



Case Report

Adverse effects of topical photodynamic therapy in rosacea – Case report

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ABSTRACT

Rosacea is a chronic and inflammatory skin condition, with relapses being a common characteristic. Its treatments are based on cosmetics, drugs, and the application of procedures based on high-powered light. Photodynamic Cosmetic Therapy (PCT) combines light, a photosensitizer (PS), and molecular oxygen present in tissues, generating photochemical reactions capable of causing tissue and vascular destruction, stimulating tissue repair. We report a case with an adverse effect caused by applying PCT, using 2 % 5-aminolevulinic acid (ALA 2 %), and irradiated with amber LED light associated with infrared radiation for the control of rosacea. A patient with subtype II rosacea underwent PCT treatment of 3 sessions at 21-day intervals, being evaluated using photographic images and Wood's lamp. In the first session of the therapy, an exacerbated inflammatory process was observed. Such an adverse event is estimated to be as a result of the patient using ointment containing corticosteroids for a short period. With the use of medications, it was possible to recover the appearance of the skin thoroughly, and after 21 days, the treatment sessions were performed again. Despite the complication that affected the patient in this study, positive effects were found after the pharmacological therapeutic measures were adopted.

1. Introduction

Rosacea is a chronic and inflammatory skin condition that presents clinical features of inflammation and excessive vascularization with repeated remissions and exacerbations being common characteristics [1].

The treatments are based on cosmetics, drugs and the application of procedures based on high-powered light [1]. Among the different treatment types, Topical PDT effectively controls vascularization and tissue remodeling, strengthening the skin protection barrier. During Topical PDT, the patient receives the endogenous PS precursor, a cream containing ALA, and, after a certain period, the affected region is irradiated, inducing the formation of reactive oxygen species (ROS) capable of activating antioxidant defense systems, as well as stimulating tissue regeneration, promoting epidermal and dermal redensification. It produces pathology management, mild to moderate inflammation levels, with quick skin recovery and offers patients greater comfort, after application of therapy [2–4].

This case study presents an atypical manifestation of a patient facing

the proposed treatment of Topical PDT using ALA 2 % irradiated with amber LED light associated with infrared radiation.

2. Case report

A 42-year-old woman presented subtype II rosacea lesions in the central region of the face, extending to the buccinator, forehead, and chin areas (Fig. 1A). She has been attempting conventional therapies for approximately 20 years, without satisfactory results, in addition to the frequent use of topical Betamethasone, a potent corticosteroid with an anti-inflammatory action.

After anamnesis, the protocol established was three sessions of Topical PDT, with irradiation 2 h after the application of the ALA 2 % formulation. In the initial evaluation, an image (Fig. 1B) was captured with Wood's lamp (Derma Scan Estek) at a wavelength in the region of 365 nm (UVA).

Initially, the face was cleaned, ALA 2 % cream (PDT-Pharma-Brazil) subsequently applied, and the patient was kept at rest in a dark environment. The waiting time was determined in line with the monitoring

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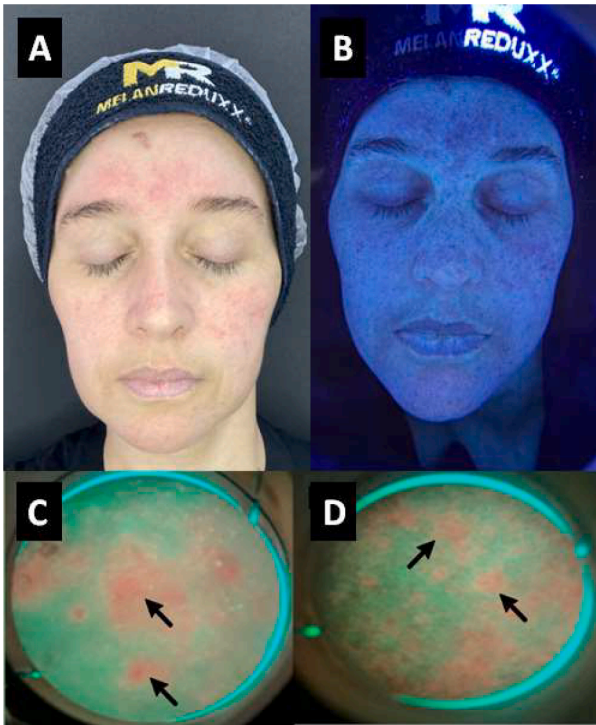


Fig. 1. (A) Image captured BEFORE treatment; (B) Initial image with Wood's Lamp aimed at clinical diagnosis and evolutionary control of pigmentation and its observed porphyrias. (C) Evidence of Protoporphyrin IX production at one hour and two hours (D) of incubation was captured with Evince.

of Protoporphyrin PpIX production through fluorescence, using the Evince equipment (MM Optics – Brazil), by 100 mW LED and with emission at 405 nm \pm 10 nm. After two hours, intense red fluorescence was observed, indicating the formation of PpIX (Fig. 1C and D).

The patient underwent irradiation using the Vénus Delta equipment (MM-Optics, Brazil), with Amber LED light emission (590 nm \pm 10 nm, 150 mW) at a fluence of 81 J/cm², associated with Infrared (IV) laser (808 nm \pm 10 nm, 100 mW), at a fluence of 2 J/cm², being applied simultaneously in 5 phases, the first continuous, and the others, pulsed phases (60 to 198 pulses per minute) totaling 5 min.

After the first Topical PDT session, mild erythema was observed. Four hours after the treatment, the patient reported the presence of intense erythema (Fig. 2A). After 24 h of Topical PDT application, the patient reported a burning sensation, the presence of blisters, and exacerbated edema, erythema, and pustules (Fig. 2B and C). After 48 h (Fig. 2D and E), there was a picture of high inflammation. To modulate the inflammation, the patient underwent topical and oral treatments with antibiotics (cephalexin 500 mg-1 tablet every 8 h for 7 days) and corticosteroids (dexamethasone 4 mg-1 tablet every 12 h for 3 days and diprogenta cream- applied 3x a day on the affected area). After the use of medication, an improvement in the inflammatory condition was observed (Fig. 2F–H) 72 h after the application of Topical PDT. After controlling the inflammation, the tissue repair process was initiated. The process of tissue desquamation began (Fig. 2I and J), and one week after Topical PDT, the appearance of the skin improved (Fig. 2K), presenting full recovery nine days after the Topical PDT and seven days after starting the drug intervention (Fig. 2L).

After the atypical manifestation and total skin recovery, the time between Topical PDT sessions was altered from 15 to 21 days, aiming at a longer time for skin recovery. During the second and third applications, sensitivity was described after application, without major complications and hyperemia in the rosacea region but with bearable sensitivity and good tolerance of the procedure.



Fig. 2. Images showing the presence of intense erythema on the skin (A), and 24 h after Topical PDT application, blisters, exacerbated edema, erythema, and pustules were present (B)–(C). 48 h after Topical PDT, persistent symptoms (D); Persistent symptoms, intense erythema, edema, and pustules (E). (F) Appearance of the face after starting drug treatment. (G) Appearance of the patient 72 h after application of Topical PDT; (H)–(J) A desquamation process is observed, followed by tissue renewal in the treated area. (K) One week after Topical PDT; (L) Total recovery nine days after Topical PDT and seven days after the start of drug intervention.

3. Discussion

This study describes the condition of a 42-year-old female patient with a history of rosacea for approximately 20 years. The patient had been using topical Betamethasone intermittently for 10 years, a corticosteroid with potent anti-inflammatory and anti-allergic action, but the patient discontinued the use of medication days before the procedure. Its prolonged use can cause adverse effects, including unusual and rare skin reactions, difficulty in healing, and even bruising, hyperemia, and hypersensitivity [4,5].

The patient presented hypersensitivity to the treatment 24 h after applying Topical PDT [4,5]. It is believed that this exacerbated inflammatory response is due to the prolonged use of steroids, providing greater sensitivity to the treated region. According to Liu et al. [5], in patients with rosacea, dermatitis, and/or inflammatory skin diseases, who frequently used medication based on corticosteroids, removing the drug from the body can influence the control of inflammation, increasing the risk of adverse effects. Some studies show positive results from the application of Topical PDT in rosacea, with a mild or moderate inflammatory response observed. However, the greater the inflammatory response, the greater the tissue repair response [2–5]. As far as we know, this study is the first to demonstrate complications after applying Topical PDT using ALA 2 % as a precursor to PpIX in the treatment of rosacea.

Despite the clinical case reported here, it is important to point out that Topical PDT is generally well tolerated but can cause unexpected reactions. It is crucial to deal with these reactions adequately so that

they do not become an impediment in the application of the therapy.

Photodynamic Therapy offers a promising approach in the treatment of rosacea, triggering beneficial effects. Amber light interacts with PpIX in mitochondria, stimulating mitochondrial biogenesis, which activates tissue healing and neovascularization. This results in the reduction of vascular effects of rosacea caused by compromised vascularization. On the other hand, infrared light indirectly interacts with PpIX in the mitochondrial respiratory chain, increasing the permeability of the cell membrane, aiding in skin hydration control. Additionally, it effectively modulates inflammation, promoting a protective skin barrier effect, which is often compromised in individuals with rosacea [6].

Although complications were observed after the first Topical PDT session, the condition was quickly controlled, restoring the health and integrity of the patient's skin. The subsequent sessions took place within a 21-day interval, with no adverse reactions or exacerbated inflammatory response being observed, also due to adequate betamethasone pause [4,5]. The result obtained after the third Topical PDT session showed an improvement in the quality of the skin, reducing the inflammatory and vascular conditions affected by rosacea.

4. Conclusion

Topical PDT effectively managed rosacea, even with complications, which can be attributed to the use of topical corticosteroids, which triggered an exacerbated inflammatory response. However, the acute inflammatory condition does not impede the continuation of the treatment. Once the complication is treated and the course of treatment is adjusted, it is possible to resume the Topical PDT.

CRediT authorship contribution statement

Priscilla Fróes Sebbe-Santos: Methodology, Investigation, Writing

– original draft. **Patrícia Miquilini:** Methodology, Data curation, Investigation. **Juliana Guerra Pinto:** Writing – review & editing, Data curation. **Priscila Fernanda Campos de Menezes:** Methodology, Writing – review & editing. **Juliana Ferreira-Strixino:** Supervision, Resources, Methodology, Funding acquisition, Formal analysis, Conceptualization, Project administration, Writing – review & editing.

Declaration of Competing Interest

This text has been revised and edited as necessary and I assume full responsibility for the content of the publication.

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