

Case Report

Combination Therapy of Acitretin Capsule and Chinese Herbs for Patients with Lichen Planus Pigmentosus-Inversus*

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Lichen planus pigmentosus-inversus (LPPI) is a relatively uncommon variant of lichen planus (LP), characterized by mottled pigmentation of bluish, black or grey color on the flexural folds with or without itch. It was first described by Pock, et al⁽¹⁾ in 2001. At present, there are only 27 cases of the disease reported from 13 reports internationally.⁽²⁾ As very few cases about LPPI are reported, the diagnosis and selection of therapeutic scheme are fairly difficult for physicians. Herein, we report 3 cases who presented with LPPI, obtaining good results after Chinese medicine (CM) treatment. These cases have typical clinical and histological performance. Meanwhile, a case of melanosis is reported, which has similar clinic manifestation and is differentiated by pathological diagnosis. This report was authorized by all patients.

Case Presentation

Case 1 was a 50-year-old Chinese female, who presented with a 20-month history of insidiously developing pigmented macules along skin cleavage lines over the axillae and groin (Figure 1). This violaceous-brown macule began on the axilla skin folds without obvious inducements and then spread to the skin cleavage of groin, neck, perioral area and palm without noticeable inflammatory changes. The macules coalesced and appeared brownish reticular lines. Nails were not affected. Clinical and pathological findings supported the diagnosis of LPPI. General systemic examination revealed no abnormalities. Laboratory studies were all within normal limits. The patient had a history of 5-year diabetes and 14-year hypertension under systematic treatments. After a 3-month topical treatment of low-potency corticosteroid cream, there was little improvement. Then the patient turned to CM treatment.

Case 2 was a 63-year-old Chinese female, who presented with a 5-month history of hyperpigmented,



Figure 1. Clinical and Pathological Features of LPPI in Case 1

Notes: Multiple hyperpigmented macules and patches with a smooth surface. Lesions on the shoulder (a), palm (b), mouth (c), axillae (d), groin (e) and neck (f). A specimen from the axillae showed the nearly atrophic epidermis and basal cell degeneration of the epidermis. There was prominently pigmentary incontinence and melanophages around vessels in the upper dermis (g, hematoxylin-eosin staining, scale bar=100 μ m).

non-pruritic and symmetrical macules around submammary and axillae folds (Figure 2). The morphology and color of the lesions had no obvious difference from those in case 1. No other physical abnormalities were found. The biopsy specimen showed similar pathological changes as in case 1, except for lymphocyte infiltration in the upper dermis.

Case 3 was a 48-year-old Chinese female, who

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Figure 2. Clinical and Pathological Features of LPPI in Case 2

Notes: Hyperpigmented macules and patches located on axillae (a, b), mouth (c) and inframammary folds (d). The pathological features were similar to case 1 (e), except for prominent lymphocyte infiltration in a band-like pattern in the upper dermis (hematoxylin-eosin staining).

complained of slightly pruritic brown macules on the face, axilla and groin for almost 3 months (Figure 3). Physical examination revealed there were no other lesions on the rest of the body. It was unknown what caused the disease. The pathological features were similar to cases 1 and 2.



Figure 3. Clinical and Pathological Features of LPPI in Case 3

Notes: Hyperpigmented macules and patches located on face (a), axilla (b) and groin (c). The pathological changes were similar to those in cases 1 and 2 (d), except for more dense lymphocytic infiltration with pigmentary incontinence in the upper dermis (hematoxylin-eosin staining).

According to tongue coating, pulse and skin lesions, combined with long-term clinical observation, we considered that Shen (Kidney) deficiency and blood stasis are the main pathogenesis of the disease. Bushen Huayu Decoction (补肾化瘀汤) which was composed of *Radix Paeoniae Alba* (15 g), *Flos Carthami* (12 g), *Radix Angelicae Sinensis* (12 g), *Radix Bupleuri* (12 g), *Semen Cuscutae* (30 g), *Herba Dendrobii* (15 g), *Rhizoma Polygonati* (30 g), *Fructus Ligustri Lucidi* (30 g) and *Fructus Lycii* (30 g), twice daily, 30 min after breakfast and dinner, was used to treat abovementioned

3 cases based on the principle of invigorating Shen and promoting blood circulation. Meanwhile, the patients were also asked to take acitretin Capsules 10 mg twice daily at meals (Huapont Life Science Co., Ltd, Chongqing, China; No. 2014033, 2014036). After 3 months' treatment, colors of the hyperpigmented macules and patches became noticeably lighter.

Case 4 was a 30-year-old Chinese female patient presented with 1-year history of gray-brown macules and patches on her jaw, neck and upper extremity without subjective symptom. She had no relevant medical or familial history. A biopsy specimen was obtained from the hyperpigmented lesions on the upper extremity and revealed pigmentary incontinence with few infiltration of numerous melanophages and lymphohistiocytes (Figure 4). Differ from the above 3 cases of LPPI, this patient's histopathology results revealed basal cell liquefaction. On this basis, a diagnosis of Riehl's melanosis was made. We also tried Bushen Huayu Decoction treatment for 3 months, but there was no obvious clinical effect. It can be concluded that although LPPI and Riehl's melanosis had the similar clinical manifestations, they are two different diseases.

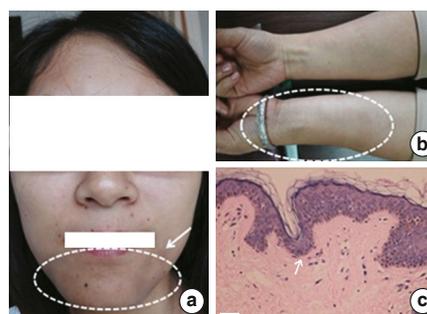


Figure 4. Clinical and Pathological Features of Riehl's Melanosis in Case 4

Notes: Clinical photographs of patients with similar dark brown macules and patches on the jaw (a) and upper extremity (b). However, the skin punch biopsy taken from the right arrow position showed typical melanosis without basal cell liquefaction (c, hematoxylin-eosin staining, scale bar=100 μ m).

DISCUSSION

LPPI most commonly happens in the axilla and groin, tending to be bilateral in the majority of patients. Other skin folds can also be involved occasionally, such as inner wrist,⁽³⁾ neck,⁽²⁻⁴⁾ inframammary folds,⁽¹⁻⁴⁾ popliteal regions,⁽³⁻⁷⁾ waist, abdomen,^(2,3) and auricular regions.^(7,8) Similar to LP, LPPI is characterized by intense basal vacuolization histologically, while LPPI

has a unique characteristic: epidermal atrophy, hydropic degeneration of the basal layer, variable density of lymphocyte infiltration, pigmentary incontinence and melanophages in the superficial dermis.^(4,7,9)

The main differential diagnosis includes lichen planus pigmentosus,⁽¹⁰⁾ which produces lesions located in sun-exposed areas and tends to affect dark-skinned races, while LPPI's typical clinical manifestation is hyperpigmented lesion(s) located in non-sun exposed, intertriginous and flexural areas. Despite the similarities in pathophysiological examination, LPPI differs from classic LPP in that there is intense epidermal atrophy without reactive acanthosis.⁽⁴⁾ Furthermore, ashy dermatosis is one of the most difficult differential diagnoses. It presents with erythematous borders on the edges of the lesions and tends to affect the trunk and limbs, rather than the regions affected by LPPI. In pathology, ashy dermatosis differs from LPPI in the epidermic atrophy with irregular hydropic degeneration on the basal layer and the absence of epidermic hyperplasia.⁽¹¹⁾ In addition, figurate erythema, axillary granular parakeratosis, contact and occupational dermatoses with hyperpigmentation, post-inflammatory hyperpigmentation, lichenoid toxic dermatitis should also be considered.^(3,7,11)

Currently, little has been known about the cause and mechanism of LPPI. In our cases, case 1 had been suffering from hypertension for 14 years and diabetes mellitus for 4 years. Two cases of LPPI arose in association with longstanding lichen planus-inversus.⁽¹²⁾ A patient infected hepatitis C virus (HCV) was reported in 2009 by Bennassar, et al⁽⁴⁾. Though it had been reported that HCV was related to some subtypes of LP, specifically to the mucosal erosive variant,⁽¹⁰⁻¹²⁾ little was known about its relationship with LPPI. Ghorbel, et al⁽¹³⁾ suggested captopril, furosemide and nifedipine could induce lichenoid eruptions. Besides, some researchers thought that LPPI was the result of direct T-lymphocyte mediating cytotoxic activity against basal keratinocytes.^(4,6,9,14,15) Less HLA-DR antigen expression led to the rapid regression of the lichenoid infiltrate, the minimal pruritus and limited duration of the inflammatory process in LPPI.^(4,6,16) Moreover, the lesions could improve or disappear spontaneously within several months without any treatment.^(4,6,13)

There were few articles related to the treatment of LPPI by Western medicine. Topical treatment was the main treatment option. However, some cases were resistant to this method. Kim, et al⁽¹⁷⁾ used 1% topical tacrolimus twice daily for 4 weeks to treat LPPI, lesions revealed no change. Another 2-week application of clobetasol propionate ointment showed insignificant response. Bennassar, et al⁽⁴⁾ used calcineurin inhibitor, 0.05% clobetasol propionate cream and 0.1% tacrolimus to treat 4 cases with LPPI lesions, but there was little improvement. Dizen Namdar, et al⁽⁹⁾ reported only moderate improvement was found in their patients by the treatment of mometasone furoate twice daily lasting for almost 3 months. Similarly, high-potency corticosteroid therapy only resulted in partial improvement.⁽¹⁸⁾ Among 2 Japanese patients, discontinuation of wearing tight underclothes resulted in disappearance of the lesions.⁽¹⁹⁾ There are no specific drugs and treatment methods for LPPI.

CM treatment has achieved good results in LPPI. Liao, et al⁽²⁰⁾ used Huayu Decoction (化瘀汤) to treat 6 patients with LPPI and achieved good results. Zhan, et al⁽²¹⁾ pointed out that lichen planus was caused by Gan (Liver) and Shen deficiency and qi stagnation blood stasis according to CM theory. Modified Gouqi Dihuang Decoction (枸杞地黄汤) was used for the treatment. Liuwei Dihuang Decoction (六味地黄汤), an important component, could fight against aging, oxidation and improve the immunity function. Chinese herbs which were used for promoting blood circulation, such as *Radix Salviae Miltiorrhizae*, *Radix Paeoniae Rubra*, and *Caulis Spatholobi*, could improve the microcirculation and blood capillary permeability, and reduce inflammation and tissue edema. The patient was cured after 2 months of continuous administration, and no recurrence occurred after 2 years follow-up. Feng, et al⁽²²⁾ summarized recent literatures, and found *Tripterygium wilfordii Hook.f* and *Tripterygium hypoglaucom (Devl. Hutch)* had a good effect on treating LP, by adjusting T cells to produce anti-inflammatory and immunomodulatory effect. Through observation of the above treatments, less side effects were found.

To cure a disease, we must fully understand its etiology and pathogenesis, however, the clinical reports about LPPI are still very few and rarely involve theoretical study so far. Herein, we reported

3 cases of LPPI treated by combination therapy of acitretin Capsule and Chinese herb. The skin lesions improved markedly, and no obvious toxic and side effects were found. The combined therapy of CM and Western medicine might be a better treatment option for LPPI.

Conflict of Interest

The authors declared that there was no conflict of interest.

Author Contributions

Chen Y drafted the manuscript and followed up the patient. Guo DJ and Xue L contributed to write the manuscript and search the literature. Mao JY, Wu MF, Xu R, Li X and Li B contributed to manuscript revision. Li FL treated and evaluated the patients. All authors read and approved the final manuscript for publication.

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