Original Article

The Role of Lasers in Connective Tissue and Inflammatory Dermatoses: A 10-Year Retrospective Review of 60 Patients in a UK Tertiary Laser Clinic

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Abstract

Introduction: The role of lasers in the treatment of standard therapy-resistant inflammatory dermatoses and connective tissue disorders has been controversial and evidence supporting the role of lasers in this setting is scarce. **Objective:** To assess the efficacy of lasers in the management of inflammatory dermatoses and connective tissue disorders (CTD). **Materials and Methods:** A retrospective case review of all inflammatory dermatoses/connective tissue diseases treated in a tertiary laser clinic between March 2010 and 2020 was undertaken. **Results:** A total of 60 cases (48 = female) were included and the average age was 51 years (range 21 to 74). The following conditions were treated: scleroderma *n* = 22 (37%), granuloma faciale *n* = 10 (17%), sarcoidosis *n* = 8 (13%), discoid lupus erythematosus *n* = 7 (12%), and systemic lupus erythematosus *n* = 2 (3%). Other diagnoses included necrobiosis lipoidica, pyoderma vegetans, hypertrophic lichen planus, and dermatomyositis. The most common type of laser used was pulsed dye laser (PDL) in *n* = 41 (68%) cases. Eight (13%) patients received treatment with the carbon dioxide (CO_2) laser. The most common site treated was the face. A good response with a marked reduction of signs was seen in 62% of patients while 10% of the patients did not respond to laser treatment. Self-limiting complications included purpura and hyperpigmentation. **Limitations:** Lack of objective assessment and outcome measures. **Conclusions:** This is the largest cohort of patients to have undergone laser treatment for inflammatory dermatoses/connective tissue disease. Based on this retrospective review, we conclude that lasers can be a useful adjunct in the management of otherwise difficult-to-treat selected inflammatory and connective tissue diseases.

Keywords: *Alexandrite laser, carbon dioxide laser, connective tissue disease, inflammatory dermatoses, Neodymium-doped yttrium aluminum garnet, pulsed dye laser, recalcitrant*

Introduction

Cutaneous manifestations of connective tissue disorders and inflammatory dermatoses can often be resistant to conventional therapies. Although the role of laser devices in dermatology is progressively expanding, their role in treating connective tissue diseases (CTD) and inflammatory processes remains controversial.[1] Generally, the mainstay of treatment of CTD includes antimalarials, systemic corticosteroids, and immunosuppressive medication. To minimize the side effects associated with systemic therapies and for recalcitrant cases,[2] alternative modalities including cryotherapy,[3] dermabrasion,[4] and laser treatments, mainly pulsed dye laser (PDL),[5] have been reported.

In addition to treatment challenges, there is a significant psychological burden in patients living with CTD, attributed to the chronic, recalcitrant nature of the disease, visibility of lesions, and the level of associated disfigurement that the patients experience.[6-8] Therefore, laser treatment offers a useful alternative and adjunctive treatment modality in certain cases to help address these difficulties.

Materials and Methods

Study design

We carried out a retrospective case review identifying all patients with connective tissue disorders or inflammatory conditions treated in a consultant dermatologist-led tertiary laser center from March 2010 to March 2020.

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Patient selection and outcomes

Case notes of all adult and pediatric patients who underwent laser treatment for their CTD were reviewed. The following data were extracted: demographics, diagnosis, site, type of laser used and the number of sessions, previous or concurrent treatments, recurrence rate, reported complications, comorbidities, and outcomes.

We defined outcomes based on the improvement of cutaneous signs on a scale of good, minimal, or no response. The outcome was assessed by the treating laser specialists. The recurrence rate was defined as patients who were re-referred for repeat treatment of the same condition.

Results

Demographics

Sixty cases with a female predominance (n = 48) were identified and the average age was 51 years (range 11 to 74). Three patients were classed as having Fitzpatrick skin phototype IV, the majority had skin phototype II. The mean duration of disease prior to attending the laser assessment clinic was 7 years (range 1 to 30).

Diagnoses and concurrent treatments

The most common CTD diagnoses were limited cutaneous systemic sclerosis (n = 12; 20%), granuloma faciale and diffuse systemic sclerosis (n = 10; 17% each), sarcoidosis (n = 8; 13%), discoid lupus erythematosus (DLE) (n = 7; 12%), and systemic lupus erythematosus (SLE) (n = 2; 3%). A summary of the results is seen in Table 1. Other diagnoses treated included necrobiosis lipoidica, pyoderma vegetans, hypertrophic lichen planus, and sclerodermatomyositis.

Previous or concurrent treatments used to manage cutaneous signs of CTD were reviewed for each patient. Three patients (5%) had received previous immunosuppressive treatment including cyclophosphamide, methotrexate, and cyclosporine. During treatment, seven patients (12%) were taking prednisolone to treat their underlying CTD diagnosis; in one patient, this was for a non-CTD diagnosis. The most common concurrent treatment was hydroxychloroquine (n = 7; 12%). There were a small number of patients (n = 2, 3% each) on systemic agents such as azathioprine, mycophenolate mofetil, dapsone, and thalidomide. There were nine patients (16%) using either tacrolimus 0.3%/0.1% ointment or clobetasol propionate ointment.

Laser treatment

PDL was used in 41 patients (68%) and eight patients (13%) received carbon dioxide (CO_2) laser. Five patients (8%) received a combination of CO_2 and PDL. Neodymium-doped yttrium aluminum garnet laser (Nd:YAG) was used in two patients (3%) and alexandrite laser was combined with PDL n = 3 (5%) or with CO_2 n = 1 (2%) or with Nd:YAG n = 1 (2%). A mean of four or five sessions was required [Table 1].

The commonest sites treated were the cheeks (n = 36; 60%), followed by the nose (n = 17; 28%). Other high-impact sites treated were the lips (n = 6; 10%), forehead/temples (n = 6; 10%), neck (n = 5; 8%), and dorsum of hands (n = 9; 15%). Other body sites treated were the chest (n = 8; 13%), back (n = 3; 5%), and shins (n = 3; 5%). Parameters used for PDL were 7.5–9 J/cm^2, 7 mm spot, 595 nm, dynamic cooling device (DCD) 30:20. Parameters used for CO_2 laser were 10–14 W, 4–6 mm spot, 10600 nm, scanner, and silk touch resurfacing mode.

Treatment outcomes, adverse events and recurrence

The level of efficacy was defined based on the level of clearance of cutaneous signs as judged by the treating clinician. Patients were deemed to have a good response if they had complete clearance of their skin lesions, moderate response if they demonstrated partial clearance, and no response if there was minimal or no discernible improvement. The majority of patients demonstrated complete clearance with good response (n = 37; 62%), moderate response was seen in 15%, and no response in 22% of patients. Out of the three patients with Fitzpatrick skin phototype IV, a good response was seen in two patients treated with CO_2 laser for sarcoidosis and granuloma faciale, respectively. One patient treated with PDL for diffuse cutaneous systemic sclerosis showed no response to treatment.

The most common complication was bruising (n = 4; 7%) and three patients (5%) showed pigmentary changes. One patient developed ulceration leading to scarring. Recurrence 12 months after the final treatment of their inflammatory skin condition was seen in 18 patients (30%).

Discussion

We present one of the largest cohorts of patients with refractory CTD and inflammatory skin conditions treated with lasers. The majority of our patients achieved good outcomes for visible sites such as the face [Figures 1-3], neck, and dorsum of the hands, which tend to be associated with the highest level of psychological burden.[9]

The use of laser therapy in this setting has been considered controversial due to the limited data available. There are several reports of success in the use of lasers in lupus erythematosus (LE), which encompasses systemic SLE, acute, subacute, and chronic cutaneous LE, which include DLE. Characteristically, LE affects the face with the classical malar/butterfly rash, but also the extensor surfaces of the arms, neck, shoulders, and upper chest. Although SLE entails a multi-organ system involvement, the cutaneous predominance is reflected in 4 out of

Table 1: Summary of patient characteristics, laser treatment, response, adverse events, and recurrence

Sex	Age	Diagnosis	Year of laser assessment	Type of laser	Site	Number of laser sessions	Outcome	Complications	Recurrence
M	44	Sarcoidosis	2015	CO_2	upper lip and nose	2	good response	0	N
M	30	Granuloma faciale	2013	CO_2	nasal vestibules	2	good response but residual	0	Y
F	58	DLE	2014	CO_2 (resurfacing of scar) and PDL	nasal tip	2	good result from CO_2, no response to PDL	0	N
M	36	DLE (hyperpigmentation)	2016	CO_2 & alexandrite	left upper lip	test patch	no response	0	N
F	29	Diffuse cutaneous systemic sclerosis	2014	PDL	face	1	minimal response	hyperpigmentation, bruising	Y
F	21	Necrobiosis lipoidica	2010	PDL Candela-V beam	shins	3	minimal response	0	unknown
M	50	Lupus pernio	2016	PDL	nose	3	good response	0	N
F	67	Post-mesotherapy granulomas	2015	PDL	cheeks	1	minimal response	0	N
F	43	Limited cutaneous systemic sclerosis	2012	PDL	face, neck, and forehead	5=face and 8=chest & arms	good response	0	Y
F	64	DLE	2009	PDL & alexandrite	face	21	moderate response	0	Y
F	51	SLE	2012	PDL & alexandrite	cheeks, nose, and chin	7	good response	hyperpigmentation, purpura	Y
M	61	Granuloma faciale	2017	PDL	upper lip	5	minimal response	0	Y
F	27	Sclerodermatomyositis	2017	PDL	cheeks	2	no response	0	N
F	43	Lupus-induced cribriform scarring on chin	2011	CO_2 & PDL	chin	3	good response but required punch excisions of deeper scars	0	N
F	55	Pyoderma vegetans	2016	CO_2	left cheek	1	good response	0	Y
F	54	Sarcoidosis	2017	CO_2 & PDL	nose	CO_2=1, PDL=3	good response	0	N
F	45	DLE	2017	PDL	nose	3	good response	0	N
F	58	Discoid/tumid lupus	2011	PDL	face	20	good response	0	Y
M	71	Granuloma faciale	2011	CO_2	nose	1	good response	0	Y
F	59	Limited cutaneous systemic sclerosis	2010	PDL	face	7	good response	0	N
F	32	Atypical necrobiosis	2015	PDL	right temple	3	good response	0	N
F	54	Granuloma annulare	2010	PDL	left dorsum of hand	4	good response	0	N
M	62	Granuloma faciale	2009	CO_2 (combined resurfacing and fractionated)	right cheek	11	good response	0	N
F	52	Granuloma faciale	2014	CO_2 & PDL	right cheek	3	good response	0	N
M	40	Granuloma faciale	2008	PDL	bilateral temples	7	good response	0	Y
F	55	Limited cutaneous systemic sclerosis	2011	PDL	face, hands, and chest	5	good response	mild purpura	N
F	21	Morphea (hyperpigmented)	2011	Alexandrite & PDL	right lower cheek	5	good response to both	mild hyperpigmentation 2' alexandrite which resolved	N

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Table 1: Contd...

Sex	Age	Diagnosis	Year of laser assessment	Type of laser	Site	Number of laser sessions	Outcome	Complications	Recurrence
F	66	DLE	2009	PDL	cheeks, nose, and chin	6	good response	mild swelling post 5th Tx that resolved	N
F	68	Jessner's lymphocytic	2014	PDL	chest wall	5	good response	0	N
F	55	Limited cutaneous systemic sclerosis	2012	PDL	face	4	good response	0	N
F	57	Orofacial granulomatous disease	2016	PDL	upper lip, left cheek	6	minimal response on upper lip	0	Y
F	58	Limited cutaneous systemic sclerosis	2016	PDL	face, neck, upper chest, and upper limbs	6	good response	0	N
F	67	Limited cutaneous systemic sclerosis	2017	PDL	lips, face, and hands	4	minimal response	0	N
M	42	Granuloma faciale	2011	PDL	scalp	4	minimal response	0	N
F	57	Sarcoidosis	2005	PDL	cheeks, nose, and ear lobe	9	good response	0	Y
F	69	Sarcoidosis	2007	PDL	left cheek	4	no response	0	Y
F	53	Limited cutaneous systemic sclerosis	2012	PDL	nose and cheeks	7	moderate response	0	N
M	65	Limited cutaneous systemic sclerosis	2008	PDL	face	7	good response	0	Y
F	48	Limited cutaneous systemic sclerosis	2016	PDL	face, upper chest, neck, and forearms	7	good response	0	N
F	58	Diffuse cutaneous systemic sclerosis	2015	PDL	face, neck, dorsal of hands	4	moderate response	0	N
M	74	Hypertrophic lichen planus	2013	CO_2	right shin	1	good response	0	Y
F	49	Limited cutaneous systemic sclerosis	2011	PDL	forehead, cheeks	6	good response	0	N
F	60	Limited cutaneous systemic sclerosis	2011	PDL	lips, cheeks, nose	7	moderate response	0	N
F	42	Diffuse cutaneous systemic sclerosis	2016	PDL	face, upper chest	4	no response	0	N
F	55	Limited cutaneous systemic sclerosis	2014	PDL	face	5	moderate response	purpura resolved	N
F	60	SLE	2012	PDL	face, arms, and back	3	good response	0	Y
F	57	Limited cutaneous systemic sclerosis	2016	PDL	face, V-neck, and hands	5	good response	0	N
F	56	Granuloma faciale	2012	CO_2	nasal alar	3	moderate response	0	N
F	50	Limited cutaneous systemic sclerosis	2016	PDL	central face, upper chest wall	5	good response	0	N

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Table 1: Contd...

Sex	Age	Diagnosis	Year of laser assessment	Type of laser	Site	Number of laser sessions	Outcome	Complications	Recurrence
F	59	Limited cutaneous systemic sclerosis	2015	PDL	nose and forehead	4	good response	purpura lasting 1/12	Y
M	57	Granuloma faciale	2008	CO_2	cheeks	3	good response	0	N
F	52	Granuloma faciale	2014	PDL & CO_2	cheeks	PDL 5-no response CO_2-2	no response	0	N
F	23	Necrobiosis lipoidica diabeticorum	2009	PDL	shins	2	good response	ulceration but healed with minimal scarring	Y
F	63	Limited cutaneous systemic sclerosis	2018	PDL	cheeks and nose	6	good response	0	N
F	50	Limited cutaneous systemic sclerosis	2018	PDL	cheeks and nose	5	good response	0	N
F	68	Diffuse systemic sclerosis	2008	PDL	face	4	good response	0	N
F	30	Ulerythema ophryogenes	2009	PDL	cheeks and eyebrows	4	good response	blistering, pigmentation	Y
F	20	Urticaria pigmentosa	2010	Nd:YAG 1064	chest, back, neck	4	good response	0	N
F	11	Urticaria pigmentosa	2010	Nd:YAG 53_2,1064, alexandrite	back	2	no response	0	N
F	52	Sarcoidosis	2018	PDL	nose	4	some response	0	N

Figure 1: Systemic Lupus Erythematosus treated with PDL and alexandrite laser. (a) On the left pre-treatment and (b) On the right post-treatment

Figure 2: Granuloma faciale treated with PDL and CO_2 laser. (a) On the left pre-treatment and (b) On the right post-treatment

Figure 3: Sarcoidosis treated with PDL and CO_2 laser. (a) On the left pre-treatment and (b) On the right post-treatment

the 11 criteria involving cutaneous manifestations.[10] Telangiectasia and dyspigmentation often persist even after the cutaneous signs have resolved. Conventional therapies often do not address the cutaneous signs, as evident from our cohort of patients.

The use of lasers in LE has been most well documented in the medical literature. There are fourteen published studies describing the efficacy of laser and adverse events seen. Eight of those studies used PDL, including in two

prospective case series and the rest used either argon 514, CO_2, or erbium-doped YAG or Nd:YAG. The prospective studies reviewing the use of PDL found 12 of 19 patients demonstrated complete resolution of their cutaneous disease.[1] The third prospective study found PDL resulted in a statistically significant decrease in Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) from a mean of 4.4 to 1.3 after only three treatment sessions. The findings described in the literature echo our results as no recurrence was seen in the majority of patients for nearly 10 months and the side effect profile included self-limiting hyperpigmentation and only single cases of permanent pigmentary changes/scarring.[5] The evidence indicates that PDL is an effective and safe method in optimizing these patients' outcomes.[11] Raulin *et al*.[12] challenged as to why PDL has not been incorporated into the conventional treatment algorithms in the context of LE and suggested that in part dermatologists may not be aware or appreciate the full use of lasers and therefore do not implement laser therapy in their treatment regimes. We would agree that we anticipated having treated more LE patients in our laser clinic, but it is possible that cases were not referred due to a lack of awareness.

The most common condition treated in our cohort of patients was scleroderma, which entails systemic and localized sclerosis or morphea. To the best of our knowledge, there are 11 published articles reviewing the use of laser therapy in scleroderma or morphea with predominantly case reports and the largest case series involving eight patients with facial telangiectasias.[1] We present the largest cohort with a total of 23 patients having localized or diffuse sclerosis and a single case of hyperpigmented morphea on the face of a child.

Facial telangiectasias seem to be the main sign that is successfully treated with the use of PDL as also demonstrated in our patients. However, the development of telangiectasias is inherent to the pathogenesis of scleroderma, and therefore, recurrence can be expected. Halachmi *et al*.[13] reported that the number of PDL treatments required for scleroderma-related telangiectasia versus sporadic telangiectasia is twofold higher. They performed skin biopsies and compared to normal skin were found to have thickened vessels and thickened collagen fibers in the reticular and deep dermis. Therefore, laser therapy is proposed as an adjunct to systemic treatment in controlling recalcitrant disease and it highlights the importance of addressing patient expectations with regard to the recurrence of signs. Our experience and the literature suggest complete resolution of signs for a period of six months to two years.[14]

A systematic review by Wat *et al*.,[15] looking at the role of IPL in dermatological disease, examined 11 studies relating to its use in telangiectasias (benign essential telangiectasia, telangiectasia of the lower limbs, hereditary hemorrhagic telangiectasia, radiotherapy-induced telangiectasia, postsurgical telangiectasia, and telangiectasia associated with systemic sclerosis). They concluded that IPL was an excellent treatment option that could be compared to the gold standard PDL. A within-subject randomized trial comparing IPL and laser treatment for telangiectasia in patients with systemic sclerosis found that PDL had superior outcomes in appearance, although IPL had fewer side effects.[16] In our cohort of patients, although IPL was not utilized, scleroderma-related telangiectasia was successfully treated with PDL.

Furthermore, the use of ablative and fractional ablative CO_2 lasers in scleroderma has been reported to be successful in treating contractures, rhytides, and calcinosis of the digits.[17-19] However, it is important to note the pathogenesis in scleroderma and morphea, which are considered to induce a profibrotic state, driven by cytokines including interleukins 4 and 6 and transforming growth factor beta.[20] Poor wound healing is a concern in view of the underlying microvascular disease and profibrotic state; therefore, ablative and resurfacing lasers may lead to higher adverse events.[21]

PDL and CO_2 laser have also been reported as effective treatment modalities for the cutaneous manifestations of dermatomyositis. Typical skin findings include poikiloderma, Gottron's papules over joints, periorbital macular erythema, eruptions over the shoulders or lateral hips, calcinosis cutis, and fissured hyperkeratotic plaques over the hands. These are often resistant to medical therapy.[22] However, there are cases reporting the successful use of PDL in the treatment of poikiloderma[23,24] and Gottron's papules[25] where a 70% improvement was noted, with no recurrence after three years. Fractional ablative CO_2 laser has also successfully been used in the treatment of ulcerating calcifications in dermatomyositis by causing liquefaction.[26] In our cohort, one patient with sclerodermatomyositis, an overlap syndrome of scleroderma and dermatomyositis/polymyositis, underwent treatment with PDL laser to telangiectasia of the cheeks but showed no response after three treatments.

There is a paucity of literature specifically examining laser treatment of CTDs in ethnic skin, including differences in recurrence rate compared with fair skin types. However, in general risk of post-procedure dyschromia and scarring is known to be greater in the skin of color, owing to structural and functional differences. Recommendations when treating Fitzpatrick skin types IV–VI include the use of longer wavelength lasers, lower fluences, treatment densities, and longer pulse durations to reduce the risk of thermal injury to the epidermis.[27,28] The three patients in our cohort with Fitzpatrick skin type IV did not experience any laser treatment-related complications, although one patient did not respond to treatment.

We have treated several different granulomatous/infiltrative processes in our laser clinic including sarcoidosis, granuloma faciale, granuloma annulare, Jessner's lymphocytic infiltrate, and pyoderma vegetans. Sarcoidosis was one of the more common conditions treated, including cases of lupus pernio. There have been 10 published articles consisting of case reports and a case series (n = 3) reviewing the use of laser therapy in sarcoidosis with five patients being treated with PDL and five with CO_2 laser in the remodeling of lupus pernio. We present the largest case series of sarcoidosis patients (n = 8) who were treated with laser, predominantly PDL but in a single case combination of PDL and CO_2 was used for lupus pernio. The response was less impressive compared to other conditions seen in our series with 37% showing resolution of their signs but 25% showing no response at all. Triamcinolone injection was used in 37% of patients while also having laser therapy. The literature review suggests that sarcoidosis has the greatest association with adverse events.[29] However, our patients only reported self-limiting purpura and no scarring was noted.

Treatment of granuloma faciale (GF) has been considered disappointing over the years, with case series suggesting the effective use of PDL. A case report of recurrent GF, and as seen in our cohort of patients, combining CO_2 with PDL has had an excellent cosmetic outcome with a longer-lasting effect and no evidence of scarring.[30] In conditions such as recalcitrant granuloma faciale, the primary role of the CO_2 laser is to reduce the thickness of the plaques. It would seem from our cohort that the lesions while considered inflammatory do not recur nor are exacerbated by this treatment.

Necrobiosis lipoidica (NL) is considered a challenging condition to manage despite a plethora of modalities reviewed over the years. Case reports reviewing the use of PDL have reported laser therapy to be overall ineffective.[31] We report three cases of recalcitrant NL including an atypical case occurring on the face, with two of those patients showing good response to PDL with no complications. There have been a limited number of reports of granuloma annulare (GA) being successfully treated with PDL, fractional photothermolysis (FP), and excimer laser.[32] From our experience, PDL showed complete resolution of lesion on the dorsum of the hand.

Conclusion

We present the largest case series of patients undergoing laser treatment for cutaneous manifestations of their inflammatory or connective tissue disease. The majority of the patients treated had lesions affecting high-impact sites such as the face and chest. Several studies have demonstrated the immense and prolonged psychological impact associated with the chronic nature and visibility of their disease. Our case series have shown the safety and effectiveness of the use of PDL in CTD-related telangiectasias; however, it is important to address patient expectations, as these tend to recur due to the nature of the condition. CO_2 was found to be useful in granuloma faciale. The use of lasers can complement conventional treatments in improving overall cosmetic outcomes and quality of life.

Abbreviations

- PDL = Pulsed dye laser
- CO_2 = Carbon dioxide laser
- Nd:YAG = Neodymium-doped yttrium aluminum garnet
- CTD = Connective tissue disease
- DLE = Discoid lupus erythematosus
- SLE = Systemic lupus erythematosus
- GF = Granuloma faciale
- GA = Granuloma annulare
- DLQI = Dermatology Life Quality Index.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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