



Photobiomodulation Therapy for Multiple Painful Fixed Drug Eruptions: The First Case Report

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Abstract

Introduction: Fixed drug eruption (FDE), a very specific adverse drug reaction and one of the most common types of drug eruption, generally resolves spontaneously within 7-10 days upon withdrawal of the causative agent; however, extensive and severe cases may also require systemic drug therapy. The present study aimed to report a case in which a broad spectrum of severe, painful lesions of FDE was managed with photobiomodulation therapy (PBMT).

Case Report: A 31-year-old Caucasian woman presented with many extremely painful mucocutaneous lesions of FDE which had arisen 8 days before, following a long period of hospitalization. The lesions were not responsive to either corticosteroids or analgesics within 5 days, and then seven daily sessions of PBMT were proposed. Pain alleviation was achieved on the 1st day of PBMT, and the lesions showed an advanced course of healing on the 3rd day. Within 7 days of PBMT, the lesions were almost completely repaired. In a 3-month follow-up period, no relapse of any FDE lesion was reported.

Conclusion: PBMT may be a promising strategy for the management of painful lesions of FDE refractory to conventional medication therapy. However, further studies are needed to confirm this hypothesis.

Keywords: Fixed drug eruption; Autoimmunity; Photobiomodulation therapy.



Introduction

Fixed drug eruption (FDE), a very specific adverse drug reaction and one of the most common types of drug eruption,¹ is characterized by either only one or a small number of erythematous or violaceous circular patches, plaques, or bullae with a dusky grey center^{2,3} that relapse on the same sites following exposure to the causative agent.⁴ Although the lesions may be self-limiting and present with no symptoms,^{4,5} in some cases, they may rupture easily, leading to erosions or ulcers.⁶ Overall, long-lasting or even permanent hyperpigmentation is noted after the resolution of the lesions.⁴

The FDE management is based on the severity of the reaction.⁷ The lesions may diminish or relieve upon withdrawal of the causative agent; however, systemic antihistamines associated with topical corticosteroids are generally necessary. Extensive and severe cases may require systemic corticosteroids, and if open wounds are present, oral antibacterials should be administered to prevent secondary infection.¹ Besides that, as with other severe allergic reactions, intensive supportive care and

maintaining fluid and electrolyte balance should also be considered.⁷

Photobiomodulation therapy (PBMT), a non-invasive treatment modality generally used to mitigate pain, stimulate wound healing, and control inflammation,^{8,9} has already proven its efficiency in modulating immunologic processes as well.¹⁰ Thus, the present paper aimed to report a case in which a broad spectrum of severe, painful lesions of FDE was managed with PBMT.

Case Report

A 31-year-old Caucasian woman presented seven extremely painful mucocutaneous lesions that had arisen about 8 days before, following a long period of hospitalization (microvascular decompression for trigeminal neuralgia). Oral analgesics were not effective enough for pain relief. The worst provoked pain (in contact) from the ulcers was “10” on a 0 to 10-point visual analog scale (VAS). No other systemic or local disease, pathology, or syndrome was present.

The patient reported that similar episodes had already

occurred many other times (i.e., lesions with different clinical features which arise suddenly at the same sites and heal with residual hyperpigmentation) and the diagnosis of FDE had been made clinically and by skin biopsy to rule out differential diagnoses; however, the causative agent had never been identified. She also told us that the lesions had been generally self-limited and recovered without treatment within 5 days, but, when necessary, systemic and topical corticosteroids had been highly effective for full remission (20 mg oral prednisolone and 0.05% topical clobetasol, three times daily). From her point of view, she had never presented a severe episode like that.

After clinical examination, mucocutaneous lesions inducing spontaneous pain and of variable sizes, colors, and surface features were present throughout the body:

1. 4 cm × 3 cm lesion on the buttocks (at right) - erythematous, circular, and slightly raised spot, with colors ranging from brown to a dark shade of red (Figure 1A);
2. 3.5 cm × 2 cm lesion on the hip (at right) - reddish, erythematous, circular, and slightly raised blister (Figure 1B);
3. 2 cm × 1 cm lesion on the thigh (at left) - reddish-brown, erythematous, circular, and slightly raised spot (Figure 1C);
4. 4 cm × 3 cm lesion around the umbilicus - reddish, erythematous, circular, and slightly raised spot (Figure 1D);
5. 1.5 cm × 1 cm lesion on the knee (at left) - reddish-brown, erythematous, circular, and slightly raised spot (Figure 1E);
6. 1.5 cm × 1 cm lesion on the cheek (at right) - reddish, erythematous, circular, and slightly raised spot (Figure 1F);
7. 1 cm × 0.5 cm lesion on the upper lip (at right) - erythematous, circular, and slightly raised blister,

bright red in color (Figure 1G).

Once the administration of oral and topical corticosteroids had been unsuccessful in healing the lesions and oral analgesics had failed to alleviate pain (for approximately 5 days), seven daily PBMT sessions were proposed as an adjuvant. This laser treatment was promptly initiated at the first medical appointment (Table 1). Twenty illumination points were distributed according to lesion size (lesion 1=5 points; lesion 2=5

Table 1. Device Information and Irradiation/Treatment Parameters

Features	Information
Manufacturer	MMOptics® Ltda
Model identifier	Twin Flex III Evolution
Number of emitters	One emitter
Emitter type	InGaAlP
Type of laser	Diode
Operation mode	Continuous
Center wavelength	660 nm
Exposure duration	10 s
Delivery system	Optical fiber
Energy density	25 J/cm ²
Energy per point	1 J
Number of points irradiated	20 points
Total radiant energy	20 J
Peak radiant power	100 mW
Average radiant power	100 mW
Focus spot area	0.04 cm ²
Beam spot size on the target	0.04 cm ²
Irradiance on the target	2.5 W/cm ²
Application technique	Skin contact
Number and frequency of treatment sessions	1 week, daily sessions
Beam divergence	No

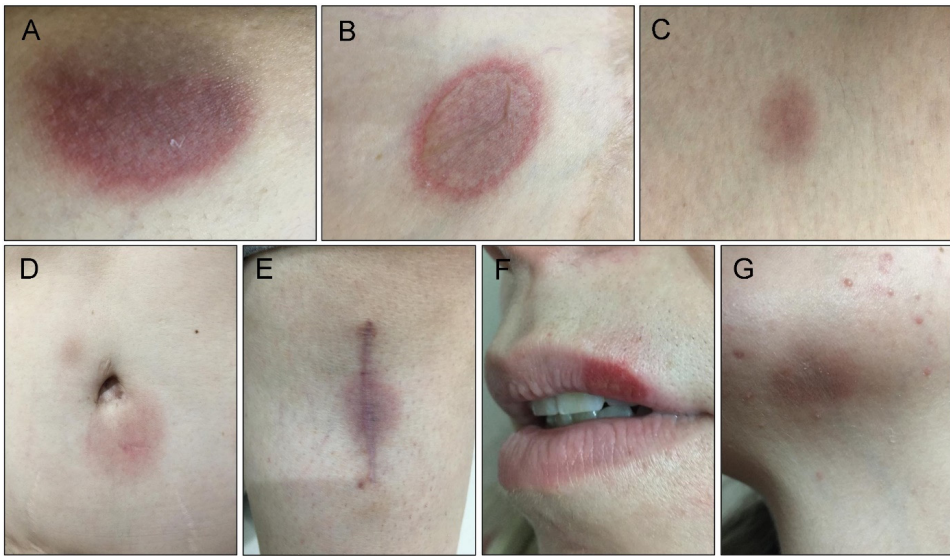


Figure 1. Clinical Presentation of Multiple Painful Fixed Drug Eruptions: 8 Days Following the Onset (the first medical appointment).

points, lesion 3 = 1 point; lesion 4 = 5 points; lesion 5 = 2 points; lesion 6 = 1 point; lesion 7 = 1 point).

Although the laser handpiece induced pain momentarily due to direct contact with the injured tissues, immediate pain alleviation (worst score, VAS scale = "6") was achieved on the 1st day of PBMT and analgesics were no longer needed. On the 3rd day, all the lesions were in an advanced course of healing; that is, epithelialization on the blister areas and mitigation of inflammation signs on the spot areas were noted (worst score, VAS scale = "4"). On the 4th day, the patient reported complete pain relief (worst score, VAS scale = "0"). After the 1st week of PBMT, the lesions showed almost complete recovery (Figure 2A-G) and both corticosteroids could be gradually tapered to withdrawal. She was also advised to seek medical help to identify accurately the causative agent by further challenge tests. In a 3-month follow-up period, no relapse of any mucocutaneous lesion was reported.

Discussion

The current paper presented a broad spectrum of severe, painful lesions of FDE not responsive to oral and topical corticosteroids, which had been administered for 5 days. Besides that, oral analgesics were also not effective for pain relief. FDE, unlike that, is recognized as an immunological cutaneous adverse reaction⁴ that generally resolves spontaneously within 7-10 days upon withdrawal of the causative agent,¹¹ information that makes this report very unusual and interesting.

Although systemic antihistamines and topical corticosteroids are necessary for most patients with FDE, extensive and severe cases - as shown herein - may also require systemic corticosteroids and even antibiotic drugs.¹ The rationale for using PBMT was based on both the ineffectiveness of conventional medication therapy commonly recommended and the uncertainty about the

causative agent of the lesions (probably a drug received during the hospitalization period). To the best of the authors' knowledge, there is no other study regarding the benefits of any phototherapeutic approach for lesions of FDE.

The general benefits of PBMT are largely described in the literature. It is considered a conservative, safe, painless, and low-cost treatment option¹² due to its capacity for modulating some events of the inflammatory response, mitigating pain, and promoting healing.^{9,13} In Dermatology, laser therapy has long been used for aesthetic purposes but its anti-inflammatory effects have recently gained attention - especially for immune-mediated cutaneous diseases.¹⁰ Although PBMT seems to influence immune cell infiltration in both animal models and human skin, the heterogeneity among the few available studies makes it impossible to reach definitive conclusions about the exact mechanisms and clinical advantages of PBMT in immunological cutaneous adverse reactions.¹⁰

Considering only such studies in humans, a phototherapy approach with 830 nm and 633 nm was used for psoriasis (a chronic, recurrent, immune-mediated disease with manifestations in the skin) and showed 90% to 100% clearance of recalcitrant lesions. The author suggested that the results were probably based mainly on the effects of the light energy at 633 nm in recruiting many Th1 and Th2 skin-homing T-cells, which might help to replace the rogue T-cell population and eliminate the psoriatic vicious circle.¹⁴ Likewise, radiation at 600-1600 nm was used for treating alopecia areata - a chronic and recurrent autoimmune disorder that affects hair follicles - and showed a success rate of 46.7%; however, the authors did not present any conclusive evidence of the immunologic mechanisms of light treatment.¹⁵ On the other hand, more recently, it has been suggested that PBMT may

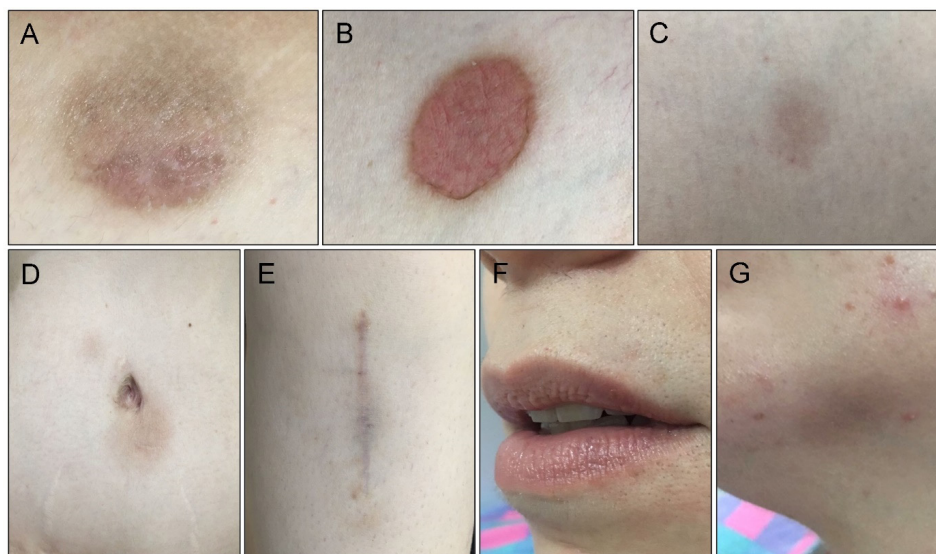


Figure 2. Clinical Presentation of Multiple Painful Fixed Drug Eruptions: One Week of Photobiomodulation Therapy (15 days following the onset of the lesions).

induce metabolic reprogramming in the regulation of the innate inflammatory response, involving mainly both macrophage activation and function and resulting in a less inflammatory environment – where the T-cell attack against the hair follicle would also be reduced.¹⁶

The findings from the current study are encouraging; however, they should be interpreted with caution. Although case reports are suitable to present novel clinical findings and to create novel hypotheses on pharmacological strategies, as well as being highly applicable for conditions in which other study designs are not feasible, they may present bias that could affect the outcomes reported, given all the unavoidable limitations (e.g., the retrospective, nonblinded, and nonrandomized study design).¹⁷ Future studies should therefore be designed with both a representative number of patients and a particular emphasis on laser parameters, as the protocol proposed herein was empirically developed considering mainly our experience in managing orofacial lesions of different natures and the features of our laser device.

Conclusion

PBMT may be a promising strategy for the management of painful lesions of FDE refractory to conventional medication therapy. However, further studies are needed to confirm this hypothesis and to identify the best laser parameters for it.

Acknowledgments

The findings and conclusions of this case report are the responsibility of the authors.

Competing Interests

No potential conflict of interest was reported by the authors.

Ethical Approval

The patient gave informed consent.

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