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Case Series

Clinico-histopathological profile of acral hyperpigmentation in skin of colour- A case series and review of literature

Ramya N Gowda[1], Sahana P Raju[2]*, Megha S A[1]

[1]*Dept. of Dermatology, Dr. B.R. Ambedkar Medical College Hospital, Bengaluru, Karnataka, India*
[2]*Dept. of Dermatology, SABVMCRI, Bowring and Lady Curzon Hospital, Bengaluru, Karnataka, India*

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ABSTRACT

Acral melanosis refers to increase in melanin pigmentation, in a diffuse, reticulate or focal pattern over the distal portions of the limbs and the head. The underlying causes are broadly classified as genetic or acquired, including various causes like hereditary, infections, inflammatory conditions, traumatic, neoplasms, drug induced and miscellaneous causes.

We present seven cases of acral pigmentation with their clinical features, dermoscopy and histopathological findings. Here is an attempt to understand the subject better with the etiological classification and review of literature.

1. Introduction

Acral pigmentation refers to the presence of pigmentation on the outer parts of the upper and lower limbs as well as facial regions. It is caused by multiple underlying causes which can be broadly classified as genetic or acquired. The causes are further delineated in Table 1. It also serves as an important clue and aids in diagnosis of underlying nutritional and metabolic conditions, in the absence of other symptoms. Acral, especially pigmentation over the face is a major cause of stress and anxiety which adversely affects quality of life, especially in skin of colour. The development of pigmentation is influenced by variations in basal epidermal melanin content and skin type, with darker skin tones experiencing these changes more frequently and severely. This article presents 7 cases of acral hyperpigmentation, offering insights into their causes, clinical manifestations, dermoscopic features, and histopathological findings.[1–4]

2. Case Series

2.1. Lichen planus pigmentosus (LPP)

Lichen Planus Pigmentosus (LPP) is a subtype of lichen planus that predominantly affects individuals with skin phototypes III-V,[4] commonly appearing in the third to fourth decades of life. Characterized by chronicity with periods of exacerbation and remission, LPP has various identified causes, including an unknown antigen triggering a lichenoid inflammatory reaction, UV irradiation, mustard oil (containing a potential photosensitizer - allyl thiocynate), and amla oil (mainly in Indian skin). Clinically, patients exhibit oval or round macular hyperpigmentation in sun-exposed areas such as the forehead, temples, and neck, ranging from slate grey to brownish black, presenting in diffuse, reticular, blotchy, and perifollicular forms. LPP can also manifest in skin folds like axillae and groin (LPP inversus). Although typically asymptomatic, there is a rare unilateral linear variant following blaschko's lines. Dermoscopic features include dots and globules, exaggerated pseudo-reticular pattern

* *Corresponding author*.
E-mail address: sahanapraju@gmail.com (S. P. Raju).

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and peri-follicular pigmentation.[5,6] Histopathological examination reveals basal layer vacuolation with epidermal atrophy, melanophages in the superficial dermis and perivascular lymphocytic infiltrate.[7] Differential diagnosis include lichen planus (actinic, inverse variant), erythema dyschromicum perstans, post inflammatory hyperpigmentation, lichenoid drug eruption. Treatment options such as photoprotection, topical tacrolimus 0.1%, topical and systemic corticosteroids, topical vitamin D have been tried with variable success.

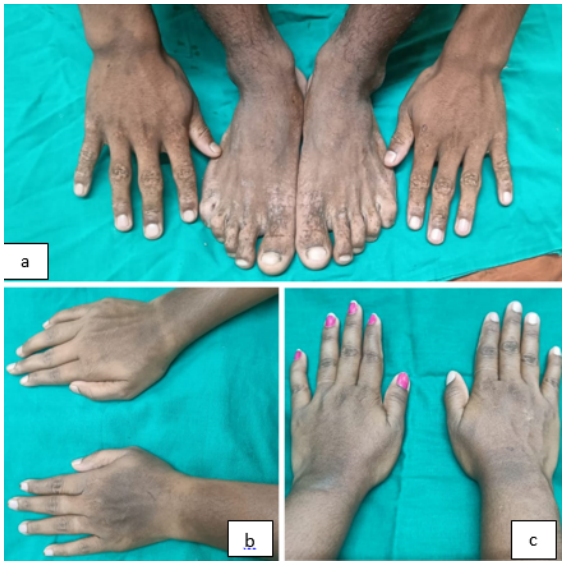

Figure 1: a: Hyperkeratosis with reticulate hyperpigmentation affecting dorsum of hands and feet; **b** & **c:** Hyperpigmentation of dorsum of hands and PIP/DIP

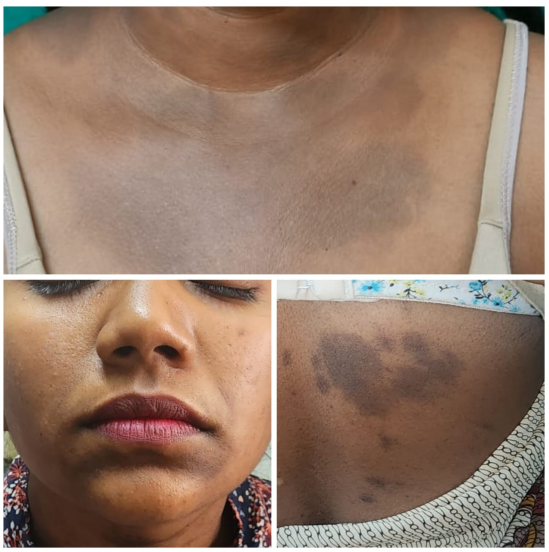

Figure 2: Hyperpigmentation involving face (seborrheic areas), neck, chest and back

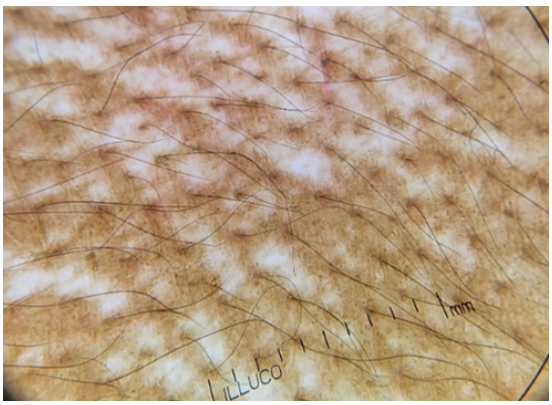

Figure 3: Dermoscopy of acral pigmentation showing peri-follicular and interspersed areas of hyperpigmentation.

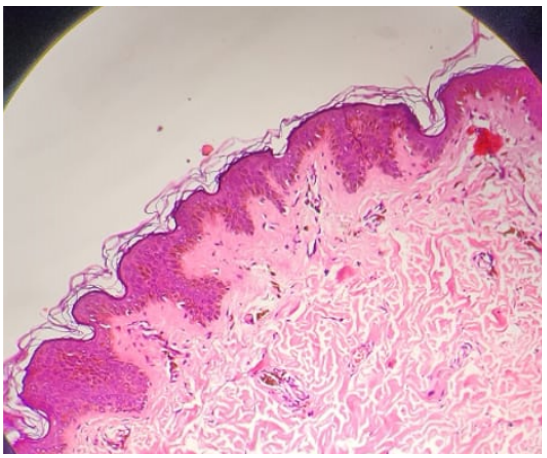

Figure 4: Histopathology showing increased basal cell layer pigmentation with melanin incontinence.

2.2. *Vitamin B12 deficiency associated pigmentation*

Vitamin B12 (cobalamin) is a water soluble B complex vitamin.[8] It is obtained through dietary sources such as eggs, milk, beef, liver and organ meats. It is a critical co-enzyme involved in DNA, proteins, lipid and carbohydrate metabolism.[8] Deficiency may arise due to intrinsic factor deficiency, achlorhydria, ileac disease, malnutrition, malabsorption syndromes, or a strict vegetarian diet.[9] The patients present with anemia, neurological manifestations such as loss of vibration, proprioception, spasticity, paraplegia, urinary incontinence, mucocutaneous features such as glossitis, angular cheilitis, localised or diffuse hair depigmentation and cutaneous hyperpigmentation of face, nails, acral pigmentation involving hands and feet, palmar creases and flexural surfaces.[8,10] The pathogenesis of cutaneous hyperpigmentation due to vitamin B12 deficiency is poorly understood. Decreased vitamin B12 causes decrease in glutathione levels which leads to decrease in inhibitory effect on tyrosinase enzyme,

Table 1: Causes of acral hyper-pigmentation [1–3]

Hereditary	• Reticulate acropigmentation of Kitamura
	• Naegeli-Franceschetti-Jadasson syndrome
	• Amyloidosis cutis dyschromica
	• DUH
	• Dermatopathia pigmentosa reticularis
	• Dyschromatosis symmetrica hereditaria
	• EBS with mottled pigmentation
Nevi	• Blue nevus
	• Junctional melanocytic nevus
Infections	• Tinea nigra
	• PKDL
	• Secondary syphilis
Inflammatory conditions	• Prurigo pigmentosa
	• Pigmented contact dermatitis (Riehl's melanosis)
	• Lichen planus pigmentosus
Traumatic	• Sub-corneal hematoma
	• Talon noire
Neoplasms	• Acral lentiginous melanoma
Drug-induced	• Antibiotics (Tetracycline, HCQs , clofazimine)
	• Anti-retro viral drugs (Zidovudine)
	• Chemotherapeutics
	• OCP's
	• Heavy metals
	• Antidepressants – amitryptilline
	• Anti-arryhtmics - amiodarone
Deposition disorder	• Amyloidosis
Miscellaneous	• Post-inflammatory hyperpigmentation
	• Laugier -Hunziger syndrome
	• Hemochromatosis

thus leading to increased melanogenesis.[10] Vitamin B12 deficiency also causes defective melanin transfer from melanocytes to adjacent keratinocytes.[8] Blood tests reveal macrocytic anemia, hyper-segmented neutrophils and reduced serum vitamin B12.[9] Histopathology shows hyperkeratosis, increased melanin granules in the basal layer, scattered melanophages, and

perivascular lymphocytic infiltrates in the upper dermis.Histopathology shows hyperkeratosis, increased number in melanin granules of the basal layer, scattered melanophages along with perivascular lymphocytic infiltrates in upper dermis.[11] Treating the underlying cause reverses the hyperpigmentation. Conditions such as pernicious anemia, impaired absorption require parenteral vitamin B12 administration. In other cases, oral supplementation of 1-2 mg daily in the initial months, followed by gradual tapering, is recommended.[8]

2.3. Dyschromatosis symmetrica hereditaria

Dyschromatosis symmetrica hereditaria, also known as reticulate acropigmentation of Dohi (RAD), is a rare autosomal dominant inherited disorder caused by a mutation in the double-stranded RNA-specific adenosine deaminase gene. This gene encodes an RNA editing enzyme. Patients with RAD develop progressive hyperpigmented and depigmented macules, typically in a reticulate pattern, primarily on the dorsal extremities. Freckle-like macules are also present on the face, with onset in infancy or early childhood and a tendency to increase in size until adolescence. Hyperpigmented lesions exhibit increased melanin pigment at the basal layer, while hypopigmented lesions show decreased or absent melanin pigment. Differential diagnosis includes reticulate acro-pigmentation of Kitamura (RAPK), characterized by hyperpigmented, atrophic, angulated macules primarily on the hands, gradually extending over the extremities, and rarely involving the face. Breaks in the epidermal ridge pattern and palmar pits are characteristic of RAPK.[12–16] Although there is no effective treatment for these conditions, various agents including topical retinoids, azelaic acid and Er:Yag laser have been successfully tried.[17]

2.4. Talon noir

Talon noir is a condition marked by painless petechial lesions, commonly found in acral body sites. Its distinct presentation involves merging macules forming a blackened purpuric plaque, leading to its naming by French dermatologist Peachey. The pathogenesis is attributed to

Table 2: Summary of clinical , dermoscopic and histopathological findings.

S.No.	Age/ Sex	Clinical features	Dermoscopic findings	Histopathology	Diagnosis
1.	18/M	Reticulate pattern of light and dark coloured macules to patches on extremities bilaterally. Few discrete hyperpigmented macules in the centro-facial area involving the nose and cheeks.	Reticulate pigment network in a honeycomb pattern against pinkish brown background with focal hypo and hyperpigmentation.	Epidermis exhibits suprapapillary atrophy, mild papillomatosis and basket weave hyperkeratosis. The rete ridges are mildly elongated with pigmented basal cells. Mild superficial perivascular chronic infiltrates present.	Acropigmentation of Dohi
2.	36/F	Diffuse hyperpigmentation over the dorsum of hands and distal one third of extensor aspect of forearms bilaterally along with few flat topped skin coloured to hyperpigmented papules with scaling.	Clustered faint brown dots with white to brown scales over a light brown background.	Epidermis exhibits mild basket weave hyperkeratosis, mild atrophy of the stratum malphigii, focal lymphocytic exocytosis and mild patchy vacuolar alteration of the basal cell layer. Mild lymphocyte predominant superficial and deep perivascular chronic inflammation present.	Polymorphic Light Eruption
3.	29/F	Diffuse hyperpigmentation over the face, neck, upper chest, back and dorsum of hands bilaterally.	Reticulate pattern of brown to blue grey dots and globules over a light to dark brown background.	Epidermis exhibits mild basket weave hyperkeratosis and atrophy of stratum malphigii. The papillary dermis exhibits mild interstitial lymphocyte predominant chronic inflammatory infiltrates with admixed melanophages.	Lichen planus pigmentosus
4.	18/F	Diffuse hyperpigmented patches on extremities involving the dorsal proximal interphalangeal joint creases and along the transverse creases of the neck.	Homogenous black pigmentation and exaggerated lattice like pattern along the furrows.	Stratified squamous epithelium exhibiting hyperkeratosis, parakeratosis, hyperplasia with basal cell degeneration. Dermis shows perivascular lymphohistiocytic cell infiltrate with proliferating blood vessels.	Erythema Dyschromicum perstans
5.	44/F	Well to ill defined brownish grey macules to patches over the upper chest and back.	Brown to bluish grey globules arranged in an irregular pattern over a bluish grey background.	Atrophic epidermis with mild basal cell vacuolation and increased melanin pigmentation. Upper dermis shows pigment incontinence, melanophages and perivascular lymphocytic infiltrates.	Vitamin B12 Induced pigmentation
6.	45/M	Multiple brown to black hyperpigmented macules of varying sizes over lips and buccal mucosa. Longitudinal ridges over all fingernails with a longitudinal band of melanonychia over the fingernail of right thumb.	Granules in shades of brown and grey-blue are dispersed over a background of whitish-pink, accompanied by scattered linear and dotted vasculature Brown black longitudinal band of pigmentation with a brown background with parallel thin lines.	Accumulation of melanin in the basal layer of keratinocytes with increase in the number of melanophages in the papillary dermis. The nail matrix exhibits hyperplasia with melanin granules in the upper dermis, heightened melanin in the basal layer, and an elevated presence of melanin pigment in the nail plate.	Laugier-Hunziker syndrome
7.	40/F	Solitary well-defined, hyperpigmented , dark brown to black plaque with a smooth surface, regular margins and a central area of ulceration over the right heel.	Homogenous global pattern with reddish black colour pigment with minute hemorrhagic punctate macules in the periphery.	Epidermal hyperkeratosis and acanthosis with intraepidermal hemorrhages. Telangiectatic vessels and extravasation of erythrocytes in papillary dermis.	Talon Noir

shearing forces in activities such as sports or climbing, causing damage to papillary dermal blood vessels and blood seepage to the epidermis.Talon noir is a condition that presents with asymptomatic petechial lesions, trauma-related and mostly found in acral body sites.[18] The most typical appearance of this clinical entity is the presence of coalescing macules forming a blackened purpuric plaque. It was precisely this appearance that gave rise to the denomination of the dermatosis, termed by the French dermatologist Peachey as talon noir, which means black heel.[19] The aetiology can be explained by damage of the papillary dermal blood vessels due to shearing forces related to sports activity, climbing, or any kind of repetitive microtrauma that eventually leads to the leakage of blood from the dermis to the epidermis.[20,21] Differential diagnoses usually include acral melanoma, acral nevi, plantar wart, pyogenic granuloma, angiokeratoma, corn, and tinea nigra.[22,23] Dermoscopy, a non-invasive procedure, can differentiate talon noir from melanoma preoperatively as the former shows homogenous reddish globular structures.[24] Acral melanoma, on the contrary, shows a typical parallel ridge pattern with irregular pigmentation.[21,25,26] Confirmation of diagnosis can be done by histopathological examination, which shows hyperkeratosis, presence of blood in the stratum corneum and extravasated erythrocytes in the papillary dermis.[18] It is a benign condition which usually subsides within few weeks by avoiding sports activity or any kind of repetitive trauma and using well-cushioned shoes, thick socks and lubrication. Exanthema associated capillary fragility can be benefited from vitamin C supplementation.[27–29]

2.5. Acral melanoma

2.6. Laugier–Hunziker syndrome (LHS

Laugier–Hunziker syndrome (LHS) is a pigmentary condition involving lips, oral mucosa, and acral areas, commonly linked with longitudinal melanonychia.[30] Typically observed in middle-aged adults around 50 years old, it is more prevalent in women, especially among Whites, notably the French and Italians.[31,32] LHS manifests as asymptomatic brown to black macules, usually less than 5 mm in diameter, over the lips, buccal mucosa, hard palate, and occasionally other oral areas.[31,32] Nail involvement occurs in 50–60% of cases, presenting as single or double stripes or complete nail pigmentation.[31,33–37] Dermoscopic examination reveals linear brown pigmentation and multiple brown dots in regular pattern on mucosal lesions. Histologically, there is hyperpigmentation of basal keratinocytes with melanin-laden macrophages. A key differential diagnosis is Peutz–Jeghers syndrome (PJS). Cosmetic treatments for LHS involve cryosurgery, Q-switched Nd:YAG, and Q-switched alexandrite laser therapy, with sun protection crucial for prevention.[38]

3. Conclusion

Acral pigmentation has a varied aetiology, either being a part of generalized pigmentation or being more local. It causes significant distress, especially facial pigmentation in patients with skin of colour. A detailed history, thorough examination and use of dermoscope, histopathology is required to arrive at a diagnosis. Treatment options include identification of underlying deficiencies, use of sunscreens, topical depigmenting agents and various lasers.

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5. Conflict of Interest

None.

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Author biography

Ramya N Gowda, Post Graduate

Sahana P Raju, Assistant Professor

Megha S A, Post Graduate

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