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Case report: Pemphigus foliaceus in 15-Year-Old Girl with Response to Oral Corticosteroid Therapy and Anti-inflammatory Nd:YAG Laser Irradiation

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ABSTRACT

Pemphigus foliaceus (PF) is a rare autoimmune bullous dermatosis in the pediatric population. We report the case of 15-year-old girl who was diagnosed with PF four months following the onset of her symptoms. Oral and topical corticosteroid therapy have proven to be effective but would predispose patients to infections. Bacterial skin infections detected in our patients were due to Methicillin-resistant Staphylococcus aureus, Klebsiella spp, and Candida albicans. We introduce long pulse Nd:YAG laser as novel therapy like "selective photoantisepsis" for inhibition of bacterial and fungal growth.

Key words: pemphygus foliaceus, Nd:YAG laser, anti-inflammatory property, wound healing.

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I. INTRODUCTION

Pemphigus foliaceus (PF) is an autoimmune blistering disorder that is characterized by scaly, crusted, and erosive erythematous lesions, which rarely develop into erythroderma. It is anecdotally described in the pediatric population, but in cases of sporadic PF in children, patients often have a distinct configuration as arcuate, circinate, and/or polycyclic. The differential diagnosis of non-endemic PF includes bullous impetigo, IgA pemphigus, drug eruption, sub-corneal pustular dermatosis, lupus erythematosus, and seborrheic dermatitis may be considered. There are no strict therapeutic guidelines for PF in children. It is suggested that the first line of systemic corticosteroid needs to be combined with antimicrobial therapy in case of expected secondary bacterial or fungal contamination as a complication from prolonged use of immunosuppressive therapy over the months.

II. CASE

A 15-year-old girl visited our clinic, complaining of diffuse erythroderma with scales and erosions in various locations around her body, predominant on scalp, face, neck, chest, back, gluteal area, and flanks. There was no mucosal involvement. The patient did not review any medication usage before the onset of skin manifestation. Skin lesions were painful with a burning sensation as well as with superficial sores and areas greasy yellowish crusting over the facial and body area. Nikolsky's sign was positive. Bilateral submandibular and axillary lymph nodes were palpable, mobile, and non-tender.

Figure 1: (a) Dermatology status on the face and neck before starting the laser treatment showed blistering, oozing, and crusting lesions measuring 0.8 x 2cm. (b) Ongoing assessment showed complete regression of the lesions with light post-inflammatory hyperpigmentation.

The symptoms gradually worsened over a period of 4 months, and became widespread, under the treatment with long doxycycline, azithromycin and topical fusidic acid therapy. Oral antibiotic therapy was not successful, antimicrobial resistance occurs, bacteria and fungi colonization change over time and no longer responded to medicines making clinical picture of PF harder, with increasing the risk of disease spread. Physical examination revealed erosive, severe edematous erythematous lesions with abundant exudates, profuse scaling, and crusting (Fig.1a, 2a, 2c, 3a).

Investigation: A biopsy specimen from a fresh lesion on the neck showed acanthosis, dyskeratotic cells, and exudation. The granulation layer was preserved and expanded with detached degenerated keratinocytes and an expanded exudate. The epidermis showed reactive

hyperplasia. Around the superficial vascular plexus there was a scarce to moderate mononuclear infiltrate. No migration of inflammatory cells and eosinophils.

Figure 2. (a, b) A close-up view of a skin lesion on the back and upper limb with multiple blistering lesions. (c,d) Resolution of lesions with resudual post-inflammatory hyperpigmetnation, 8 weeks after initialisation of laser treatment

Direct immunofluorescence (DIF) showed a deposition of IgG and C3 on the epidermal intercellular space. The patient tested positive for anti-desmoglein (DSG) 1 IgG measured by ELISA (>1,000 U/mL) and negative for Anti DSG 3 (Invitrogen, Thermo Fisher Scientific).

Bacterial swabs were collected from clinically infected lesions on the face, scalp, neck, and lower body area. Isolates showed the growth of Methicillin-resistant Staphylococcus aureus, and Pseudomonas aeruginosa, on the chest and lower back areas, with Klebsiella spp and Candida albicans on the face and scalp area.

Blood tests: total blood count, C-reactive protein, fibrinogen, T3, T4, TSH, Anti TPO Ab, Anti TG Ab, C3, C4, C1q, liver function tests, urea and electrolytes, glucose, antinuclear antibody, urinalysis, and blood pressure were within normal limits.

After admission, we initiated a treatment of prednisone (1 mg/kg/day) for 15 days with pantoprazole 20 mg twice a day, ciprofloxacin 500 mg per day, probiotics, with topical gentamicin ointment twice a day control culture of skin swabs were collected again from the face, scalp, neck and lower back area. The clinical picture was improved following treatment; however, the annular erythema, collarette scales, and small pin head-like pustules emerged on the patient's mid-face area, with crusting in scalp area and ongoing itching and oozing lesions on the lower back. KOH examination has shown persistent Klebsiella spp, and Candida albicans colonization on the face and scalp area, and persistent bacterial colonization of Klebsiella spp on lower back area.

Figure 3. (a) Skin close up of ruptured bullous lesion in the upper limb, leaving open sore

Afterwards, oral antibiotic therapy was stopped because of severe gastritis and profuse diarrhea. Admission of prednisone was reduced gradually to (0.5 – 0.25 mg/kg·day), for next 15 days with pantoprazole 20 mg twice a day, continuing with probiotics, while topical betamethasone cream 1:2 twice daily and zink-emollient cream two times daily was prescribed.

In the same visit, we started laser protocol with long pulse Nd:YAG laser (Fotona Dynamis SP platform, Ljubljana, SLO). The following parameters were followed for face and body areas: spot size of 4mm, pulse width of 25ms, fluence of 35 J/ cm^2, frequency of 1 Hz in 8 to 10 circular movements on each eroded area, with chill air cooling twice weekly for 4 weeks initially, then once per week for 4 weeks. For scalp area, because of the preservation of hair follicles, parameters were modified to spot size of 4mm, pulse width of 0.1ms, fluence of 10 J/ cm^2, and frequency of 2 Hz in 10 parallel and linear movements.

Gradually, serum titer of the anti-Dsg1 antibody was significantly degraded 8 weeks after initiation of therapy. Three weeks after initiation of Nd:YAG laser

therapy, erosions were epithelized, while crusting lesions on scalp and erythema on the forehead were still present until the sixth week of laser therapy. The patient reported a notable reduction of itch and oozing in the second week of laser treatment. Following resolution of skin lesions, KOH examination yielded negative results in all retested areas.

Complete healing with an absence of erythema and any sign of acute skin inflammation observed at the end of 12 weeks following drug initiation. Post-inflammatory hyperpigmented patches developed on different body sites. The patients continued to be under regular follow-up (Fig. 1b, 2b, 2d). Six months after the laser treatment, mild hyperpigmentation was barely visible.

III. DISCUSSION

In this patient, the clinical features suggest pemphigus foliaceous, confirmed by the widely acceptable immunopathological criteria. The goal of the treatment was to promote healing as well as to limit bacterial contamination and new blister development.

The common cause of severe complications in patients with blistering skin conditions is septicemia which is usually secondary to cutaneous bacterial, virus, or fungal infection, which might be facilitated by systemic corticosteroids and immunosuppressive adjuvant drugs that are often administered for these patients.

In this study, Nd:YAG laser irradiation was applied for the reduction of fungal and bacterial contamination and promotion of healing of erosive lesions. Lasers can reduce the number of both gram-negative and gram-positive bacteria with anti-microbial and bactericidal effects, which was confirmed by several studies [1].

Nd:YAG laser therapy in in vivo studies, such as the one conducted by Kozarev, have shown improvement and even cure of onychomycosis caused by Candida albicans, Candida albicans, and Trichophytons[2]. Nd:YAG laser for the treatment of chronic paronychia improves skin appearance regarding erythema and swelling of their proximal nail folds [3,4]. The efficacy of laser irradiation has been confirmed against Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Enterococcus faecalis [5]. Nd:YAG laser light interaction with microorganism cells show contracting or shrinking of the cell with changes in deoxyribonucleic acid, which leads to inhibition of bacterial growth and metabolic inactivation [6].

It was clear that Nd:YAG laser manipulates the bacteria morphology. Nd:YAG lasers may provide selective photoantisepsis by killing bacteria, since the absorption of laser energy and laser thermal killing effects, at the near infra-red laser light of 1,064-nm wavelength is estimated to be 100-fold greater in pathogens than it is in surrounding gingival soft tissues [7].

Near-infrared laser (NIR) light can cause photoexcitation of endogenous microbial porphyrin molecules contained in microorganisms, evoking oxidative damage through reactive oxygen species, which have a high killing potential for bacteria, fungi, and viruses [8].

Yin et al reported that high-intensity Nd:YAG laser therapy on chronic wounds is of significant efficacy and far superior to conventional wound dressing [9]. NIR light photons interact with a specific photoreceptor, while absorbed light energy is transferred to a photosystem molecule where convert photon's energy into chemical energy, ending with the conversion of ADP to ATP. NIR laser light healing process stimulation is the result of significant induction of production the collagen, granulation tissue, and glycosaminoglycans in the extracellular matrix. Significant anti-inflammatory effects are based on the modulation of an inflammatory response, through interleukin secretion and cytokine production visible in exudation and proliferation capacity, and on the other side through inhibition of cyclooxygenases and lipoxygenases by modulation of prostaglandin and prostacyclin secretion [9,10].

During and after laser irradiation, treatment did not cause marked discomfort but significantly reduced itch and burning sensation, indicating that laser is a well-tolerated procedure. No side effects were observed.

IV. CONCLUSIONS

This case report demonstrates that a long-pulsed Nd:YAG laser treatment in repeated exposure was effective in the context of treating an infected wound. Nd:YAG laser-based anti-microbial treatment can significantly reduce the quantity of Candida albicans, Staphylococcus aureus and Klebsiella spp without any discomfort, no side effects, and might be an alternative to the systemic and topical administration of antimicrobial drugs, in cases where these agents are contraindicated.

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