

Case Report

Methylene blue-mediated antimicrobial photodynamic therapy: A novel strategy for digital dermatitis-associated sole ulcer in a cow – A case report

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1. Introduction

Sole ulcer (SU) is one of most prevalent causes of lameness in dairy cows, being responsible for negative economic and welfare implications. Early identification and effective treatment are essential to reduce clinical complications [1]. In our understanding, an ideal approach for treatment of infected SUs should not cause side effects, induce antimicrobial resistance or environmental damages, neither lead antibiotic residues in milk or meat.

In this context, antimicrobial photodynamic therapy (aPDT) has arisen as an innovative approach to treat local infections in veterinary practice [2]. aPDT combines a photosensitizer (PS) with light and oxygen. In this study, we investigated methylene blue (MB)-mediated aPDT to treat a dairy cow suffering from an infected SU.

2. Case report

An adult crossbreed cow presenting clinical lameness (locomotion score 4) for 15 days and unsuccessfully treated with anti-inflammatory drugs was admitted at the teaching hospital of University of São Paulo. The animal was restrained in lateral recumbency on a hydraulic tilt table chute for diagnosis and treatment procedures. A detailed clinical examination revealed a digital dermatitis (DD)-associated SU in the lateral claw on the left hind foot. Clinically, the lesion presented a full thickness defect in the epithelium, malodorous, painful, with irregular

borders, and draining blood in the disruption site at the heel bulb, with approximately 1 cm of diameter. A rigid probe was inserted into the lesion to identify the extent and depth of the infection in the internal structures of the digit. The bone surface of the third phalanx was not involved, and a large extent of loose horn was present indicating the infected pathway through the solar corium tissue.

After cleaning and claw trimming, the loose horn and necrotic tissue were removed under regional anesthesia, exposing an extensive lesion. Subsequently, an orthopedic block was fixed to the sound digit on the same foot to reduce weight bearing through the damaged claw (Fig. 1A). To carry out aPDT, we topically administered about 10 mL of MB aqueous solution at a concentration of 0.1% (Sigma-Aldrich, USA) on the lesion. After 10 min of pre-irradiation time to allow PS uptake, we irradiated punctually the lesion with a diode laser emitting $\lambda = 660$ nm, fluence of 140 J/cm^2 , 4 J and 40 s per point, 100 mW, and fluence rate of 3.5 W/cm^2 (Therapy XT, DMC[®], Brazil) (Fig. 1B). Then, the lesion was protected by a bandage to reduce environmental contamination. A pain support treatment was done with a nonsteroidal anti-inflammatory drug (Meloxicam, 0.5 mg/kg, SID) during the first three days. The animal was maintained in a soft deep shaved wood bedding to reduce the pressure on the claw lesion. aPDT and bandage were repeated once a week until complete recovery of the lesion, and if the block got lost between changes of bandages it was immediately re-attached. Clinical evaluation was based on locomotion score, reduction of injured area and inflammatory signs, and time for complete healing

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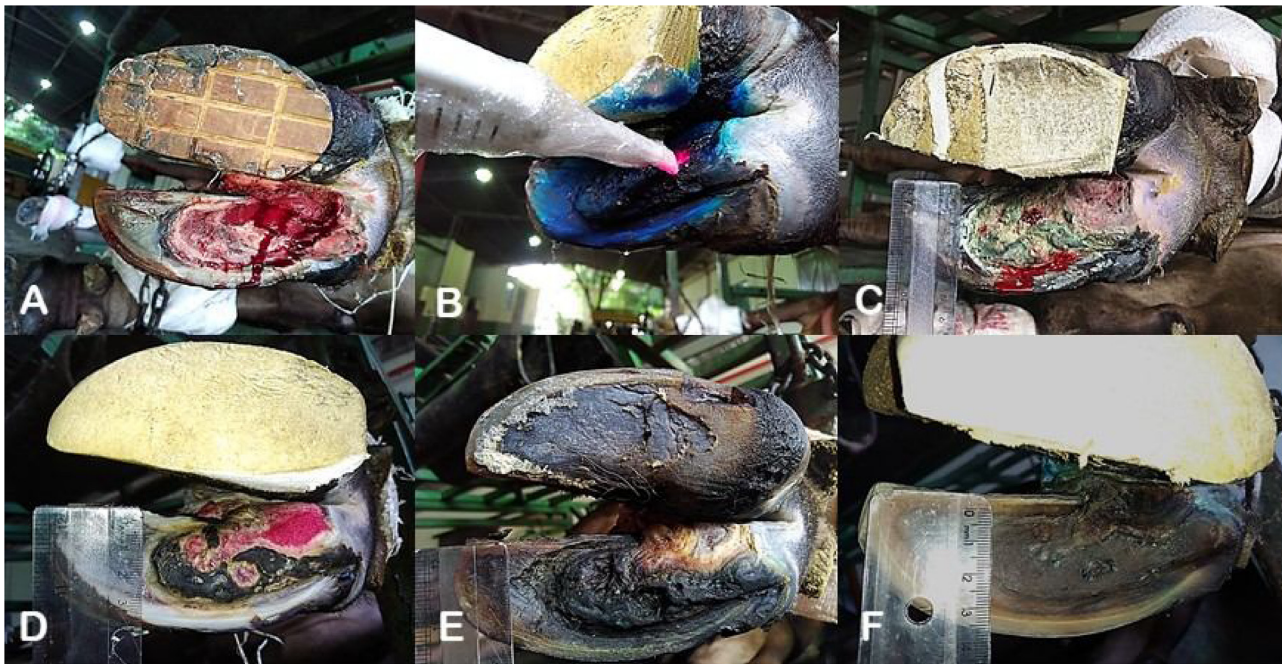


Fig. 1. Representative images of DD-associated sole ulcer treated by aPDT. Initial lesion after cleaning, claw trimming, and necrotic tissue debridement (A); application of the photosensitizer MB and irradiation with the diode red laser (B); Lesion aspect one week (C), 21 days (D), 35 days (E), and 57 days (F) following aPDT showing significant improvement and recovery of the lesion at the end of treatment.

(i.e., new hard horn tissue covering the entire lesion).

New horn and granulation tissues were present from the margin to the center, respectively, and the recovery area was remarkably visible following the first week post-aPDT (Fig. 1C). After 21 days, we noticed a significant reduction in inflammation and lesion size by about 70% (Fig. 1D) as well as a clinical improvement of the lameness. After a month, the sole was covered by irregular soft keratin with no bleeding signs and a small single lesion on interdigital heel (Fig. 1E). The completed healing was achieved after 57 days (locomotion score 2) (Fig. 1F). Moreover, no adverse effects were observed during the follow-up period.

3. Discussion

In our study, aPDT proved to be a suitable option to treat DD-associated SU, which exhibited complete healing after 57 days. Severe lesions require between 40 and 60 days for complete reepithelization [3]. However, MB-mediated aPDT presented longer healing time than that reported by Kofler et al. (38 days) [4]. This difference could be explained by environmental and intrinsic factors of lesion (e.g., housing, bedding, extension of lesions and by the type of surgical treatment and aftercare) [5].

Our findings showed that MB-mediated aPDT promoted complete healing after 8 sessions. In this respect, we performed aPDT only once a week to be feasible with the bandage replacement, however, if we shorten the interval between aPDT sessions, the complete healing could occur faster.

There is no consensus on the best treatment for SU. Therapeutic trim associated with the use of block on the sound claw is the most reported method for favorable clinical outcomes [1]. Literature has also reported the use of topical antibiotics to avoid contamination and secondary abscess formation [3], but the administration of antibiotics remains controversial [1].

In this study, we ratify the use of aPDT in Veterinary Medicine and emphasize a non-antibiotic option for this disease. Interestingly, other

recent studies addressing aPDT for infectious diseases in food-producing animals showed promising results [2], being recognized as an attractive approach by European Medicines Agency (EMA) and European Food Safety Authority (EFSA) [6].

Although aPDT is not yet in the mainstream veterinary practice, it could represent a cost-effective treatment for SU, and other claw diseases (e.g., bovine digital dermatitis, toe lesions, etc.) opening a new avenue in this setting. We hope this preliminary study will be helpful for large animal clinicians and scientists and contribute as a stimulus for further research on aPDT in Veterinary Medicine.

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