookworms in the egg or larval phase. In the egg phase, which then enters the skin, it will hatch and become a larva. Adult hookworms can only live in the intestines of animals, whereas in humans the larvae of worms cannot complete their natural life cycle because the larvae do not have enough collagenase enzymes to penetrate the basement membrane and invade the dermis so that the larvae become trapped in the skin tissue, migrate along with the epidermis and leave a rash. linear or serpiginous to form a tunnel (burrow). The incubation period for CLM generally occurs between 10-15 days and can heal on its own, in some case reports it was reported that the larvae died within a period of 4 weeks to several months [11,12] In this case the patient still felt itching which could be caused by the larva invasion. deeper and hit several areas at once.

The appearance of the lesion in the early stages is in the form of erythematous papules, then it develops into erythema macules that are elongated and elevated to form a serpiginous image (2-4 mm in diameter) and tunnels. The predilection for CLM lesions is generally found in the dorsal areas of the arms, inferior extremities, and soles of the feet which have a high risk of contact with hookworm eggs [13]. In the right region of the genus and cruris, macules and hyperpigmented patches appear in the serpiginous shape. The patient's skin lesions appeared in susceptible areas to the external environment and the morphology of the skin lesions was characteristic, so we diagnosed the patient with CLM.

The diagnosis of CLM is based on physical examination of the morphology of typical skin lesions in the form of serpiginous erythema papules accompanied by itching to heat, a history of direct exposure to contaminated soil or sand and living in endemic areas. In this case, a skin biopsy was not performed because it was not specific enough to know the exact location of the worm larvae [12]. Non-invasive investigations

that can be done to help make the diagnosis in the form of a dermoscopy, in which a brownish-yellow transparent area appears that is arranged segmentally resembling a worm shape and several spots blood vessels [14] The results of the dermoscopic examination in the patient showed a hyperpigmented brownish macula in the serpiginous shape which supported the diagnosis of CLM, but in this case, it did not form a segmental area.

The management of CLM includes non-medical and medical, where some preventive efforts that can be done include the use of footwear when doing outdoor activities, avoiding direct skin contact with contaminated soil or sand, if you have a pet, a dog or cat must regularly clean its fur from feces contamination and check with the veterinarian and maintain a clean environment, especially those living in tropical and sub-tropical climates [15]. The main medical therapy in CLM is using anti-worm drugs both topical and systemic. Topical drugs that can be used in CLM include 10% albendazole ointment or 10% -15% tiabendazole ointment for 5-10 days. Both drugs are more effective when applied in an occlusive manner, but in cases, with large lesions, they cannot give maximum results. The first-line oral therapy for CLM is ivermectin at a dose of 0.15-0.2 mg/kg/day (200 µg / kg/day) for 1-2 days, while the second line that can be given is albendazole 400 mg/day for 3 days. but the results are less than optimal when compared to ivermectin because ivermectin has a broader spectrum and is effective at all stages including eggs, but the availability of this drug is still very limited in health facilities, including in Indonesia [16,17].

Treatment in some cases of CLM may consider using frozen surgical therapy with liquid nitrogen, especially in small or small amounts of lesions. Side effects that can occur with the procedure include pain during spraying and topical anesthesia can be given to improve patient comfort, erosive wounds after spraying, and not being able to kill larvae precisely because it is difficult to determine the exact presence of larvae in the epidermal layer [18] The study conducted by Kapadia et al. on 18 CLM patients showed different results, where 9 people who received single albendazole therapy experienced a clinical improvement of 78% while 9 people who received combination therapy of oral albendazole and cryosurgery using liquid nitrogen experienced complete healing by 100% [19].

#### 4. CONCLUSION

The main principle of CLM management is using anti-worm drugs such as albendazole, but these drugs have not been able to provide a maximum cure rate. Choosing a combination therapy modality with cryosurgery can be considered as an alternative in cases of resistant CLM.

#### CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### ETHICAL APPROVAL

Research ethical issues including informed consent, anonymity, and confidentiality, were addressed carefully during the study process. The research ethical clearance approval letter was obtained from the Research Ethics Committee at Dr. Moewardi Hospital, Surakarta, Indonesia, No. 970/XI/HREC/2021, on February 2<sup>nd</sup>, 2021.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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