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Case Report

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Photobiomodulation Therapy in Improving Quality of Life in Kindler Syndrome: A Case Study

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Abstract

Introduction: Kindler syndrome (KS) is a rare genetic disorder characterized by skin fragility, acral blister formation, diffuse cutaneous atrophy, photosensitivity, palmoplantar hyperkeratosis, pseudosyndactyly, and alopecia. Oral manifestations include limited mouth opening, which adversely affects oral hygiene, chewing, and swallowing, significantly impacting the quality of life of affected individuals.

Methods: A 26-year-old male with KS was referred for the management of reduced mouth opening, presenting with an interincisal distance of 19 mm. This was a critical concern for facilitating prosthetic rehabilitation. The patient underwent Photobiomodulation (PBM) therapy as a non-invasive treatment modality aimed at improving trismus.

Results: Following PBM therapy, the patient's mouth opening improved significantly from 19 mm to 23 mm. This enhancement allowed for the initiation of prosthetic rehabilitation.

Conclusion: PBM therapy is a promising treatment for managing trismus in KS by breaking down abnormal collagen deposits and reducing collagen synthesis, effectively addressing the underlying pathology. It offers significant improvements in mouth opening, which can enhance oral hygiene, nutritional intake, and overall quality of life. This non-invasive approach provides a viable option for patients with KS who require prosthetic rehabilitation.

Keywords: Kindler syndrome; Poikiloderma; Hereditary acrokeratotic; Trismus; Photobiomodulation therapy.

Introduction

Kindler Syndrome (KS), described first by Theresa Kindler in 1954, is a rare autosomal recessive genodermatosis disease caused by a functional mutation in the FERMT1 (KIND1) gene on chromosome 20p12.3, characterized by epidermolysis bullosa and congenital poikiloderma.[1-3] It also affects oral mucosa, leading to lesions such as blisters and erosions, ulcerations, and atrophy. Intraorally, KS is particularly characterized by a greater predisposition to periodontal diseases, which occur earlier and progress faster than in the general population as shown in a study by Blanchet et al.[4] One of the oral manifestations of this syndrome is limited mouth opening due to abnormal deposits of type VII collagen which can greatly affect the day-to-day activities of the patient.[1]

Photobiomodulation (PBM) therapy is the therapeutic use of non-ionizing light at near infrared frequencies to modulate biological activity. Previously, the term used was "low-level laser therapy" which was later replaced by "photobiomodulation" by the North American Association of Laser Therapy (NAALT) and the World Association of Laser Therapy (WALT) in 2014.[4] PBM therapy modulates biological processes at molecular and cellular levels, enhancing tissue healing and repair.[5-7] One mechanism involves stimulating plasminogen production, which promotes tissue remodelling and breaks down abnormal collagen deposits.[5] Another mechanism involves decreased production of pro-inflammatory cytokines (IL-1α, IL-1β, TNFα) and TGFβ, thereby reducing collagen synthesis.[6,8] This makes PBM therapy a promising intervention for trismus, a condition where limited mouth opening impairs quality of life. The success achieved in the present case can help the oral physicians in clinically managing KS if they encounter any case in their practice. The application can also be extended to the clinical management of similar conditions.

Case Presentaion

A 26-year-old male diagnosed with KS was referred by a prosthodontist to us for the management of reduced mouth opening, necessary for prosthetic rehabilitation. The patient reported a gradual reduction in mouth opening since the age of 10 years, which progressively worsened with age. This was accompanied by difficulty in chewing, swallowing and maintaining oral hygiene. As a part of the manifestation of KS, the patient also gave a history of bullae formation on the skin of legs, hands, and face in that order, which started at the age of 3 years

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and was usually limited to the body area exposed to sunlight. The formation of new bullae ceased after the age of 13 years; however, he continued experiencing skin inflammation when exposed to sunlight. He also revealed a history of ulceration on oral mucosa, swelling and bleeding from gums, and tooth mobility. The patient had a history of multiple extractions due to tooth mobility. The patient had been on medication for the skin lesions since childhood.

Clinical Findings

Extraoral examination revealed poikiloderma on the hands, forearms, feet, face and neck, atrophy of skin, multiple bullous lesions on the dorsal surface of hands at metacarpophalangeal joint and interphalangeal joint (Figure 1a-b), and alopecia. Intraoral examination revealed the ulceration of buccal mucosa, gingival inflammation, bleeding, desquamation, and recession (Figure 1c-d), blanching of palatal mucosa, and limited mouth opening with an interincisal distance of 19 mm (Figure 2a).

Diagnostic Assessment

The patient had a previous biopsy report with histopathological findings suggestive of KS. The timeline of the case is illustrated in Figure 3. The orthopantomogram (OPG) revealed multiple missing teeth, severe secondary dental caries in a root canal-treated mandibular right first molar, root remnants of the mandibular right second molar, and malaligned mandibular left second premolar and molars. Generalized moderate-to-severe periodontitis was noted (Figure 4).

Therapeutic Intervention

Apart from periodontal management, PBM therapy of 980 nm soft diode with a power setting of 1watt was initiated, and it involved non-contact mode sessions of 3-4 minutes per area over 8 sessions with 3-day intervals.

Follow-up and Outcomes

At the end of the therapy, patient's mouth opening improved from 19 mm to 23 mm (Figure2a-b) in a span of 4 weeks, and there was complete remission of oral ulceration. He could then undergo prosthetic rehabilitation and was advised to perform mouth exercises and scheduled for regular follow-ups after prosthetic rehabilitation.

Discussion

KS is a rare autosomal recessive genodermatosis disease characterized by bullous poikiloderma.[9] It is also known as Congenital Bullous Poikiloderma and was included into the revised epidermolysis bullosa (EB) classification in 2007 based on its biological and clinical characteristics, establishing KS as a rare EB subtype. Since KS was first described in 1954, around 400 cases have been reported worldwide, affecting individuals of any geographic origin and both sexes. Clinical features of KS are as follows: blister formation since birth, mainly on extremities due to trauma or sun exposure, which decreases with age; skin atrophy with a thin, wrinkled appearance; photosensitivity; poikiloderma with reticular telangiectasia and mottled pigmentation; axillary freckling; hyperkeratosis of the palms and soles, sometimes resulting in the loss of fingerprints; pseudosyndactyly; and eye issues such as

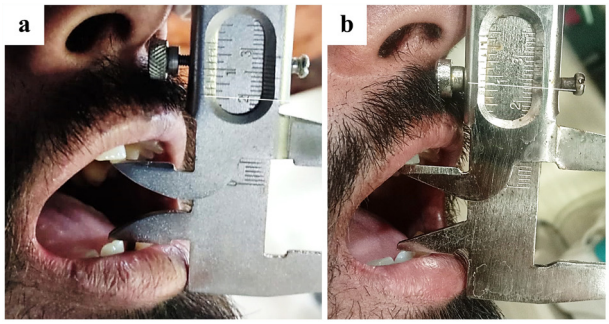

Figure 2. Inter-incisal Distance; (a) before PBM therapy, (b) after PBM therapy

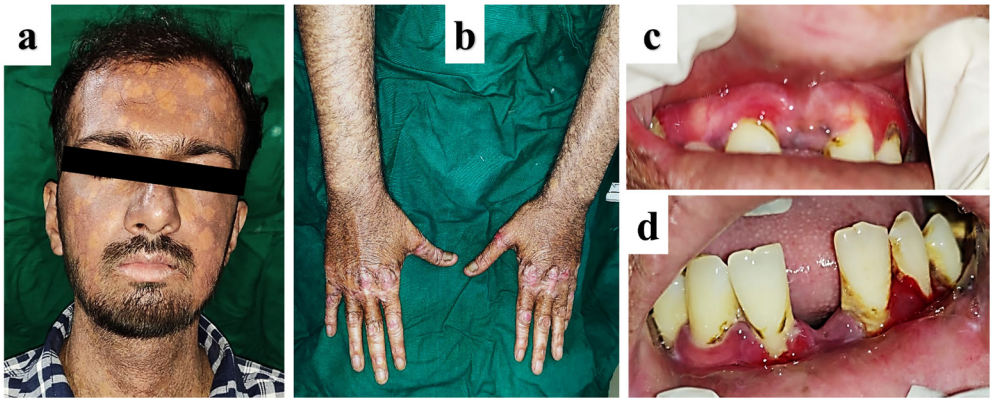

Figure 1. Clinical Features; (a) poikiloderma in face (diffuse hyper and hypopigmentation of skin), (b) multiple bullous lesions on the dorsal surface of hands, (c) inflammation, bleeding, desquamation and recession of gingival of the maxillary anterior region, (d) inflammation, bleeding, desquamation and recession of gingival of the mandibular anterior region

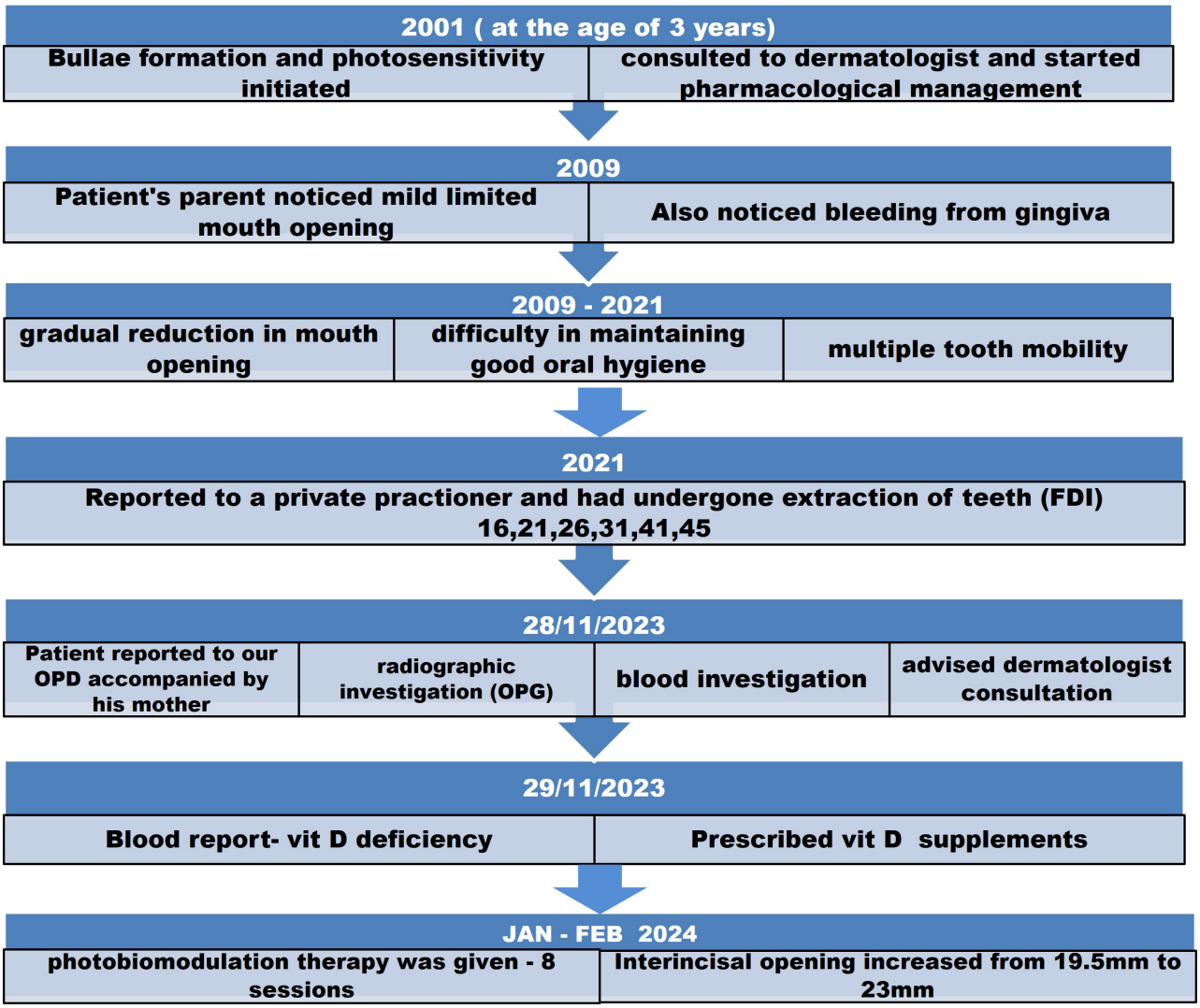

Figure 3. Timeline

conjunctivitis, corneal erosion, and ectropion of the lower eyelids.[1]

Despite the existing documented cases, there is limited dental literature on the condition. Dental findings have been discussed in few dermatological and paediatric publications, but they lack the depth of discussion.[1]

In 1996, Wiebe et al[10] reported a case of KS with dental findings, including premature loss of teeth, fragile bleeding gingival, severe periodontal bone loss, haemorrhagic mucositis, labial leukokeratosis, and limited mouth opening which severely affects quality of life by compromising oral hygiene, chewing, and swallowing, and increasing the risk of aspiration.[1]

The diagnosis of KS is based on clinical findings and molecular genetic testing of the FERMT1 gene. Forman et al reported histopathological and immunofluorescence features. Histopathologic features include hyperkeratosis, atrophy of epidermis, presence of oedema in dermis, leakage of pigment from cells, loss of rete ridges, and presence of clear spaces within basal epidermal cells. Also, few cases show the presence of cytoid bodies.[11] An important feature is the presence of splits at different levels, including intraepidermal, junctional, and dermal, most frequently at the lowermost portion of the basal layer, and associated collagen depositions within the clefts are unique ultrastructural findings.[1,9] Immunofluorescence microscopy shows type VII collagen was found abnormally deep in the connective tissue in both inflamed and noninflamed tissue. The elevated expression of type VII collagen may be due to alterations in the epithelial cells which release pro-inflammatory cytokines (IL-1α, IL-1β, TNFα) and TGF-β stimulating fibroblast type VII collagen production or may result from genetic defects in the COL7A1 gene,[12,13] and these genes are upregulated by TGF-β.[14] However, a report describing two Japanese KS patients with abnormal type VII collagen in the dermis showed no mutation in the COL7A1 gene.

The malignant transformation rate of this syndrome

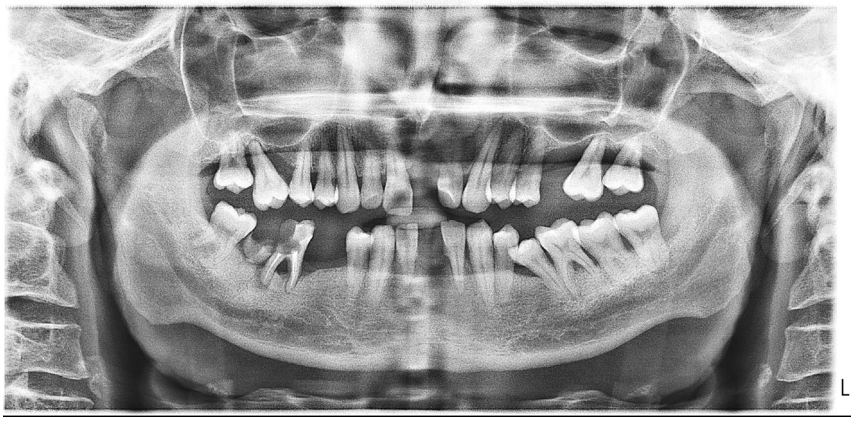

Figure 4. OPG

is about 50%, mostly transforming into squamous cell carcinoma of skin (lip) and oral mucosa (hard palate).[1,15] The management of patients with KS generally involves a multidisciplinary approach, and dentists should be included in the team for oral management and considerations.[1,11] Oral care typically focuses on periodontal management and minimizing mucosal trauma, often resulting in tooth extractions. However, our literature review found no reports or studies on managing limited mouth opening in this syndrome. Laser PBM therapy was developed in the 1960s. It has analgesic and anti-inflammatory effects and stimulates a repair mechanism in wound healing.[6] It is non-invasive, non-thermal and safe. It has no systemic effects, shows faster pain reduction, and does not cause mechanical cellular damage. It is an alternative therapy for reducing pain and burning sensation in oral mucosal conditions. It has a variable mechanism of action, primarily acting on cytochrome-c-oxidase in mitochondria which release nitric oxide (which is a competitive inhibitor of oxygen) from the binding site of oxygen, increasing reactive oxygen species and ATP production, which results in improving mitochondrial respiration, cell metabolism, gene transcription, thus enhancing tissue remodelling and wound healing process.[6]

PBM therapy acts on fibroblasts and keratinocytes by decreasing the release of inflammatory cytokines (IL-1α, IL-1β, TNFα, and leukoregulin) and TGF-β and decreasing collagen synthesis by deactivating COL7A1 gene transcription.[6,8,16] It also stimulates plasminogen production, which is converted to plasmin by a plasminogen activator (Its level increases due to decreased TGF-β). Plasmin stimulates the activation of pro-collagenase, which results in an increased level of collagenase, leading to increased collagen degradation. Thus, PBM therapy offers a novel solution for the management of limited mouth opening by breaking down abnormally deposited collagen VII in connective tissues and reducing collagen formation.

Conclusion

The presented case study highlights how trismus in KS can be effectively managed by PBM therapy mostly by breaking down abnormal collagen deposits and reducing collagen formation, significantly improving mouth opening and enhancing oral hygiene, nutritional intake, and overall quality of life. However, a clinical trial in future studies including larger sample size and histopathological correlation will further strengthen the claim of managing trismus in similar conditions using PBM therapy.

Patient Perspective

The patient gave positive feedback regarding an improvement in quality of life with improved mastication, swallowing and maintenance of oral hygiene, which was difficult previously due to reduced mouth opening.

Authors' Contribution

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Investigation: Farha Khatoon, Sunil Surendraprasad Mishra, Vaishnavi Shailesh Sawant, Anupama Anand Chavan.
Methodology: Farha Khatoon, Sunil Surendraprasad Mishra, Vaishnavi Shailesh Sawant, Anupama Anand Chavan.
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Supervision: Sunil Surendraprasad Mishra.
Validation: Farha Khatoon, Sunil Surendraprasad Mishra.
Visualization: Farha Khatoon, Sunil Surendraprasad Mishra.
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Writing–review & editing: Sunil Surendraprasad Mishra.

Competing Interests

The authors declare no conflict of interest.

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Patient's Consent

Written informed consent was obtained from the patient.

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