



Methylene blue-mediated antimicrobial photodynamic therapy for canine dermatophytosis caused by *Microsporum canis*: A successful case report with 6 months follow-up

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ABSTRACT

Dermatophytosis is a superficial skin infection that widely affects companion animals. *Microsporum canis* is one of the most prevalent species isolated from dogs and cats, and because of the serious zoonotic potential, short-term treatment regimens are preferred to prevent the spread of disease either by direct contact or through contamination of the environment. Antimicrobial photodynamic therapy (APDT) has emerged as a promising strategy able to kill effectively a wide range of pathogens in a short period with minimal morbidity. In this case report, a 7-year-old male dog was diagnosed with dermatophytosis caused by *M. canis*. Methylene blue-mediated antimicrobial photodynamic therapy (MB-APDT) was applied over the lesions in two sessions with an interval of 7 days. The dog successfully healed, achieving a complete clinical cure after 21 days, without reports of recurrence after a follow-up period of 6 months. Therefore, MB-APDT could be a potential ally of small animal clinicians to treat superficial fungal diseases and should be further explored in Veterinary Medicine.

1. Introduction

Dermatophytosis, also known as *tinea* or ringworm, is a fungal infection of the skin caused by dermatophytes (*Microsporum* sp., *Epi-dermophyton* sp., and *Trichophyton* sp.). It is the most frequent fungal infection of companion animals, causing superficial skin lesions associated with pleomorphic clinical signs. Due to its infectious and contagious nature, it can be transmitted to humans, highlighting the zoonotic potential of these fungi [1,2]. In small animal practice, treatment is strongly recommended to shorten the course of the disease and also to prevent the spread of dermatophyte agents to other animals and humans [1,2]. In pets, dermatophytosis can be topically or systemically treated in a long-term regimen, depending on clinical presentation. However, the outcomes may range by several individual factors, and recurrence cases are frequently reported [1,2].

Methylene blue (MB) is a cationic dye that is activated by red light, and in the presence of molecular oxygen generates a considerable amount of reactive oxygen species (ROS) that lead to microbial inactivation [3]. MB-mediated antimicrobial photodynamic therapy (MB-APDT) stands out as an interesting approach for superficial

infections in different areas of health science, including Veterinary Medicine, with promising results [3]. Indeed, the literature is vast regarding MB-APDT against a broad range of microorganisms, highlighting the broad spectrum of this therapeutic approach. In this regard, MB-APDT can inactivate both spores and hyphae of dermatophyte agents [4]. Thus, MB-APDT could become an ally of small animal clinicians to treat skin infections since it has been considered a cost-effective therapy without causing adverse effects.

So far as our knowledge goes, the use of MB-APDT has not yet been explored for dermatophytosis in pets, which encourages us to investigate its clinical effectiveness. Herein, we report a case of canine dermatophytosis caused by *M. canis* successfully treated by MB-APDT.

2. Case report

A Pekingese 7-year-old male dog was presented with nonpruritic ulcerated skin lesions with a crusty covering in the lower back (Fig. 1A). After cleaning the region, it was observed two well-defined round-shaped lesions with areas of hair loss (alopecia), erythema, and inflammatory reactions (Fig. 1B). The clinical suspicion was dermatophytosis,

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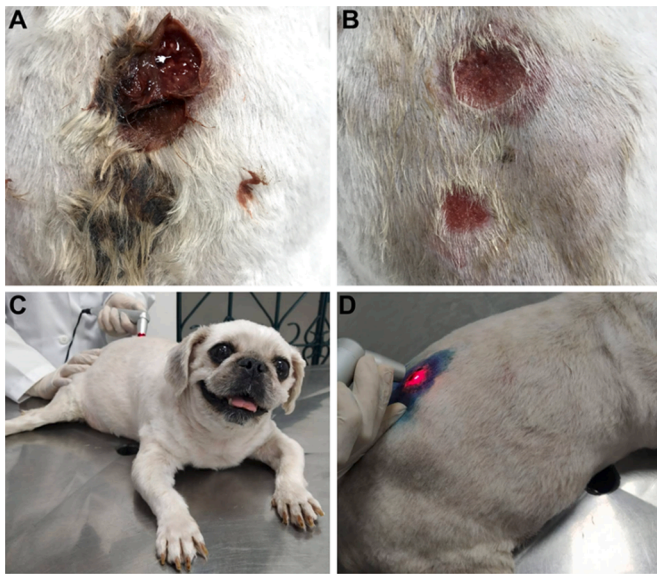


Fig. 1. Representative images of dermatophytosis in a dog infected with *M. canis*. Clinical presentation of lesions before (A) and after (B) cleaning, followed by MB-APDT sessions (C and D).

further confirmed by a fungal culture that identified *M. canis* growth.

Medical records revealed that the animal was previously treated with systemic glucocorticoid therapy due to a chronic condition of osteoarthritis. Biochemical markers revealed abnormalities in liver enzymes, displaying increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase. Lesions were exclusively treated with MB-APDT. In brief, topical administration of 3 mL of

MB aqueous solution at a concentration of 500 μM (Sigma-Aldrich, USA) was directly performed on the wounds through a syringe. After 10 min, we irradiated punctually the lesions with a diode laser emitting a wavelength of 650 nm, radiant exposure of 30 J/cm^2 , 6 J and 150 s per point (total of 4 points), 40 mW, spot size 0.2 cm^2 , and irradiance of 200 mW/cm^2 (STARLaser®, Microdont, SP, Brazil) (Figs. 1C and D).

The dog was monitored every week for 4 weeks, then every month for 6 months. The areas of both lesions were significantly reduced by 4-fold, showing small circular patches, keeping the round ring shape characteristics 7 days post-treatment (Fig. 2A). After 14 days, the upper lesion was reduced by approximately 90%, displaying a very small wound at the center of infection, whereas in the lower one no wounds were observed (Fig. 2B).

On the 21st day, no erythema or inflammatory signs were noticed in both lesions, suggesting that the lesions were completely healed (Fig. 2C). Interestingly, hair regrowth around the lesions was observed within one month after healing, achieving a complete coverage in 2 months, which was sustained for the evaluated period (6 months) (Figs. 2D-E).

3. Discussion

In this case report, we have demonstrated that MB-APDT was very effective to treat a dog with dermatophytosis, achieving successfully wound healing in a short period, and sustained for 6 months without recurrence.

The most common treatments of dermatophytosis in pets comprise a combination of topical and systemic drugs in a long-course regimen [1, 2]. However, oral antifungals in high concentrations might promote multiple side effects, including vomiting, anorexia, and increased levels of AST and ALT, thereby resulting in hepatotoxicity [1,2]. The treated dog had already shown abnormal liver enzymes, owing to the previous glucocorticoid administration. Therefore, topical MB-APDT could be

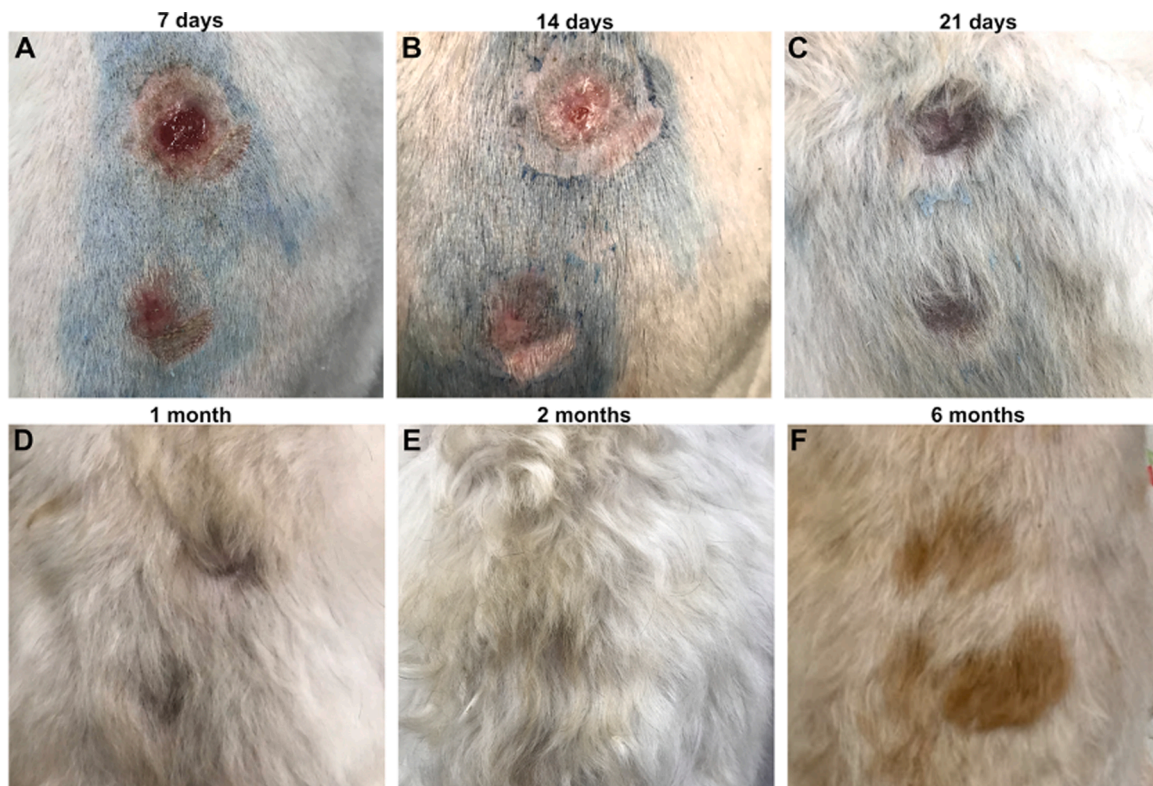


Fig. 2. Representative images of MB-APDT outcome in a dog suffering from dermatophytosis caused by *M. canis*. (A) 7 days after the first MB-APDT session. (B) 14 days after the first MB-APDT session and 7 days after the second one. (C) 21 days after the first MB-APDT session and 14 days after the second one. (D, E, and F) 1, 2 and 6 months after the first MB-APDT session, respectively.

considered a safe and efficient alternative to prevent further systemic adverse effects.

The association of topical therapy is usually recommended to shorten the duration of treatment and avoid further contamination, hence preventing the zoonotic risks either via direct contact or through the spread of pathogens in the environment [1,2]. Despite that, the current solution/shampoos should be applied twice weekly, and topical creams are mostly used on a daily regimen, for several weeks, which can be expensive and/or time-consuming [1,2].

Remarkably, APDT achieved a satisfactory clinical outcome in only 2 sessions showing complete clinical healing after 21 days, with minimal intervention, and without side effects. This is an encouraging result since, in general, commercially available drugs promote clinical cure within 4 weeks or months after therapy [1,2].

Yet, considering that APDT is a non-invasive technique, it could reduce animal distress, improving their welfare, which is desirable for a good prognosis. Indeed, it has been demonstrated that increased levels of cortisol caused by chronic stress might play an important role in the downregulation of immune response, hence contributing to the progress of dermatophytosis infection [2]. Thus, as a low-stress handling procedure, APDT ensures the patient's well-being during the treatment, resulting in a better outcome. Additionally, MB-APDT has also been shown to be a time-saving and cost-effective therapy, overcoming the major drawbacks of the conventional treatments of dermatophytosis [5].

In summary, this is the first case report describing a successful therapeutic strategy using MB-APDT for the treatment of dermatophytosis in a dog. Our findings support the results of previous studies that have shown MB-APDT to be effective against dermatophytes *in vitro* [4] and also shed light on the use of MB-APDT as a promising approach in small animal practice. In this regard, some recent studies have already

demonstrated that APDT could be an ally to treat infections in companion animals [6,7]. This is a case report and *in vitro* antimicrobial sensitivity testing might prove of value when examined in larger series. Finally, we hope that this case report encourages small animal clinicians and researchers to further explore the use of such promising therapy in Veterinary Medicine.

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