

# Telmisartan-Induced Lichen Planus Eruption Manifested on Vitiliginous Skin

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### PRACTICE POINTS

- Lichen planus (LP) is a T-cell-mediated autoimmune disease that affects the skin and often the mucosa, nails, and scalp.
- The etiology of LP is unknown. It can be induced by a variety of medications and may spread through the isomorphic phenomenon.
- Immune factors play a role in the development of LP, drug-induced LP, and vitiligo.

To the Editor:

A 39-year-old man with a history of hypertension and vitiligo presented with a rapid-onset, generalized, pruritic rash covering the body of 4 weeks' duration. He reported that the rash progressively worsened after developing mild sunburn. The patient stated that the rash was extremely pruritic with a burning sensation and was tender to touch. He was treated with beta-methasone valerate cream 0.1% by an outside physician and an over-the-counter anti-itch lotion with no notable improvement. His only medication was telmisartan-hydrochlorothiazide (HCTZ) for hypertension. He denied any drug allergies.

Physical examination revealed multiple discrete and coalescent planar erythematous papules and plaques involving only the depigmented vitiliginous skin of the forehead, eyelids, and nape of the neck (Figure 1A), and confluent on the lateral aspect of the bilateral forearms (Figure 1B), dorsal aspect of the right hand, and bilateral dorsi of the feet.

Wickham striae were noted on the lips (Figure 1C). A clinical diagnosis of lichen planus (LP) was made. The patient initially was prescribed halobetasol propionate ointment 0.05% twice daily. He reported notable relief of pruritus with reduction of overall symptoms and new lesion formation.

A 4-mm punch biopsy was performed on the left forearm. Histopathology revealed LP. Microscopic examination of the hematoxylin and eosin-stained specimen revealed a bandlike lymphohistiocytic infiltrate that extended across the papillary dermis, focally obscuring the dermoepidermal junction where there were vacuolar changes and colloid bodies. The epidermis showed sawtooth rete ridges, wedge-shaped foci of hypergranulosis, and compact hyperkeratosis (Figure 2).

On further questioning during follow-up, the patient revealed that his hypertensive medication was changed from HCTZ, which he had been taking for the last 8 years, to the combination anti-hypertensive medication telmisartan-HCTZ before the onset of the skin eruption. Due to the temporal relationship between the new medication and onset of the eruption, the clinical impression was highly suspicious for drug-induced eruptive LP with Köbner phenomenon caused by the recent sunburn. Systemic workup for underlying causes of LP was negative. Laboratory tests revealed normal complete blood cell counts. The hepatitis panel included hepatitis A antibodies; hepatitis B surface, e antigen,

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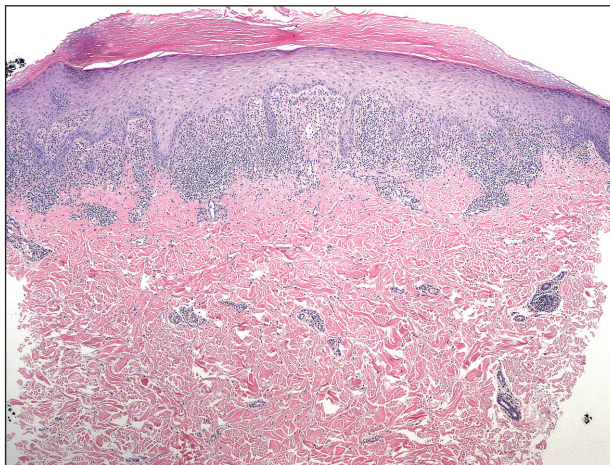
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**Figure 1.** Confluent shiny erythrovioleaceous papules and plaques on the photodistributed vitiliginous skin of the posterior aspect of the neck (A). Numerous shiny erythrovioleaceous papules coalescing into confluent plaques on photodistributed vitiliginous skin of the bilateral lateral forearms (B). Netlike lacy white lines (Wickham striae) on the lower mucosal lip with mild edema on the upper and lower lips (C).



**Figure 2.** Histopathology of a specimen from the left forearm revealed a bandlike lymphohistiocytic infiltrate that extended across the papillary dermis, focally obscuring the dermoepidermal junction. The epidermis showed sawtooth rete ridges, wedge-shaped foci of hypergranulosis, and compact hyperkeratosis (H&E, original magnification  $\times 40$ ).



**Figure 3.** Four weeks after discontinuation of telmisartan-hydrochlorothiazide, the patient noted near-complete resolution of lichen planus and subtle perifollicular repigmentation on the posterior aspect of the neck (A). He exhibited marked reduction of lichen planus on the bilateral lateral arms as well as perifollicular repigmentation of vitiliginous areas (B).

and core antibodies; hepatitis B surface antigen and e antibodies; hepatitis C antibodies; and antinuclear antibodies, which were all negative.

The patient continued to develop new pruritic papules clinically consistent with LP. He was instructed to return to his primary care physician to change the telmisartan-HCTZ to a different class of antihypertensive medication. His medication was changed to atenolol. The patient also was instructed to continue the halobetasol propionate ointment 0.05% twice daily to the affected areas.

The patient returned for a follow-up visit 1 month later and reported notable improvement in pruritus and near-complete resolution of the LP after discontinuation of telmisartan-HCTZ. He also noted some degree of perifollicular repigmentation of the vitiliginous skin that had been unresponsive to prior therapy (Figure 3).

Lichen planus is a pruritic and inflammatory papulosquamous skin condition that presents as scaly, flat-topped, violaceous, polygonal-shaped papules commonly involving the flexor surface of the arms and legs, oral mucosa, scalp, nails, and genitalia. Clinically, LP can present in various forms including actinic, annular, atrophic, erosive, follicular, hypertrophic, linear, pigmented, and vesicular/bullous types. Koebnerization is common, especially in the

linear form of LP. There are no specific laboratory findings or serologic markers seen in LP.

The exact cause of LP remains unknown. Clinical observations and anecdotal evidence have directed the cell-mediated immune response to insulting agents such as medications or contact allergy to metals triggering an abnormal cellular immune response. Various viral agents have been reported including hepatitis C virus, human herpesvirus, herpes simplex virus, and varicella-zoster virus.<sup>1-5</sup> Other factors such as seasonal change and the environment may contribute to the development of LP and an increase in the incidence of LP eruption has been observed from January to July throughout the United States.<sup>6</sup> Lichen planus also has been associated with other altered immune-related disease such as ulcerative colitis, alopecia areata, vitiligo, dermatomyositis, morphea, lichen sclerosis, and myasthenia gravis.<sup>7</sup> Increased levels of emotional stress, particularly related to family members, often is related to the onset or aggravation of symptoms.<sup>8,9</sup>

Many drug-related LP-like and lichenoid eruptions have been reported with antihypertensive drugs, antimalarial drugs, diuretics, antidepressants, nonsteroidal anti-inflammatory drugs, antimicrobial drugs, and metals. In particular, medications such as captopril, enalapril, labetalol, propranolol, chlorothiazide, HCTZ, methyl dopa, chloroquine, hydroxychloroquine, quinacrine, gold salts, penicillamine, and quinidine commonly are reported to induce lichenoid drug eruption.<sup>10</sup>

Several inflammatory papulosquamous skin conditions should be considered in the differential diagnosis before confirming the diagnosis of LP. It is important to rule out lupus erythematosus, especially if the oral mucosa and scalp are involved. In addition, erosive paraneoplastic pemphigus involving primarily the oral mucosa can resemble oral LP. Nail diseases such as psoriasis, onychomycosis, and alopecia areata should be considered as the differential diagnosis of nail disease. Genital involvement also can be seen in psoriasis and lichen sclerosis.

Treatment of LP is mainly symptomatic because of the benign nature of the disease and the high spontaneous remission rate with varying amount of time. If drugs, dental/metal implants, or underlying viral infections are the identifiable triggering factors of LP, the offending agents should be discontinued or removed. Additionally, topical or systemic treatments can be given depending on the severity of the disease, focusing mainly on symptomatic relief as well as the balance of risks and benefits associated with treatment.

Treatment options include topical and intral-lesional corticosteroids. Systemic medications such

as oral corticosteroids and/or acitretin commonly are used in acute, severe, and disseminated cases, though treatment duration varies depending on the clinical response. Other systemic agents used to treat LP include griseofulvin, metronidazole, sulfasalazine, cyclosporine, and mycophenolate mofetil.

Phototherapy is considered an alternative therapy, especially for recalcitrant LP. UVA1 and narrowband UVB (wavelength, 311 nm) have been reported to effectively treat long-standing and therapy-resistant LP.<sup>11</sup> In addition, a small study used the excimer laser (wavelength, 308 nm), which is well tolerated by patients, to treat focal recalcitrant oral lesions with excellent results.<sup>12</sup> Photochemotherapy has been used with notable improvement, but the potential of carcinogenicity, especially in patients with Fitzpatrick skin types I and II, has limited its use.<sup>13</sup>

Our patient developed an unusual extensive LP eruption involving only vitiliginous skin shortly after initiation of the combined antihypertensive medication telmisartan-HCTZ, an angiotensin receptor blocker with a thiazide diuretic. Telmisartan and other angiotensin receptor blockers have not been reported to trigger LP; HCTZ is listed as one of the common drugs causing photosensitivity and LP.<sup>14,15</sup> Although it is possible that our patient exhibited a delayed lichenoid drug eruption from the HCTZ, it is noteworthy that he did not experience a single episode of LP during his 8-year history of taking HCTZ. Instead, he developed the LP eruption shortly after the addition of telmisartan to his HCTZ antihypertensive regimen. The temporal relationship led us to direct the patient to the prescribing physician to discontinue telmisartan-HCTZ. After changing his antihypertensive medication to atenolol, the patient presented with improvement within the first month and near-complete resolution 2 months after the discontinuation of telmisartan-HCTZ.

Our patient's LP lesions only manifested on the skin affected by vitiligo, sparing the normal-pigmented skin. Studies have demonstrated an increased ratio of CD8<sup>+</sup> T cells to CD4<sup>+</sup> T cells as well as increased intercellular adhesion molecule 1 at the dermal level.<sup>10,16</sup> Both vitiligo and LP share some common histopathologic features including highly populated CD8<sup>+</sup> T cells and intercellular adhesion molecule 1. In our case, LP was triggered on the vitiliginous skin by telmisartan. Vitiligo in combination with trauma induced by sunburn may represent the trigger that altered the cellular immune response and created the telmisartan-induced LP. As a result, the LP eruption was confined to the vitiliginous skin lesions.

Perifollicular repigmentation was observed in our patient after the LP lesions resolved; the patient's

vitiligo was unresponsive to prior treatment. The inflammatory process occurring in LP may exert and interfere in the underlying autoimmune cytotoxic effect toward the melanocytes and the melanin synthesis. It may be of interest to find out if the inflammatory response of LP has a positive influence on the effect of melanogenesis pathways or on the underlying autoimmune-related inflammatory process in vitiligo. Further studies are needed to investigate the role of immunotherapy targeting specific inflammatory pathways and the impact on the repigmentation in vitiligo.

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## REFERENCES

- Pilli M, Zerbini A, Vescovi P, et al. Oral lichen planus pathogenesis: a role for the HCV-specific cellular immune response. *Hepatology*. 2002;36:1446-1452.
- De Vries HJ, van Marle J, Teunissen MB, et al. Lichen planus is associated with human herpesvirus type 7 replication and infiltration of plasmacytoid dendritic cells. *Br J Dermatol*. 2006;154:361-364.
- De Vries HJ, Teunissen MB, Zorgdrager F, et al. Lichen planus remission is associated with a decrease of human herpes virus type 7 protein expression in plasmacytoid dendritic cells. *Arch Dermatol Res*. 2007;299:213-219.
- Requena L, Kutzner H, Escalonilla P, et al. Cutaneous reactions at sites of herpes zoster scars: an expanded spectrum. *Br J Dermatol*. 1998;138:161-168.
- Al-Khenaizan S. Lichen planus occurring after hepatitis B vaccination: a new case. *J Am Acad Dermatol*. 2001;45:614-615.
- Boyd AS, Neldner KH. Lichen planus. *J Am Acad Dermatol*. 1991;25:593-619.
- Sadr-Ashkevari S. Familial actinic lichen planus: case reports in two brothers. *Arch Int Med*. 2001;4:204-206.
- Manolache L, Seceleanu-Petrescu D, Benea V. Lichen planus patients and stressful events. *J Eur Acad Dermatol Venereol*. 2008;22:437-441.
- Mahood JM. Familial lichen planus. *Arch Dermatol*. 1983;119:292-294.
- Shimizu M, Higaki Y, Higaki M, et al. The role of granzyme B-expressing CD8-positive T cells in apoptosis of keratinocytes in lichen planus. *Arch Dermatol Res*. 1997;289:527-532.
- Bécherel PA, Bussel A, Chosidow O, et al. Extracorporeal photochemotherapy for chronic erosive lichen planus. *Lancet*. 1998;351:805.
- Trehan M, Taylor CR. Low-dose excimer 308-nm laser for the treatment of oral lichen planus. *Arch Dermatol*. 2004;140:415-420.
- Wackernagel A, Legat FJ, Hofer A, et al. Psoralen plus UVA vs. UVB-311 nm for the treatment of lichen planus. *Photodermatol Photoimmunol Photomed*. 2007;23:15-19.
- Fellner MJ. Lichen planus. *Int J Dermatol*. 1980;19:71-75.
- Moore DE. Drug-induced cutaneous photosensitivity: incidence, mechanism, prevention and management. *Drug Saf*. 2002;25:345-372.
- Ongenaes K, Van Geel N, Naeyaert JM. Evidence for an autoimmune pathogenesis of vitiligo. *Pigment Cell Res*. 2003;16:90-100.