

## Case Report

# Fractional Photothermolysis for the Treatment of Granuloma Annulare: A Case Report

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**Background and Objective:** To date, reports on the safe and effective laser treatment of disseminated granuloma annulare (GA) are still limited.

**Study Design/Patient and Methods:** A 58-year-old Caucasian female with disseminated GA was treated with fractional photothermolysis (FP) using a 1,440-nm Nd:YAG laser. Four lesions on the patient's left upper arm were defined as the "test region" with the remaining untreated areas serving as controls.

**Results:** A complete remission was achieved after two to three treatment sessions. Treatments were well tolerated. Due to the controlled study design, a spontaneous remission was unlikely.

**Conclusion:** We conclude that FP may be a potentially efficacious therapeutic approach and should be considered in managing generalized GA. *Lasers Surg. Med.* 40:319–322, 2008. © 2008 Wiley-Liss, Inc.

**Key words:** fractional photothermolysis; granuloma annulare

## INTRODUCTION

Granuloma annulare (GA) is a relatively common idiopathic granulomatous inflammation of the dermis and subcutaneous tissue. It is characterized by groups of flesh-colored or erythematous papules which form growing rings; they can be either localized or generalized. The condition has been reported to occur after trauma, malignancy, viral infections (e.g., HIV, Varicella zoster, Epstein-Barr virus), insect bites and tuberculosis skin tests [1], indicating a probable immunological pathway of pathogenesis [2]. The condition affects patients of all age groups, but most cases of localized granuloma annulare occur in people under 30 years of age, and women are affected about twice as often as men [3]. In about 15% of cases, patients have more than 10 lesions at a time (i.e., disseminated granuloma annulare); these patients are usually either under 10 or over 40 years of age [4].

In approximately 50% of patients, single granuloma annulare lesions resolve spontaneously within months or a few years. By contrast, cases of disseminated GA can last

for more than a decade, and recurrences are common [1]. These cases clearly represent a major therapeutic challenge and many patients remain troubled by the appearance. The visible and unsightly nature of this skin condition has led to the proposal of a variety of topical and/or systemic treatment methods [5–15] (Table 1)—all with varying degrees of success and each with its own treatment-associated morbidity.

So far, there is only one case report about non-ablative laser treatment of granuloma annulare. In 2005, Sniezek et al. treated a single granuloma annulare plaque on a patient's left wrist successfully with a 585-nm pulsed dye laser [16]. Since the authors did not describe the natural course of the non-treated areas, spontaneous remission should be considered in this case.

## PATIENT AND METHODS

A 58-year-old Caucasian female presented for evaluation of multiple discrete and confluent brown papules (0.2–1 cm in diameter) on both arms, neck, chest, and abdomen (Fig. 1a). The asymptomatic lesions had been present for 3 months and had not yet been treated. The medical history was significant for post-strumectomy hypothyroidism and cardiac insufficiency (NYHA I) after mitral valve replacement due to rheumatic fever. There was no family history of similar skin findings. Medication included coumarin, L-thyroxine,  $\beta$ -blocker, and furosemide.

A biopsy specimen, which was obtained from a representative area on the right upper arm, revealed palisaded

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The authors have conducted the treatment and written the article without any contribution from other parties and bear the full responsibility for its content.

There is no conflict of interest. None of the authors of the study has financial interests of any kind or is in any way affiliated with manufacturers, wholesalers or retailers of the device under investigation.

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**TABLE 1. Therapeutic approaches proposed for disseminated granuloma annulare (in alphabetical order)**

Treatment	Author(s)	No. of cases	Outcome
Cyclosporine A (immunosuppressive agent)	Spadino et al. [5]	4	“More or less” complete clearance
Chloroquines (anti-malaria drug)	Simon and von den Driesch [6]	1	Complete clearance
Dapsone (anti-leprosy drug)	Steiner et al. [7]	10	Four complete, three partial remissions
Fumaric acid esters (anti-psoriasis drug)	Eberlein-König et al. [8]	8	Four complete, three partial remissions
Infliximab (TNF- $\alpha$ inhibitor)	Hertl et al. [9]	1	Complete clearance
Isotretinoin (retinoid)	Looney and Smith [10]	Meta-analysis	Effective, but with serious side effects
Niacinamide (vitamin B3)	Ma and Medenica [11]	1	Complete clearance
Pimecrolimus (topical immunosuppressive agent)	Rigopoulos et al. [12]	1	Partial clearance
Tacrolimus (topical immunosuppressive agent)	Jain and Stephens [13]	1	“Successful”
UVA1 phototherapy	Schnopp et al. [14]	20	50% “excellent or good”
Vitamin E/zileuton (5-lipoxygenase inhibitor)	Smith et al. [15]	3	Complete clearance

granulomas with histiocytes and giant cells around degenerated collagen fibers and mucin in the upper dermis. These findings supported the diagnosis of granuloma annulare. The patient underwent a work-up, including a metabolic profile (to rule out diabetes mellitus), and the results were all within normal limits.

After a full discussion of treatment options, she was offered topical and oral PUVA therapy but declined because of the associated risks. The patient agreed to a trial of fractional photothermolysis (FP) on a limited area. Four GA

lesions on the patient’s left upper arm were defined as the “test region” of treatment (Fig. 1a), with the untreated areas serving as a control to avoid misinterpreting a spontaneous remission as a successful treatment. The patient was treated using a 1,440-nm Nd:YAG laser (Affirm™, Cynosure, Westford, Massachusetts) which utilizes a microarray of lenses with a 10 mm beam to create distinctive treatment zones. The treatments were performed at settings of 6 J/cm<sup>2</sup>, 3 milliseconds pulse duration, and 2 full passes with a 25% overlap in conjunction with a cold-air cooling device (Cryo5™ set at level 5, Zimmer Medizin Systeme, Neu-Ulm, Germany). No other anesthesia was required. Care was taken to ensure tip contact with skin during all treatment pulses, as the microarray of lenses requires contact so it can properly focus and distribute energy for effective treatment.

## RESULTS

After two treatment sessions (3 weeks apart), the test areas showed a marked clinical improvement (i.e., height and diameter of the lesions were decreased), whereas the control regions remained unchanged or had even progressed (Fig. 1b). All treatments were well tolerated by the patient. The only side effects we observed included transient edema which resolved in 4–6 hours and prolonged erythema lasting 3–4 weeks. The patient has since undergone a total of three treatment sessions of the other GA lesions on both arms, neck, chest, and abdomen, with complete clearance within a follow-up of 8 months (Fig. 1c).

## DISCUSSION

This report is unique since it is the first reported case of fractional photothermolysis for the treatment of granuloma annulare. After a total of two to three treatment sessions with a fractional device, we were able to achieve complete remission of all treated lesions without changes in skin

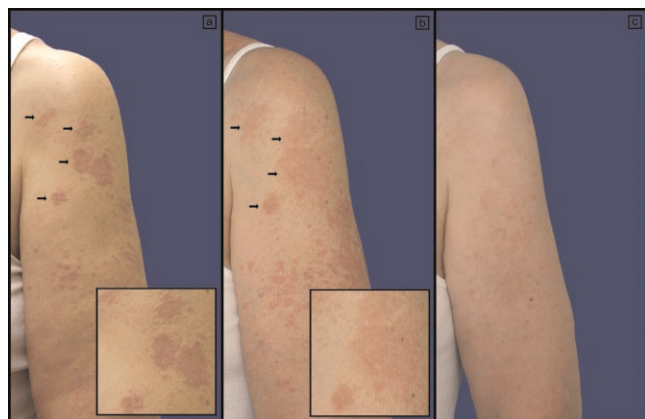
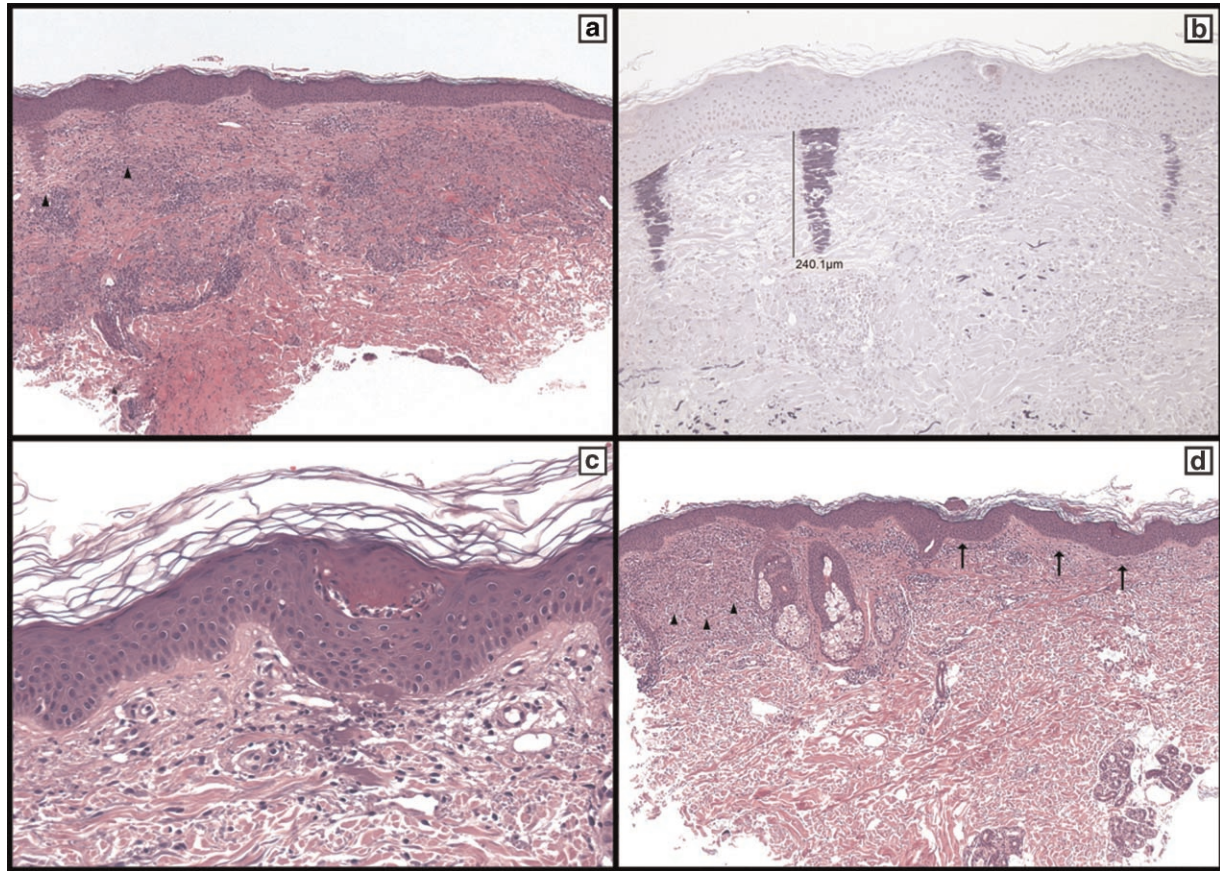


Fig. 1. **a:** Granuloma annulare before treatment was initiated. The arrows indicate the locations which were subsequently treated as test sites. The inset displays a magnification of the test sites. **b:** Ten days after two fractional photothermolysis treatment sessions of the test sites (6 J/cm<sup>2</sup>, 3 milliseconds, 10 mm, 2 passes). The test sites show a complete remission, while the non-treated areas increased in size and number. Note the erythema following the test laser sessions. The inset displays a magnification of the test sites. **c:** Eight months after three fractional photothermolysis sessions of the complete arm. Complete remission of all treated lesions.



**Fig. 2. a:** Histopathological section of granuloma annulare 24 hours post-laser treatment (Hematoxylin & Eosin, magnification  $\times 10$ ): well delineated micro-columns of coagulation penetrated into the dermis, reaching superficial foci of granuloma annulare (arrow heads). **b:** The zones of thermal damage were approximately 250–300  $\mu\text{m}$  apart, with each lesion approximately 70  $\mu\text{m}$  in diameter and 240  $\mu\text{m}$  in depth (elastic stain, magnification  $\times 40$ ). **c:** Dyskeratotic cells in the epidermal part of the MTZ and a button-like eosinophilic

material containing melanin and dermal content just below the stratum corneum (microscopic epidermal necrotic debris, MEND) (Hematoxylin & Eosin, magnification  $\times 100$ ). **d:** Tissue was excised 3 weeks after treatment (Hematoxylin & Eosin, magnification  $\times 10$ ). Arrow heads show residual granulomas in non-treated areas. The epidermis has already reepithelialized with minimal necrotic epidermal residues in the treated areas (arrows). The MENDs are nearly extruded.

texture or other long-term side effects. Spontaneous remission was unlikely since the test areas were treated first and remained the only ones to respond to treatment while the other areas continued to spread.

FP as referenced in this case report was first described by Manstein et al. and focuses on the principle of micro-island damage by producing microarrays of energy in distinct foci throughout the treated region [17]. FP induces a wound healing response in the dermis [18] that has been utilized for cosmetic applications and, more recently, medical ones as well [19–21]. However, the literature has reported relatively little scientific validation of the acute histopathological skin changes and wound healing response which fractional laser treatment can effect.

To illustrate the effect of FP on granuloma annulare, lesions located away from the test site were selected in order to avoid any confounding influence of the biopsy per se. They were then treated using the same parameters

as described above and subsequently excised 24 hours and 3 weeks post-laser treatment. Histological examination (Fig. 2) shows columns of coagulation in the range of 50–100  $\mu\text{m}$  in diameter along with localized epidermal separation contained within the column width. The 1,440-nm radiation from the laser is strongly absorbed by the tissue, typically up to a depth of 240–350  $\mu\text{m}$ . The short duration of the laser pulse insures that the energy within the high fluence zone is well localized. This is why histology of areas that have undergone 2 passes do not show diffuse coagulation, even at the relatively high fluences used in this study. The main effect one would expect from this admittedly aggressive treatment is increased inflammation and greater healing response. This may be the reason for the prolonged erythema that has been observed. Also, a possible reason for this side effect is the changed wound healing response in tissue with GA compared to normal skin.

In the present case, the lesions' clearing is most likely due to the stimulation of controlled, non-specific wound healing processes that "rebuild" the skin in the treated areas. This assumption is supported by anecdotal reports showing a resolution of lesions after trauma, local injections, biopsies, and cryotherapy [22,23].

As is apparent from Figure 2a, zones of thermal coagulation reached only superficial foci of granuloma annulare. On the other hand, we know from histological studies that exposures at 6 J/cm<sup>2</sup> show deep dermal remodeling below the papillary dermis [24]. We also know from animal models that a potential controlling factor (prostaglandin E<sub>2</sub>, PGE<sub>2</sub>) is released by macrophages and inhibits granuloma formation of granulomatous diseases. Wolter et al. [25] demonstrated that the capacity of macrophages to release PGE<sub>2</sub> is decreased in patients with sarcoidosis (which represents another palisaded granulomatous dermatosis). Conceivably, FP-induced inflammation might attract macrophages releasing high levels of PGE<sub>2</sub>. The exact mechanism of action, however, remains to be discovered.

In conclusion, FP offers a possible remedy with minimal side effects for the highly unsatisfactory condition of granuloma annulare therapy that is marked by patients demanding treatment and lesions that are often refractory. The present case report is intended to inspire additional studies and discussions. It should be noted that its efficacy must be confirmed by further studies, but such studies are definitely warranted by the encouraging results of this case report.

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