

Acquired Macular Pigmentation of Unknown Etiology

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ABSTRACT

Acquired macular pigmentation of unknown etiology is a new umbrella term that encompasses a group of diseases that, while having similar clinical and histological features, their true entities are controversial, and a global consensus regarding these conditions is still lacking. The conditions comprised by the term are ashy dermatosis, erythema dyschromicum perstans, lichen planus pigmentosus, and idiopathic eruptive macular pigmentation. In this review, we compare the clinical and histological features of these conditions that comprise acquired macular pigmentation of unknown etiology, as well as review their responses to treatment.

KEYWORDS: Hypermelanosis, hyperpigmentation, lichen planus, pigmentation disorders

In clinical practice, the terms *ashy dermatosis* (AD), *erythema dyschromicum perstans* (EDP), *lichen planus pigmentosus* (LPP) and *idiopathic eruptive macular pigmentation* (IEMP) are potential differential diagnoses when encountering hyperpigmentation of the skin with unknown etiology and without any sign of preceding or concurrent inflammation. A definite diagnosis, however, might prove to be challenging, as these conditions contain overlapping clinical and histological features, and it seems the terms are often used interchangeably. It is worthwhile to update the available information on this group of diseases in order to improve treatment outcomes and patient knowledge of disease prognosis.

Recently, AD, EDP, and IEMP have been grouped together under the umbrella term *acquired macular pigmentation of unknown etiology*. Using this classification, AD, EDP, and IEMP are all considered to have unknown etiologies, with AD and EDP separated according to the existence of an erythematous border. LPP, however, was classified as having a known etiology.¹ Although LPP has a recognized connection with lichen planus, its pathogenesis and triggers are still largely unproven. Thus, in our opinion, LPP should also be considered to have an unknown etiology and be included under the umbrella term.

In an attempt to clarify the similarities and differences between the individual conditions that make up this disease group, we collected and reviewed all relevant publications and summarized clinical and histological features, current diagnostic criteria, and available treatment options of each condition. However,

the answer as to whether these conditions truly represent unique clinical entities or are different variations of the same disease is still inconclusive.

ASHY DERMATOSES AND ERYTHEMA DYSCHROMICUM PERSTANS

Clinical features. *Ashy dermatoses.* The recognition of hyperpigmentation of the skin without any preceding inflammatory skin lesions, proven triggers, or causative agents can be dated back several years. The term *ashy dermatosis* was first used by Ramirez in 1957 to describe asymptomatic macular lesions with various “shadings of grayish pigmentation,” with an insidious onset and no sex predilection, in young adult patients.² These symmetrical, hyperpigmented lesions are typically located on the trunk, neck, and upper extremities, and are most commonly observed on patients with Fitzpatrick skin type IV³ (Figure 1). The lesion size can vary from 1-cm macules to very large patches. Itchiness has been reported as a symptom by approximately 16 percent of the patients.³

Erythema dyschromicum perstans. In 1961, shortly after Ramirez’s publication, Convit et al⁴ observed similar lesions to those of AD but with raised, narrow, erythematous borders that characteristically disappear in a few months. Later, Sulzberger⁵ proposed the term *erythema dyschromicum perstans*, and commented that the narrow red border indicates an active phase. While most current literature reports AD and EDP as one entity, some researchers, based on diagnosis algorithms, consider the erythematous border to be a distinguishing

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feature in EDP.^{1,6} Of note, authors of a retrospective study of 68 patients with EDP reported that only 17.6 percent of the patients observed the peripheral erythematous border.³ This finding indicates that the presence of an erythematous border can vary from patient to patient, and whether it is present relies on the observations of the patient and/or timing of consultation. EDP has been diagnosed in prepubertal children, as well as adults, and shares numerous overlapping features with idiopathic eruptive macular pigmentation (discussed later).^{7,8}

Histological features. Biopsies taken from AD/EDP in numerous studies have shown similar histopathological findings. The epidermis can appear as hyperkeratotic or atrophic, sometimes with apoptotic keratinocytes. Frequently, there is basal vacuolar degeneration and a focal or lichenoid pattern with colloid bodies along the dermoepidermal junction. Primary histological findings include pigment incontinence and melanophages in the dermis, along with mild-to-moderate superficial perivascular lymphohistiocytic infiltration. According to Chang et al,³ EDP can be subdivided into active lesions with predominant basal vacuolar degeneration and lymphocytic infiltration and inactive lesions with melanophages and pigment incontinence in the dermis.³ Table 1 summarizes the main clinical and histological findings of AD/EDP from previous studies.

Etiology. Though the cause of AD/EDP is unknown, it is plausible that multiple environmental and genetic factors participate in the pathogenesis of the disease. One study of Mexican patients showed that AD has an important genetic predisposition and is associated with HLA-DR4 subtype*0407.⁹ Another study detected an expression of cluster of differentiation (CD) 54 and major histocompatibility complex class II (HLA-DR) in the keratinocyte basal cell layer, as well as an increase in the expression of CD36 in the strata spinosum and granulosum and CD69 and CD94 in the dermal cell infiltrate.¹⁰

So far, reported triggers of AD/EDP include parasite infection, chemicals (e.g., ammonium nitrate, fungicide, pesticide, X-ray contrast, cobalt allergy, oral antibiotics, benzodiazepines endocrinopathies).^{7,11–14} Recently, Chua et al¹⁵ reported three cases of ashy dermatoses induced by omeprazole.¹⁵



FIGURE 1. Symmetrically distributed grayish macular pigmentation on the trunk in ashy dermatosis

Diagnostic criteria and classification.

There is currently no accepted or widely implemented diagnostic criteria for AD/EDP used in clinical practice. However, some practical recommendations have been made in the past. Zaynoun et al⁶ proposed a simple classification for AD, and described the condition as idiopathic, eruptive, hyperpigmented macules, irrespective of the histological presence of interfacial dermatitis at the time of examination. A diagnosis of EDP is considered in patients with lesions similar to those of AD, but with a history of or active presence of erythematous borders. Other conditions—namely LP, LPP, actinic LP, postinflammatory hyperpigmentation, drug-induced melanodermas, and mastocytosis—have been classified as “simulators” of AD.⁶

After studying 68 patients with EDP, Chang et al³ proposed a list of clinical signs in the diagnosis of AD/EDP. Unlike Zaynoun et al,⁶ Chang et al considered AD and EDP to be the same entity and recommended that a diagnosis of AD/EDP is warranted when the following criteria are met:³

1. Except for occasional slight itching, the lesions remain asymptomatic.
2. Some of the lesions have an easily observable, nonelevated, erythematous border.
3. The lesions can appear on exposed or unexposed areas.
4. The lesions do not involve the mucosa.
5. The lesions rarely improve.

Treatment and prognosis. Various oral and topical treatment modalities have been

given to patients, but often with disappointing outcomes (Table 1). The most popular agent used is still topical corticosteroid, followed by triple-combination creams (e.g., fluocinolone acetonide, hydroquinone, tretinoin).³ Some positive results were reported with clofazimine and dapsone,^{16,17} while isotretinoin and various pigment lasers, in recent case reports, have shown significant lesion clearance.^{18–20} Additional, well-controlled clinical trials are necessary to determine the most effective treatment. Overall, a majority of patients (49%) did not show any significant improvement after a follow-up period of more than one year.

LICHEN PLANUS PIGMENTOSUS

Clinical features. Originally described in India,²¹ LPP has been reported in various parts of the world, including Mexico, Kuwait, and Turkey.^{18,21–25} LPP presents as ill-defined, slate-gray to brownish-black macules found on sun-exposed areas, predominantly on the face and neck, flexural folds, and, rarely, on oral mucosa (Figure 2).¹⁸ The insidious hyperpigmentation occurs in adults with Fitzpatrick Skin Types III to IV and occasionally becomes mildly pruritic. An interesting feature of LPP, which distinguishes it from other conditions in this group, is that it can have different morphological patterns. The rash has been described as diffuse, reticular, blotchy, perifollicular, follicular, linear,²³ and zosteriform. The presence of LPP on intertriginous areas are termed *lichen planus pigmentosus-inversus* (LPP-inversus).²²

TABLE 1. Main clinical and histological findings of AD/LPP from previous studies

STUDY TYPE	NO. OF PATIENTS (M:F) RACE	MEAN AGE AT ONSET	MORPHOLOGY	MOST COMMON LOCATION	ADDITIONAL FEATURES	MUCOSAL INVOLVEMENT	ASSOCIATIONS	HISTOLOGY	TREATMENT AND OUTCOME
Ramirez (1967) ²									
Retrospective descriptive study	139	Early adulthood	>1cm ash color with various shadings of grayish pigmentation	N/A	N/A	N/A	N/A	Hydropic or liquefaction degeneration of the basal cell layer, dermal melanosis, perivascular lymphohistiocytic infiltration	Treatment unknown
Convit et al. (1961) ⁴									
Case series	5 (3:2)	Range of 11–36 years	>few cm grayish color; poorly defined	Trunk, limbs, face	Raised erythematous margins, occasional moderate pruritus, some hypopigmentation on grayish background	Spared	None	Slight follicular hyperkeratosis, hydropic degeneration of the basal layer, pigmentary incontinence, superficial perivascular lymphohistiocytic infiltration, melanophages	Penicillin 15–20 million units; broad-spectrum antibiotics, sulfones, corticosteroid; all refractory to treatment
Vega et al. (1992) ²⁴									
Comparative observational study	20 (6:14) Mexican	33.6 years	Ash color, gray-blue, blackish-brown	Face, upper trunk, and neck	Raised erythematous margin in eight patients (40%)	N/A	None	Hyperkeratosis, epidermal atrophy, basal vacuolization, perivascular infiltration, melanophages	Topical keratolytics, topical corticosteroid, chloroquine diphosphate; mean follow-up at 4 months; no improvement
Silverberg et al. (2003) ⁷									
Retrospective descriptive study	8 (4:4) Caucasian, Hispanic, and African-American	5.2 years	0.5–2 cm, gray to blue	Neck and trunk	N/A	N/A	Suspected medication in two cases	Dermal melanin and melanophages, mild vacuolar degeneration, superficial lymphocytic infiltration	3 patients were treated (topical steroid & selenium sulfide lotion); 5 showed complete clearance (average 2.5 years)
Torrelo et al. (2005) ⁸									
Retrospective descriptive study	14 (6:8) Caucasian and Hispanic	6.9 years	Ash color	Trunk (100%)	None	Spared	None	Vacuolar changes (mostly peripheral to the lesion), colloidal bodies, perivascular infiltration, melanophages, (center of the lesion), pigmentary incontinence	No treatment; 50% improvement or resolution in prepubertal patients (follow-up: 0.3–5 years)
Chang et al. (2015) ³									
Retrospective descriptive study	68 (29:39) Korean	39.9 years	Blue-gray	Trunk (69.1%)	Peripheral erythematous border in 17.6%; itching and sign of inflammation in 16.1%	Spared	Suspected medication in three cases	Dermal melanophages and pigmentary incontinence (83.8%), lymphocytic infiltration (73.5%), increased epidermal melanin (58.8%), basal vacuolar degeneration (48.5%), colloid bodies (26.5%)	Various treatment; topical steroid most common; 43.1% slight to fair improvement (mean follow-up: 17.9 months)

M:F: male:female; AD/EDP: ashy dermatosis/erythema dyschromicum perstans; N/A: not applicable

Despite LPP sharing similar features with AD/EDP, Vega et al²⁴ found significant clinical differences and concluded that LPP and AD/EDP are indeed two separate conditions.²⁴ The shade of rash in LPP tends to be dark brown instead of grayish, the distribution is less likely to be symmetrical, and associated pruritus is more common.²⁴ In addition, involvement of the oral mucosa, previously described as having a diffuse or speckled pattern, is exclusive to LPP.²⁶ Nevertheless, the differentiation between AD/EDP and LPP is still a subject of controversy. Daoud and Pitterlkow²⁷ report that AD/EDP and LPP represent an overlap in the phenotypic spectrum of lichenoid inflammation in darkly pigmented skin.²⁷

Histological features. A review of skin biopsies obtained from 65 patients with LPP showed that perivascular infiltration, basal cell degeneration, and presence of melanophages were the most common findings (81.5%, 78.5%, and 63%, respectively).²⁴ Other epidermal changes include hyperkeratosis and atrophy. In general, histological findings of LPP resemble those found in AD/EDP and thus cannot be differentiated based on histological basis alone.²⁴ Table 2 summarizes the main clinical and histological findings of LPP from previous studies.

Etiology. LPP is frequently associated with lichen planus (ranging from 9–27%) and hepatitis C infection (up to 60.6%), contributing to the theory that LPP is a rare variant of lichen planus.¹⁸ Apart from that, patients have reported a history of using mustard oil, amla oil (a common remedy used for body massage and hair dressing in India), henna, and hair dye.^{18,26} However, a temporal relationship between the use of these agents and the development of LPP could not be established. Approximately 17.7 percent of the patients diagnosed with LPP experienced darkening of the pigmentation after exposure to sunlight.²⁶ This finding, together with its predilection for sun-exposed areas, supports the notion that ultraviolet radiation might play a role in the pathogenesis of LPP, perhaps affecting an unknown photosensitizing agent. Other conditions that have been linked to LPP are frontal fibrosing alopecia, acrokeratosis of Bazex, and minimal change nephrotic syndrome.^{28–31}

Diagnostic criteria. Until now, there have not been proposed diagnostic criteria or classifications for LPP.

Treatment and prognosis. Similar to AD/EDP, LPP is refractory to treatment. However, topical and systemic corticosteroids, oral vitamin A, and pigment lasers have resulted in favorable outcomes.^{32–35} In a prospective study of 33 patients with LPP, 53.8 percent showed improvement in pigmentation after 16 weeks of topical tacrolimus.¹⁸ Interestingly, in a small number of patients with positive hepatitis C virus serology, a significant improvement was achieved after a year of antiviral medication.¹⁸

IDIOPATHIC ERUPTIVE MACULAR PIGMENTATION

Clinical features. In 1978, the term *idiopathic eruptive macular pigmentation* emerged.³⁶ Compared with those of AD/EDP and LPP, IEMP lesions are smaller, well-defined, discrete, hyperpigmented macules, often less than 3 cm in diameter (Figure 3). They appear on the trunk and extremities, almost exclusively in healthy young children and adolescents, without any associated pruritus or involvement of the oral mucosa.³⁷ IEMP lesions can vary from brown to ash-colored, and sometimes the surface of the lesion is velvety with papillomatosis, similar to acanthosis nigricans.³⁸ IEMP can be diagnosed with or without the appearance of papillomatosis.

The most distinguishing feature of IEMP is that the lesions resolve without treatment within several months to years. Interestingly, the condition seems to exist in both dark and light skin phototypes, as opposed to AD/EDP and LPP, which more typically present in individuals with darker skin. Torrelo et al⁷ and Silverberg⁸ both observed that young patients who develop AD/EDP are more likely to be Caucasian and the lesions seem to resolve spontaneously.^{7,8} This raises the suspicion that some of the reported cases of AD/EDP in younger Caucasian children might actually have been IEMP.

Histological features. IEMP is an epidermal, hypermelanotic condition, unlike AD/EDP or LPP. The most striking finding is increased melanin in the basal cell layer. Basal cell vacuolization and lichenoid reactions are always absent, and the inflammation in the dermis can be very mild with few melanophages.³⁹ Table 3 summarizes the main clinical and histological findings of IEMP from previous studies.

Etiology. While the pathogenesis of IEMP remains unknown, the most logical theory links it to hormonal factors, due to its predominance in children and young adults.³⁷ IEMP has

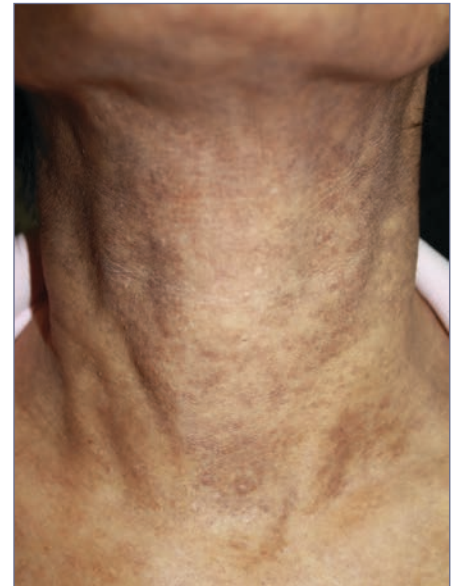


FIGURE 2. Ill-defined slate-gray to brownish macules on the neck in lichen planus pigmentosus

also been hypothesized to be related to an autoimmune phenomenon, as described in a case report of a 33-year-old Caucasian woman with a history of Hashimoto's thyroiditis who developed biopsy-proven IEMP during her second pregnancy.⁴⁰

Diagnostic criteria. Within the group of acquired macular pigmentation of unknown etiology, IEMP is the only condition with well-documented diagnostic criteria. The original criteria, proposed by Sanz de Galdeano et al⁴¹ include the following:

1. Eruption of brownish, nonconfluent, asymptomatic macules involving the trunk, neck, and proximal extremities in children and adolescents
2. Absence of preceding inflammatory lesions
3. No previous drug exposure
4. Basal cell layer hyperpigmentation of the epidermis and predominant dermal melanophages without visible layer damage or lichenoid inflammatory infiltrate
5. Normal mast cell count.

Since the publication of these criteria, they have been used regularly in case reports.

In 2007, Joshi et al³⁹ reviewed 24 case reports of IEMP and proposed a revised diagnostic criteria that incorporates a papillomatosis variant and emphasizes the main histological findings.³⁹ The new criteria are as follows:

1. Eruption of brownish-black, discrete,

TABLE 2. Main clinical and histological findings of LPP from previous studies

STUDY TYPE	NO. OF PATIENTS (M:F) NATIONALITY	MEAN AGE AT ONSET	MORPHOLOGY	MOST COMMON LOCATION	ADDITIONAL FEATURES	MUCOSAL INVOLVEMENT	ASSOCIATIONS	HISTOLOGY	TREATMENT AND OUTCOME
Bhutani et al. (1974)									
Case series	40 Indian	12–50 years	Slate blue to steel gray	Face, upper extremities, abdomen	Mild-to-moderate pruritus in 20 patients	Spared	Coincidental lichen planus in 11 patients (27%)	Basal cell degeneration, abundant melanin pigment in basal and spinous layers, dermal inflammatory infiltration composing of lymphocytes and histiocytes (continuous band and colloid bodies), pigmentary incontinence	Topical corticosteroid, systemic corticosteroid, antihistamine; 4 of 11 showed improvement after a few weeks
Vega et al. (1992)									
Comparative observational study	11 (6:5) Mexican	46 years	Dark brown	Face	Pruritus in 7 patients (62%)	N/A	Coincidental lichen planus in 1 patient (9%)	Hyperkeratosis, epidermal atrophy, basal vacuolization, perivascular infiltration, melanophages	Topical corticosteroid, keratolytics, 10% dimethyl sulfoxide, griseofulvin, prednisolone, retinoids, chloroquine; 1 patient showed resolution (with topical corticosteroid)
Kanwar et al. (2003)									
Retrospective descriptive study	124 (56:68) Indian	26 years for men, 38 years for women	Slate gray to brownish-black	Face and neck	Different patterns of pigmentation: diffuse (77.4%), reticular (9.7%), blotchy (7.3%), perifollicular (5.6%), mild–moderate itching (31.5%), burning sensation (6.5%)	Four patients had oral mucosal involvement	Coincidental lichen planus in 19 patients (15.3%)	Hyperkeratosis (13.8%), thinning of the epidermis (7.7%), basal cell degeneration (78.5%), perivascular infiltration (81.5%), melanophages (63%), band-like infiltrate in the upper dermis (18.5%)	N/A
Al-Mutairi and El-Khalawany (2010) ¹⁸									
Prospective descriptive study	33 (21:12) Kuwaiti	34 years	Violet blue, blackish-brown	Face and neck	Different patterns of pigmentation: diffuse (54.5%), reticular (21.2%), linear (6.1%), perifollicular (3%), inversus type in 21.2%, mild pruritus in 27.3%	One patient had oral mucosal involvement	Coincidental lichen planus in 8 patients (24.2%); serology for hepatitis C was positive in 20 patients (60.6%)	Melanin incontinence (100%), hyperkeratosis (34.2%), epidermal thinning (39.5%), vacuolar degeneration (44.7%), keratinocyte apoptosis (34.2%)	16 weeks of topical tacrolimus in 13 patients; 53.8% showed improvement; 2/20 patients with positive HCV serology showed LPP clearance after antiviral therapy
Sindhura et al. (2016) ²⁵									
Retrospective descriptive study (emphasis on follicular variant)	91 (28:63) Indian	37.5 years	Slate gray	Face and neck	Different patterns of pigmentation: diffuse (49.4%), reticular (13.2%), blotchy (10.9%), perifollicular (9.9%); atypical variants included segmental, linear, flexural, and follicular (16.5%)	N/A	Lichen planopilaris of the scalp in 2 patients	Biopsy result shown for follicular type: follicular plugging, focal basal cell vacuolization, increased basal layer melanin, moderate-dense perifollicular lymphohistiocytic infiltration	Treatment for follicular type: oral dexamethasone 2.5mg twice a week 1% mometasone fluorate cream, 0.1% tacrolimus ointment; 1 patient showed improvement

M:F: male:female; LPP: lichen planus pigmentosus; N/A: not applicable

nonconfluent, asymptomatic macules and/or slightly raised plaques that resemble acanthosis nigricans and involve the face, neck, trunk, and proximal extremities, with complete resolution after months to years

2. Affects mostly children and adolescents (i.e., those in the first two decades of life)
3. Epidermal hypermelanosis with or without papillomatosis as the main histological finding with an absence of dermal inflammation
4. A lack of numerous dermal melanophages and no presence of interface changes (The presence of either of these is considered negative findings and might be considered to be against the diagnosis of IEMP.)
5. Absence of preceding inflammatory lesions
6. No previous drug exposure
7. Normal mast cell count

Treatment and prognosis. IEMP has an unremarkable prognosis and is usually self-limited. The lesions will gradually resolve on their own, typically within a period of several months to a few years. So far, there is no documentation of any recurrences. This information might be useful when providing advice to patients or parents of young patients.

Following our review, we summarized the main similarities and differences of AD/EDP, LPP, and IEMP in Table 4.

DIFFERENTIAL DIAGNOSIS FOR ACQUIRED MACULAR PIGMENTATION OF UNKNOWN ETIOLOGY

There is a wide range of differential diagnoses when patients present with hyperpigmentation of the skin, and clinicians can often make the correct diagnosis only after taking a history and performing a thorough physical examination. Occasionally, skin biopsies can aid in the diagnosis. Some dermatological conditions share similar features with AD/EDP, LPP, and IEMP and should be ruled out before considering this group of diseases. When melanocytosis and/or melanophages are seen on histology, acquired dermal melanocytosis, including the late-onset naevus of Ota or Ito, should be considered. Systemic conditions such as hyperthyroidism and Addison's disease can also present with macular hyperpigmentation, as can effects from systemic drugs such as amiodarone and minocycline.¹ Postinflammatory hyperpigmentation is common, especially after conditions like



FIGURE 3. Multiple discrete brownish macules in a seven-year-old girl, consistent with idiopathic eruptive macular pigmentation

cutaneous lupus erythematosus, graft-versus-host disease, and prurigo pigmentosa.

The most important condition to rule out is pigmented contact dermatitis or Riehl's melanosis, as avoidance of the contact allergen is an essential part of the treatment plan. This rare noneczematous variant of contact dermatitis manifests as hyperpigmentation in dark-skinned individuals, resulting from repeated contact of a very small amount of allergen. It is believed that the amount of contact allergen is not enough to mount the usual epidermal spongiosis and inflammation of the skin, but instead causes basal liquefaction, gradually dropping melanin pigment to the upper dermis.⁴² The hyperpigmentation can be reticulated, with shades of slate gray, grayish brown, and bluish brown (Figure 4A). The lesions typically occur on the site of contact. Examples include over-covered areas in a patient allergic to an optical whitener in washing powder or on the face and neck in cases of a fragrance allergy.⁴² The most common allergens are detected in fragrances, cosmetics, textile dyes, washing powders, and rubber products. Examples include naphthol AS (dye for textile), and hydroxycitronellal and benzyl salicylate (both fragrances) (Figure 4B).⁴² It is worthy to note that, unlike the typical contact dermatitis, the hyperpigmentation can persist even after discontinuation of exposure to the allergen.⁴³

When a history of a possible contact allergen is gathered, patch testing might be the next logical step. A prospective study performed various screening patch tests on Israeli patients suspected to have pigmented contact dermatitis, revealing that the majority had a positive result with European standard series (16 out of 26 patients, 10 of whom were relevant), with fragrance mix being the most common allergen.⁴⁴ In another study from Thailand, eight out of 10 patients with clinical pigmented contact dermatitis had a positive patch test result. The most common allergens were nickel sulfate hexahydrate, cobalt(II) chloride hexahydrate, and fragrance mix II.⁴⁵

After taking into account these differential diagnoses, we would like to propose a simple approach to diagnosing acquired dermal hyperpigmentation, as shown in Figure 5.

CONCLUSION

The term *acquired macular pigmentation of unknown etiology* depicts a group of hyperpigmented conditions with overlapping features. AD and LPP share the same histological picture of pigmentary incontinence, basal vacuolization, and superficial perivascular infiltrate, but differ in terms of clinical pattern. IEMP, on the other hand, has more definite histological findings, mainly showing epidermal hypermelanosis with or without papillomatosis. A wide range of other systemic and dermatologic

TABLE 3. Main clinical and histological findings of IEMP from previous studies

STUDY TYPE	NO. OF PATIENTS (M:F) NATIONALITY	MEAN AGE AT ONSET	MORPHOLOGY	MOST COMMON LOCATION	ADDITIONAL FEATURES	MUCOSAL INVOLVEMENT	ASSOCIATIONS	HISTOLOGY	TREATMENT AND OUTCOME
Degos et al. (1978) ³⁶									
Case series	7 French	Children and teenagers	5–25mm erythematous, brown, ash color	Neck, trunk, and limbs	N/A	N/A	N/A	Hyperpigmentation of the basal cell layer, mild lymphohistiocytic superficial perivascular infiltration	N/A
Galdeano et al. (1996) ⁴¹									
Case series	5 (2:3) French	8 years	3–20 mm, light brown, brown	Neck, trunk, and limbs	Normal mast cell count	Spared	N/A	Increased pigmentation of the basal cell layer, pigmentary incontinence, mild perivascular lymphohistiocytic infiltration	No treatment given; 4 patients showed spontaneous fading
Jang et al. (2001) ³⁷									
Case series	10 (6:4) Korean	10.5 years	Mostly 3–10 mm, brown or gray	Trunk and extremities	N/A	Spared	None	Normal epidermis, Increased pigmentation of the basal layer, pigmentary incontinence, melanophages, mild superficial perivascular lymphohistiocytic infiltration	No treatment given; 9 patients had resolution in 2 months to 5 years
Joshi (2007) ³⁸									
Case series	9 (7:2) Indian	9.9 years	< 2–3 cm, dark brown, brownish-black	Trunk and extremities	Some lesions had velvety surface similar to acanthosis nigricans	N/A	None; no obesity, no acanthosis nigricans elsewhere	Papillomatosis of the dermis, increased melanin in the basal layer, sparse perivascular lymphocytic infiltration	Topical corticosteroid; all resolved in six to eight months

M:F: male:female; IEMP: idiopathic eruptive macular pigmentation; N/A: not applicable

conditions should be included in the differential diagnosis, especially noneczematous pigmented contact dermatitis. Additional large-scale studies are required for the development of practical diagnostic criteria and treatment guidelines.

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TABLE 4. Summary of clinical and histological patterns

PARAMETER	AD/EDP	LPP	IEMP
Age at onset	Young adult	Young adult	Prepubertal children
Sex	No predilection	No predilection	No predilection
Skin type	Darker	Darker	Lighter
Onset	Insidious	Insidious	Insidious
Symptoms	Asymptomatic	Mild pruritus	Asymptomatic
Color	Blue-gray	brown-gray	Dark brown
Size and border	Large patches, can be diffuse or well-defined with elevated erythematous border	Few centimeters, diffuse	Smallest 3–25mm, well-defined
Distribution	Trunk most common, followed by face and neck	Face and neck most common, followed by trunk; can be on intertriginous areas	Trunk and extremities
Subtype	N/A	For morphology: diffuse reticular, linear, perifollicular, follicular; for distribution: segmental, inversus	With or without papillomatosis
Mucosal involvement	None	Rare	None
Association	Not proven	Lichen planus in 9–27%, lichen planopilaris, hepatitis C infection	Not proven
Clinical course	Chronic, refractory to treatment	Chronic, refractory to treatment	Spontaneous recovery in a few months to years
Histology	Mainly basal vacuolization, pigmentary incontinence and melanophages	Mainly basal vacuolization, pigmentary incontinence and melanophages	Mainly increased pigmentation of the basal cell layer (epidermal hypermelanosis)

AD/EDP: ashy dermatoses/erythema dyschromicum perstans; LPP: lichen planus pigmentosus; IEMP: idiopathic eruptive macular pigmentation; N/A: not applicable

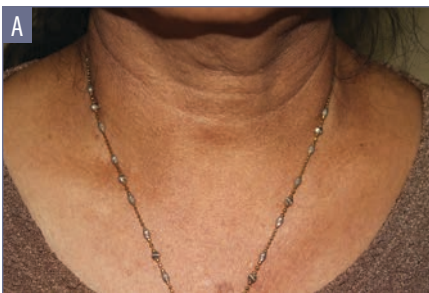


FIGURE 4. A) Pigmented contact dermatitis in a patient with history of prolonged cosmetic products use; B) The patient's patch test was positive for benzyl salicylate on Day 28.

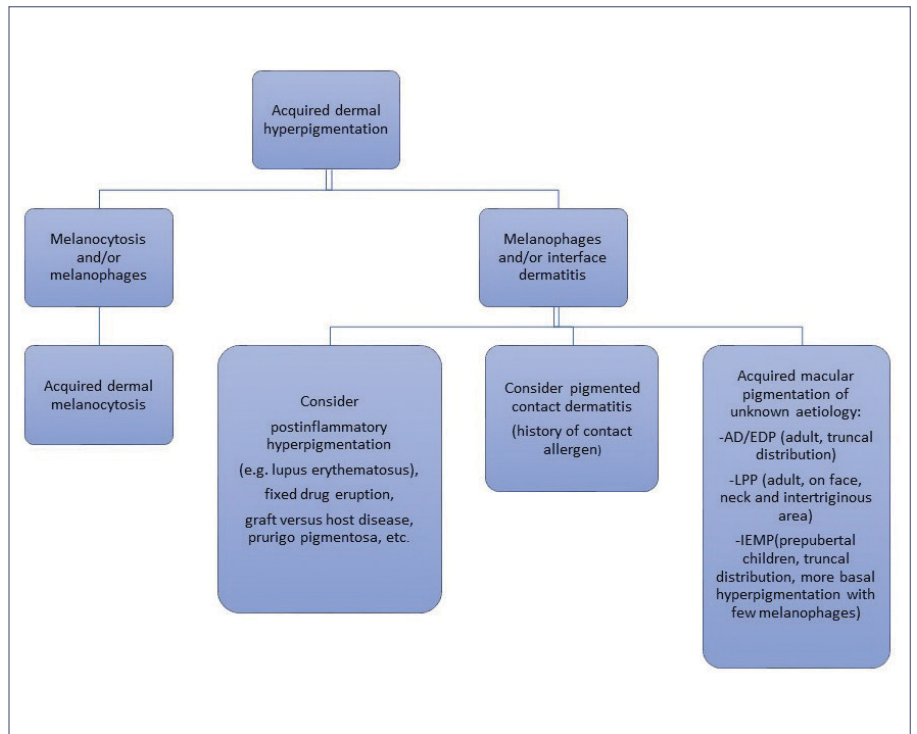


FIGURE 5. Considerations for diagnosing acquired dermal hyperpigmentation

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