

Urticaria Induced by Laser Epilation: A Clinical and Histopathological Study With Extended Follow-Up in 36 Patients

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Background: Laser epilation is the most common dermatologic light-based procedure in the world. We describe a unique side effect of the procedure: a delayed persistent urticarial rash.

Patients and methods: We conducted a retrospective study involving 13,284 patients who received laser epilation at our clinics from January 2006 through March 2010 with 755 nm alexandrite laser (MiniGentleLase, Gentlelase, and GentleMax, Candela). Using patient clinical data and photos that were recorded on a standard side-effect report chart, we identified patients with suspected urticaria. Those patients were then followed for a period that ranged from 12 to 63 months. Only patients who could be diagnosed, treated, and followed by the dermatologist at our clinics were included in the study. Patients diagnosed or treated by other physicians or nurses and those without clinical photos or insufficient follow-up data were not included.

Results: We identified 36 patients who developed a severe, itchy, persistent hive rash on the treated area 6–72 hours after treatment. Eruption occurred most often on the legs (31 cases), followed by the groin (11 cases), axillae (eight cases), forearms (one case), and upper lip (one case). The eruption consisted of a hive rash with multiple pruritic perifollicular papules and confluent plaques on the treated area. Most patients required oral corticosteroids to control the symptoms. Lesions resolved in 7–30 days. The urticaria occurred mostly after the first treatment (26 cases), and was recurrent in subsequent treatments. Pretreating with oral corticosteroids prevented or limited the eruption. Thirty-three of the 36 patients reported a history of allergic rhinitis or some other allergy. Skin biopsies on four patients showed edema and a deep, dense dermal infiltrate consistent with lymphocytes mixed with eosinophils in a perivascular and occasionally perifollicular pattern in the mid and lower dermis.

Conclusions: Persistent urticaria is a rare side effect of laser epilation. Rupture of the hair follicle by laser heat may trigger a delayed hypersensitivity reaction in a subset of predisposed allergic patients. An antigen from the disrupted hair follicle may be the triggering factor. To prevent this side effect, we recommend that laser

epilation in allergic patients be preceded by an extended laser patch test, which should be evaluated 24–48 hours later. Preventive prednisone should be prescribed to patients who develop an urticarial rash on the test area. *Lasers Surg. Med.* © 2012 Wiley Periodicals, Inc.

Key words: allergy to hair; itchy rash; laser hair removal; photoepilation; preventive prednisone; side effects; urticaria

INTRODUCTION

Laser epilation is currently the most common dermatologic light-based procedure in the world. It is performed with three types of lasers that operate within the red or infrared wavelength region (alexandrite, diode, and Nd-Yag) and with nonlaser intense pulsed lights (IPL) devices (500–1,200 nm wavelength flashlamps) [1]. Laser epilation is done in both medical and non-medical settings and by caregivers with various levels of medical and technical education. The procedure's most common side effects are hyperpigmentation and hypopigmentation secondary to burning, as well as hair stimulation [1–3]. We describe a series of 36 patients who developed a unique side effect, a delayed and persistent urticarial rash, from laser epilation after a long follow-up.

PATIENTS AND METHODS

For this retrospective study, a total of 13,284 patients, 1,311 males and 11,973 females, were treated with laser epilation at the Dermitek Clinic in Bilbao and the Sinpelo Clinic in Madrid from January 2006 through March 2010. Patient ages ranged from 12 to 79 years; their Fitzpatrick skin phototypes ranged from I to IV. The most commonly treated areas were the axillae (91%), the groin (64%), and the legs (34%). Three alexandrite lasers (MiniGentleLase,

Conflicts of interest: none.

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Gentlelase and GentleMax, Candela) were used: 755 nm, 18-mm spot size, and 3-msecond pulse duration. Fluences ranged from 10 to 16 J/cm², depending on the skin phototype; most were within the 12–14 J/cm² range. A dynamic cooling device was used with cryogen spray settings of either a 40-msecond spray with a 30-msecond delay or a 30-msecond spray with a 20-msecond delay.

Patient clinical data and photos were recorded on a specific side-effect report chart common to the clinics. Patient ages ranged from 20 to 47 years; their Fitzpatrick skin phototypes ranged from II to IV. All 36 patients were evaluated by a dermatologist. Those patients whose cases fulfilled a common clinical pattern were then followed for a period that ranged from 12 to 63 months. Suspicious itchy rashes with incomplete data were discharged. Four of the 36 patients were biopsied on a lesion of one leg in a random area.

RESULTS

Of the 13,284 patients treated, 36 (35 women and one man) were found to have developed a delayed and severe persistent urticarial eruption, which started 6–72 hours after treatment. Patient results are summarized in the Table 1. Morphologically, the rash consisted of multiple perifollicular urticarial papules with a tendency to be confluent in larger irregular urticarial plaques (Figs. 1 and 3). The papules and plaque lesions left occasional patches of normal skin. The number of lesions corresponded with the density of hair follicles. These lesions were always limited to the treated area; they did not extend to other parts of the body. None of the patients had a systemic reaction, such as angioedema or anaphylaxis.

The eruption was severely pruritic and persistent. The duration of the lesion was an average of 10–30 days without treatment. When treated with oral prednisone, either alone or combined with antihistamines, the lesions resolved in 5–10 days. All lesions resolved completely without postinflammatory hyperpigmentation or hypopigmentation. A few cases left temporary mild hyperpigmentation secondary to scratching.

Urticaria occurred in 26 patients (72.22%) after the first laser epilation treatment session, in five patients (13.88%) after the second session, in four patients (11.1%) after the third session, and in one patient (2.8%) after the fourth session.

In all 36 patients, the skin reaction was normal immediately after the laser treatment. Patients reported that the eruption started 6 hours to 5 days after treatment (average delay was 19:33 hours). In patients with eruptions who had subsequent laser epilation treatments, the lesions appeared at about the same time or earlier after the second treatment.

In seven of the 10 cases of patients who developed urticaria for the first time after their second, third, or fourth laser session, the laser settings used in the session that triggered the rash were identical to those used in the earlier “normal” sessions; in three of the cases, the settings were lower. None of these 10 cases had used higher

settings during the treatments that immediately preceded the development of urticaria than were used in the previous normal sessions.

Urticaria occurred on the legs in 31 of the 36 cases (86%) of 7,210 treatments, on the bikini area in 11 of the 36 cases (30.55%) of 8,634 treatments, on axillae in eight of the 36 cases (22%) of 10,069 treatments; on forearms in one; on the upper lip in one. Nineteen of the 31 patients (61%) with affected legs had been treated in other areas that were not affected. Eleven of the 31 patients (35%) with affected legs had other areas affected besides the legs. Only in two patients were areas of fine hair (upper lip, forearms) affected.

Previous allergies were reported by 33/36 patients. The most frequent allergies were allergic rhinitis to dust mites (15/31) and allergic rhinitis to pollen (hay fever; 12/31). Among the other reported allergies were those to food, cat hairs, textiles, cosmetics, medications, and sunlight.

No patient had a history of urticaria from cold or heat.

Histopathology

Biopsies performed on four patients showed edema and a deep and dense infiltrate consistent with lymphocytes mixed with eosinophils in a perivascular and occasionally perifollicular pattern in the mid and lower dermis (Fig. 2).

Other Tests

Lesions were not reproduced with the laser on a non-hairy area of internal aspect of the arm in four patients. Lesions were not reproduced with the cryogen spray alone in three patients on areas affected and non-affected by the urticaria.

Treatment

To control the severe itch, most patients were treated with oral prednisone (30–40 mg) in the morning, plus an antihistamine at night (25 mg of hydroxyzine or 10 mg of cetirizine). Some patients preferred not to take prednisone; they were treated with an antihistamine and a topical corticosteroid cream (Adventan cream, Schering) for 7 days. Treatment with oral prednisone resulted in a faster resolution of the urticaria.

Follow-Up

Seven of the 36 patients stopped laser epilation treatments after the first session because of the rash. The remaining 29 patients continued with more sessions despite being advised of a possible recurrence of the urticaria. The follow-up period of these 29 patients ranged from 12 to 63 months. The number of subsequent sessions ranged from 1 to 12, with an average number of 5.

Of these 29 patients, 19 were treated with preventive prednisone. The dosage was 30 mg/day for 3 days starting the day of the treatment session, followed by 15 mg/day for 3 more days. Twelve of the 19 preventively treated patients did not have recurrence after following treatments; seven patients did have recurrence, although of milder intensity. (See Table 1 for details of patient treatment during the follow-up period.)

TABLE 1. Follow-Up and, Effects of Pretreatment With Oral Corticosteroids on Patients With a History of Delayed Persistent Urticarial Rash Induced by Laser Epilation

Patient	Laser-epilation-treated areas with urticaria	Laser-epilation-treated areas without urticaria	Treatment session when urticaria initially occurred (Bx = Biopsy)	No. of post-urticaria laser-epilation treatments	Preventive medication given before subsequent sessions	Recurrence of urticaria	Follow-up urticaria
1	Legs, axillae		1st (Bx)	0			
2	Legs	Bikini	1st (Bx)	0		Yes, abandons	
3	Legs, bikini	Upper lip	1st	1 big test area			
4	Legs, axillae		1st	0			
5	Legs		3rd	10	No	Yes	Progressively less
6	Legs, forearm		1st	3	Prednisone	No	
7	Legs		1st	8	Prednisone	No	3rd time no urticaria
8	Lower legs, bikini	Axillae	1st	1 big test area		Yes, abandons	
9	Legs	Bikini, axillae	1st	7	Prednisone	No	
10	Legs	Bikini	1st	9	Prednisone	Yes	Progressively less
11	Legs, bikini axillae		1st (Bx)	7	Prednisone	Yes	Progressively less
12	Legs		1st	2	Prednisone	No	
13	Lower legs, axillae	Between eyebrows	2nd	1 big test area		Yes, abandons	
14	Legs	Bikini, axillae	1st	5	Prednisone	No	5th time no urticaria
15	Lower legs	Bikini, axillae	1st	5	Prednisone	No	
16	Legs, bikini		1st	5	Prednisone	Yes	Progressively less
17	Legs	Bikini	4th	7	Prednisone	No	
18	Lower legs	Bikini, axillae	2nd	6	Prednisone	Yes	Progressively less
19	Lower legs	Bikini, axillae	1st	8	No	Yes	Progressively less
20	Lower legs	Bikini, axillae	3rd	4	Prednisone	No	5th time no urticaria
21	Bikini		1st	2	No	Yes	
22	Lower legs, bikini, axillae		1st	5	Prednisone	No	
23	Legs	Bikini, axillae	3rd	12	No	Yes	Progressively less
24	Bikini, axillae		1st	4	Prednisone	No	
25	Lower legs		2nd	5	Prednisone	No	
26	Pubis, bikini	Legs, axillae	2nd	4	No	No	
27	Lower legs, bikini, axillae		1st	3	Prednisone	Yes	Progressively less
28	Legs	Bikini, axillae	1st	3	Prednisone	Yes	
29	Legs	Bikini, axillae	1st	4	Desloratadine	No	
30	Lower legs		2nd	2	No	Yes	Progressively less
31	Legs	Bikini, axillae	1st	4	No	Yes	Progressively less
32	Lower legs	Thighs, bikini, axillae	1st	3	Prednisone	Yes	4th time no urticaria
33	Lower legs, bikini	Axillae	3rd	4	Prednisone	No	Progressively less
34	Bikini		1st	3	No	Yes	Progressively less
35	Upper lips	Thorax, abdomen, arms	1st	1 big test area		Yes, abandons	
36	Legs		1st (Bx)	1	No	Yes	



Fig. 1. Severe urticaria 24 hours after 1st treatment (left); milder urticaria 24 hours after 2nd treatment (right) in same patient taking preventive prednisone.

Ten of the 29 patients did not want to take preventive prednisone due to corticosteroid-phobia. One of these 10 patients was treated with preventive desloratadine instead, and the urticaria did not recur. In eight of the 10 patients, the urticaria recurred.

In all patients, both those treated with oral prednisone and those not treated, the rash became progressively milder with ongoing sessions until almost complete resolution. The decrease in intensity of the urticaria was proportional to hair reduction.

In general, the urticaria was very mild after four to five additional laser epilation treatments, even when subsequent treatments maintained the same laser settings. After these four to five treatments, preventive prednisone could be withdrawn. Some itch and mild erythema still occurred in some patients, but these symptoms usually could be controlled with a topical corticosteroid cream administered alone or in combination with an antihistamine.

In some patients the time of onset of the rash occurred earlier after subsequent laser treatments. For example, patient 14 developed urticaria 6 days after her first laser treatment, but only 12 hours after her second treatment. In other patients, however, the time of onset of the rash was similar after the first and subsequent treatments.

DISCUSSION

The 36 cases in this series showed a common clinical pattern. The urticaria presented as a severe pruritic eruption consisting of urticarial papules and large plaques. It occurred several hours or days after treatment and persisted for one to several weeks. It was more

frequent on the legs and in thick-hair (bikini, axillae) areas, but fine-hair areas were also involved. It was limited to the treated area, and occurred in one or several treated areas of the same patient.

The onset of the urticaria was most frequent after the first laser epilation treatment, but the rash sometimes occurred for the first time after a second, third, or, more rarely, fourth treatment. Once it appeared, the urticaria tended to repeat in subsequent treatments, although the evolution was to a milder or almost completely disappearing rash. The urticaria was prevented or limited with oral prednisone.

Almost all patients (33/36) in our study reported a history of allergies, especially allergic rhinitis caused by dust mites, which is the most prevalent type of allergy in the general population [4]. Dust mites have been observed in the hair of animals [5], and heat may expand antigens from the mite. Why post-epilation urticaria occurs only in a subset of allergic patients is unknown. We found no characteristics to distinguish this subset from other laser-epilation patients with the same allergies. Recently, however, three sisters presented with urticaria after laser epilation in our clinics (unpublished data); all three had a history of allergic rhinitis or asthma, suggesting that the development of urticaria after laser epilation may have a genetic link.

The antigen responsible for post-epilation urticaria may be present in the hair shaft or in the follicle itself and released after the lysis by laser energy. This hypothesis is supported by several observations from our study. First, the urticaria occurred with laser epilation treatments and was limited to the treated area. Second, the urticaria

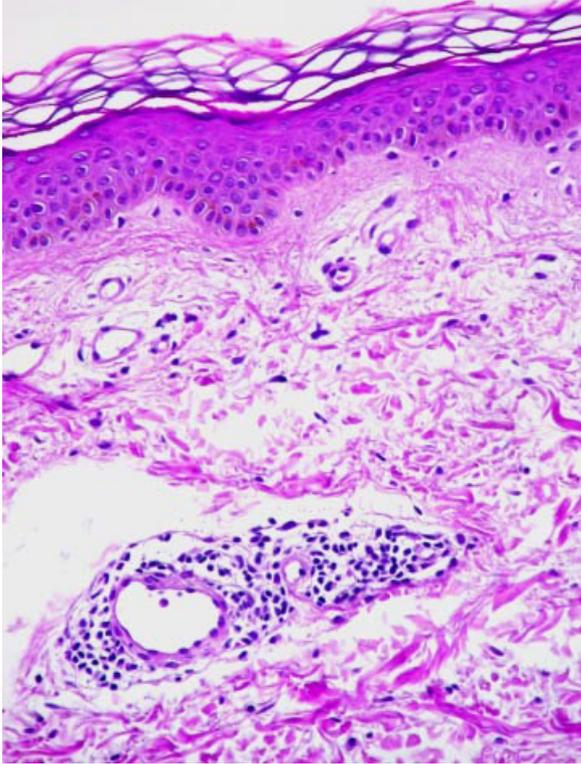


Fig. 2. Perivascular mononuclear infiltrate in reticular dermis with some eosinophils.

improved and disappeared along with progressive hair removal. In addition, the papules and lesions occurred on thick-hair areas, but were absent on areas with less or no hair, and patch tests done on the inner arms of selected patients were negative.

Histologically, the urticaria showed a dense perivascular infiltration of lymphocytes mixed with eosinophils. Inflammation was located in the mid and deep dermis, and involved the superficial vascular plexus. These findings support a hypersensitivity reaction mediated by mast cells. They also suggest that the antigen is deeply located and that the urticaria may occur only with those laser wavelengths that reach deep into the hair follicle.

Allergic reactions after treatment of tattoos with two Q-switched lasers have been described [6,7]. In those studies, unlike in ours, not only patients experienced localized but also widespread generalized urticaria outside the treatment site, and the rash appeared to result from rapid thermal expansion, which caused the tattoo pigments to become extracellular, triggering an immune response [6]. Heat alone did not induce the urticaria observed in our study, however; if so, the urticaria would have been reported with other skin treatments that use high-temperature lasers.

An *in vivo* study by Algermissen et al. [8] reported an erythematous skin response (weal and flare reactions) in 19 of 20 volunteers treated with an argon laser on the inner arms. In that study, treatment with the H1-blocker loratadine and triamcinolone cream was ineffective or non-significant, but local anaesthetics as well as neuropeptide depletion of skin with capsaicin abolished the reactions almost completely, suggesting that laser-associated transient weal and flare reactions are based primarily on a neurogenic rather than a histamine- or mast cell-dependent mechanism.

There are five previous reported cases similar to ours. Moreno-Arias et al. [9] reported a single case of persistent urticaria on the legs after laser epilation with a 810 nm diode laser. Because their patient developed ecchymotic macules after the urticaria resolved, the authors of that study suggested that the patient had urticarial vasculitis,



Fig. 3. Urticaria 24 hours after treatment with 10 J/cm² (left) and 8 J/cm² (right); 8 J/cm² shows less intensity.

although she declined a biopsy to confirm this diagnosis. None of our patients developed purpura or ecchymoses, although some patients had reddish-pigmented macules, which appeared to be secondary to scratching and resolved completely within days. Bernstein reported four cases of severe urticaria that occurred immediately after laser epilation and that lasted many days [10]. The clinical picture of all four patients was similar to that of our series of patients, although the onset of the urticaria in the Bernstein study occurred within 24 hours, unlike the longer delayed onset (6 hours to 5 days) observed in our study.

The wavelength of the alexandrite laser used in our study did not appear to play a critical role in the pathogenesis. One of our patients developed urticaria after undergoing laser epilation treatment in another center using an IPL system, and a second patient was discharged from that same center because she developed urticaria after being treated with a Lightsheer diode laser (Lumenis Ltd., Yokneam, Israel). In addition, the case described by Moreno-Arias occurred with a Lightsheer diode laser, and one of the cases described by Bernstein occurred with an Nd-Yag (Candela Corporation, Wayland, MA) laser.

The cryogen from the DCD (dynamic-cooling device) can also be ruled out as the triggering agent. We performed tests in affected patients with the cryogen alone; the urticaria was not reproduced, only transient erythema. In patients with multiple areas treated with the same cryogen settings, urticaria occurred only in a single area, and the urticaria improved in subsequent treatments using the same settings. In the Moreno-Arias case and in our case of a patient who developed urticaria after treatment with IPL at another center, contact cooling was used. In an *in vivo* study of human skin exposed to cryogen spray cooling, acute erythema and urticaria were noted 1–24 hours after exposure in 14 of 27 and three of 27 subjects, respectively [11]. Unlike in our study, the reaction was immediate and of very short duration.

We did find an association between fluence and the intensity of the urticarial reaction. It appears that the higher the fluence, the more intense the reaction (Fig. 3). In patient 4, for example, an area treated with 16 J/cm² and many clustered shots had an intense reaction, while an area treated with 12 J/cm² and fewer shots had a moderate erythema. The reaction also occurred, however, with energies as low as 8–9 J/cm², as in patient 3, or at medium levels of 10–12 J/cm².

Eighteen of our 36 patients were treated with preventive prednisone (30 mg for 3 days followed by 15 mg for 3 days). Although the prednisone was effective, seven patients had a minor recurrence; they may have needed a higher dose of prednisone. In fact, two recent patients (not included in this series) who experienced a very intense post-laser epilation reaction required 60 mg for 3–6 days to prevent a recurrence.

In all the patients in this series, the reaction was progressively less intense with subsequent treatments using the same settings. In general, after the fourth or fifth treatment most patients did not need prednisone and

managed with a corticosteroid cream. This outcome was proportional to the decrease of hair, a factor that supports the hypothesis that the antigen is located in the hair itself.

Our study has several limitations. This is a retrospective study, and some data may have been missed. Prevalence is underestimated because only those patients who could be diagnosed by a dermatologist were included. In addition, only severe cases were selected; patients with milder pruritic erythema or patients with only itchy reactions were eliminated. Patients who developed an urticarial rash on the patch test area before their first laser epilation treatment were also excluded from the study.

CONCLUSIONS

Urticaria is a rare side effect of laser epilation that seems to occur in a subset of allergic patients. To prevent this side effect, patients who are suspected of being at risk for developing this reaction should be given an extended high-energy laser patch test on an area with thick hair before undergoing treatment. The result should be evaluated 24–48 hours later, and preventive prednisone should be prescribed to patients who develop a delayed, itchy, and persistent urticarial rash in the test area. An antigen located in the deep hair follicle may be the etiological factor behind this allergic reaction. The urticaria remits with subsequent hair removal treatments.

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