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Case Report

Fractionated Ablative Laser-Assisted Methyl Aminolevulinate Photodynamic Therapy with 532-nm KTP Activation for Multiple Basal Cell Carcinomas in Gorlin Syndrome: A Case Report

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Abstract: Basal cell carcinomas (BCCs) in Gorlin syndrome are often numerous, recurrent, and difficult to manage with repeated surgery because cumulative procedures may produce substantial morbidity, scarring, and disfigurement. Methyl aminolevulinate photodynamic therapy (MAL-PDT) is an established tissue-sparing option for superficial BCC and selected thin nodular BCCs, with favourable cosmetic outcomes and the ability to treat multiple lesions during a single session. Unfortunately, conventional photodynamic therapy (PDT) is limited by inadequate photosensitizer penetration into thicker tumours and by treatment-related pain during illumination time. This report describes a novel laser-assisted PDT protocol for multiple BCCs in Gorlin syndrome that combines fractionated ablative laser pretreatment to enhance intralesional penetration of methyl aminolevulinate (MAL), followed by a 3-hour incubation and photoactivation with a 532-nm KTP vascular laser rather than conventional blue or red light. The conceptual novelty of this approach is twofold: first, ablative fractional laser creates vertical channels that markedly increase delivery of topical photosensitizer into deeper tissue; second, the activating vascular laser may plausibly provide dual benefit by both activating accumulated protoporphyrin IX (PpIX) and exerting direct vascular-directed effects that have independently shown efficacy against BCCs, all while potentially reducing treatment-related pain. Following treatment, the patient achieved excellent lesion-level clearance with no scarring or dyspigmentation, no reported pain, and 94% (51/54) lesion-level clearance at 12 months. These findings suggest that fractional ablative laser-assisted MAL delivery combined with KTP-mediated activation may represent a promising office-based, scar-sparing strategy for selected patients with multiple BCCs, especially when repeat surgery is undesirable.

Keywords: gorlin syndrome; basal cell nevus syndrome; photodynamic therapy; methyl aminolevulinate; Er:YAG; KTP

1. Introduction

Gorlin syndrome [1], also known as nevoid basal cell carcinoma syndrome [2], is an autosomal dominant disorder with loss of function of the PTCH1 tumour suppressor gene in the hedgehog signalling pathway [3]. In addition to other syndromic findings, this mutation leads to the development of numerous BCCs beginning early

in life, often on both sun-exposed and non-sun-exposed skin. Because patients may develop large numbers of tumours over time, management must balance oncologic control with preservation of function, cosmesis, and quality of life; cumulative treatment burden becomes a central management issue, particularly when lesions arise in cosmetically sensitive areas or when repeat surgery would be disfiguring.

Consensus recommendations support MAL-PDT as a useful noninvasive option in Gorlin syndrome for superficial BCC and selected nodular BCCs, particularly thinner lesions under 2 mm, as it can treat multiple lesions in a field-directed fashion while preserving tissue and usually producing little or no scarring [4]. However, several studies have identified tumour thickness and incomplete intralesional photosensitizer accumulation as major determinants of PDT failure in BCC [5,6]. Experimental and clinical studies therefore have explored methods to improve drug delivery, including curettage, microneedling, iontophoresis, and laser-assisted drug delivery [7–9]. Among these, fractionated ablative laser pretreatment has emerged as a particularly attractive strategy because it creates reproducible microscopic vertical channels that bypass the stratum corneum and facilitate deeper distribution of aminolevulinate derivatives into the epidermis, adnexa, and dermis [9].

In porcine skin, fractional carbon dioxide (CO_2) laser pretreatment before MAL application produced orders-of-magnitude greater protoporphyrin IX fluorescence and meaningful photobleaching through skin depths reaching approximately 1.8 mm, supporting the concept that inadequate drug delivery rather than light penetration is a major barrier in thicker lesions [5]. Clinical studies in actinic keratoses and nodular BCC have further shown that fractional laser pretreatment increases fluorescence and improves clinical response compared with conventional PDT alone [6,10–12].

The remaining unresolved question is whether the activating light source itself can be optimized. Conventional PDT for BCC commonly uses red light because of its deeper tissue penetration, whereas blue light is shorter but more commonly used in some 5-aminolevulinic acid (ALA) protocols. Separately, vascular lasers such as pulsed dye laser (PDL) have demonstrated efficacy as monotherapy for BCC and have also been used separately as PDT-activating sources, suggesting that a vascular-selective wavelength may contribute therapeutic benefit beyond porphyrin activation alone [13]. This case highlights a new combination approach in which a fractionated ablative laser was used to enhance MAL penetration and a 532-nm vascular laser was used to activate PpIX, potentially producing a dual-mechanism effect through simultaneous PDT and vascular targeting.

2. Case

A 76-year-old man with clinically diagnosed Gorlin syndrome (4 major clinical criteria including >2 BCCs, odontogenic keratocysts of the jaw, palmar pitting, bifid rib) had been followed closely by dermatology for 45 years; during that time we documented treatment of over 850 BCCs. Prior treatment burden was substantial and included wide local excisions, Mohs micrographic surgery, electrodessication and curettage, CO_2 laser ablation, cryotherapy, topical 5-fluorouracil, and photodynamic therapy. At the current follow-up visit, 54 separate lesions consistent with BCCs were identified on the back, including both de novo lesions as well as lesions arising at the periphery of previously treated sites. All lesions were considered clinically low risk and were located outside anatomic sites requiring primary surgical management.

Baseline clinical photography was obtained. Histopathology from four representative thicker lesions confirmed both superficial and nodular BCCs (Figure 1); other lesions had dermatoscopic findings including sharp arborizing telangiectasias, semitranslucent areas, and small erosions in keeping with BCCs. All lesions were marked, and local anesthesia was achieved with 1% lidocaine with epinephrine. Hyperkeratotic scale and crust were gently debrided, and exophytic components were superficially curetted. Each lesion, including a 3 mm margin, was then pretreated with a fractional erbium-doped yttrium aluminum garnet (Er:YAG) laser system (Fotona, Dynamis; 22 J/cm^2 fluence; 100 ms pulse duration) to create microscopic channels intended to enhance depth of penetration of the photosensitizer.

Following laser pretreatment, topical methyl aminolevulinate 16% cream (Metvix; Galderma Canada Inc., Toronto, ON, Canada) was applied under occlusion with Tegaderm film (3M). After 3 h of incubation, the occlusive film and excess product were removed. The treated sites were then illuminated with a potassium titanyl phosphate (KTP) 532 nm laser (Cynosure Lutronic, DermaV; 12 mm spot size, 5.5 J/cm^2 fluence, 10 ms pulse duration). Each lesion received three pulses total. Immediate post-procedure reactions included erythema, mild edema, and serous crusting—all expected local effects after photodynamic therapy and may be accentuated by fractionated ablative laser pretreatment. The patient denied pain with treatment (Figure 2A).

At 3-month follow-up, all 54 treated basal cell carcinomas had cleared clinically, with no evidence of lesion-level recurrence as assessed with dermoscopy (Figure 2B). Cosmetic outcome was excellent, with no scarring or dyspigmentation at treated sites. There was no infection, ulceration, or functional impairment, and the patient

reported the recovery was acceptable and preferable to prior treatment modalities. At 12 months, careful photographic and dermatoscopic review showed recurrence of 3/54 previously treated lesions, with no new lesions arising at the periphery of treated sites (Figure 2C). Overall, this corresponded to an initial clinical clearance of 100% at 3 months and a 12-month maintained lesion-level clinical clearance of approximately 94% (51/54) after one treatment session.

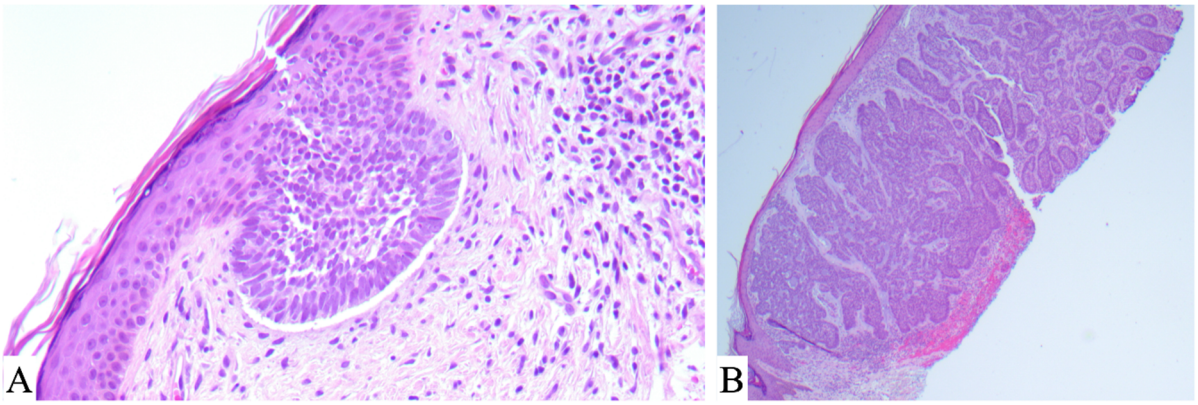

Figure 1. (**A**) Hematoxylin–eosin staining of superficial BCC demonstrating basaloid tumor nests budding from the epidermis confined to the superficial dermis, with peripheral palisading and stromal retraction clefts. (**B**) Hematoxylin–eosin staining of nodular BCC showing large dermal nests of malignant basaloid keratinocytes with peripheral palisading and a mucinous stroma containing plump spindle cells.

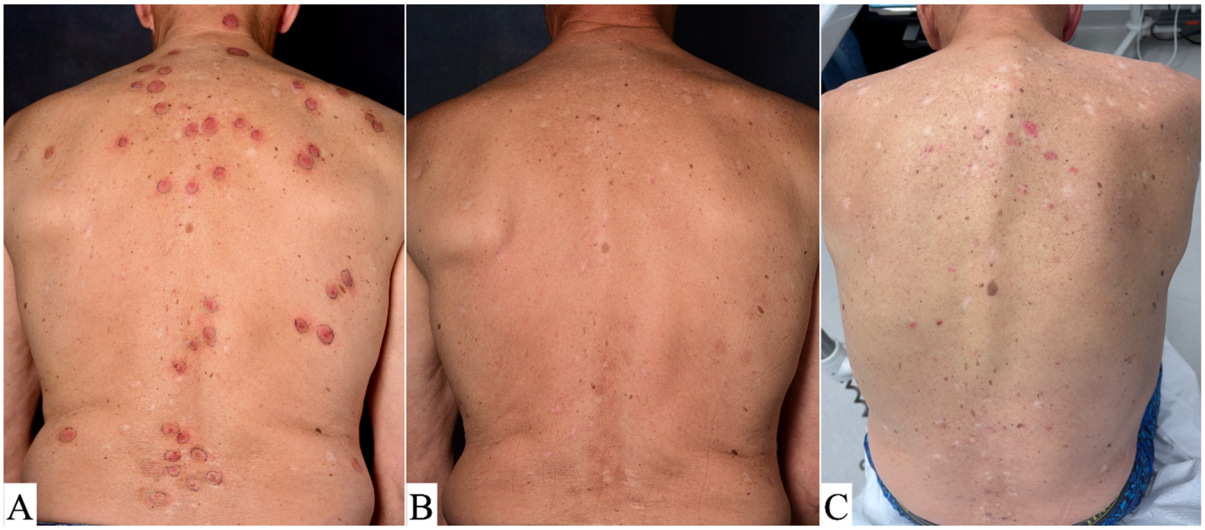

Figure 2. (**A**) Patient photograph immediately following fractionated ablative laser-assisted MAL-PDT activated by KTP laser. Note the dozens of hypopigmented scars from prior BCC treatments. (**B**) Patient photograph at 3-month follow-up. (**C**) Patient photograph at 12-month follow-up.

3. Discussion

The principal novelty of this case is not simply the use of PDT for BCC in Gorlin syndrome, which is already supported by consensus guidance and prior case series, but the specific pairing of two mechanistically complementary laser steps: fractionated ablative pretreatment to improve MAL delivery and 532-nm vascular laser activation to potentially add an independent antitumour vascular effect. To our knowledge, this specific combination has not been previously reported as a protocol for BCC in Gorlin syndrome or isolated BCCs.

The first innovative component is fractionated ablative laser-assisted drug delivery. The limitation of conventional topical PDT in nodular and thicker BCC is closely tied to insufficient penetration of ALA or MAL beyond approximately 1 mm in many lesions. Haedersdal and colleagues demonstrated that fractional CO_2 pretreatment before topical MAL dramatically increased porphyrin fluorescence in hair follicles and dermis, with photobleaching maintained from the surface to approximately 1.8 mm depth after illumination [5]. Lippert and colleagues then translated this concept clinically in nodular BCC, showing higher fluorescence in 94.6% of ablative laser-pretreated tumour halves and superior histologically confirmed clearance compared with control halves treated

without fractional laser pretreatment [6]. Review data on laser-assisted drug delivery similarly conclude that fractionated ablative CO_2 and Er:YAG systems, via creation of dermal micro-channels, can enhance the permeability and depth of penetration of topically applied agents, including ALA and MAL used for PDT [5–10,14].

The second innovative component is the use of vascular laser light as the activating source. Although peak PpIX absorption occurs in the Soret band at 410 nm, there are additional Q-band absorption peaks at longer visible wavelengths, including bands in the green-yellow (504, 538, 576 nm) and red (630 nm) portions of the spectrum; KTP 532 nm laser as the activating source may reach a portion of the 538 nm Q-band [15]. It has been shown previously that longer wavelengths allow for superior treatment of thicker lesions [16]. Moreover, the PDL literature is informative conceptually as it shows vascular lasers can function as PDT activators, supporting the biologic plausibility that visible vascular wavelengths can activate porphyrins despite lower absorption than the Soret band [13]. In addition, vascular lasers used alone have shown efficacy in BCC, likely through selective photothermolysis of tumour-associated vasculature [13]. This dual-mechanism concept may be especially relevant in BCC, where tumour survival depends not only on malignant epithelial cells but also on supporting stromal and vascular components. PDT already acts through direct tumour cell apoptosis, vascular injury, and immune activation, rather than through a single pathway alone. Using a vascular laser to activate PpIX may therefore enhance the very mechanisms already central to PDT efficacy while simultaneously delivering a wavelength long associated with vascular-selective photothermolysis. Taken together, the duality of activating PpIX and plausibly of having direct effect on tumour vasculature provides the rationale for describing this approach as dual-mechanism.

A further practical advantage is workflow. Standard blue-light ALA protocols require 14–18 h of incubation and 16 min 40 s of light exposure, whereas red-light MAL protocols typically require 2.5–4 h of incubation and 8–10 min of light exposure; both modalities are associated with significant treatment discomfort. Where available, the MAL formulation may be advantageous not only with decreased incubation time, but also with ease of application with the cream vehicle compared to the ALA solution. In the present case, KTP pulse activation was associated with a shorter illumination time, potentially improving the patient experience. Our patient denied any pain with treatment apart from initial local anesthesia prior to curettage and fractionated laser; less associated pain is certainly clinically meaningful for patients, particularly those with multiple BCCs or requiring repeated sessions.

Cosmesis is another major consideration in Gorlin syndrome. Consensus recommendations emphasize that MAL-PDT is particularly attractive in this population because it is noninvasive, repeatable, able to treat multiple lesions during the same session, and associated with little or no scarring [4]. Avoidance of scar burden is especially valuable in patients who begin developing tumours early in life and often undergo many procedures over decades. The scar-free result in this case is therefore clinically important, not merely cosmetically appealing.

This case raises the question of lesion-level recurrence. Published clearance rates range from 74–95% after 2 conventional PDT sessions separated by 2 weeks, dependent on the depth and subtype of BCC [16–18]. The low rate of lesion-level recurrence in this case is therefore encouraging, although it should be interpreted cautiously in the absence of histologic confirmation and larger comparative studies. Furthermore, in this case, a 94% sustained lesion-level clinical clearance at 12 months after one session is comparable to other PDT protocols, though with the benefit of fewer total sessions [17,18].

Several limitations should be acknowledged. First, this is a single-center experience and cannot establish superiority over conventional MAL-PDT, surgery, or other pretreatment methods. Second, although vascular-laser-mediated PDT is biologically plausible, the literature supporting KTP specifically as the activating source for BCC PDT is much more limited than the literature for conventional red-light MAL-PDT or for PDL-mediated PDT concepts. Third, because some laser-assisted PDT studies have shown greater local adverse effects despite higher efficacy, formal assessment of pain, healing time, and recurrence in a prospective series will be essential. Fourth, it is possible that BCCs may recur after 12 months of follow-up, and longer follow-up may be required to adequately prognosticate lesion-level recurrence.

Nonetheless, this report suggests a promising therapeutic direction. In carefully selected patients with multiple BCCs, especially those with Gorlin syndrome who prioritize tissue preservation and reduced cumulative scar burden, fractionated ablative laser-assisted MAL delivery followed by 532-nm KTP vascular laser activation may offer a practical, mechanistically rational, and cosmetically favourable alternative approach.

4. Conclusions

This case illustrates a novel PDT strategy for multiple BCCs in Gorlin syndrome using fractionated ablative laser pretreatment to enhance penetration of methyl aminolevulinate and 532-nm KTP vascular laser activation after a 3-h occluded incubation. The approach is innovative because it combines improved photosensitizer delivery with a vascular-selective activating wavelength that may also contribute direct antitumour benefit.

The observed outcomes of excellent initial lesion-level clearance, no scarring, little pain, low rate of lesion-level clinical recurrence, and shorter practical treatment time suggest that this protocol may be particularly valuable for patients in whom repeat or extensive surgery is undesirable. Further prospective studies should compare this method against standard MAL-PDT and other laser-assisted PDT protocols, with attention to histologic clearance, recurrence, pain, cosmesis, and optimal laser parameters.

Author Contributions

C.R.J.: conceptualization, methodology, investigation, data curation, formal analysis, visualization, writing—original draft preparation, writing—review and editing; B.K.R.: conceptualization, methodology, investigation, resources, data curation, formal analysis, visualization, supervision, writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

Ethical review and approval were waived for this study, due to the retrospective, single-case design using only de-identified information obtained during routine clinical care, with no additional interventions or identifiable private information, and therefore not constituting human subjects research requiring institutional review board review under our institution's ethics policy and applicable national regulations.

Informed Consent Statement

Written informed consent has been obtained from the patient to publish this paper including case details and clinical images.

Data Availability Statement

No novel datasets were generated. Data are contained within the article and supplementary materials. Individual-level raw data are not publicly available due to privacy and ethical constraints; de-identified data may be shared by the corresponding author upon reasonable request and will be retained for at least 10 years after publication.

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Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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