


Spanning 17 Years: Diagnostic Evolution from Lichen Planus Pigmentosus to Hyperpigmented Mycosis Fungoides

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Abstract: Lichen planus pigmentosus (LPP) and hyperpigmented mycosis fungoides (MF) represent two distinct rare cutaneous disorders. This case explores the potential association between LPP and hyperpigmented MF, a previously unreported progression. The authors report a 52-year-old male presenting with purplish-red macules on the abdomen and upper extremities subsequent to exposure to petrochemicals, initially diagnosed in 2007 with lichen planus (LP). In 2019, LPP was confirmed by histopathological evaluation of a skin biopsy obtained from an outside institution. Despite treatment with hydroxychloroquine sulfate tablets, the lesions exhibited disease progression. After 17 years, generalized hyperpigmentation gradually developed. Repeat biopsies and immunohistochemistry were performed in 2024, leading to the definitive diagnosis of hyperpigmented MF. The patient is currently managed with subcutaneous interferon alpha-2b (IFN α -2b) injections, with the rash color showing slight lightening. In conclusion, the cutaneous manifestations of MF demonstrate marked heterogeneity, requiring systematic clinical evaluation and histopathological assessment to facilitate accurate diagnosis and guide the development of stage-appropriate treatment protocols. Whether the transformation from LPP to hyperpigmented MF is rare, impossible, or a missed diagnosis remains to be further clarified with more reported cases.

Keywords: lichen planus pigmentosus, mycosis fungoides, interferon alpha-2b, hyperpigmentation

Introduction

LPP and hyperpigmented MF are immune-mediated dermatoses with overlapping clinical features and similar pathological manifestations, characterized by a lichenoid band-like inflammatory cell infiltrate.¹ While histopathology aids differentiation, early-stage MF may mimic LPP. Their possible contributing factors might be chronic skin disorders and longstanding exposure to allergens.^{2,3} A critical question remains: whether LPP can transform into hyperpigmented MF. To date, there are no such reports. We report a rare case initially diagnosed as LPP, which was ultimately confirmed as hyperpigmented MF following two dermatopathological examinations over a 17-year period. A potential contributing factor in this patient might be long-term exposure to petrochemicals during mechanical repair work. This case highlights the diagnostic challenges of differentiating LPP from MF and underscores the importance of longitudinal clinicopathological correlation in refractory hyperpigmentary disorders.

Case Presentation

A 52-year-old male mechanic with occupational exposure to petrochemicals (oil and diesel) presented with progressive hyperpigmentation. In 2007, the patient developed scattered black-red macules on the upper extremities, buttocks and abdomen (Figure 1A). At that time, a diagnosis of LP was established based on characteristic cutaneous manifestations at another medical institution. In 2019, a dermatopathological examination at an external facility confirmed LPP. Despite nearly a year of treatment with hydroxychloroquine sulfate tablets, the patient's condition failed to improve and the rash continued to worsen. Over the past year, the skin of the entire body became hyperpigmented (Figure 1B and C).

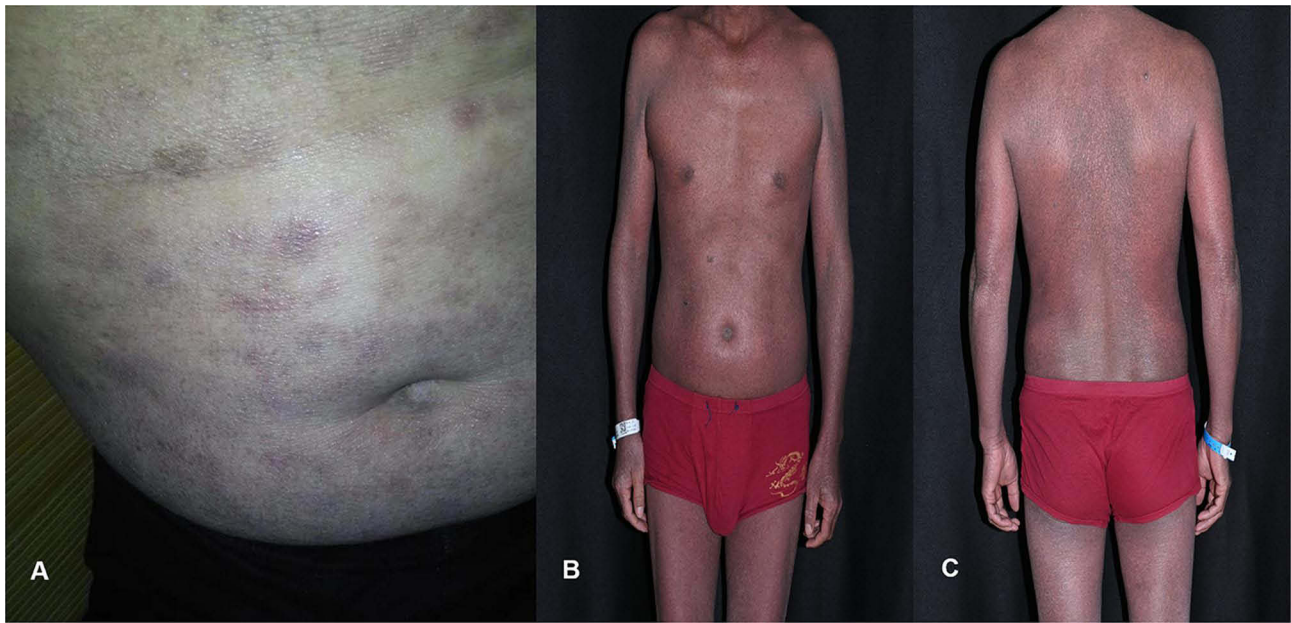


Figure 1 Black-red macules on the abdomen (A). Diffuse hyperpigmentation throughout the entire body (B and C).

A skin biopsy from the abdomen revealed a lymphocytic infiltrate obscuring the dermoepidermal junction, marked pigment incontinence, and migration of lymphocytes into the epidermis (Figure 2A and B). Reflectance confocal microscopy (RCM) showed thickening of the spinous layer, liquefaction degeneration of basal cells, vasodilation in

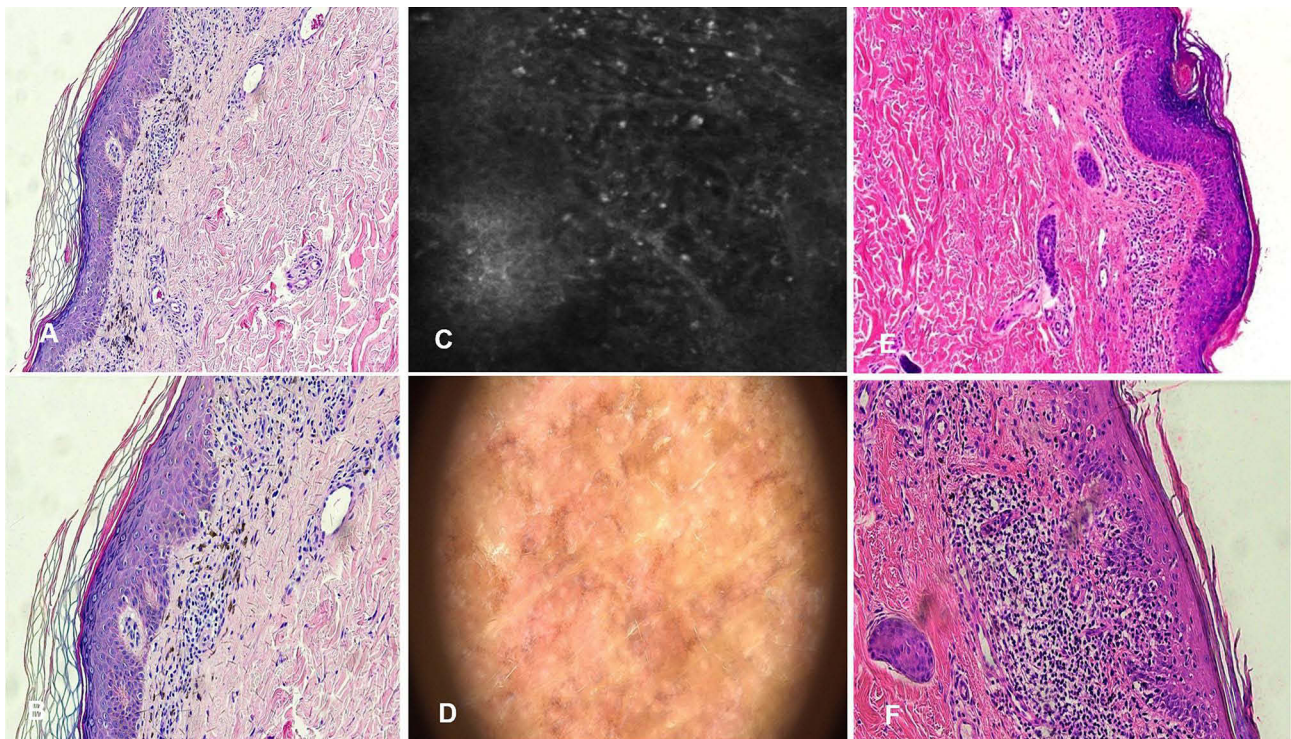


Figure 2 Initial biopsies demonstrating a lymphocytic infiltrate in the upper dermis, basal cell vacuolar changes, prominent pigment incontinence with melanophages in the upper dermis, and atypical lymphocytes in the epidermis (H&E, (A), x200; (B), x200). RCM showing thickening of the spinous layer, liquefaction degeneration of basal cells, vasodilation in the superficial dermis, and infiltration of inflammatory cells (C). Dermoscopy revealing indistinct white reticular streaks scattered among blue-gray dots with follicular plugs (D). Histopathology showing atypical lymphocytes aligned along the basal layer, perivascular spaces with melanophages in the dermis, and lymphocytes migrated into the epidermis with larger hyperchromatic nuclei (H&E, (E), x200; (F), x200).

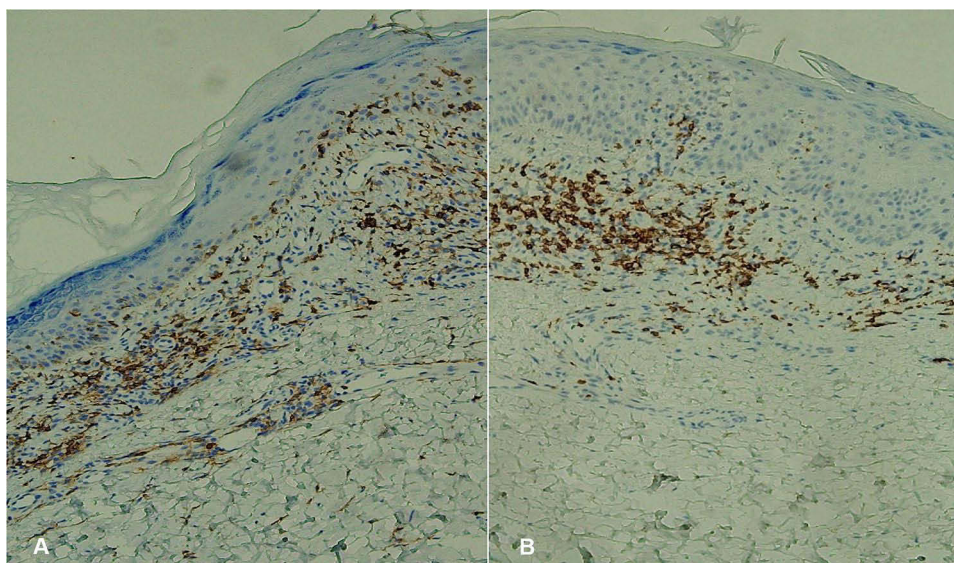


Figure 3 The immunohistochemical staining of the tumor cells were positive for CD4 ((A), x200), and partial positive for CD8 ((B), x200).

the superficial dermis, and infiltration of inflammatory cells (Figure 2C). Dermoscopy revealed indistinct white reticular streaks scattered among blue-gray dots with follicular plugs (Figure 2D). The dermatopathological examination identified abnormal lymphocyte migration into the epidermis, raising suspicion of cutaneous lymphoma. To avoid misdiagnosis, a repeat skin biopsy was recommended 2–3 months later.

A second dermatopathological examination was performed two months later and showed a denser band-like lymphocytic infiltrate in the papillary dermis. Some lymphocytes had migrated into the epidermis, exhibiting larger hyperchromatic nuclei aligned along the dermoepidermal junction, with focal basal cell vacuolar degeneration. The papillary dermis contained numerous melanophages within the dermal infiltrate (Figure 2E and F). Immunohistochemical results revealed predominantly CD3+ and CD4+ lymphocytes, with partial positivity for CD5, CD7, and CD8 in infiltrating cells, and slight positivity for CD30 (Figure 3A and B). Based on these findings and clinicopathological correlation, the diagnosis of hyperpigmented MF was confirmed. The patient is currently receiving subcutaneous injections of IFN α -2b 3 million IU thrice weekly.

Discussion

LPP is a rare variant of lichen planus (LP), first described by Bhutani in 1974.⁴ It manifests as reticular pigmentation on sun-exposed and flexural skin areas with a long clinical course.⁵ Histologically, it shows epidermal hyperkeratosis, vacuolar degeneration of the basal cell layer, perivascular lymphoid cell infiltration in the dermis, and pigment incontinence. The etiology remains unclear, though a unique lymphocyte-mediated inflammatory response is thought to play a key pathogenic role. Reported predisposing factors include sun exposure,⁵ hepatitis C virus infection,¹ and cosmetic use.⁶

Hyperpigmented MF is an extremely rare subtype of MF, presenting as hyperpigmented macules and patches. It typically affects individuals with darker skin tones, who present at a younger age than those with classic MF.⁷ Histologically, it is characterized by interface changes with melanophages on hematoxylin-eosin staining, epidermotropism, and dermal lymphocytic infiltration. Immunohistochemically, it often shows a predominantly CD8+ phenotype, while a CD4-CD8- phenotype is less frequently observed.⁸ The hyperpigmentation likely arises from interface changes and melanophage accumulation, mediated by cytotoxic CD8+ T lymphocytes targeting melanocytes and basal keratinocytes.⁸

The histopathological diagnosis of early-stage MF can be particularly challenging. In many cases, confirming clinical suspicion may necessitate multiple biopsies over an extended period, with definitive diagnosis ultimately requiring

careful clinicopathological correlation that integrates clinical presentation and histopathological findings. Table 1 outlines the clinical and histopathological criteria used to differentiate hyperpigmented MF from LPP.³

In the early stages of the disease or within initial lesions, LPP and hyperpigmented MF pose significant diagnostic challenges due to their overlapping clinical manifestations. Histopathological examination may reveal shared features, including vacuolar interface dermatitis with marked pigment incontinence. However, the clinical presentation of atrophic patches and poikilodermatous lesions shows a stronger association with MF than with LP.¹⁰ Mucosal involvement also serves as a valuable diagnostic feature in LPP. Histopathologically, the primary criterion for early identification may be the presence of atypical or enlarged lymphocytes, which are not characteristically observed in classic LPP presentation.³ Studies have shown that patients with MF initially diagnosed at an advanced stage were 4 years older than those initially diagnosed at an early stage.⁹ Combined with the natural course of MF, this implies a potential diagnostic delay and strongly suggests that these patients had lived with MF for a prolonged period without accessing medical care.

Can LPP transform into hyperpigmented MF? Unfortunately, there are no relevant studies to date. The two diseases may manifest overlapping clinical or histopathological features in certain cases. The etiology of MF remains incompletely understood. Infectious agents, occupational exposures, and genetic variations are all considered to contribute to the pathogenesis of this disease. Some studies have suggested that persistent antigenic stimulation acts as an initial trigger for lymphocyte proliferation and transformation,¹¹ but the nature of such stimulating antigens remains unclear. Research has found that the incidence of MF is higher among individuals working in industrial environments, such as the petrochemical, textile, machinery, and metal industries.¹² A European multicenter case-control study further confirmed that occupational exposure to solvents and polycyclic aromatic hydrocarbons constitutes a risk factor for the disease.¹³ In the present case, the patient reported a 19-year history of daily occupational exposure to engine oil before developing LP, which may have served as a trigger for the progression from LP to MF. Furthermore, exposure to allergens may induce not only LP but also MF. This might theoretically represent a mechanistic link between LP and MF. The limitation of this case is the inability to re-evaluate the original samples from 2007 and 2019.

Table 1 Criteria for Differentiating Hyperpigmented MF from LPP

Criteria, Clinical	Hyperpigmented MF	LPP
Age at onset	Older ⁹	Variable
Type of lesion	Patches, plaques, or tumors with hyperpigmentation, atrophy, and poikilodermatous changes	Gray-to-brown macules, papules, or patches
Lesion distribution	Typically asymmetric, often on trunk and buttocks, predilection for nonexposed areas	Usually symmetric, mainly on sun-exposed areas
Mucosal involvement	Rare	Common
Progression	Gradual, variable	Stable
Criteria, histopathologic	Band-like, lymphocytic, dense	Classic band-like infiltration, lymphocytic
Pattern of infiltrate		
Epidermotropism	Present, halo around individual lymphocyte, or around collections of them (Pautrier microabscesses)	Absent
Atypical lymphocytes	Present, at least a few epidermal lymphocytes are larger than dermal lymphocytes	Rare or absent, lymphocyte nuclei are monomorphous and small in size
Papillary dermis	Fibrotic, poikilodermatous	Normal or fibrotic
Immunophenotypic features	Predominantly CD8+	Normal
TCR gene rearrangement	Monoclonal, oligoclonal	Polyclonal
Dermoscopy	Sperm-like blood vessels (early-stage)	Blue-gray pigment granules, flaky homogeneous reddish-brown pigment
RCM	Intraepidermal hyporeflexive cells, some aggregate to form vesicle-like structures; reduced refractivity of the pigment ring at the dermo-epidermal junction.	Basal cells liquefy and degenerate, Band-like infiltration of phagocytes and predominantly lymphocytic inflammatory cells in the superficial dermis

This calls to mind another chronic inflammatory disease, psoriasis, which may potentially progress to MF. Psoriasis and MF share common pathogenic mechanisms associated with T-cell dysfunction, although the precise mechanisms underlying aberrant T-cell stimulation and migration remain under investigation. In fact, chronic psoriatic skin inflammation is associated with the continuous activation of skin T cells, which increases the risk of gene mutation accumulation and may eventually lead to the occurrence of lymphoma.^{14,15} Since T cells are overactivated lymphocytes in psoriasis, it is expected that the incidence of T-cell lymphomas (eg, cutaneous T-cell lymphoma) is higher in patients with psoriasis. In addition, psoriasis and cutaneous T-cell lymphoma may share a common genetic background, which promotes the proliferation and survival of tumor cells.¹⁴

Conclusion

From a clinical perspective, MF should be included in the differential diagnosis of any refractory hyperpigmented dermatosis. Sequential skin biopsies should be performed in patients with persistent or worsening hyperpigmentation to ensure accurate diagnosis and appropriate management. Moreover, non-invasive RCM and dermoscopy represent excellent adjunct tools, facilitating real-time dynamic monitoring. This is the first documented case of this progression. The uniqueness of the case raises the question of whether a correlation exists between LPP and hyperpigmented MF. If such a correlation is confirmed, it would necessitate a reevaluation of LPP, particularly regarding the potential for malignant transformation in patients with extensive involvement. The limitation of this case lies in the inability to re-evaluate the original samples from the past. Whether LPP can progress to MF requires confirmation with more clinical cases.

Ethics Statement

Hangzhou Third People's Hospital approved the publication of the case details.

Consent Statement

The authors certify that they have obtained all appropriate patient consent forms. The patient provided written informed consent for the publication of the case details and images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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