ACQUIRED HYPERMELANOSIS

Epidermal hypermelanosis

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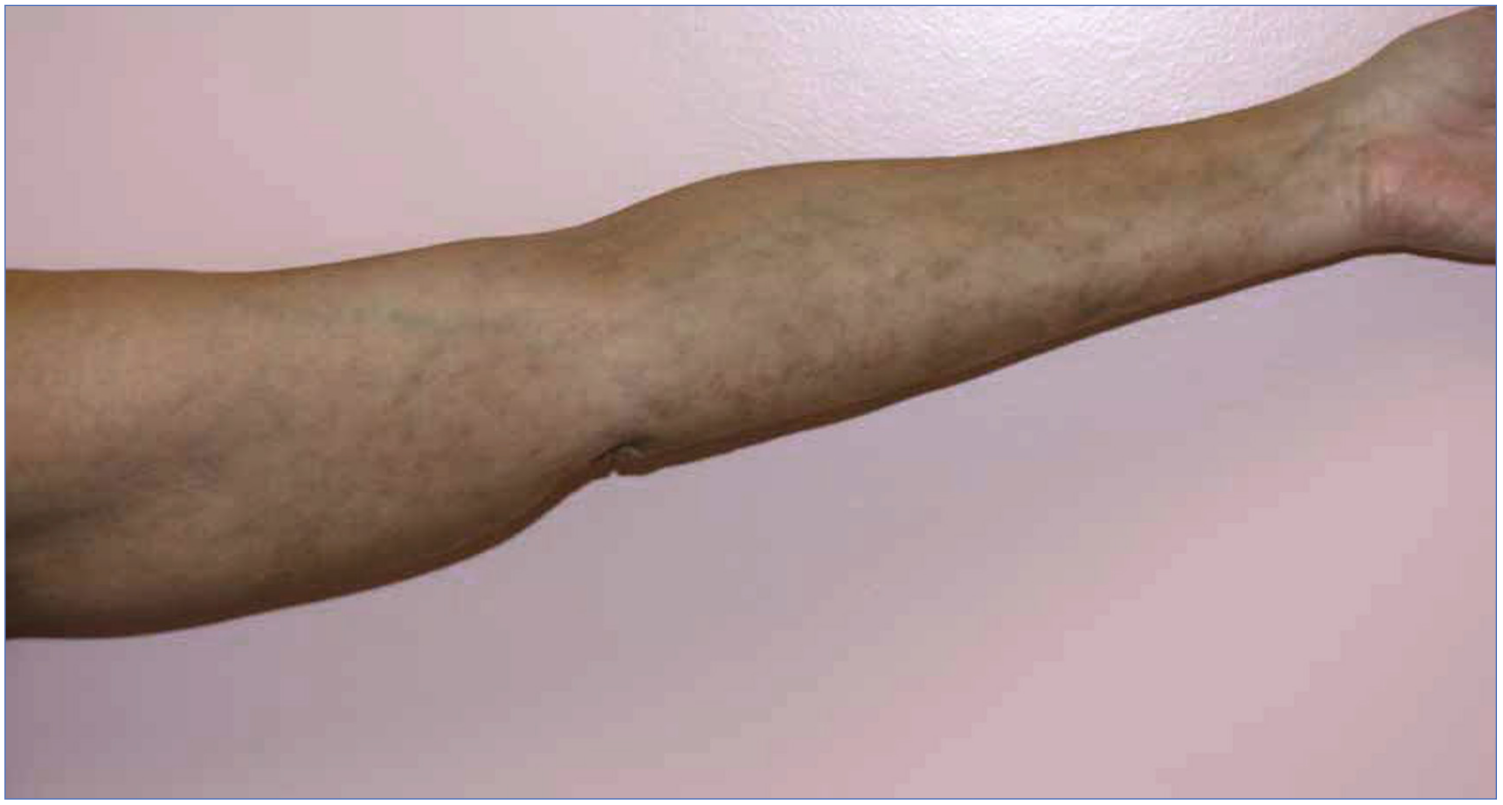
Thierry Passeron (✉)
Department of Dermatology and INSERM U1065,
University Hospital of Nice,
Nice, France
e-mail:thierry.passeron@unice.fr

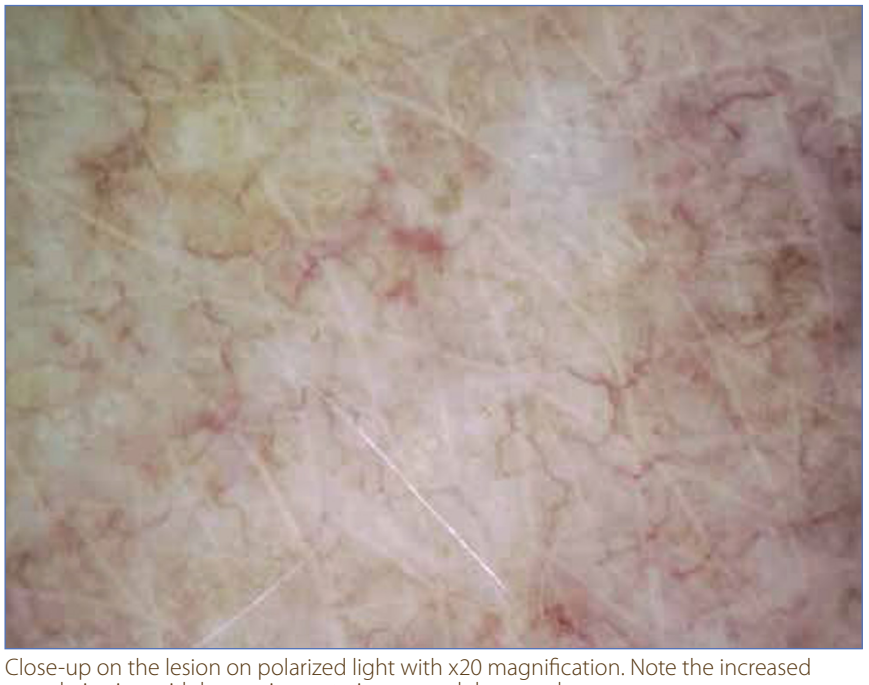
T. Passeron and J.-P. Ortonne, *Atlas of Pigmentary Disorders*, DOI 10.1007/978-3-319-10897-1_2

ACQUIRED BILATERAL TELANGIECTATIC MACULES



Irregular, dark red to brown telangiectatic macules on the arm.

Hyperpigmented and telangiectatic macules with irregular borders.



Close-up on the lesion on polarized light with x20 magnification. Note the increased vascularization with hyperpigmentation around the vessels.

EPIDEMIOLOGY

The entity has been reported very recently with 13 cases in the Korean population.
Mean patient age was 43 years (age range, 37 to 52 years) in this series with eleven men and two women.
Skin types III and IV.
The condition is probably not so rare.
We have observed the same condition in Caucasian individuals.

CLINICAL DERMATOLOGICAL PRESENTATION

Irregular, dark red to brown telangiectatic macules with progressive development. The lesions are asymptomatic.
Localization: symmetric disposition on the upper arms. Lower arms thighs, legs can be involved. The involvement of neck and trunk appears possible but rarer.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin contained in the epidermis without melanocyte proliferation.
Mild capillary proliferation and telangiectasia in the affected areas as compared to unaffected perilesional skin.
Slight perivascular inflammatory cell infiltration in the dermis.

DIFFERENTIAL DIAGNOSIS

- Telangiectasia macularis eruptiva perstans (TMEP) but Darier sign is absent (although rarely observed in this type of mastocytosis) and no increase of mast cells is observed in the dermis.
- Acquired brachial cutaneous dyschromatosis (ABCD).
- Nevoid telangiectasias.
- Solar lentigines.

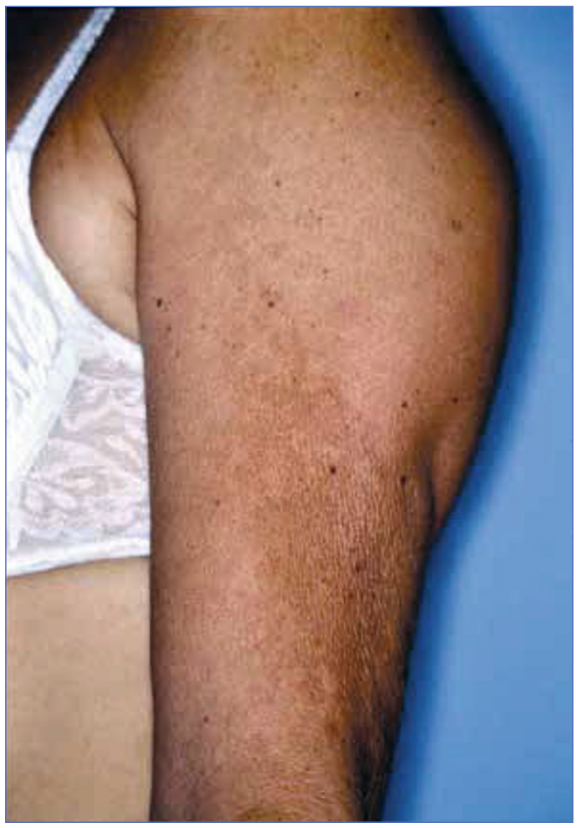
TREATMENT

No spontaneous improvement with time. Intense pulse light or laser targeting both the vascular and the pigmentary components can be proposed.

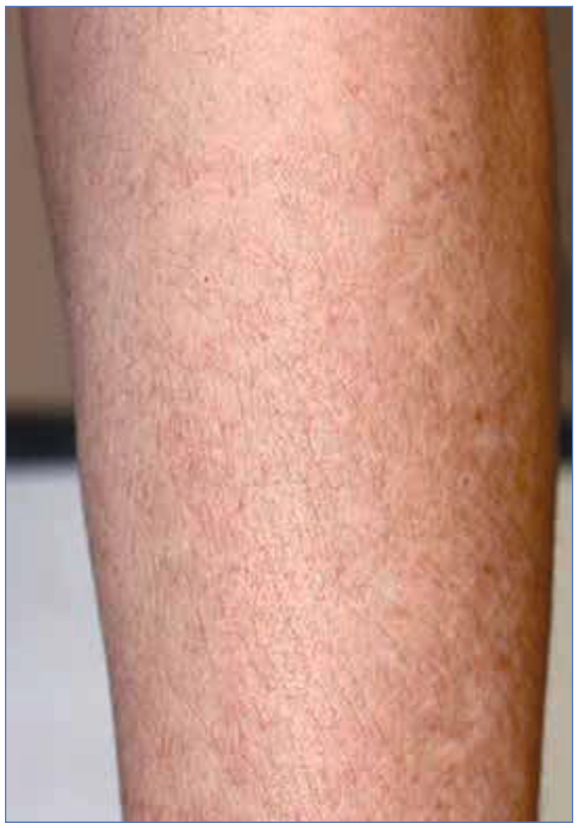
KEY REFERENCE

- Park JH, Lee DJ, Lee YJ, Jang YH, Kang HY, Kim YC. Acquired Bilateral Telangiectatic Macules: A Distinct Clinical Entity. JAMA Dermatol. 2014;150:974-7.

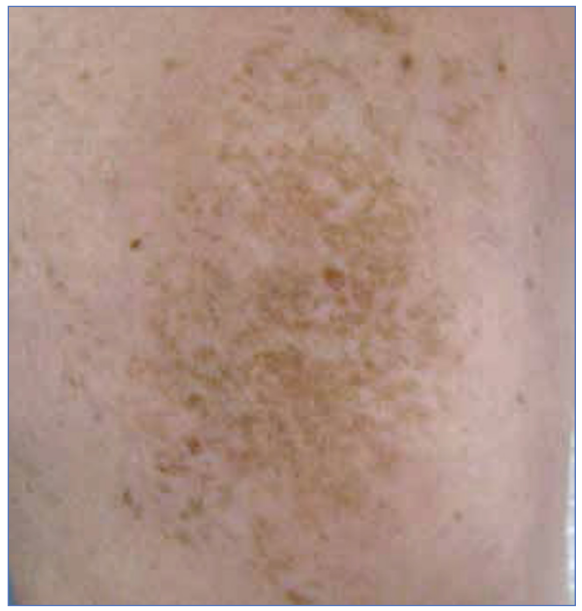
ACQUIRED BRACHIAL CUTANEOUS DYSCHROMATOSIS (ABCD)



Marked ABCD of the arm.

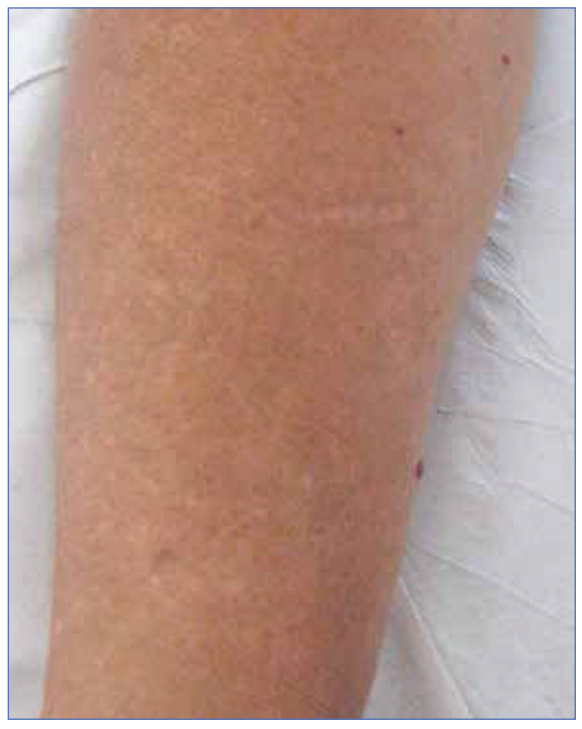


Mild ABCD of the arm.



Marked ABCD of the arm. Note the irregular borders.

Gray brown patches with geographic borders of the arm associated with hypopigmented macules.



Mild ABCD of the forearm.

SYNONYMS
Melasma of the arms.

EPIDEMIOLOGY
This disorder is not rare.
Middle-aged patients, mostly women, are affected.

PATHOPHYSIOLOGY
Unknown.
For some authors acquired brachial cutaneous dyschromatosis (ABCD) is a melasma. However, its prevalence in postmenopausal women, the presence of hypopigmented macules, the absence of a relation with estrogens, pregnancy, or hormone replacement therapy, and the frequent association with Civatte's poikiloderma suggest that ABCD is a distinct entity of melasma. A photoageing disorder maybe potentialized by the chronic use of topical cosmetic or perfumes is suspected.

CLINICAL DERMATOLOGICAL PRESENTATION
Gray brown patches with geographic borders occasionally interspersed with hypopigmented macules.
Asymptomatic.
Localization: dorsum of the forearm and sometimes of the arms. Bilateral disposition. Face and dorsum of the hand are spared.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Increased melanin found with a homogeneous pattern along the basal layer. No pigmentary incontinence. Epidermal atrophy, actinic elastosis and superficial telangiectasis are also observed.

DIFFERENTIAL DIAGNOSIS
- Dyschromatosis symetrica.
- Pigmented contact dermatitis.
- Macular amyloidosis.

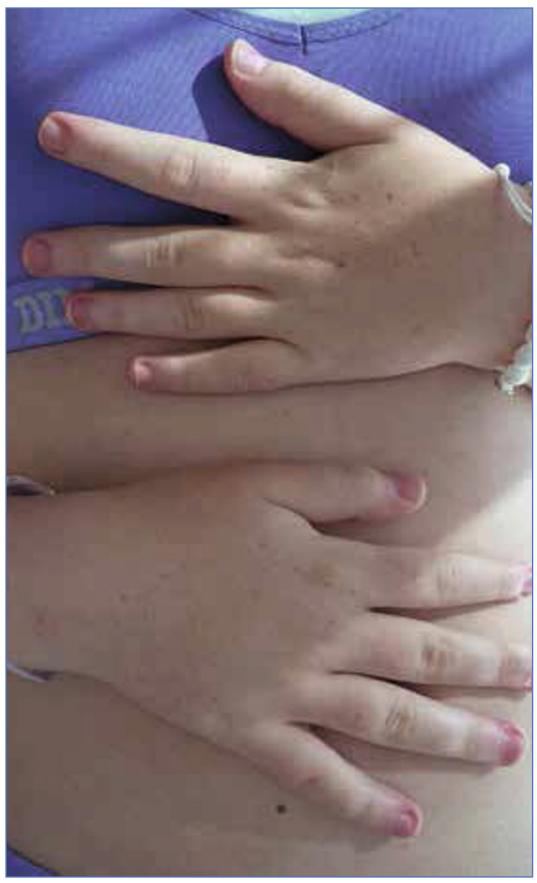
TREATMENT
Depigmentating agents, chemical peels, and lasers have been proposed but none gives truly satisfactory results. Photoprotection and avoidance of topical cosmetic and perfumes are strongly advised.

KEY REFERENCES

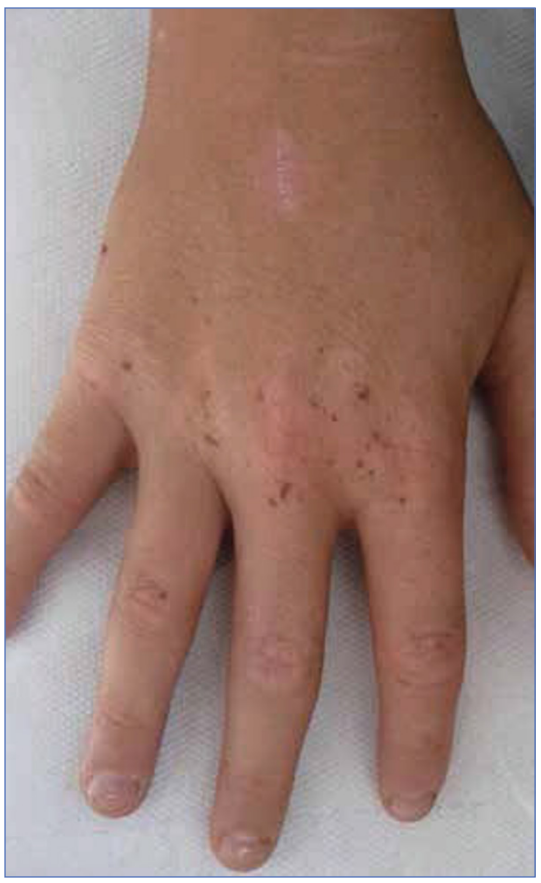
- Rongioletti F, Rebora A. Acquired brachial cutaneous dyschromatosis: a common pigmentary disorder of the arm in middle-aged women. J Am Acad Dermatol. 2000;42:680-4.
- Hu SW, Chu J, Meehan S, Kamino H, Pomeranz MK. Acquired brachial cutaneous dyschromatosis. Dermatol Online J. 2011;17:16.

ACQUIRED PIGMENTED MACULES ON FRICTION AREAS IN RED HAIR PATIENTS

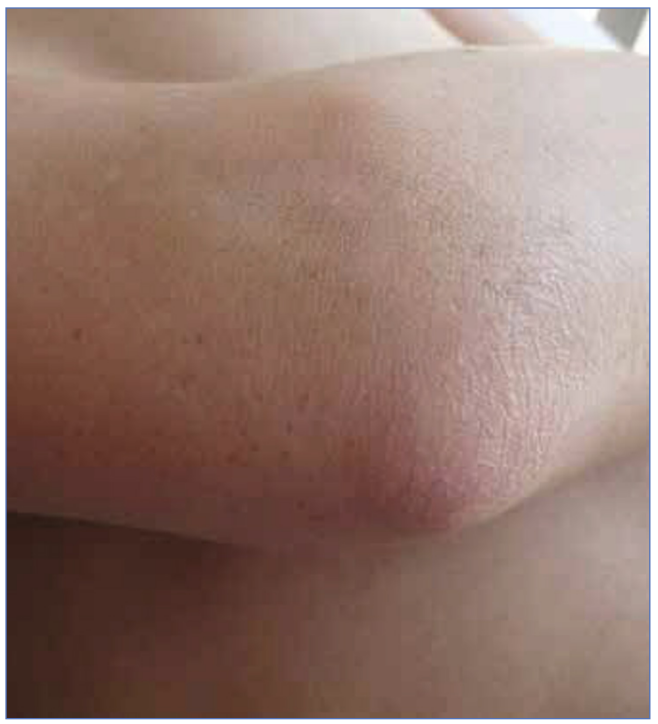
Christine Chiaverini



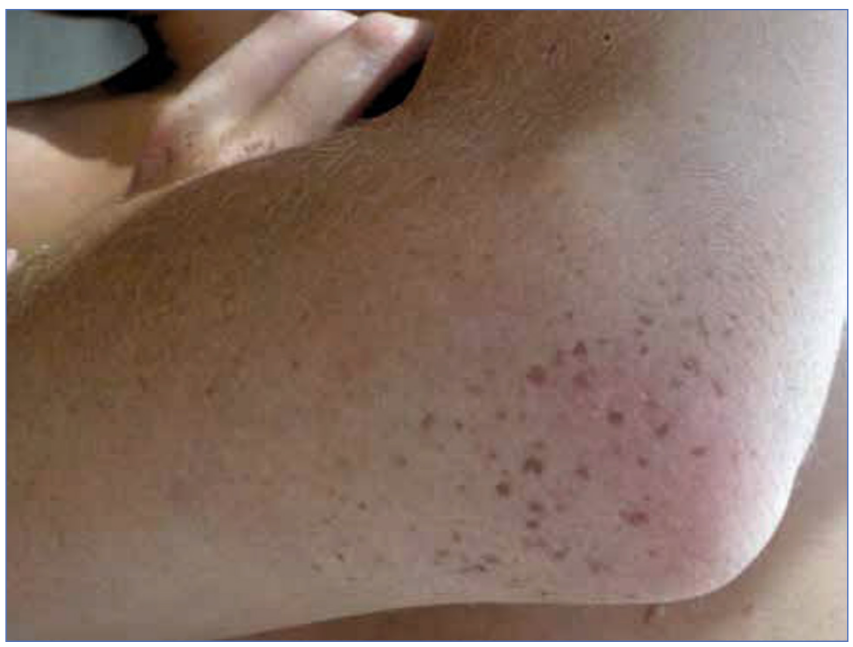
Acquired pigmented macules on the dorsum of the hand of a red haired child.



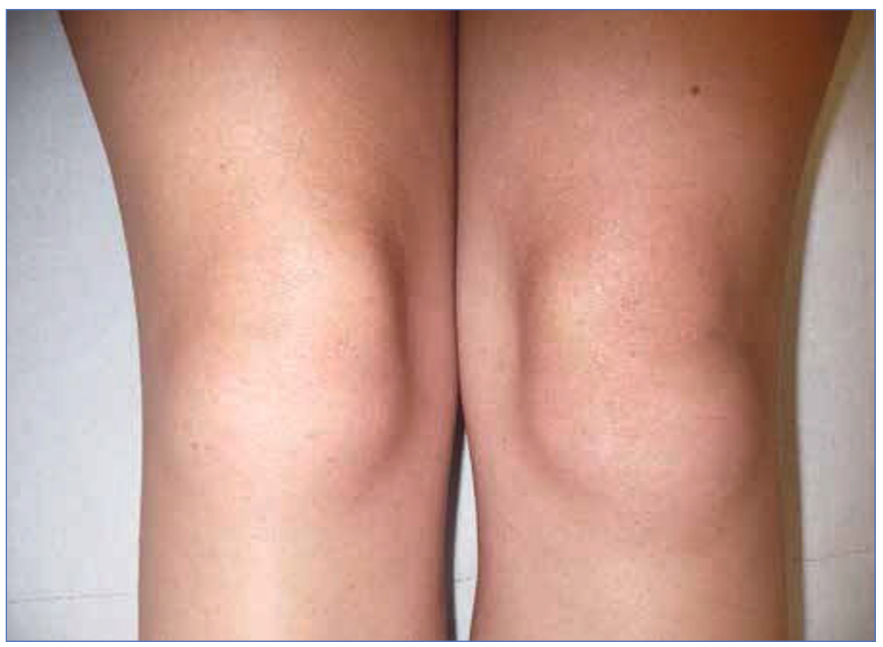
Acquired pigmented macules on the dorsum of the hand of a red haired child.



Acquired pigmented macules on the elbow of a red haired child. Note that the macules are restricted to the friction area.



Acquired pigmented macules on the elbow of a red haired child. Note the same type of lesion also located on the dorsum of the hand.



Acquired pigmented macules on the knees of a red haired child.

EPIDEMIOLOGY

Although not yet well described this entity appears to be quite common.

PATHOPHYSIOLOGY

Unknown.

CLINICAL DERMATOLOGICAL PRESENTATION

Pigmented brown or light brown macules in red haired children

More difficult to see when children become adults because of multiplication of ephelides in sun exposed areas.

Localization: macules are restricted to friction areas of the body: mostly knees and elbows, sometimes on the dorsal side of hands.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Not available.

DIFFERENTIAL DIAGNOSIS

- Ephelides.
- Lentigines.

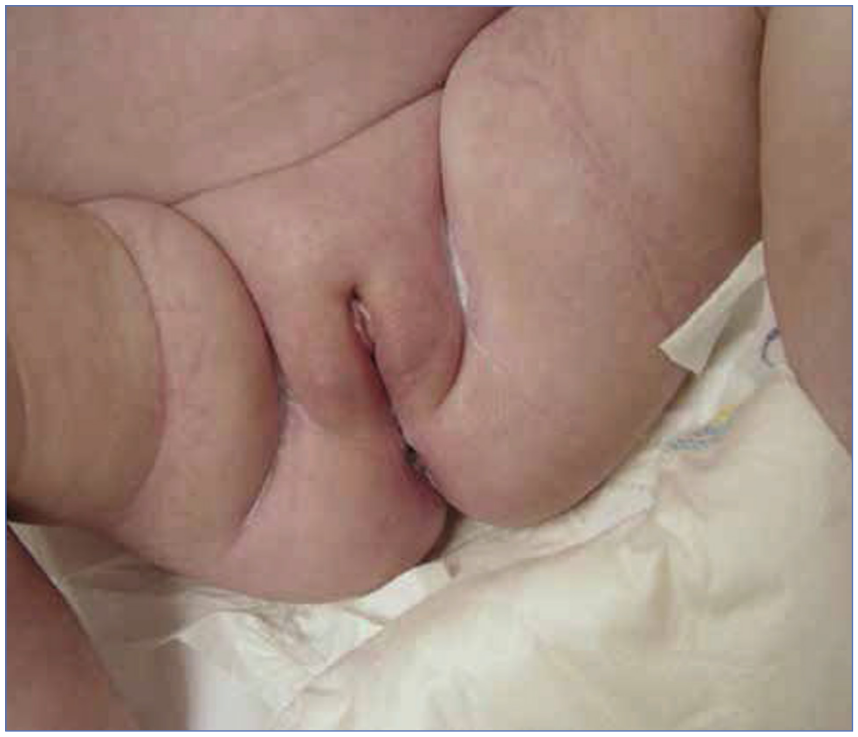
TREATMENT

Abstention.

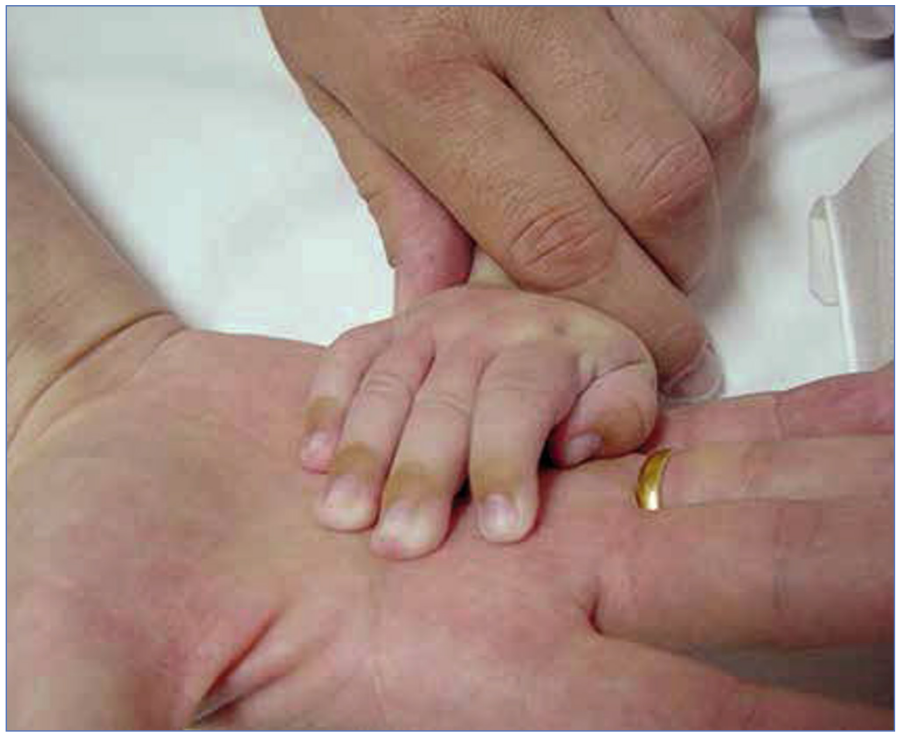
KEY REFERENCES

Personal observation.

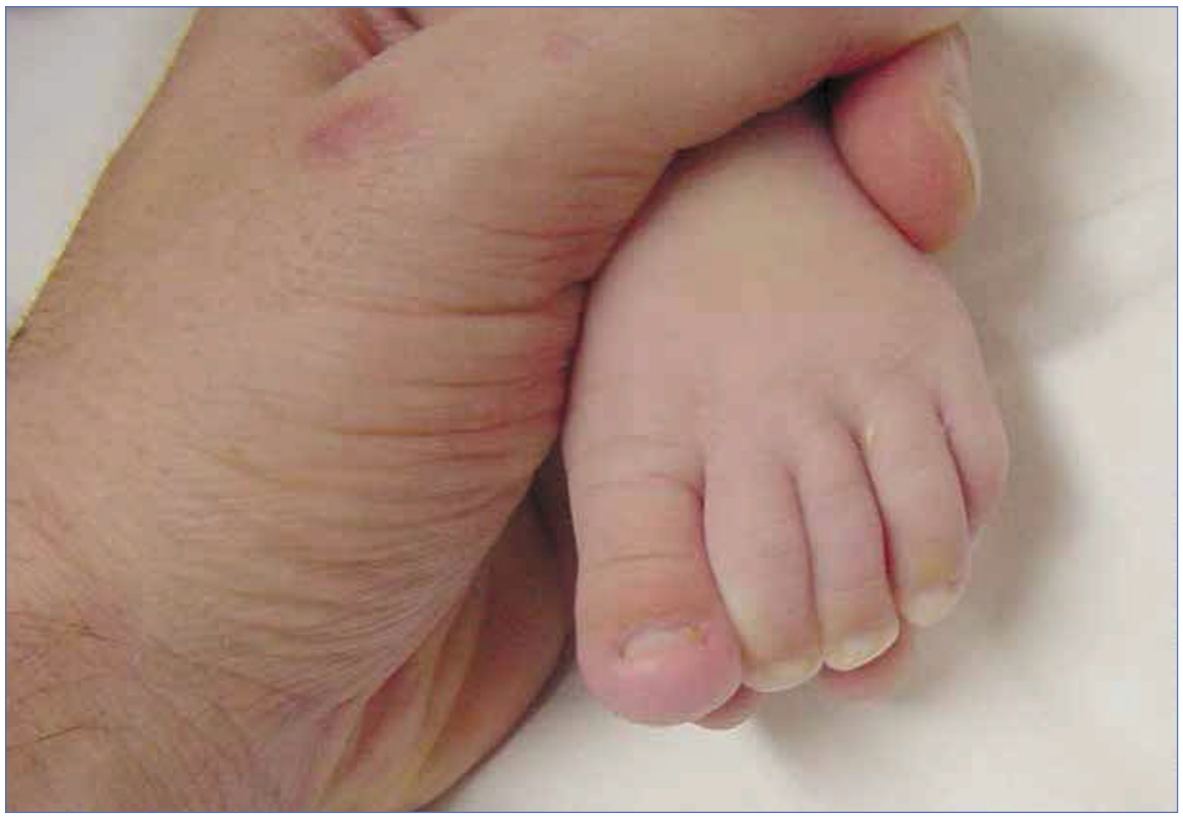
ACROMELANOSIS PROGRESSIVA



Slight hyperpigmentation of the genital area in acromelanosis progressiva (coll. Julio Guerrero Fernandez).



Progressive hyperpigmentation on acral areas of the fingers in a young infant (coll. Julio Guerrero Fernandez).



Progressive hyperpigmentation of the toes in the same infant (coll. Julio Guerrero Fernandez).

EPIDEMIOLOGY
Only a few cases have been described.

PATHOPHYSIOLOGY
Unknown.
Some hypotheses suggest that it could be an epidermal hamartoma of melanocytes.

CLINICAL DERMATOLOGICAL PRESENTATION
Asymptomatic and progressive brown to blue-black hyper-pigmentation.
Mostly seen in newborns or during the first years of life.
Initially located on the acral areas of the fingers and toes. Perianal area can be involved.
Then progression to the buttocks, genital, abdomen and thighs.
Involvement of mucous membrane has been reported once.
Nails are spared.

EXTRACUTANEOUS SIGNS
Seizures reported in one case.

HISTOPATHOLOGY
Increased number of normal melanocytes in the basal epidermis.

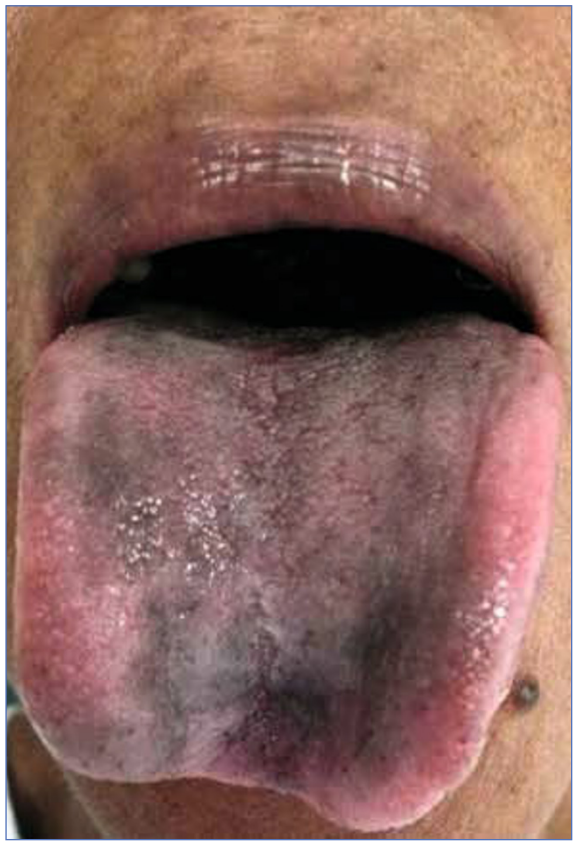
DIFFERENTIAL DIAGNOSIS
- Periungueal hyperpigmentation of the newborns.
- Reticulate acropigmentation of Kitamura.
- Acropigmentation of Dohi.

TREATMENT
None reported.
No spontaneous regression of the hyperpigmentation.

KEY REFERENCES

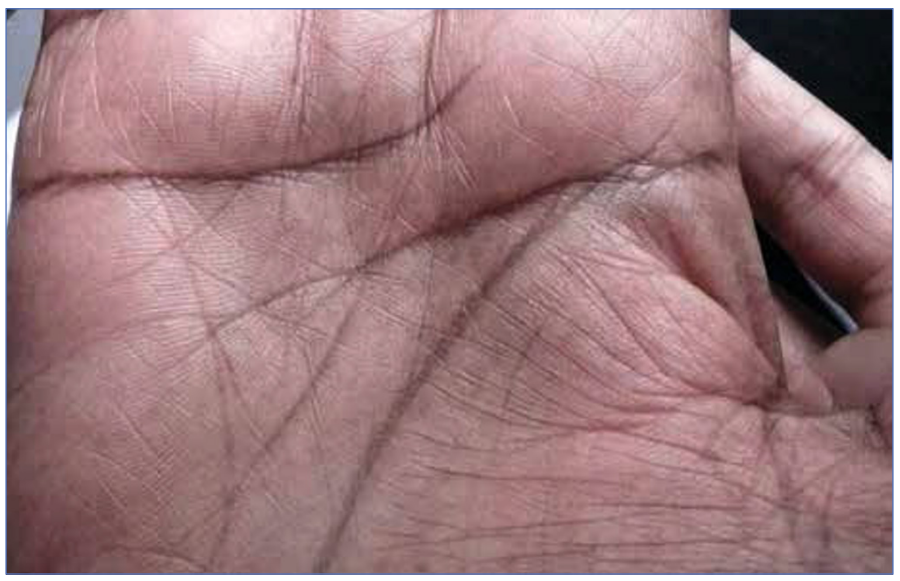
- Weidman A. Acropigmentation (acromelanosis): Report of a case. Cutis 1969:5;1119-20.
- González JR, Vázquez Botet M. Acromelanosis. A case report. J Am Acad Dermatol. 1980;2:128-31.
- Sopena Barona J, Gamo Villegas R, Guerra Tapia A, Iglesias Díez L. Acromelanosis. An Pediatr (Barc). 2003;58:277-80.

ADDISON'S DISEASE

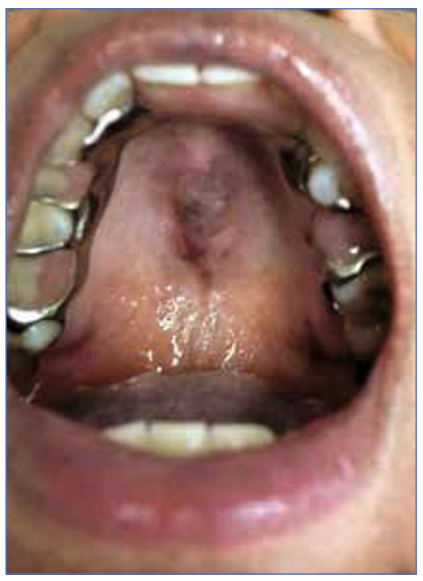


Hyperpigmentation of the tongue.

Hyperpigmentation of the extremities of the fingers associated with acquired melanonychia.



Hyperpigmentation of the palmar creases.



Hyperpigmentation of the hard palate.

EPIDEMIOLOGY

Addison's disease is an uncommon disorder affecting approximately 1 in 10,000 individuals.
There is no age, race or sexual predilection.

PATHOPHYSIOLOGY

Addison disease is caused by a deficiency of adrenocortical hormones including glucocorticoids such as cortisone, and mineralocorticoids such as aldosterone. The adrenal cortex fails to synthesize glucocorticoids appropriately, leading to an overproduction of the upstream hormones called pro-opiomelanocortin (POMC) by the hypothalamus. The POMC is the source of adrenocorticotropic hormone (ACTH) and alpha-melanocyte stimulating hormone (αMSH) that will stimulate melanogenesis.

CLINICAL DERMATOLOGICAL PRESENTATION

Brown or bronze hyperpigmentation of the skin suggestive of a deep suntan of the skin.
Mucous membranes are affected with patchy hyperpigmented macules of the buccal and gingival mucosa as well as the tongue. Acquired melanonychia is frequently observed.
In 20–40% of patients, the hyperpigmentation is the presenting symptom of their disease.
Localization: The pigmentation is usually darker in areas prone to trauma, such as palmar creases, knees and elbows, which are subjected to pressure and friction. Common areas for deeper pigmentation are the areola, axilla, perineum and genitalia.

EXTRACUTANEOUS SIGNS

Hypotension, weakness, nausea, vomiting and diarrhea.

HISTOPATHOLOGY

Increased melanin in the basal and upper layers of the epidermis, including the stratum corneum. Melanophages may be present in the upper dermis. The number of melanocytes is unchanged.

DIFFERENTIAL DIAGNOSIS

- Cushing syndrome, when the cause is an inappropriate secretion of ACTH, can lead to the same kind of hyperpigmentation. However, the extra cutaneous signs are different (hypertension, central obesity, buffalo neck, red striae, etc).
- Drug induced hyperpigmentation.
- Carcinoid syndrome.
- POEMS syndrome.

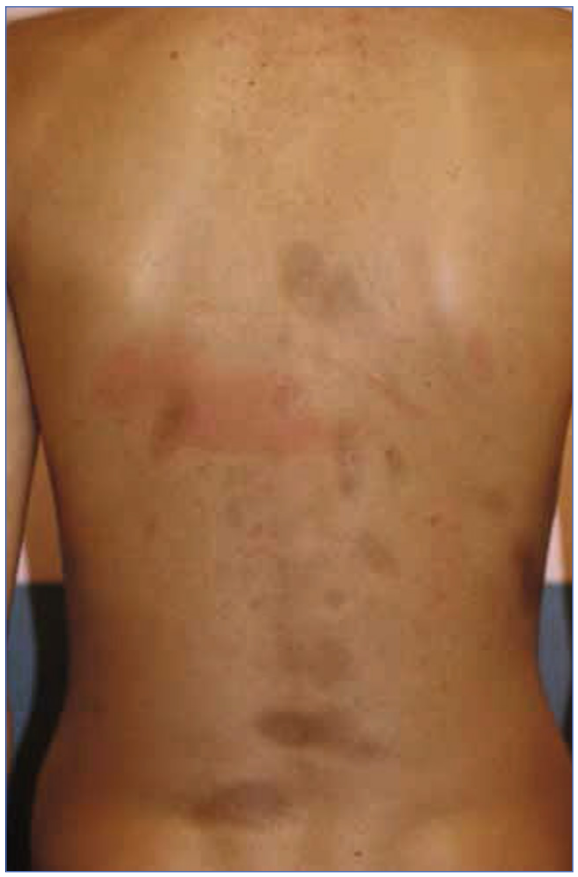
TREATMENT

Hormone replacement allows a progressive regression of the hyperpigmentation.

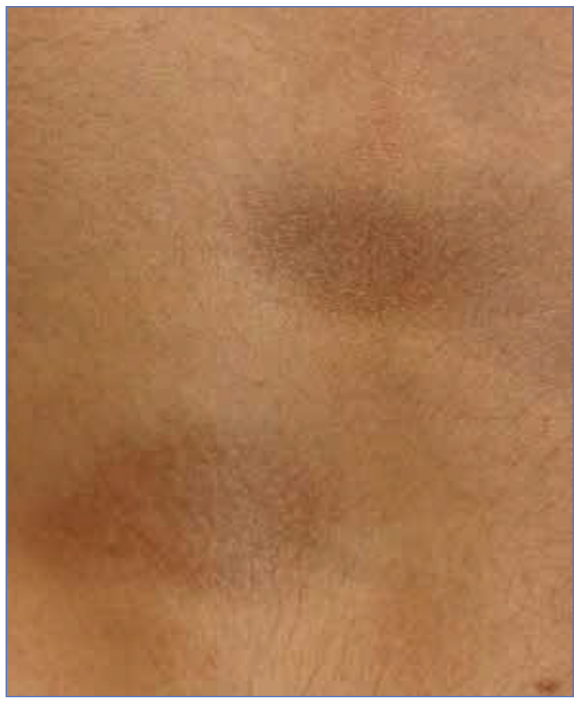
KEY REFERENCES

- De Rosa G, Corsello SM, Cecchini L, Della Casa S, Testa A. A clinical study of Addison's disease. Exp Clin Endocrinol. 1987;90:232-42.
- Kong MF, Jeffcoate W. Eigthy-six cases of Addison's disease. Clin Endorcrinol. 1994;41:757-61.

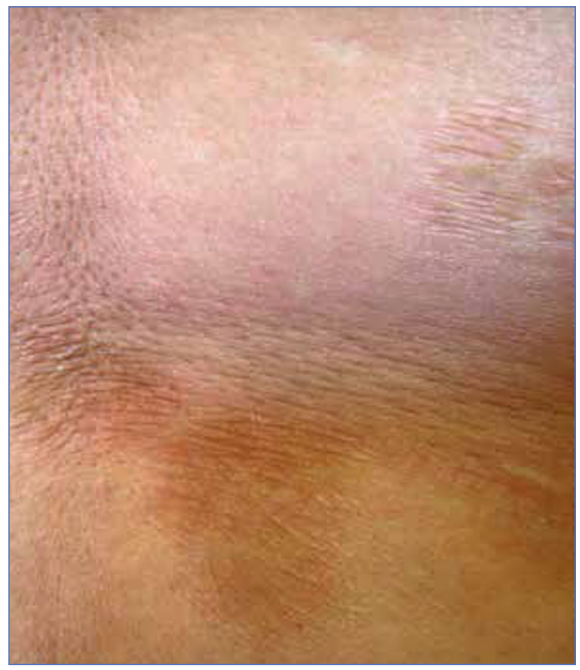
ATROPHODERMA OF PIERINI AND PASINI



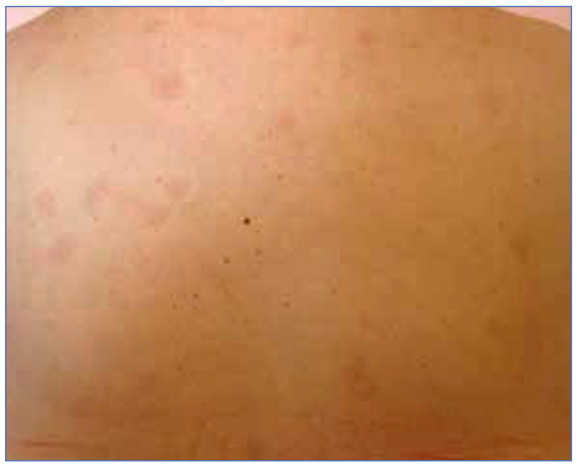
Multiple, sharply demarcated, hyperpigmented, non-indurated patches of the back.



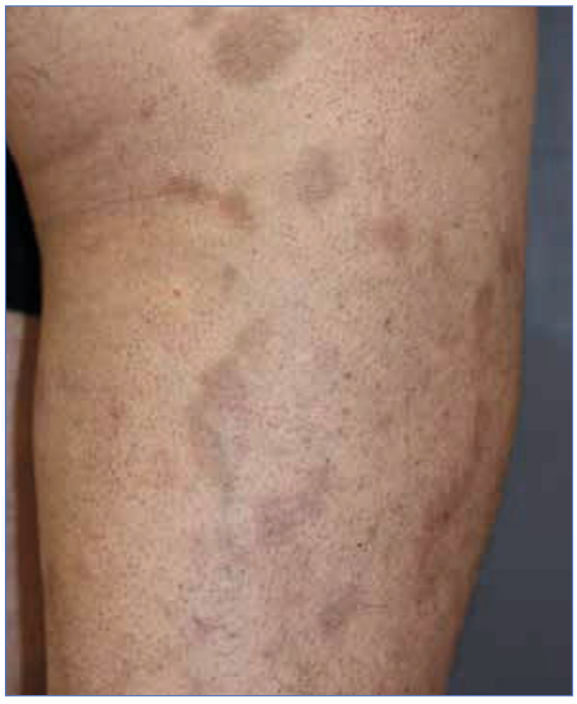
Close view of the same lesions.



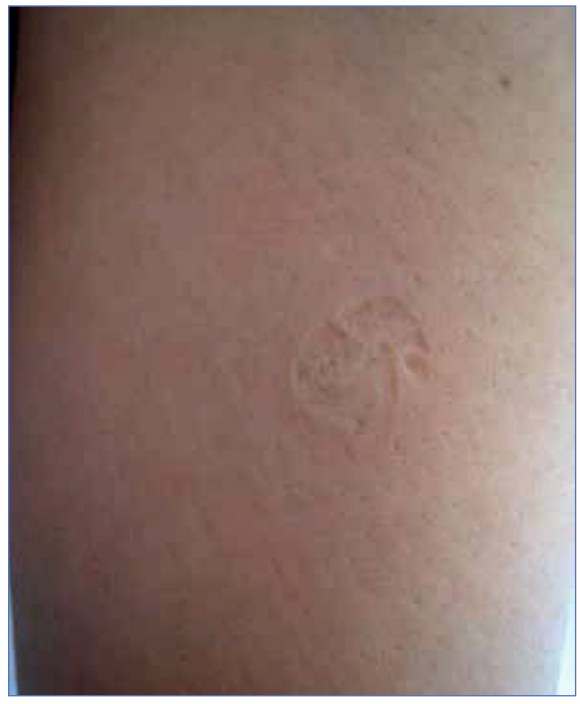
Late lesions of atrophoderma of Pierini and Pasini. Note that some lesions are still hyperpigmented when others lighten. Also note the skin atrophy.



Early lesions of atrophoderma of Pierini and Pasini.



Hyperpigmented lesions of atrophoderma of Pierini and Pasini on the arm. Note the skin atrophy associated with the hyperpigmentation.



Slightly hypopigmented lesion of atrophoderma of Pierini and Pasini of the arm. Note the sharply defined (cliff-drop) borders.

SYNONYMS

Morphea plana atrophica, dyschromic and atrophic scleroderma.

EPIDEMIOLOGY

More frequent in women than in men, with a ratio of 6:1.
More common in Caucasians than in Asians and Blacks.
Can be observed at all ages but the onset is usually during the second or third decade of life.

PATHOPHYSIOLOGY

Unknown. The role for infection with *Borrelia burgdorferi* has been suggested.

CLINICAL DERMATOLOGICAL PRESENTATION

Single or multiple, sharply demarcated, hyperpigmented, non-indurated patches.
With time the hyperpigmentation may lighten, and the lesion becomes depressed with sharply defined (cliff-drop) borders.
Size from one centimeter to large patches covering almost the entire back.
Localization: trunk and less commonly on the limbs.
Note: Hyperpigmentation is not constant and hypopigmented lesions mostly located on the upper limbs have been recently reported and appear to be not so rare.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin in the basal layers of the epidermis.
Melanophages can be observed.
Perivascular lymphohistiocytic infiltrate in the dermis with a decrease of collagen quantity and flattening of the rete pegs.

DIFFERENTIAL DIAGNOSIS

- Morphea.
- Fixed drug eruption.
- Idiopathic eruptive macular pigmentation.

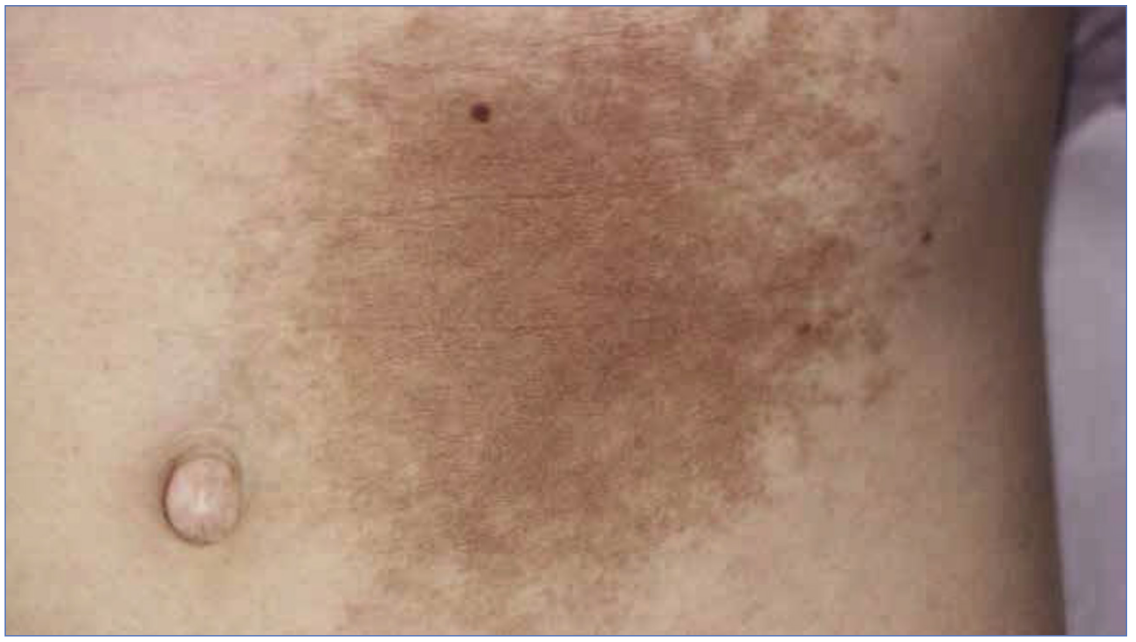
TREATMENT

No treatment is truly effective and spontaneous resolution can be observed.
High potent topical steroids can be useful in early stages.
When *Borrelia burgdorferi* antibody titer is high, some authors propose to treat it like Lyme disease with penicillin or cyclins.

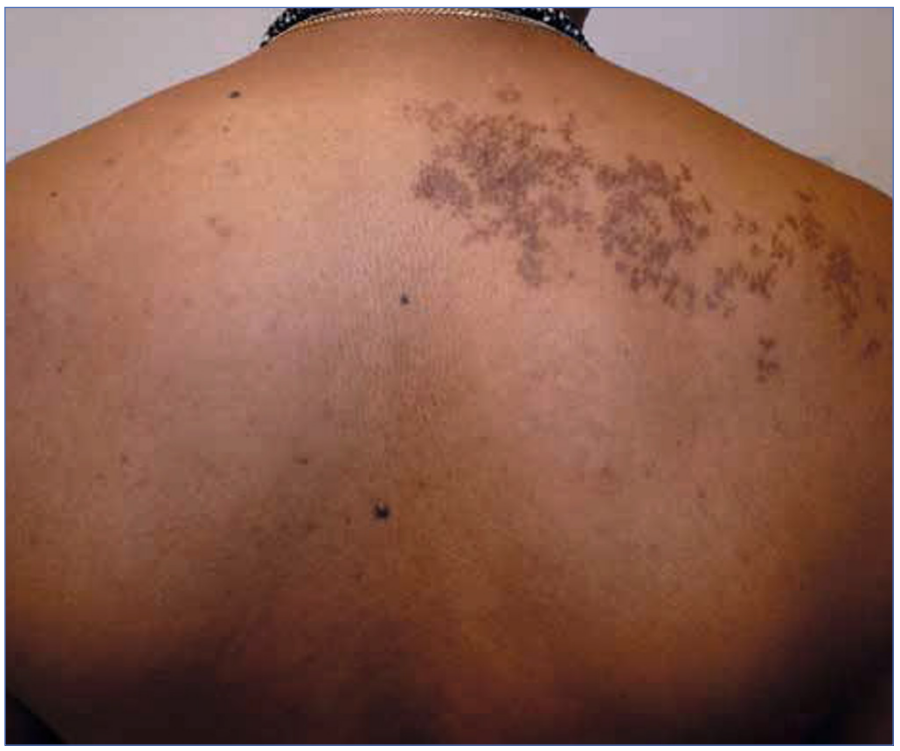
KEY REFERENCES

- Lee Y, Oh Y, Ahn SY, Park HY, Choi EH. A case of atrophoderma of Pasini and Pierini associated with borrelia burgdorferi infection successfully treated with oral doxycycline. Ann Dermatol. 2011;23:352-6.
- Saleh Z, Abbas O, Dahdah MJ, Kibbi AG, Zaynoun S, Ghosn S. Atrophoderma of Pasini and Pierini: a clinical and histopathological study. J Cutan Pathol. 2008;35:1108-14.

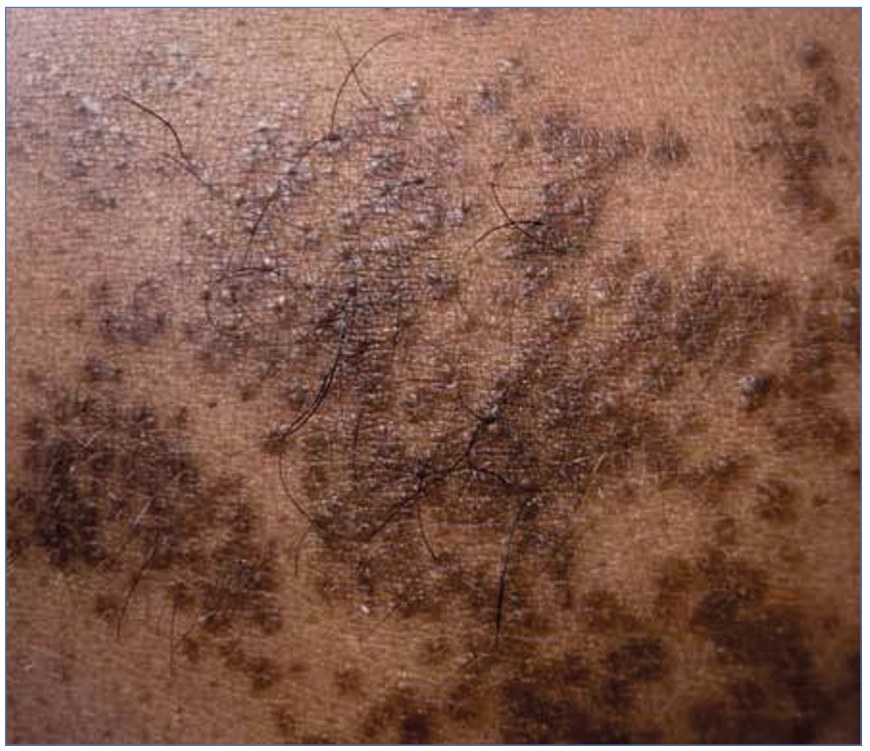
BECKER NEVUS



Becker's nevus of the abdomen. In this case no hypertrichosis was associated.



A. Becker's nevus of the right shoulder.



B. Close-up of the same lesion. Note the coarse and dark hairs associated to the hyperpigmentation.

SYNONYMS

Becker melanosis, pigmented hairy epidermal nevus.

EPIDEMIOLOGY

Becker nevus occurs in approximately 0.5% of the population. All races are affected.
A male predominance is reported, but a recent study performed in children showed the same frequency between male and female.

PATHOPHYSIOLOGY

The exact cause of the hyperpigmentation is unknown. An inability of the melanocytes to be down-regulated once stimulatory factors activate them have been reported.

CLINICAL DERMATOLOGICAL PRESENTATION

Irregular hyperpigmented macules or patches often associated with hypertrichosis.
The hair associated with Becker nevus initially develops several years after the hyperpigmentation and is often coarse and dark. Muscle hyperplasia and dermal thickening is noted.
Usual onset in the puberty period, but many cases have been reported before puberty. Becker's nevus can also be congenital.
Localization: Mostly unilateral and on the shoulders, upper arms, or anterior chest.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased basal layer pigmentation with regular acanthosis, papillomatosis, variable hyperkeratosis, dermal thickening. Absence of nevus cells nest.
Hyperplasia of hair follicles and sebaceous glands can also occur as well as lengthening and clubbing of the rete ridges.

DIFFERENTIAL DIAGNOSIS

- Congenital hairy nevi.
- Nevus of Ito.
- Café-au-lait spots.
- Linear and whorled nevoid hypermelanosis.

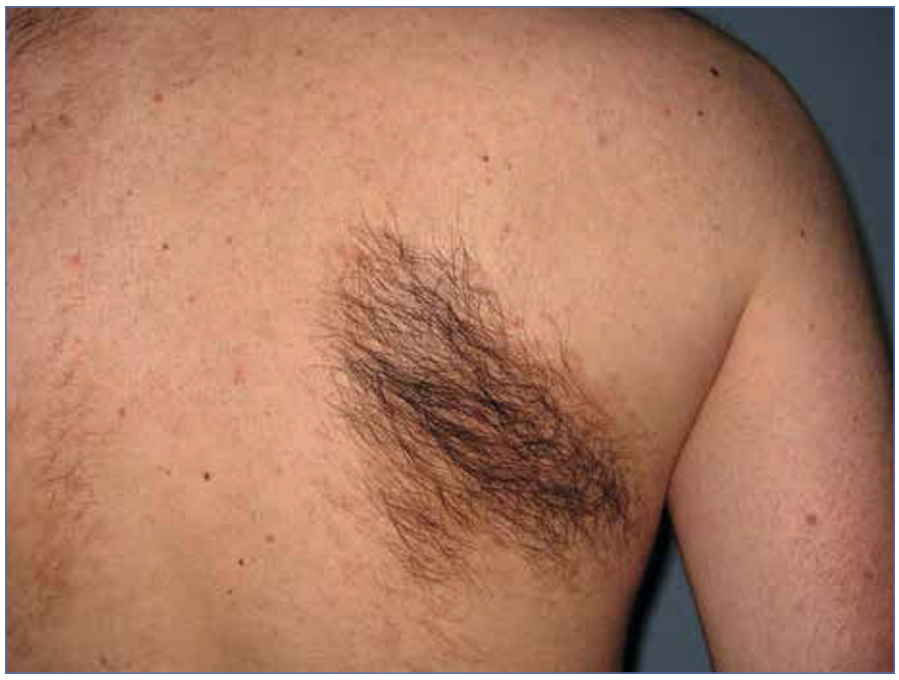
TREATMENT

Becker's nevus has no malignant potential.
For cosmetic purposes, small lesions can be treated surgically. Larger lesion can be treated with long pulsed laser for hair removal. Q-switched lasers can be used for treating the hyperpigmentation but the results are inconstant and relapses may occur.

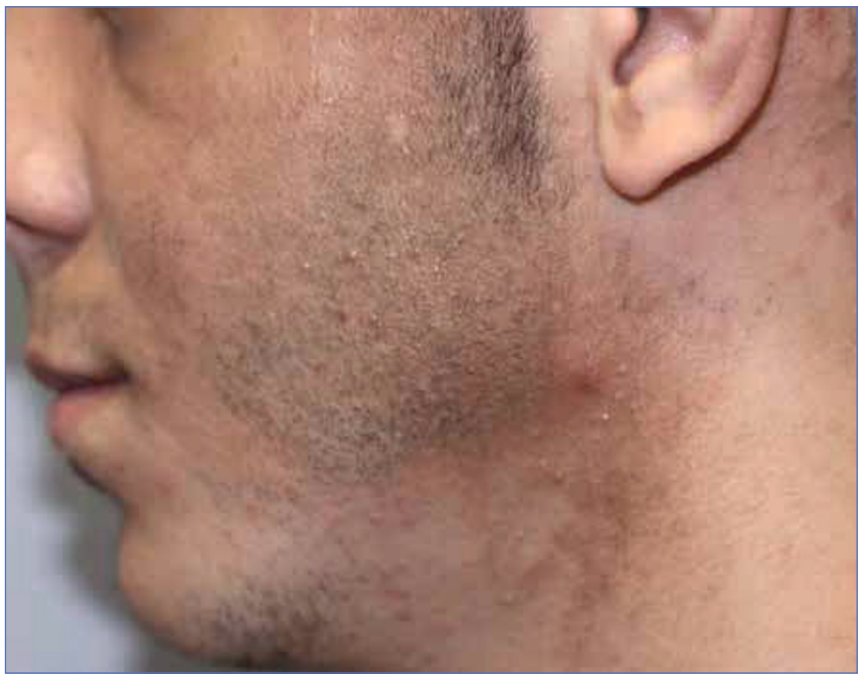
KEY REFERENCES

- Becker SW. Concurrent melanosis and hypertrichosis in distribution of nevus unius lateris. Arch Dermatol Syphil. 1949;60:155-60.
- Patrizi A, Medri M, Raone B, Bianchi F, Aprile S, Neri I. Clinical characteristics of Becker's nevus in children: report of 118 cases from Italy. Pediatr Dermatol. 2012;29:571-4.
- Polder KD, Landau JM, Vergilis-Kalner IJ, Goldberg LH, Friedman PM, Bruce S. Laser eradication of pigmented lesions: a review. Dermatol Surg. 2011;37:572-95.

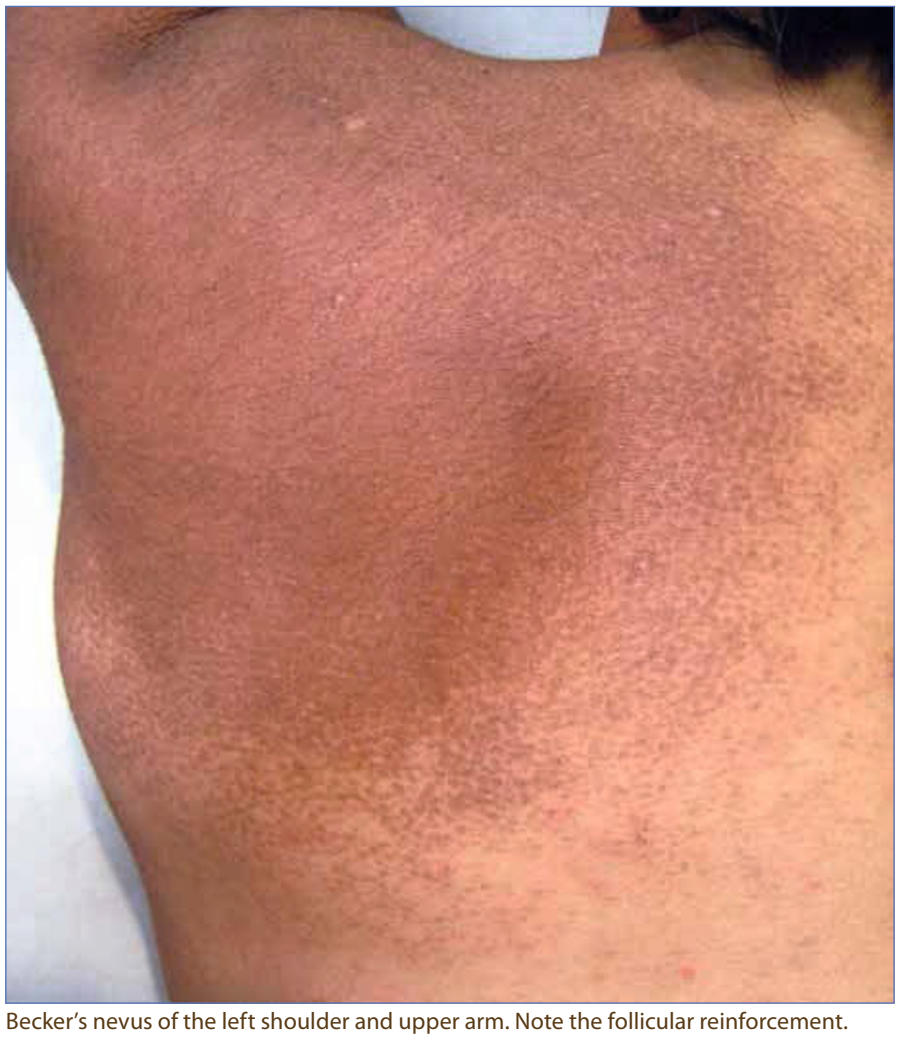
BECKER NEVUS



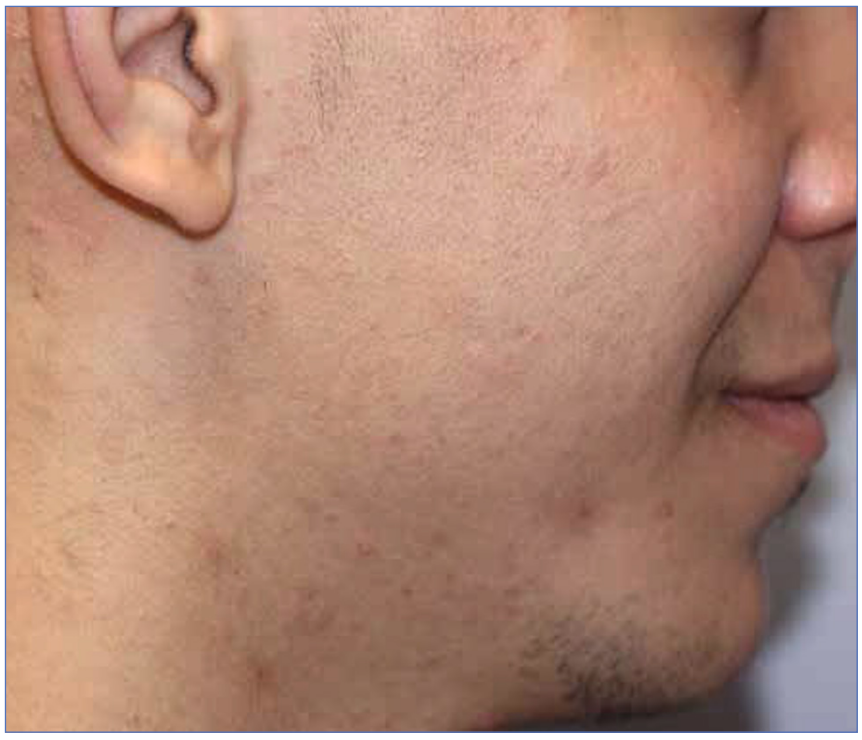
Becker's nevus of the back with marked hypertrichosis.



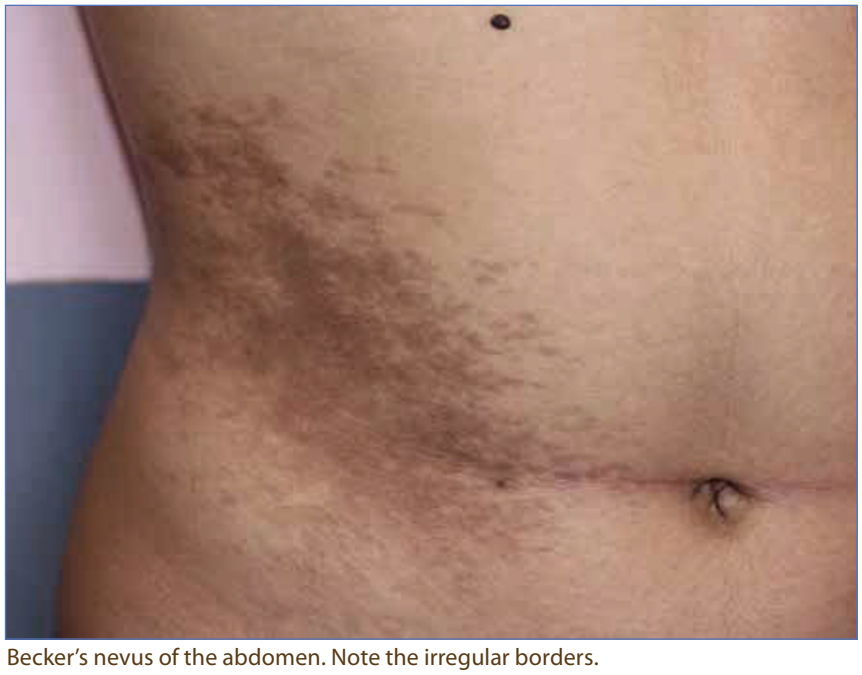
A. Involvement of the face in Becker's nevus in men can be misleading.



Becker's nevus of the left shoulder and upper arm. Note the follicular reinforcement.

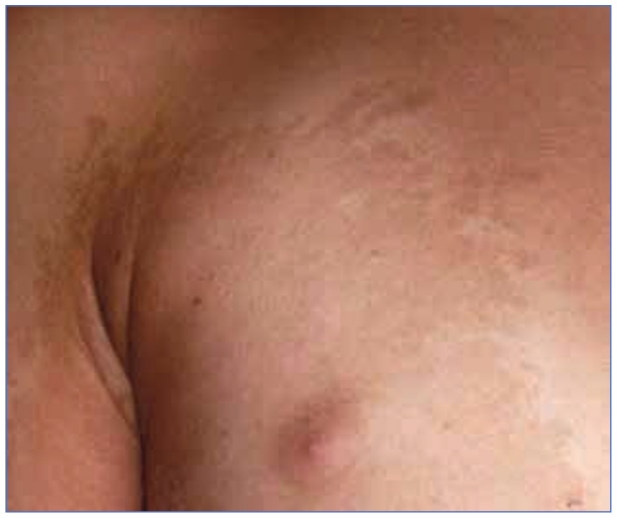


B. Opposite healthy cheek of the above male patient.

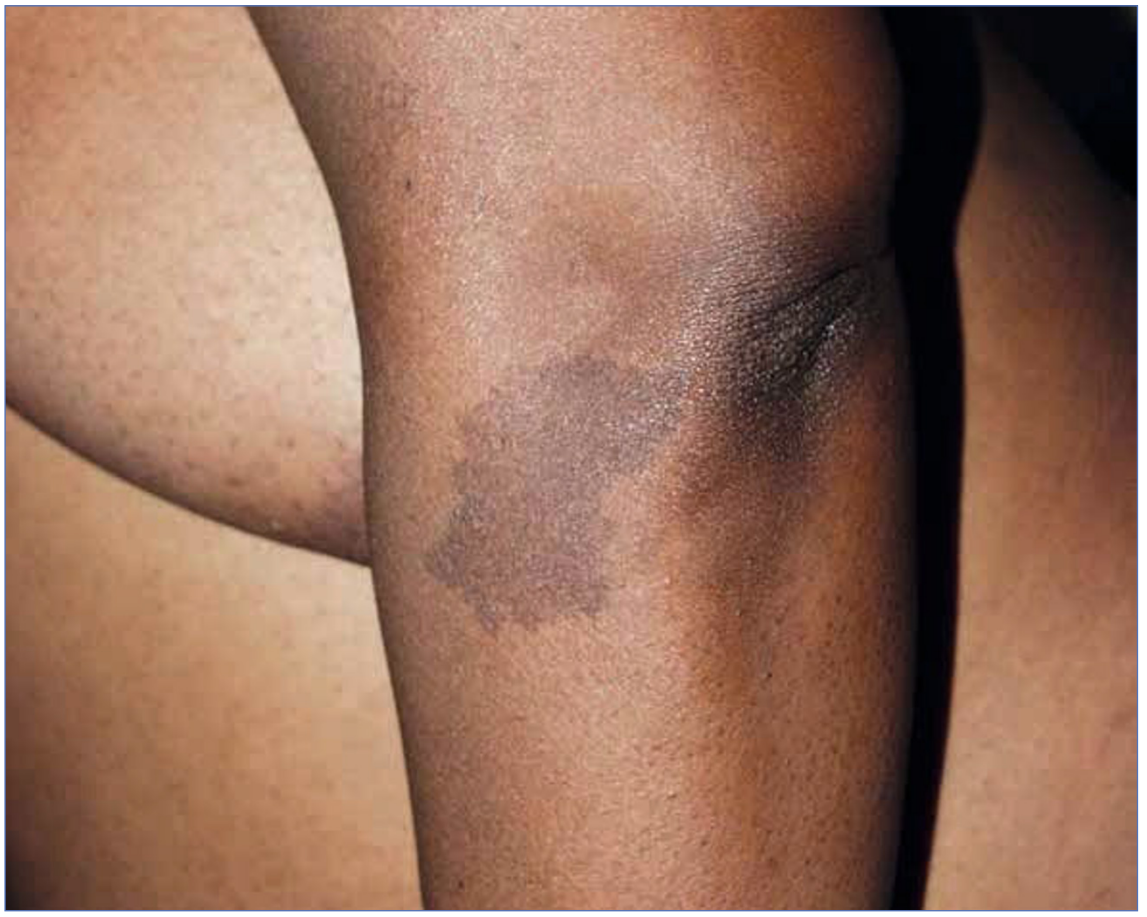


Becker's nevus of the abdomen. Note the irregular borders.

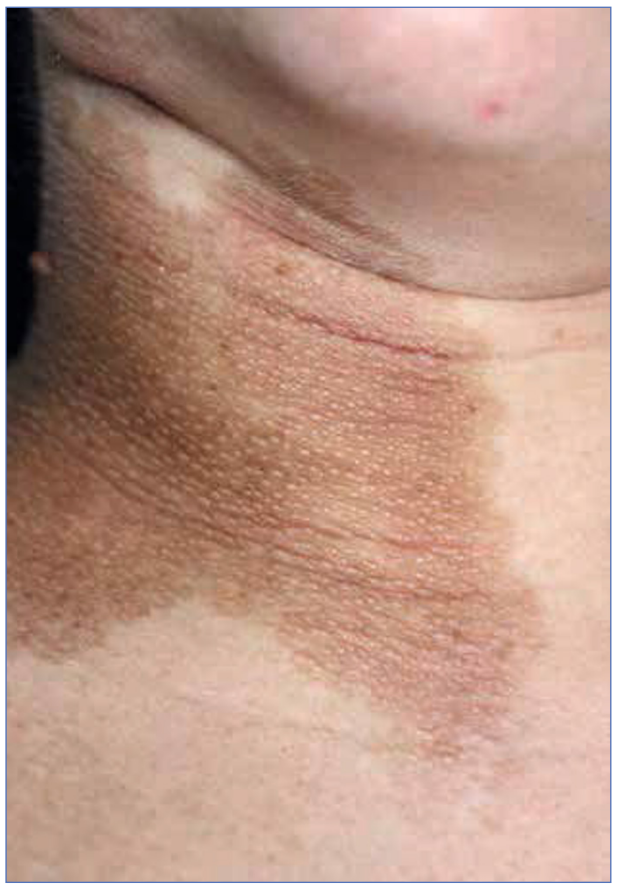
CAFÉ-AU-LAIT SPOTS



Café-au-lait spot in McCune-Albright syndrome. The jagged edges are characteristic of the diagnosis.



Isolated café-au-lait spot of the arm.



Large café-au-lait spot in neurofibromatosis type 1. Note the smooth margins.

Small café-au-lait spot associated with a nevus depigmentosus on the abdomen.

SYNONYMS

Café-au-lait macules.

EPIDEMIOLOGY

Up to one third of the general population have café-au-lait spots.
The incidence in neonates varies. They are more frequently observed in the Black population (18% in African-Americans, as compared to 0.3% in Caucasians).
No sexual predilection.

PATHOPHYSIOLOGY

The hyperpigmentation is due to a normal number of melanocytes producing more melanin.

CLINICAL DERMATOLOGICAL PRESENTATION

Light to dark brown oval or round macules to larges patches. The hyperpigmentation is uniform.
Localization: trunk, buttocks and lower limbs are mostly affected.

EXTRACUTANEOUS SIGNS

None when café-au-lait spots are isolated.
More than six lesions should prompt the search for neurofibromatosis or Legius syndrome. The margins of café-au-lait spots associated with neurofibromatosis are smooth while those of McCune-Albright syndrome have jagged edges.

HISTOPATHOLOGY

Increased epidermal melanin with normal numbers of melanocytes.

DIFFERENTIAL DIAGNOSIS

- Nevus spilus.
- Becker's nevus.
- Congenital nevus.
- Linear and whorled nevoid hypermelanosis.

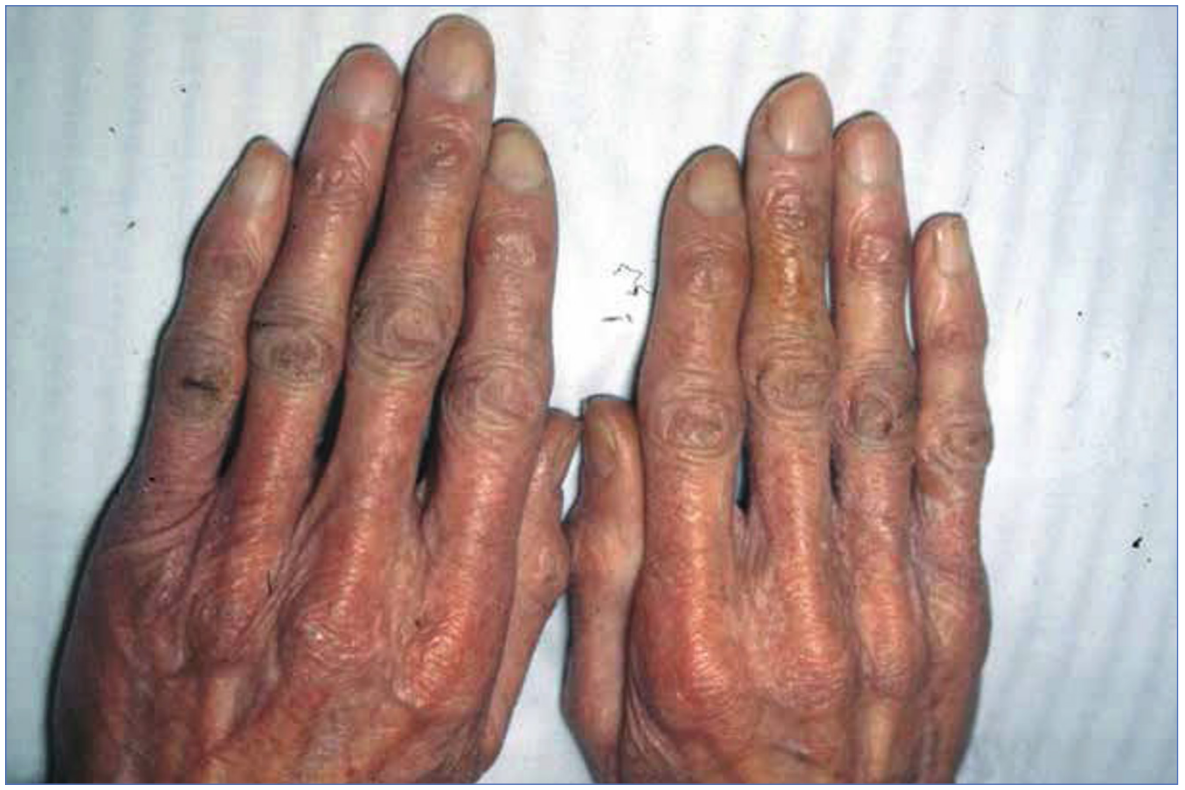
TREATMENT

Café-au-lait spots have no malignant potential.
Q-switched lasers have been proposed for aesthetic purposes but relapses are almost constant and strongly limit the interest of such an approach.

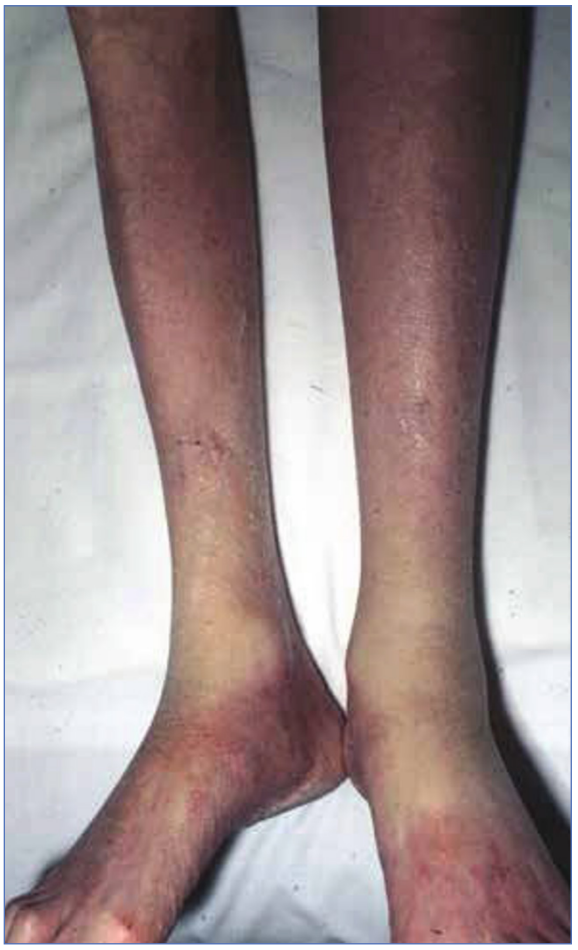
KEY REFERENCES

- Tekin M, Bodurtha JN, Riccardi VM. Café au lait spots: the pediatrician's perspective. Pediatr Rev. 2001;22:82-90.
- Shah KN. The diagnostic and clinical significance of café-au-lait macules. Pediatr Clin North Am. 2010;57:1131-53.

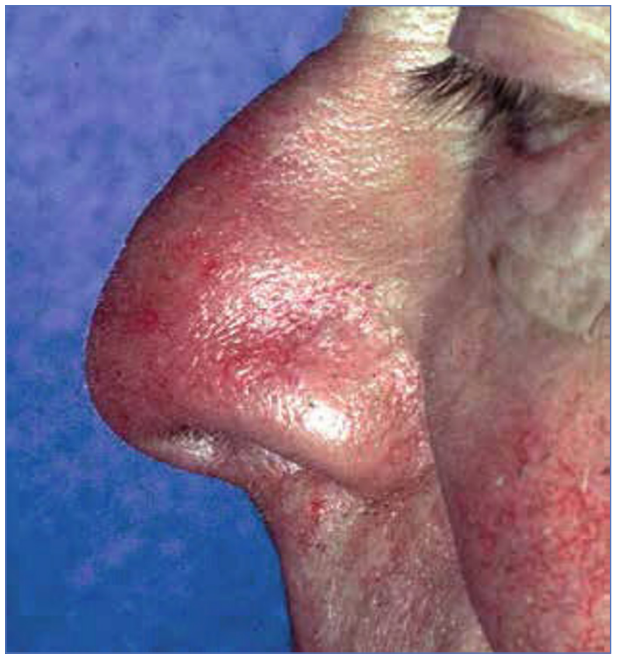
CARCINOID SYNDROME



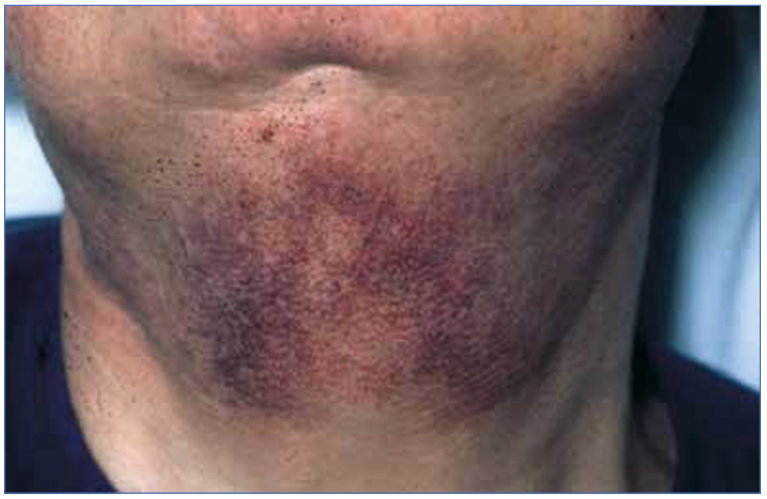
Hyperpigmentation of the sun-exposed areas in a patient with carcinoid syndrome inducing niacin deficiency and pellagra symptoms (coll. Hazel Bell).



Sclerodermoid changes on the legs (coll. Hazel Bell).



Cutaneous flushing on the face in carcinoid syndrome (coll. Hazel Bell).



Cutaneous flushing on the neck in carcinoid syndrome (coll. Hazel Bell).

EPIDEMIOLOGY

The incidence of carcinoid tumors (tumors of the diffuse endocrine system: amine precursor uptake and decarboxylation [APUD] and neuroendocrine cell system) is one to two cases per 100,000 individuals. Carcinoid syndrome occurs in less than 10% of carcinoid tumors. Most of these tumors are located in the intestinal tract (distal ileum or appendix).

PATHOPHYSIOLOGY

Due to the secretion of polypeptides and amines by the carcinoid tumors. The symptomatology depends on the type of secreted factors.

Hyperpigmentation can occur in some cases:

- Production of adrenocorticotropic hormone (ACTH) (induces a generalized hyperpigmentation similar to the one observed in Addison disease).
- Production of serotonin (a large production of serotonin used most of the available tryptophan for its production and induces a niacin deficiency and phenotype similar to the one observed in pellagra).

CLINICAL DERMATOLOGICAL PRESENTATION

Cutaneous flushing (mostly located on the face, neck and upper torso).

Hyperpigmentation: on sun-exposed area (see pellagra), or generalized (see Addison's disease). Yellow-brown and slightly atrophic plaques on the trunk, thighs, wrists and forehead is sometimes observed but the pathophysiology is unknown. Sclerodermatoid changes can be observed.

EXTRACUTANEOUS SIGNS

Diarrhea.

Palpitations, asthma, wheezing, dyspnea, low blood pressure, asthenia, dizziness are the most common symptoms.

HISTOPATHOLOGY

Carcinoid tumors consist in small round cells. The diagnosis is based on the measurement of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA). The histological examination of the hyperpigmented skin is not specific and depends on the mechanism of the hyperpigmentation (ACTH production [see Addison's disease] or niacin deficiency [see pellagra]).

DIFFERENTIAL DIAGNOSIS

- Addison's disease and pellagra are the two main differential diagnoses for the hyperpigmentation.

TREATMENT

Treatment of the carcinoid tumor: surgery, somatostatin analogs (octreotide), interferon-alpha (IFNα).

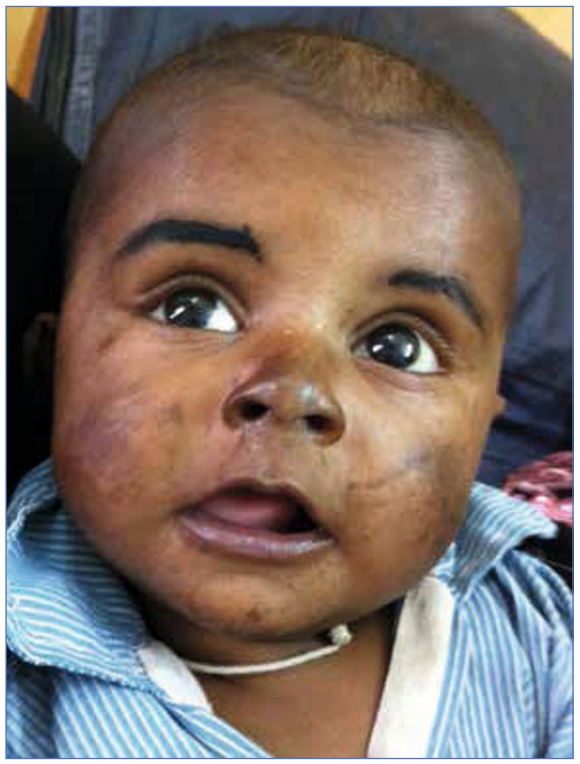
Symptomatic treatment (H_1 and H_2 antagonists, nicotinamide and niacin supplements).

KEY REFERENCES

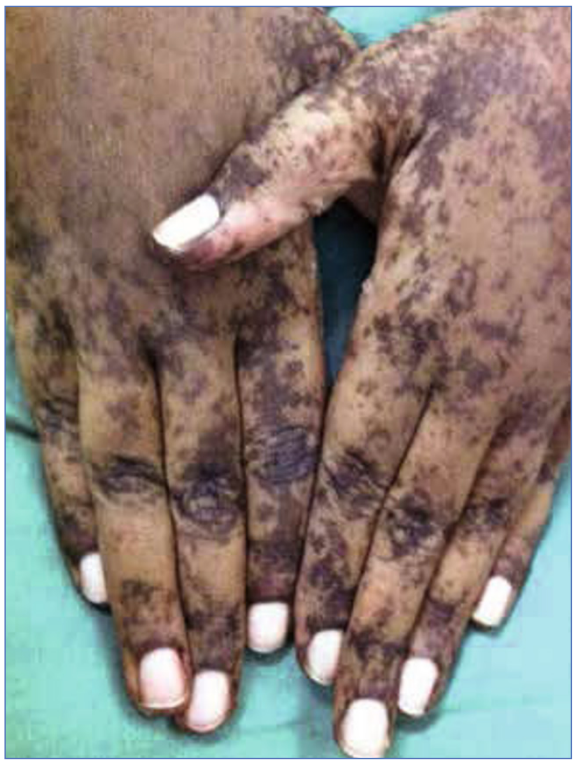
- Gartner LA, Voorhess ML. Adrenocorticotropic hormone-producing thymic carcinoid in a teenager. Cancer. 1993;71:106-11.
- Feingold KR, Elias PM. Endocrine-skin interactions. Cutaneous manifestations of adrenal disease, pheochromocytomas, carcinoid syndrome, sex hormone excess and deficiency, polyglandular autoimmune syndromes, multiple endocrine neoplasia syndromes, and other miscellaneous disorders. J Am Acad Dermatol. 1988;19:1-20.

CHIKUNGUNYA

Arun Inamadar



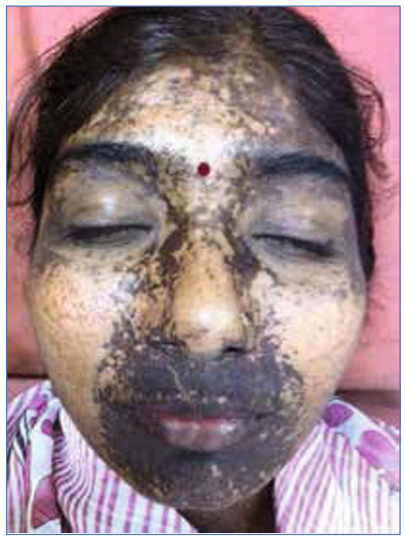
Flagellate hyperpigmentation secondary to chikungunya viral fever (coll. Arun Inamadar).



Acral hyperpigmentation secondary to chikungunya viral fever (coll. Arun Inamadar).

Lentiginous facial hyperpigmentation in a young child with chikungunya viral fever (coll. Arun Inamadar).

Diffuse acral hyperpigmentation secondary to chikungunya viral fever (coll. Arun Inamadar).



Lentiginous centro-facial hyperpigmentation secondary to chikungunya viral fever (coll. Arun Inamadar).

EPIDEMIOLOGY

Chikungunya is a mosquito-borne viral disease first described during an outbreak in southern Tanzania in 1952. Chikungunya has been identified in nearly 40 countries in Asia, Africa, Europe and also in the Americas. The disease occurs in Africa, Asia and the Indian subcontinent.

All age groups are affected, including newborns.

PATHOPHYSIOLOGY

The proximity of mosquito vector breeding sites to human habitation is a significant risk factor for chikungunya.

Both *Aedes aegypti* and *Aedes albopictus* have been implicated in large outbreaks of chikungunya. Whereas *A. aegypti* is confined within the tropics and sub-tropics, *A. albopictus* also occurs in temperate and even cold temperate regions.

CLINICAL DERMATOLOGICAL PRESENTATION

Some of the cutaneous features are observed during the acute stage of the illness, and others during convalescence or thereafter. Pigmentary changes is the most common cutaneous finding (42%):

- Lentiginous centro-facial eruption are the most frequent signs.
- Diffuse hyperpigmentation of the face and extremities are frequently observed.
- Flagellate hyperpigmentation is rarer.

Maculopapular eruption and intertriginous aphthous-like ulcers are observed in 33% and 21% of cases, respectively

Lesions with significant morbidity are generalized vesiculobullous eruptions (2.75%), found only in infants, lymphedema, and intertriginous aphthous-like ulcers. Exacerbation of existing dermatoses, such as psoriasis, and unmasking of undiagnosed Hansen's disease are observed.

EXTRACUTANEOUS SIGNS

Chikungunya is characterized by an abrupt onset of fever frequently accompanied by joint pain. Other common signs and symptoms include muscle pain, headache, nausea, fatigue and rash. The joint pain is often very debilitating, but usually lasts for a few days or may be prolonged for weeks.

HISTOPATHOLOGY

Lymphocytic vasculopathy is seen.

DIFFERENTIAL DIAGNOSIS

- Dengue fever and any other viral illness with fever and joint pain.

TREATMENT

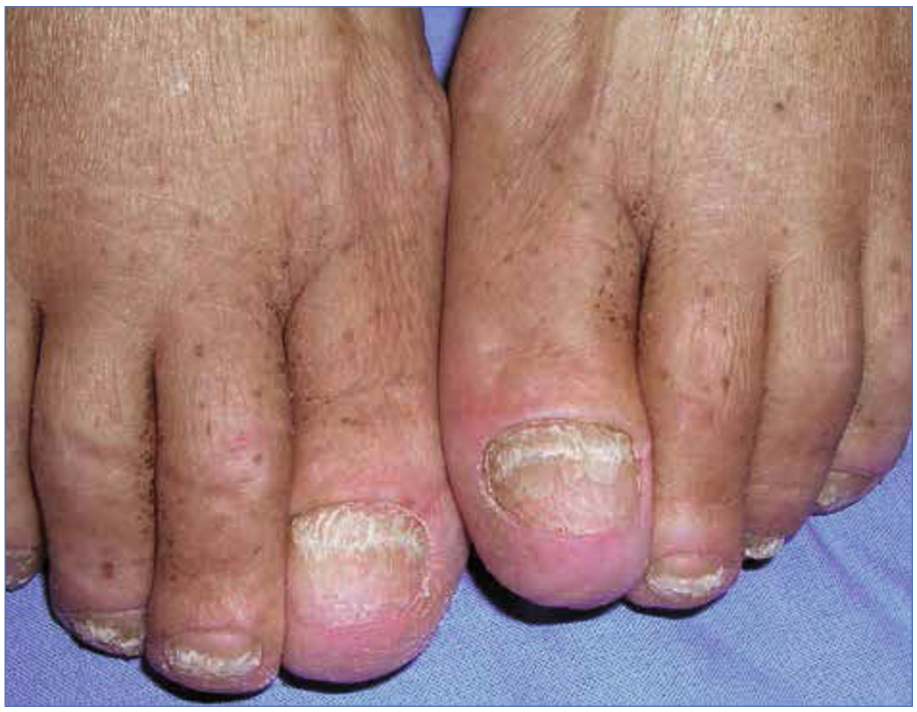
There is no specific antiviral drug treatment for Chikungunya.

Treatment is directed primarily at relieving the symptoms, including the joint pain using antipyretics, optimal analgesics and fluids.

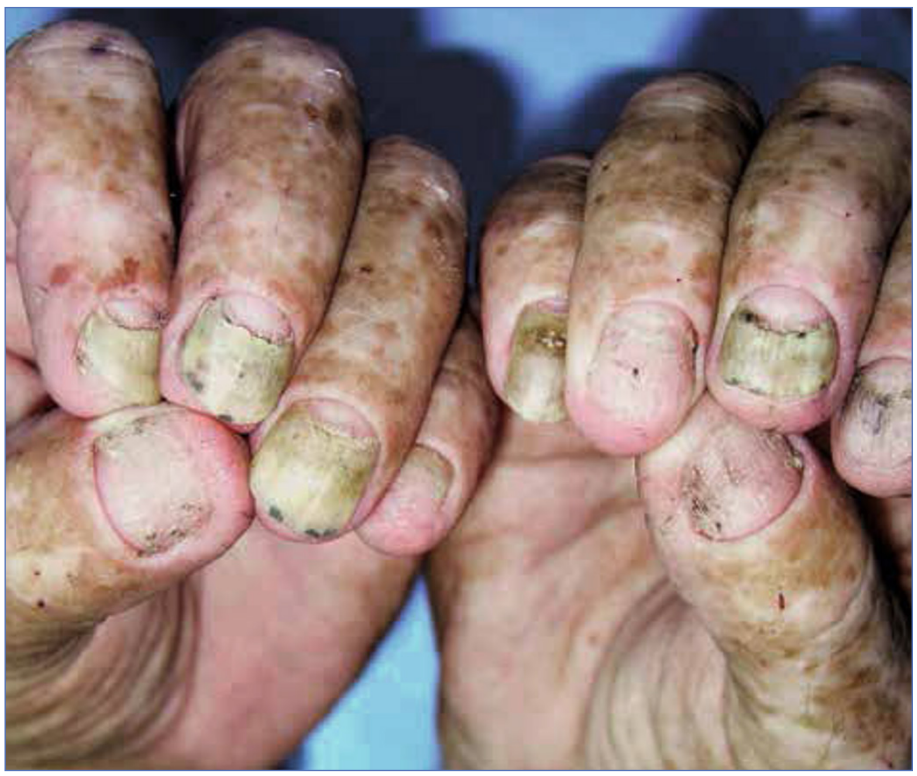
KEY REFERENCES:

- Gibney KB, Fischer M, Prince HE, Kramer LD, St George K, Kosoy OL, Laven JJ, Staples JE. Chikungunya fever in the United States: a fifteen year review of cases. Clin Infect Dis. 2011;52:e121-6.
- World Health Organization. Outbreak and spread of chikungunya. Wkly Epidemiol Rec. 2007;82:409-15.
- Inamadar AC, Palit A, Sampagavi VV, Raghunath S, Deshmukh NS. Cutaneous manifestations of Chikungunya fever: observations made during a recent outbreak in south India. Int J Dermatol. 2008;47:154-9.

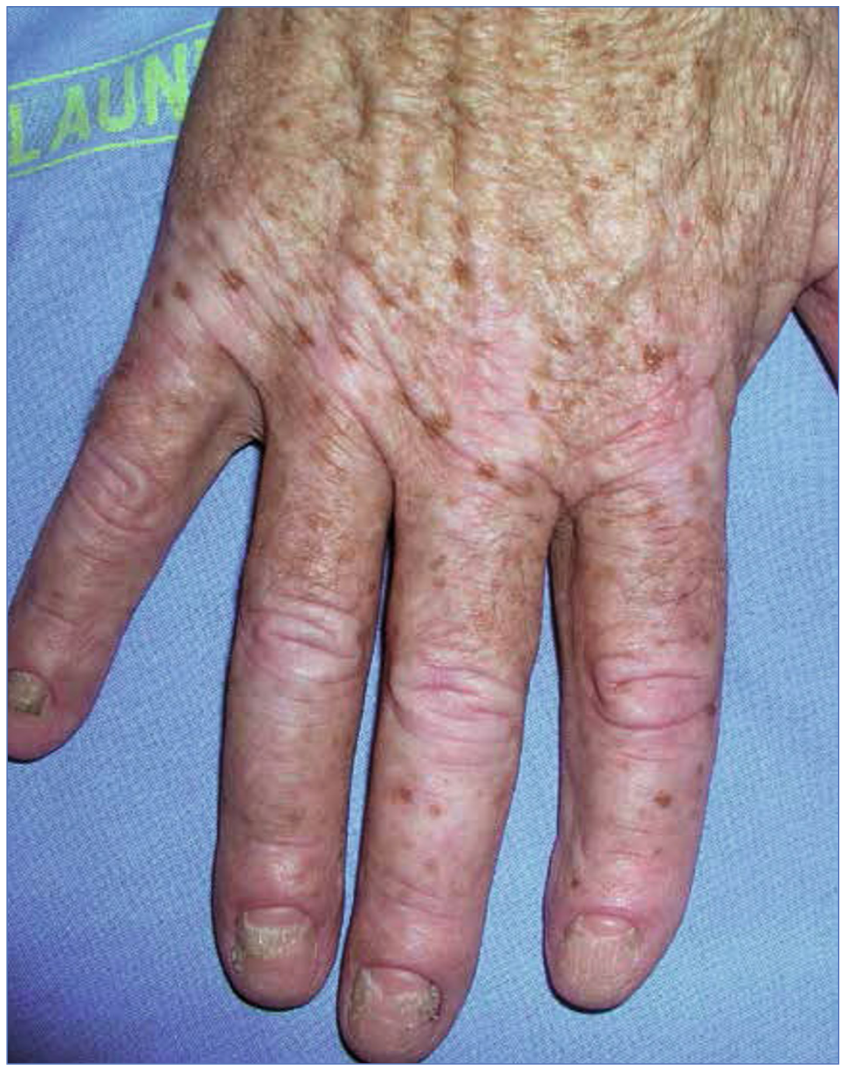
CRONKHITE-CANADA SYNDROME



Light brown macules of the feet associated with dystrophic nails (coll. BM Piraccini).



Marked dystrophic changes of the fingernails associated with hyperpigmented macules (coll. BM Piraccini).



Multiple brown macules of the hands in Cronkhite-Canada syndrome (coll. BM Piraccini).

SYNONYMS

Polyposis, skin pigmentation, alopecia and fingernail changes.

EPIDEMIOLOGY

Rare condition with only 400 cases worldwide reported in literature.
Adults are mostly affected but cases in children have been reported.

PATHOPHYSIOLOGY

Unknown. An autoimmune process is suspected. Some familial cases have been reported.

CLINICAL DERMATOLOGICAL PRESENTATION

Light to dark brown macules and patches.
Localization: Generalized. Palms and soles can be involved first.
Dystrophic changes of the fingernails.
Alopecia.

EXTRACUTANEOUS SIGNS

Gastrointestinal polyposis, diarrhea, weight loss, and abdominal pain.

HISTOPATHOLOGY

Increased melanin in the epidermis. Normal or slight increase of melanocytes. Dermal melanosis can be observed.
Slight thickening of the epidermis with compact hyperkeratosis.

DIFFERENTIAL DIAGNOSIS

- Gardner syndrome.
- Bannayan-Riley-Ruvalcaba syndrome.
- Peutz-Jeghers syndrome.

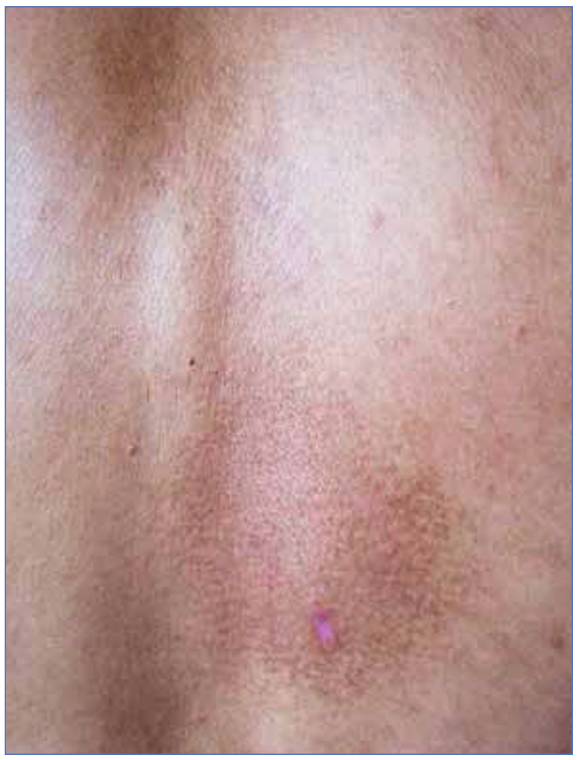
TREATMENT

Nutritional support and corticosteroids.

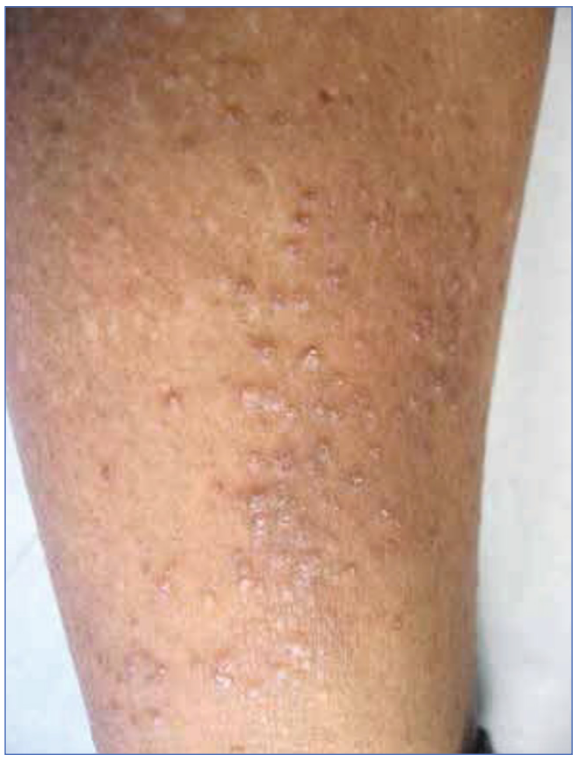
KEY REFERENCES

- Kao KT, Patel JK, Pampati V. Cronkhite-Canada syndrome: a case report and review of literature. Gastroenterol Res Pract. 2009;619378.
- Ortonne JP, Bazex J, Berbis P. Cronkhite-Canada disease. Discussion apropos of a case and study of the pigmentation. Ann Dermatol Venereol. 1985;112:951-8.

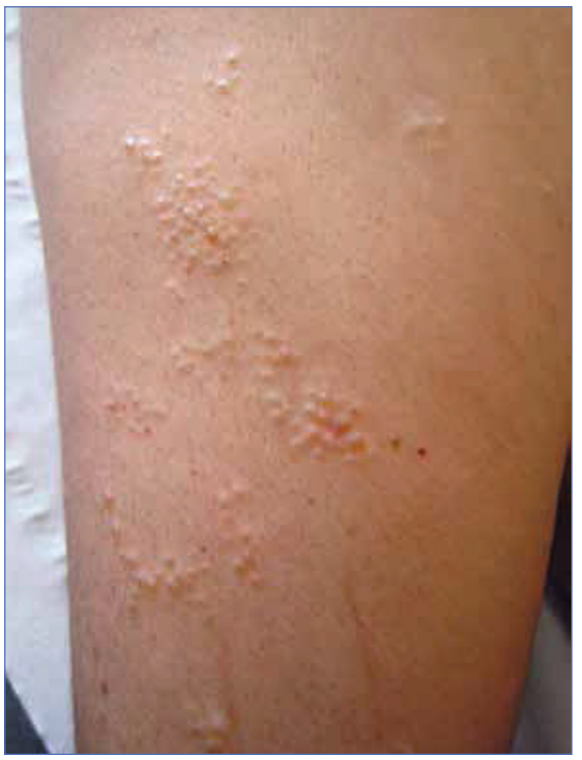
CUTANEOUS AMYLOIDOSIS



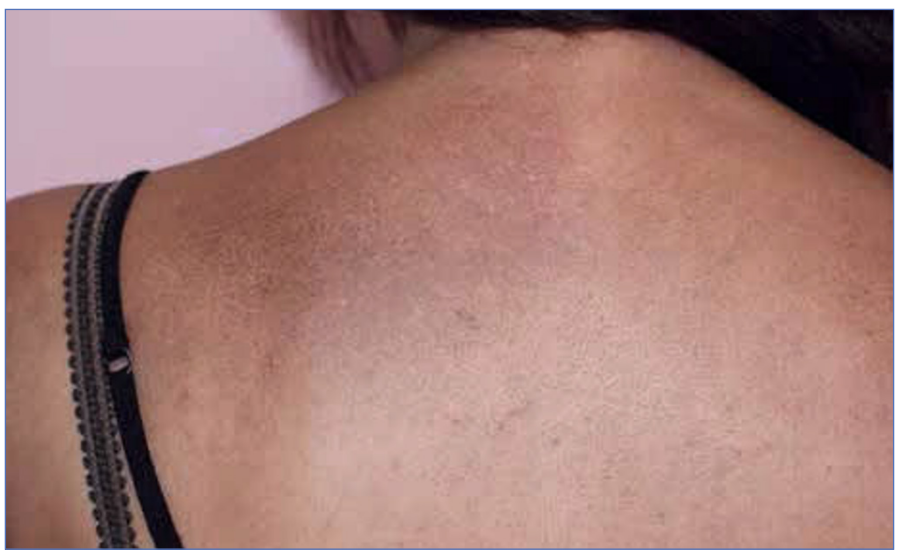
Macular amyloidosis presenting as reddish-brown hyperpigmentation of the back. The coalescence of the small macules leads to poorly defined borders.

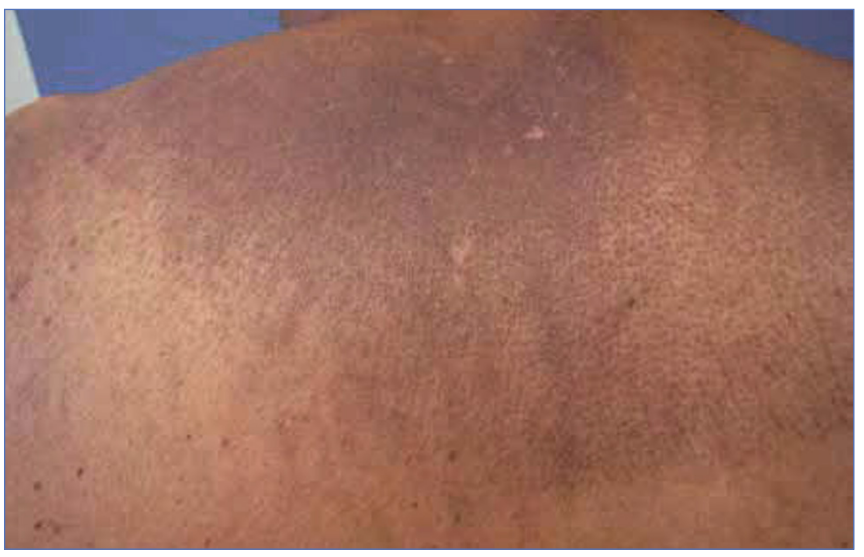


Flesh-colored and mildly keratotic papules of lichen amyloidosis.



Flesh-colored papules in micronodular amyloidosis.





Friction amyloidosis due to the chronic use of a massage glove. Note the predominance of the lesions on the left part of the upper back in right-handed patients.

EPIDEMIOLOGY

Cutaneous amyloidosis is seen throughout the world but is more common among Asians, Middle-Easterners and Latin Americans.
Mostly in adults, but all ages may be affected.
Macular amyloidosis is more frequent in women while lichen amyloidosis is more frequent in men.

PATHOPHYSIOLOGY

Amyloid deposits could come from the transformation of necrotic epidermal cells into amyloid by dermal macrophages. One other explanation could come from a secretion of amyloid by disrupted basal epidermal cells. Those amyloid deposits then bind to antikeratin antibodies.
Constant friction and rubbing with brush or towel may cause macular amyloidosis (also called friction amyloidosis).

CLINICAL DERMATOLOGICAL PRESENTATION

The two most common types of cutaneous amyloidosis are macular and lichen amyloidosis.

- Macular amyloidosis:
  Brown to reddish-brown small macules with poorly defined borders.
  Asymptomatic to severe pruritus.
  Localization: mostly in the inter scapular area. Arms are the second most frequent localization.
- Lichen amyloidosis:
  Flesh-colored papules which coalesce into flat-topped, mildly keratotic plaques.
- Nodular amyloidosis:
  Unique or few flesh-colored or yellowish papules or nodules. Localization: Face, scalp and extremities.
  Constant and severe pruritus.

EXTRACUTANEOUS SIGNS

No sign of systemic amyloidosis.
Localized cutaneous amyloidosis is frequently observed in patients with multiple endocrine neoplasia (MEN) type 2a.

HISTOPATHOLOGY

Amyloid deposits revealed by staining such as Congo red or thioflavin-T, and located within the dermal papillae. In nodular amyloidosis the amyloid deposits extend into the deeper dermis and sometimes in the subcutis.
Presence of dermal melanophages.

DIFFERENTIAL DIAGNOSIS

- Post-inflammatory hyperpigmentation.
- Nevus of Ito, ashy dermatosis for macular amyloidosis.
- Prurigo nodularis, lichen planus and pretibial myxedema for lichen amyloidosis.

TREATMENT

The treatment remains difficult for all forms of cutaneous amyloidosis.
Acitretin, low-dose cyclophosphamide, mechanical and laser assisted dermabrasion, and fractional ablative laser have been reported for treating lichen amyloidosis.
Topical steroids, topical tacrolimus, cyclosporine and Q-switched lasers have been used for macular amyloidosis.
Surgery and CO_2 laser have been proposed for nodular forms.
Antihistamines are usually poorly effective against pruritus, but some successes have been reported with ultraviolet B (UVB).
Avoiding friction is mandatory for treating friction amyloidosis and usually allows a slow and progressive improvement of the lesions.

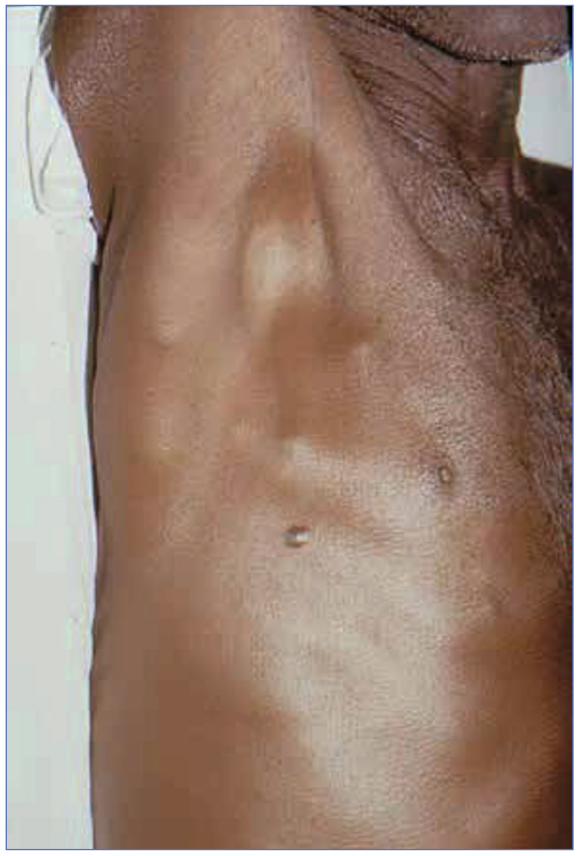
KEY REFERENCES

- Breathnach SM. Amyloid and amyloidosis. J Am Acad Dermatol. 1988;18:1-16.
- Schreml S, Szeimies RM, Vogt T, Landthaler M, Schroeder J, Babilas P. Cutaneous amyloidoses and systemic amyloidoses with cutaneous involvement. Eur J Dermatol. 2010;20:152-60.

DIFFUSE MELANOSIS IN MALIGNANT MELANOMA

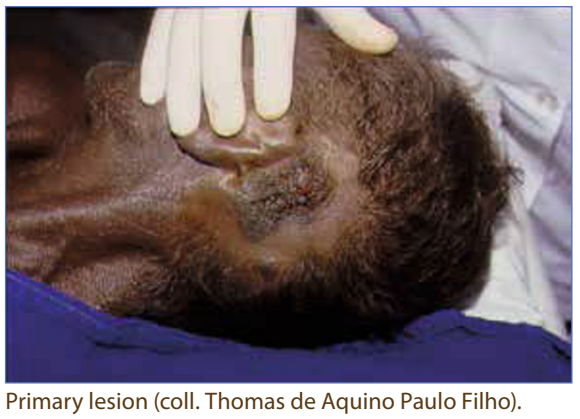
A. Diffuse melanosis associated with metastatic melanoma (coll. Thomas de Aquino Paulo Filho).

B. Same patient 8 months before disease onset (coll. Thomas de Aquino Paulo Filho).

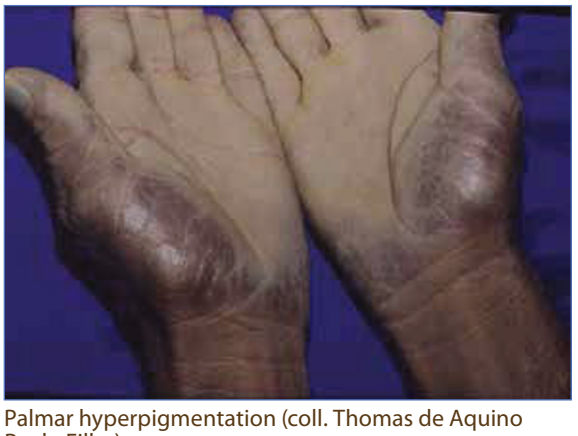


Cutaneous and lymph node metastases (coll. Thomas de Aquino Paulo Filho).

Darkened urines (note at the right control urine of unaffected subject) (coll. Thomas de Aquino Paulo Filho).



Primary lesion (coll. Thomas de Aquino Paulo Filho).



Palmar hyperpigmentation (coll. Thomas de Aquino Paulo Filho).

EPIDEMIOLOGY
Exceptional occurrence in patients with metastatic melanoma.

PATHOPHYSIOLOGY
Excessive production of alpha-melanocyte stimulating hormone (αMSH) (from the tumor) in combination with hepatocyte growth factor (HGF) and endothelin-1 (ET-1) (released from distinct site of metastasis) is suspected. This would induce a synergistic response of normal and malignant melanocytes resulting in enhanced proliferation, melanogenesis, and motility.

CLINICAL DERMATOLOGICAL PRESENTATION
Asymptomatic progressive slate-blue hyperpigmentation
Localization: entire skin. Sclera can also be affected.

EXTRACUTANEOUS SIGNS
Darkened urine due to melanuria.

HISTOPATHOLOGY
Mostly melanophages associated with an increased melanin contained in keratinocytes and proliferation of normal melanocytes and melanoma cells.

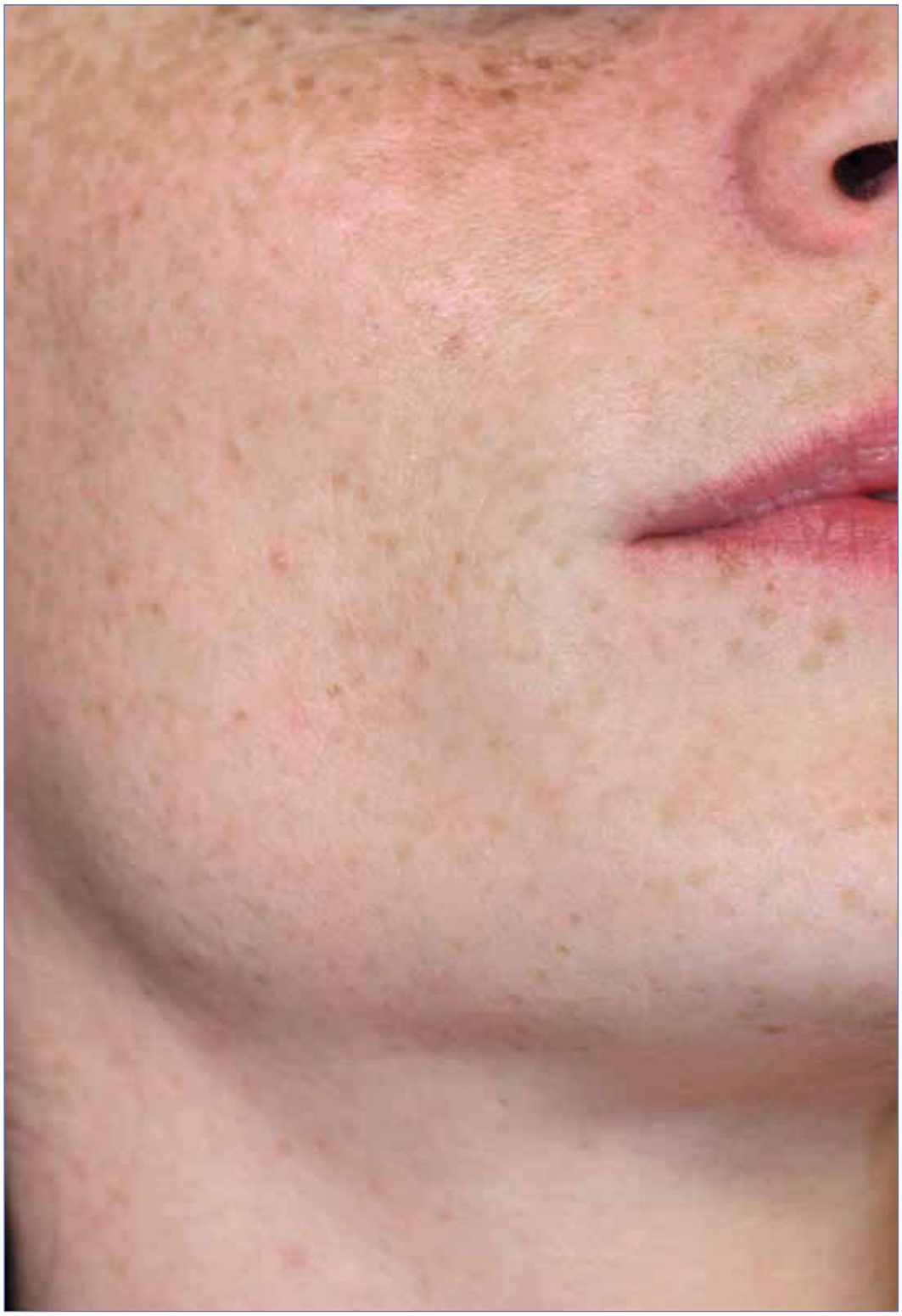
DIFFERENTIAL DIAGNOSIS
- Addison's disease.
- Hemochromatosis.
- Argyria.

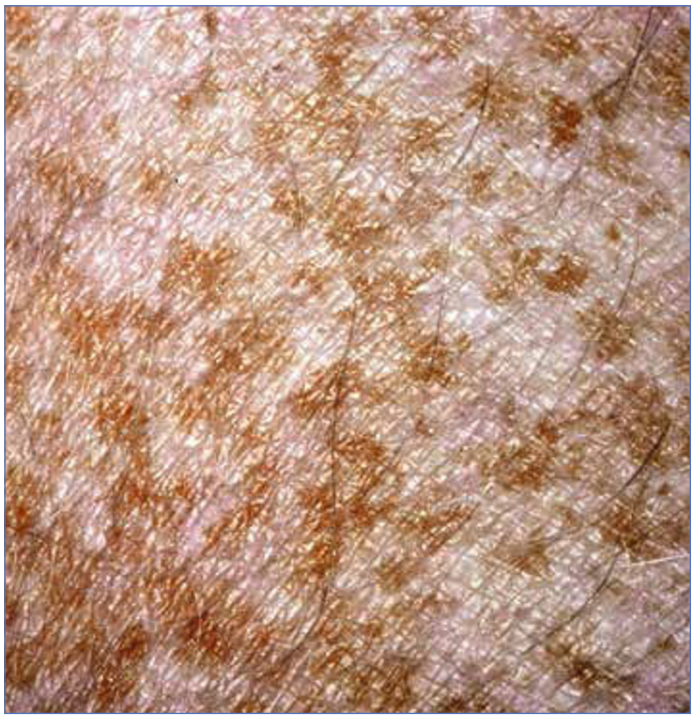
TREATMENT
None reported.
Effective treatment of the metastatic disease should improve the condition.

KEY REFERENCES

- Bork K, Korting GW, Rumpelt HJ. Diffuse melanosis in malignant melanoma. Hautarzt. 1977;28:463-8.
- Paulo Filho Tde A, da Trindade Neto PB, Reis JC, Bartelt L, da Costa SA. Diffuse cutaneous melanosis in malignant melanoma. Dermatol Online J. 2007;13:9.

EPHELIDES





Ephelides in close-up.

Multiple ephelides on the face.
Note the increased proportion on the malar area that is more exposed to the sun and the absence of spots beneath the chin.
While lentigos can affect the lips, note that ephelides spare them.

SYNONYMS
Freckles.

GENETICS
Ephelides are genetic in origin following an autosomal dominant pattern. A relationship between melanocortin-1 receptor (MC1-R) gene variants and ephelides has been demonstrated. Carriers of one or two MC1-R gene variants had a three and eleven times increased risk of developing ephelides, respectively.

EPIDEMIOLOGY
Ephelides are much more frequent in red- or blond-haired and fair skinned individuals.
Boys and girls are equally affected.

PATHOPHYSIOLOGY
Ephelides are strongly associated with the MC1-R gene. The MC1-R is the receptor of α-MSH that activates the cyclic adenosine monophosphate (cAMP) pathway, which is the main pathway of melanogenesis. Decreased activity of this pathway due to allelic variations in the MC1-R gene, promotes the production of pheomelanins (brown-red pigments that promote oxidative stress) instead of eumelanins (dark brown pigment with photoprotective properties).

CLINICAL DERMATOLOGICAL PRESENTATION
Light brown and uniform macules from 1 to 5 mm.
Asymptomatic.
Onset may be at any time but it often early in children with an increased number into young adulthood and a progressive decrease in older ages.
Localization: Only on sun-exposed area. Mucous membrane, palms and soles are spared.

HISTOPATHOLOGY
Increased pigmentation in the basal layers of the epidermis. Large numbers of mature melanosomes and dendritic melanocytes are present in dark-skinned individuals. The normal number of melanocytes and the absence of elongations of the rete ridges contrast with the histological features observed in solar lentigines.

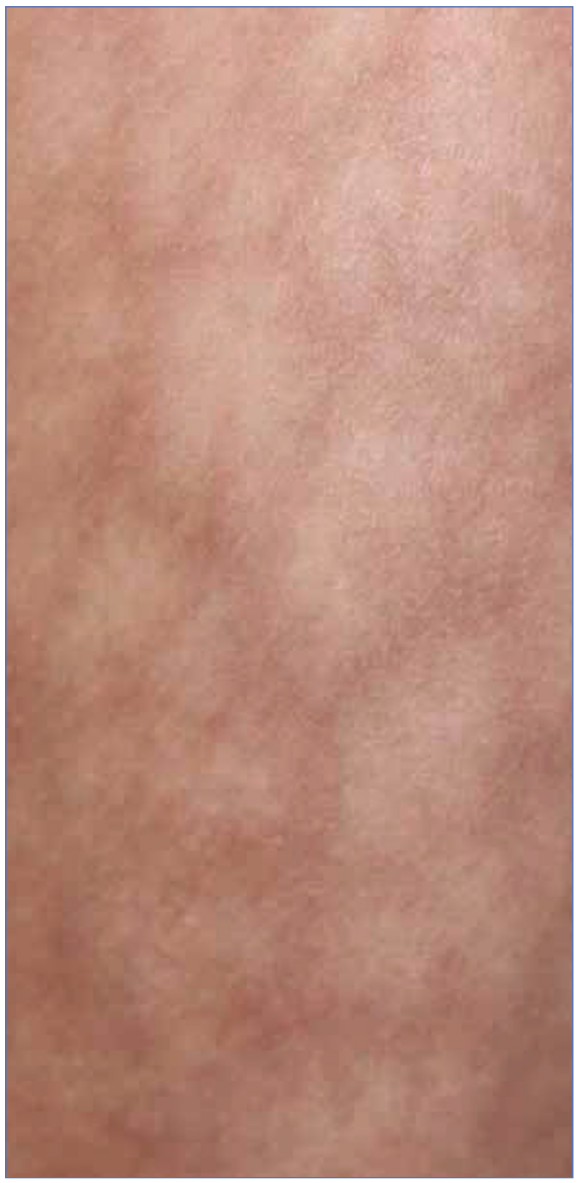
DIFFERENTIAL DIAGNOSIS
- Lentigines.

TREATMENT
Sun avoidance with protective clothing and sunscreens. For cosmetic reasons topical depigmenting creams, peeling, cryotherapy and lasers (Q-switched 532 nm is preferable) can be used. Relapses are constant and strongly limit the interest of such treatments.

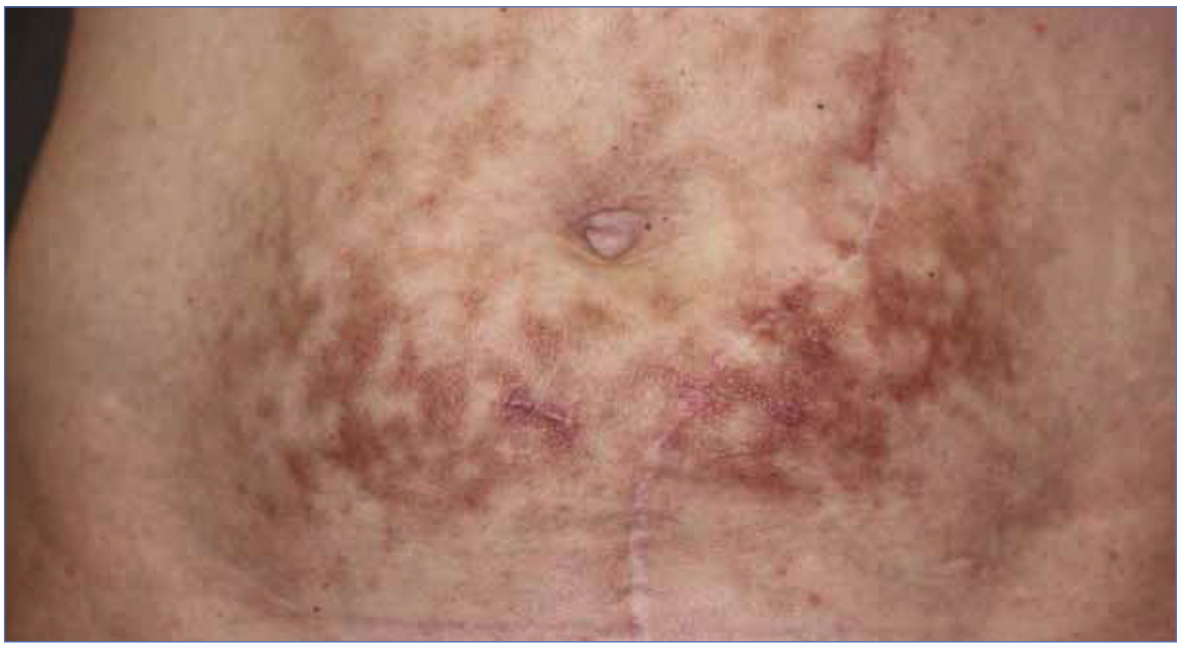
KEY REFERENCE

- Bastiaens M, ter Huurne J, Gruis N, Bergman W, Westendorp R, Vermeer BJ, Bouwes Bavinck JN. The melanocortin-1-receptor gene is the major freckle gene. Hum Mol Genet. 2001;10:1701-8.

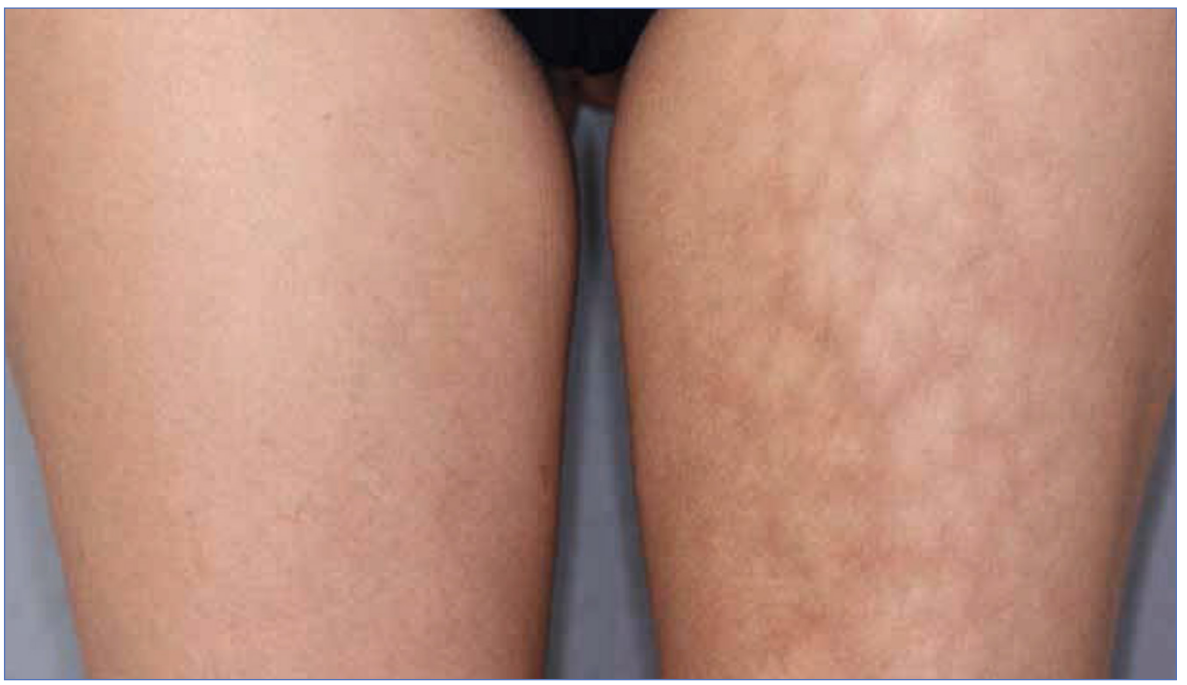
ERYTHEMA AB IGNE



Typical reticulated hyperpigmented pattern.



Erythema ab igne due to the use of heat pads to relieve abdominal pain. Erythema is still present and has come to be associated with the hyper-pigmentation.



Erythema ab igne of the thigh due to the chronic use of a laptop always put down on the same thigh.

SYNONYMS

Ephelis ab igne, erythema a colore, ephelis ignealis, erythema coloricum, livedo reticularis a colore, toasted skin syndrome and fire stains.

EPIDEMIOLOGY

Erythema ab igne (EAI) used to be a rare condition that was mostly observed in patients using heating pads or falling asleep in front of a stove. The use of localized heat to relieve back pain and the use of laptops are responsible for the increased frequency.
Affects all races and skin types.
More frequent in adults and in women.

PATHOPHYSIOLOGY

EAI is due to a long-term exposure to heat below the threshold for thermal burn leading to a cutaneous hyperthermia around 45°C. The pathogenesis leading to the hyperpigmentation is poorly understood.

CLINICAL DERMATOLOGICAL PRESENTATION

Macular erythema with reticulated pattern at early stages. The hyperpigmentation may take up to 3 weeks to appear after the heat exposure.
Brown macular hyperpigmentation with a very suggestive reticular ('livedoid') pattern localized in the area exposed to the heat.
Bullous reaction, and poikiloderma with epidermal atrophy, telangiectasia and hyperkeratosis can be observed in chronic cases.
Itching or burning can be reported.
Localization: Back and thigh are the most frequent localization.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin in the epidermis with melanophages and hemosiderin in the dermis.
Atrophy of the Malpighian layer, with dermal vasodilatation.
Epidermal dysplasia and epidermal vacuolization with elastosis can be observed in advanced cases.

DIFFERENTIAL DIAGNOSIS

- Livedo reticularis.
- Cutis marmorata.

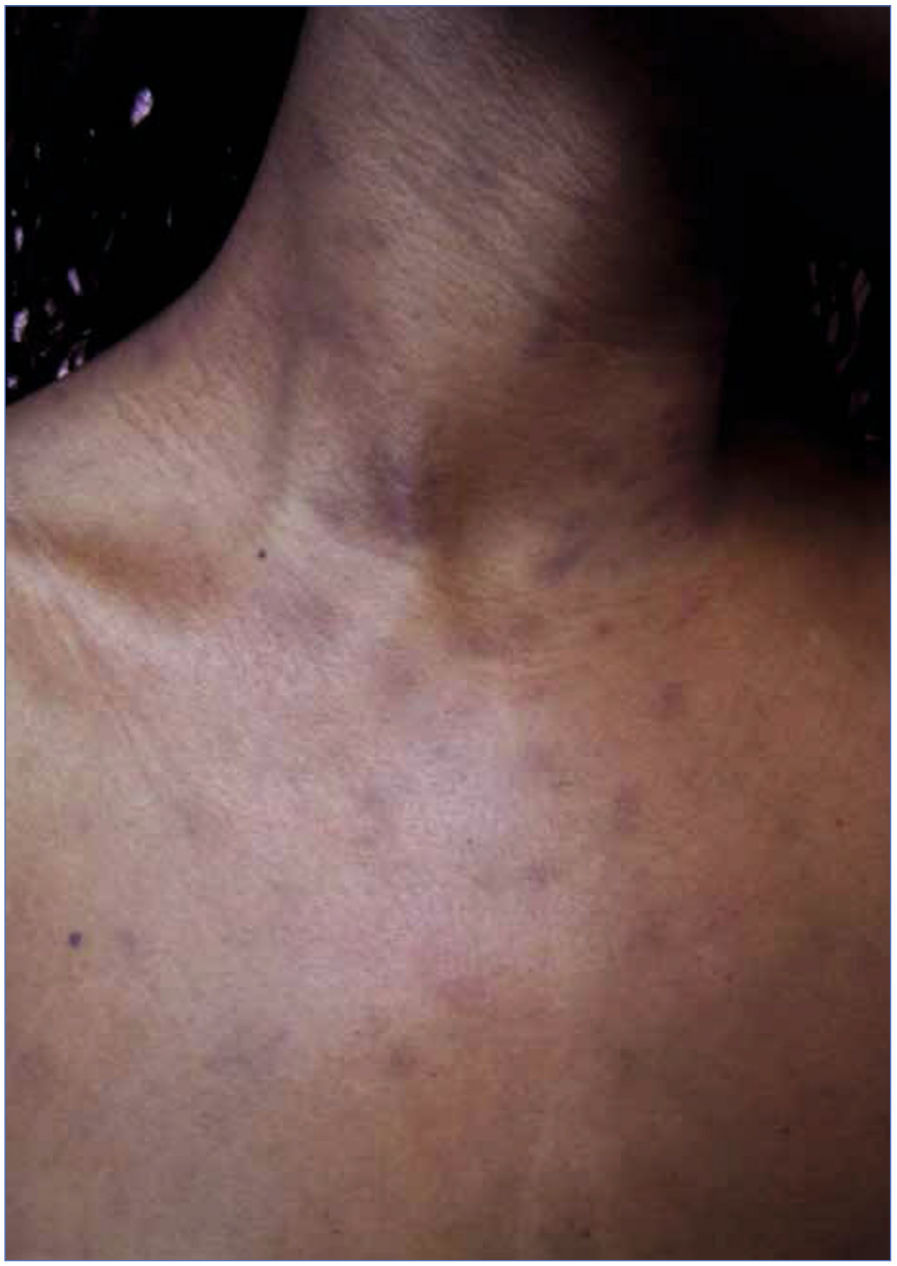
TREATMENT

Removal of the offending heating device.
The possible development of cutaneous squamous cell carcinoma or Merkel cell carcinoma require a dermatologic follow-up.
Topical tretinoin, 5-fluorouracil cream, and more recently Q-switched laser approaches have been reported to improve the condition.

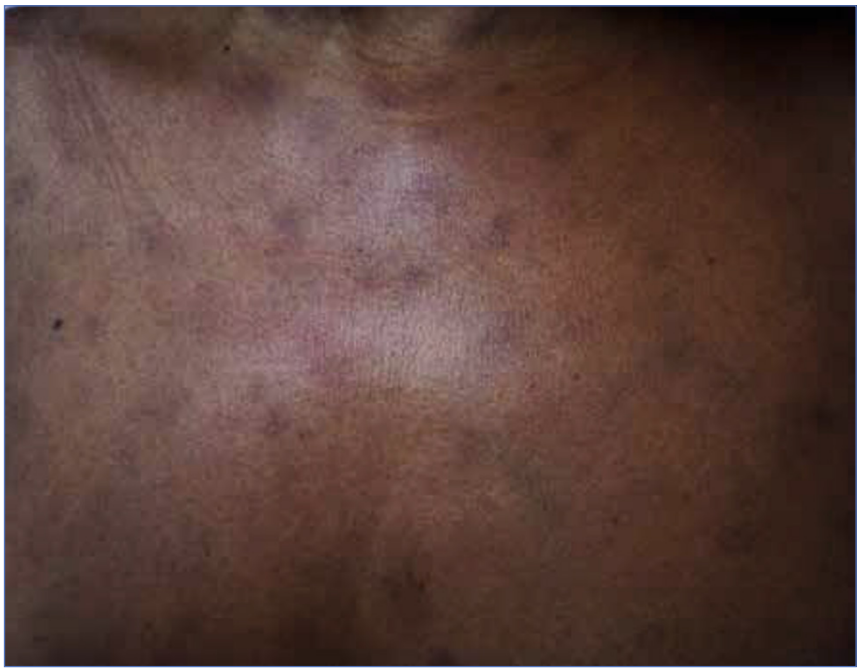
KEY REFERENCES

- Sahl WJ Jr, Taira JW. Erythema ab igne: treatment with 5-fluorouracil cream. J Am Acad Dermatol. 1992;27:109-10.
- Cho S, Jung JY, Lee JH. Erythema ab igne successfully treated using 1,064-nm Q-switched neodymium-doped yttrium aluminum garnet laser with low fluence. Dermatol Surg. 2011;37:551-3.

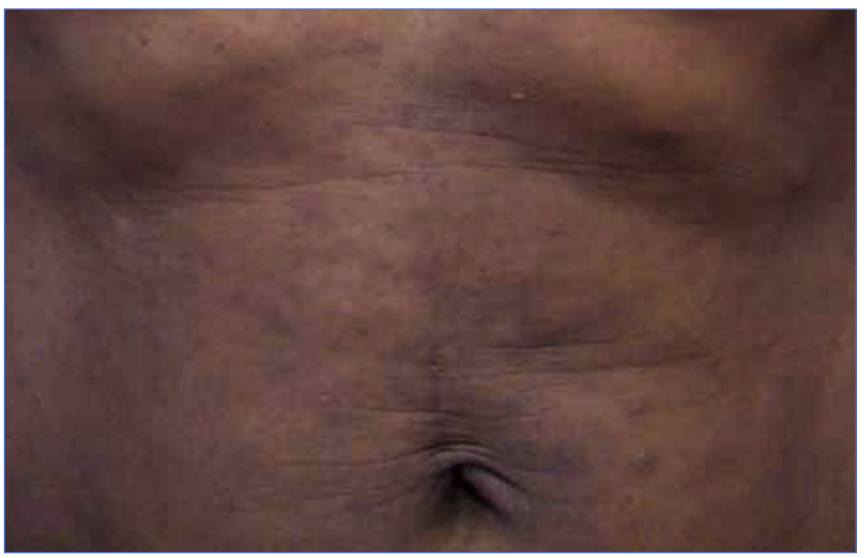
ERYTHEMA DYSCHROMICUM PERSTANS



Brown-blue macules of the neck and the upper trunk.



Erythema dyschromicum perstans of the trunk.



Diffuse eruption spreading to the abdomen.

SYNONYMS
Los Cenicientos (ashen ones), ashy dermatosis.

EPIDEMIOLOGY
Mostly reported in intermediate skin types (Latin America) but can be observed worldwide and in all skin types.
Slightly more frequent in females.
All ages can be affected but most cases are observed in children and young adults.

PATHOPHYSIOLOGY
Unknown.
Could be a variant (with subclinical inflammation of lichen planus pigmentosus).

CLINICAL DERMATOLOGICAL PRESENTATION
Ashy hyperpigmented macules (blue-brown to gray color).
Asymptomatic.
Usually no inflammation, but a slight erythema can be observed at the edges of the lesions.
Localization: symmetrical distribution on the trunk, the neck and the face. Limbs can be affected but palms, soles and mucous membrane are spared.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Increased melanin in the epidermis and melanophages in the dermis.
Atrophic epidermis with spongiosis, perivascular lymphohistiocytic infiltrate, and lymphocytic exocytosis in early lesions.

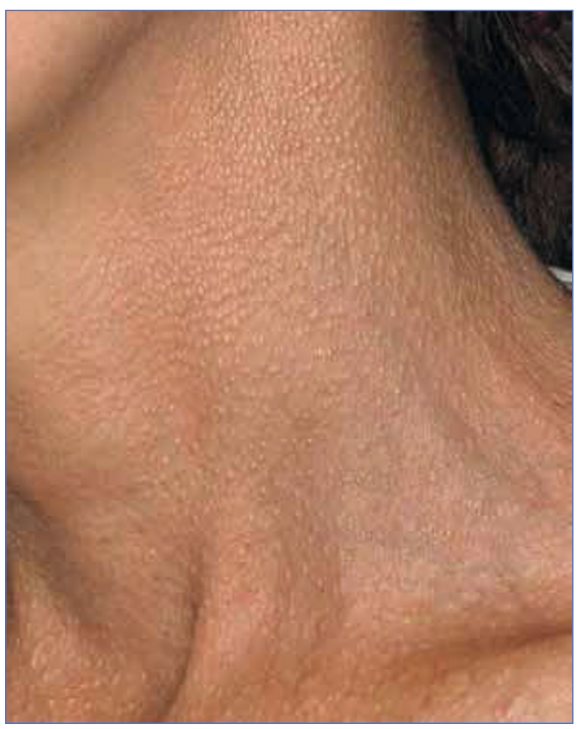
DIFFERENTIAL DIAGNOSIS
- Lichen planus pigmentosus.
- Idiopathic eruptive macular pigmentation.
- Post-inflammatory hyperpigmentation.
- Fixed-drug eruption.
- Mastocytosis.

TREATMENT
None is truly effective.
Clofazimine at 100 mg/d with progressive decrease after 1 month can be useful in early stages.
Topical steroid might be useful if inflammation is observed.
Sun protection is usually advised.

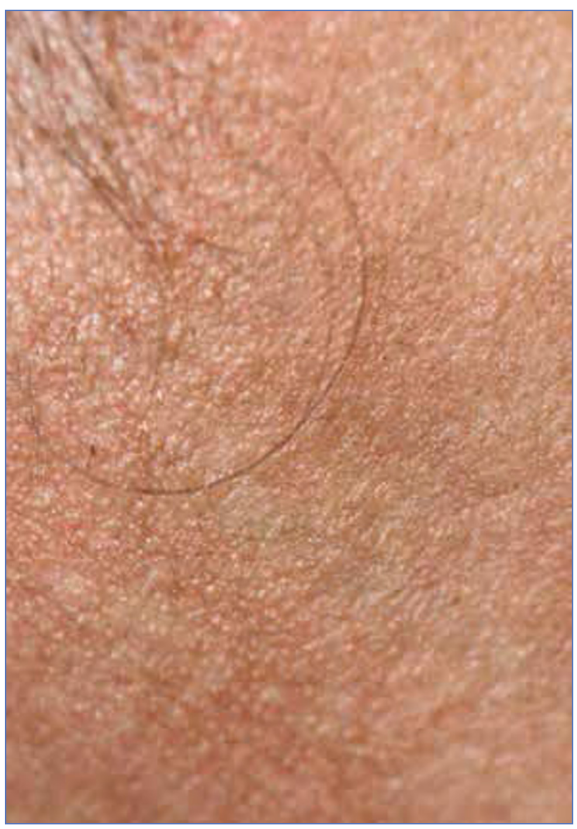
KEY REFERENCES

- Osswald SS, Proffer LH, Sartori CR. Erythema dyschromicum perstans: a case report and review. Cutis. 2001;68:25-8.
- Baranda L, Torres-Alvarez B, Cortes-Franco R, Moncada B, Portales-Perez DP, Gonzalez-Amaro R. Involvement of cell adhesion and activation molecules in the pathogenesis of erythema dyschromicum perstans (ashy dermatitis). The effect of clofazimine therapy. Arch Dermatol. 1997;133:325-9.
- Piquero-Martín J, Pérez-Alfonzo R, Abrusci V, Briceño L, Gross A, Mosca W, Tapia F, Convit J. Clinical trial with clofazimine for treating erythema dyschromicum perstans. Evaluation of cell-mediated immunity. Int J Dermatol. 1989;28:198-200.

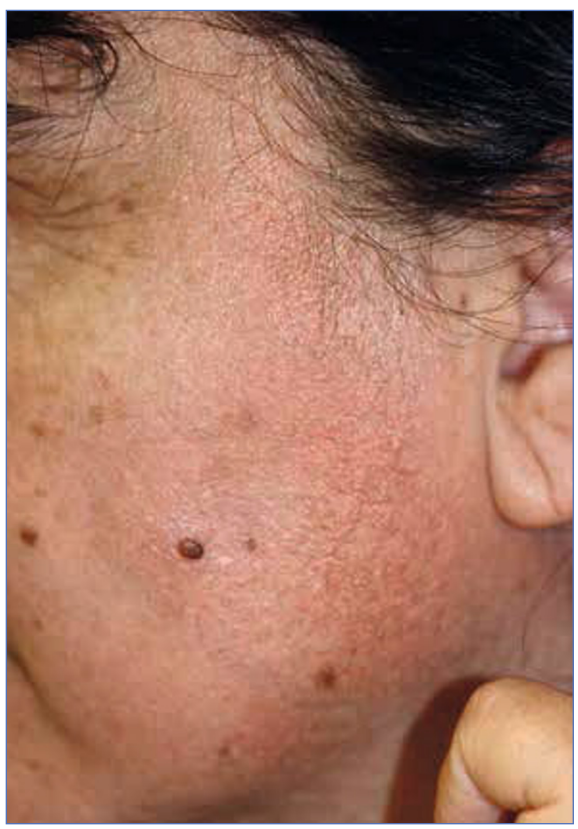
ERYTHROMELANOSIS FOLLICULARIS FACIEI ET COLLI



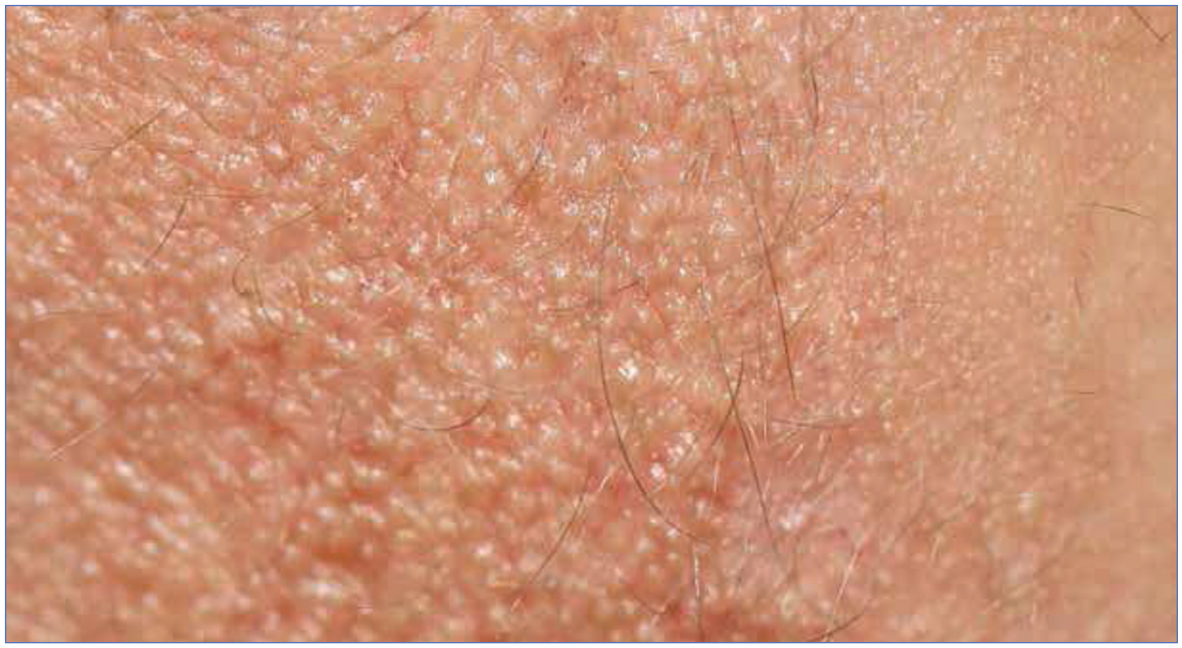
Erythromelanosis follicularis faciei and colli affecting the neck.



Erythromelanosis follicularis faciei and colli. The hyperpigmentation is more marked here.



Erythromelanosis follicularis faciei and colli affecting the face of a woman.



Close-up of the lesions.
Note the association of erythema, mild pigmentation and the multiple follicular papules.

EPIDEMIOLOGY

Sporadic with only a few cases reported (only one familial case observed).
Onset at puberty.
Mostly young and middle-aged men are affected but also seen in adult females.

PATHOPHYSIOLOGY

Unknown.

CLINICAL DERMATOLOGICAL PRESENTATION

Triad of erythema, hyperpigmentation and follicular papules.
Asymptomatic.
Localization: pre-auricular area then progressive spreading to the cheeks and neck. In most cases bilateral and symmetric disposition.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Hyperpigmentation of the basal layers of the epidermis.
Perifollicular parakeratosis.
Mild to moderate superficial lymphohistiocytic infiltrate of the dermis with vascular ectasia.

DIFFERENTIAL DIAGNOSIS

- Ulerythema ophyrogenes (the lack of atrophy and scarring in erythromelanosis follicularis faciei et colli allows to differentiate this entity to ulerythema ophyrogenes).
- Riehl melanosis.
- Melasma.
- Poïkiloderma of Civatte.
- Erythrose peribuccale pigmentaire of Brocq.
- Becker nevus.

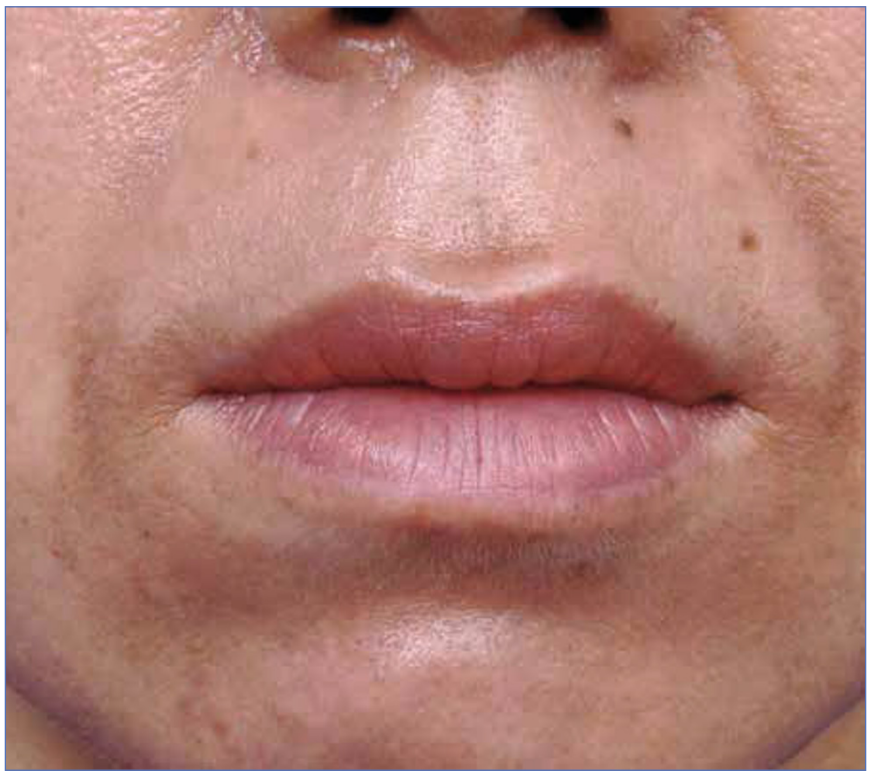
TREATMENT

Topical retinoic acid or topical tocalcitol.
Isotretinoin at 1 mg/d and laser have been proposed.
Anecdotic successes have been reported with intense pulse light and pulsed dye laser.

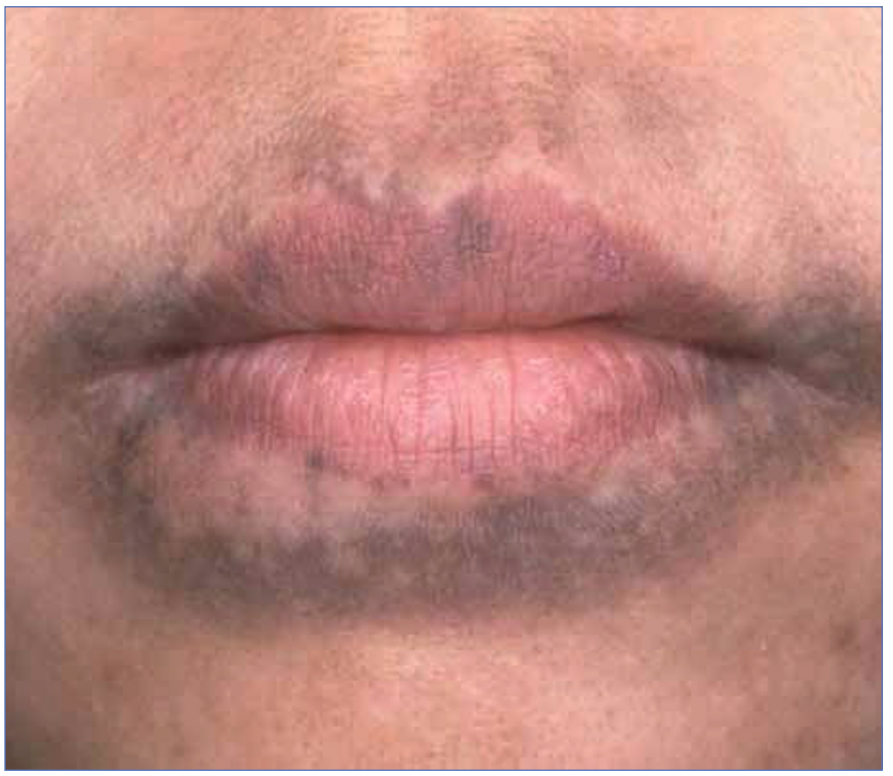
KEY REFERENCES

- Sardana K, Relhan V, Garg V, Khurana N. An observational analysis of erythromelanosis follicularis faciei et colli. Clin Exp Dermatol. 2008;33:333-6.
- Yañez S, Velasco JA, González MP. Familial erythromelanosis follicularis faciei et colli-an autosomal recessive mode of inheritance. Clin Exp Dermatol. 1993;18:283-5.

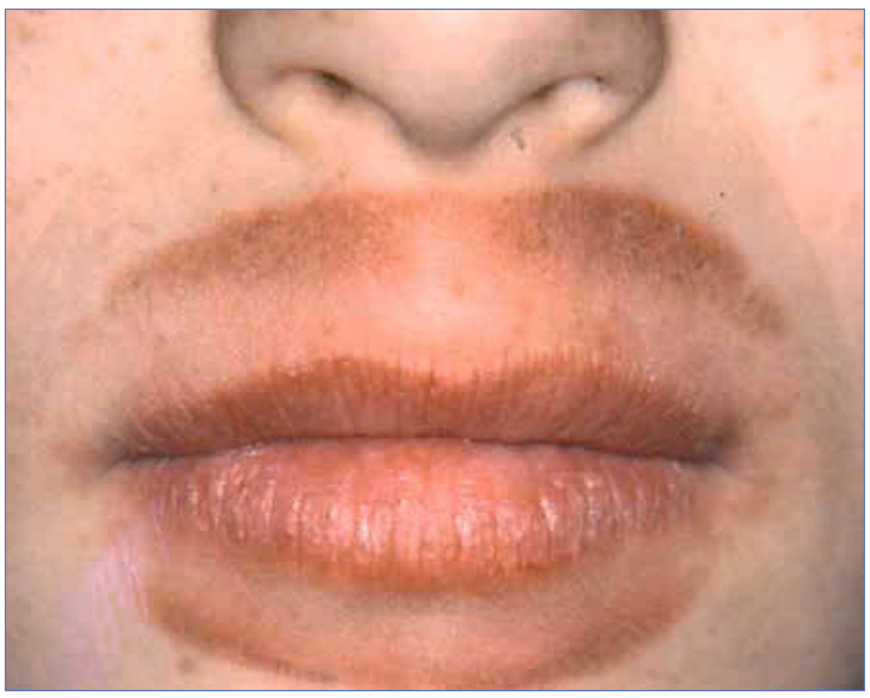
ERYTHROSE PÉRIBUCCALE OF BROCQ



Erythrose péribuccale of brocq (coll. Hee Young Kang).



Erythrose péribuccale of Brocq (coll. Hee Young Kang).



Brown hyperpigmentation restricted to the peri oral area suggestive of érythrose péribuccale of brocq.

SYNONYMS

Erythrosis pigmenta faciei, erythrosis pigmentosa peribuccalis, melanosis perioralis et peribucalis.

EPIDEMIOLOGY

Only a few cases have been reported.
Mostly observed in women.

PATHOPHYSIOLOGY

Unknown. Chronic sun exposure and fragrances are suspected to play a role in the occurrence of this affliction.
Clinical dermatological presentation.
Brown pigmentation often with erythema at early stages then gray-bown pigmentation.
Increased vascularization with telangiectasia may be seen on the hyperpigmented areas.
Scaling and loss of vellus hair can be observed.
Localization: central face and mostly perioral with a thin unaffected line at the border of the lips.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin in the basal layers of the epidermis and melanophages in the dermis.
Vascular dilatation and perivascular lymphohistiocytic infiltrate in the dermis.

DIFFERENTIAL DIAGNOSIS

- Post inflammatory hyperpigmentation.
- Perioral dermatitis.
- Melasma.

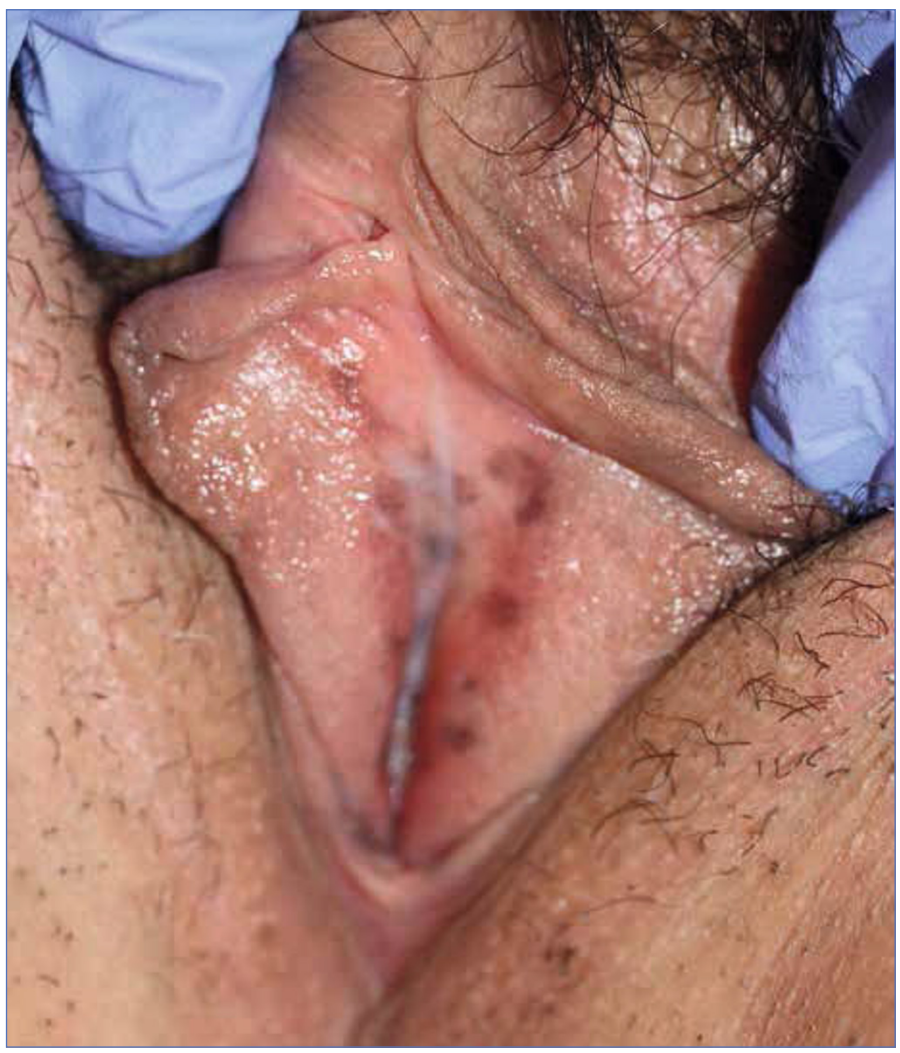
TREATMENT

Sun protection and avoidance of cosmetics and fragrances.
Blanching creams are rarely effective.

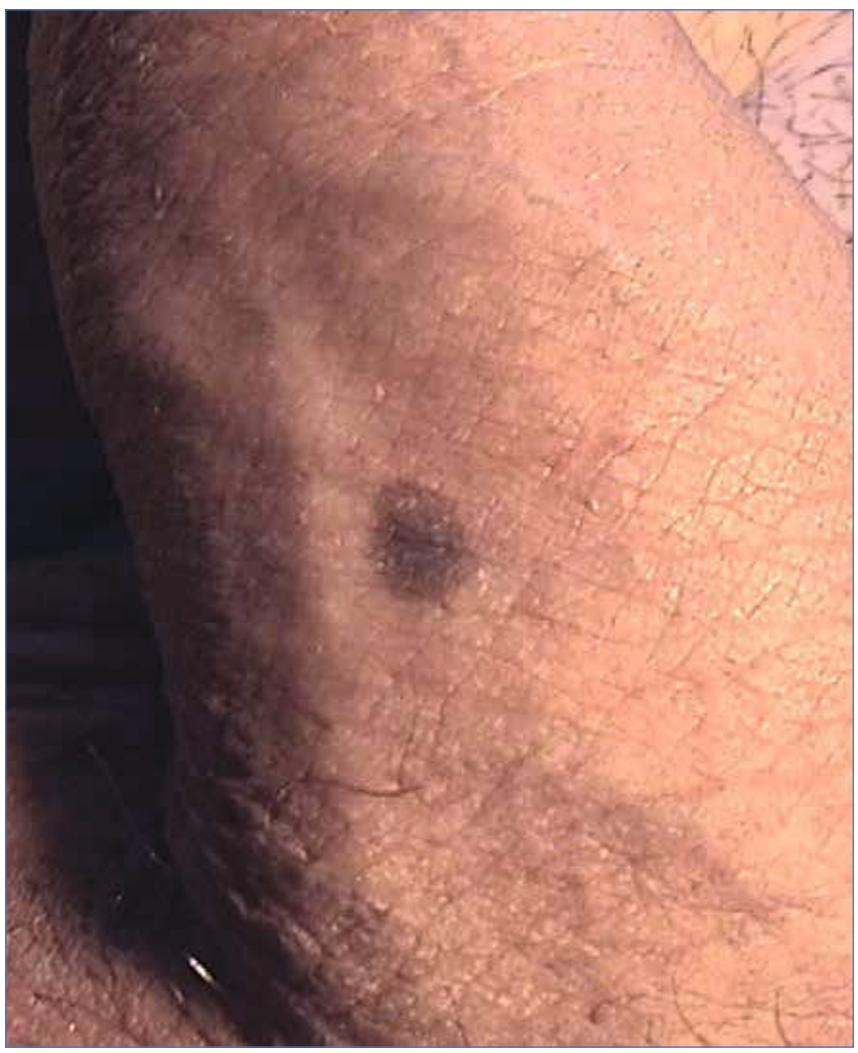
KEY REFERENCES

- Cohen EL. Erythrosis pigmentosa peribuccalis. Br J Dermatol Syph. 1948;60:203-11.
- Brocq L. L'erythrose pigmentée peri-buccale. Presse Med 1923;13:728-729.

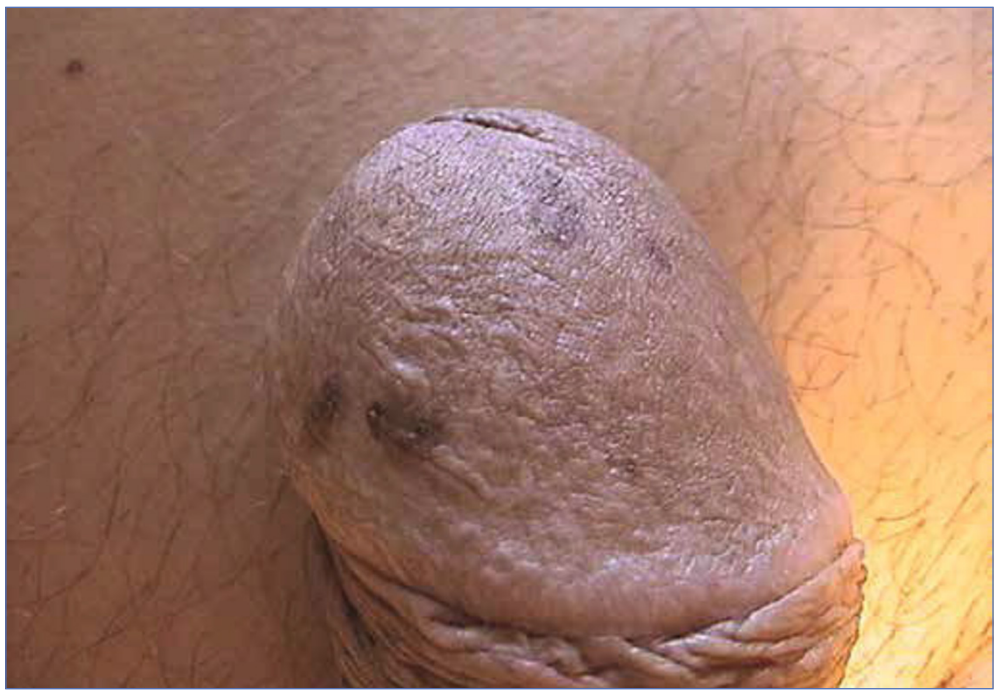
GENITAL MELANOSIS



Genital melanosis of the vulva.



Homogeneous hyperpigmented macule in genital melanosis.



Genital melanosis of the penis.

SYNOMYMS
Vulvar melanosis, penile melanosis, penile lentigo.

EPIDEMIOLOGY
Common lesions observed in 3 to 7% of the population.
Both vulvar and penile lesions can be observed.

CLINICAL DERMATOLOGICAL PRESENTATION
Hyperpigmented macules.
The lesions are asymptomatic.
Localization: penis, scrotum, vulva, vagina.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Epithelial hyperplasia, elongation of epidermal ridges, and basal keratinocyte hyperpigmentation with few melanophages.
An epidermal melanocytic proliferation, without nest formation, can be noted.

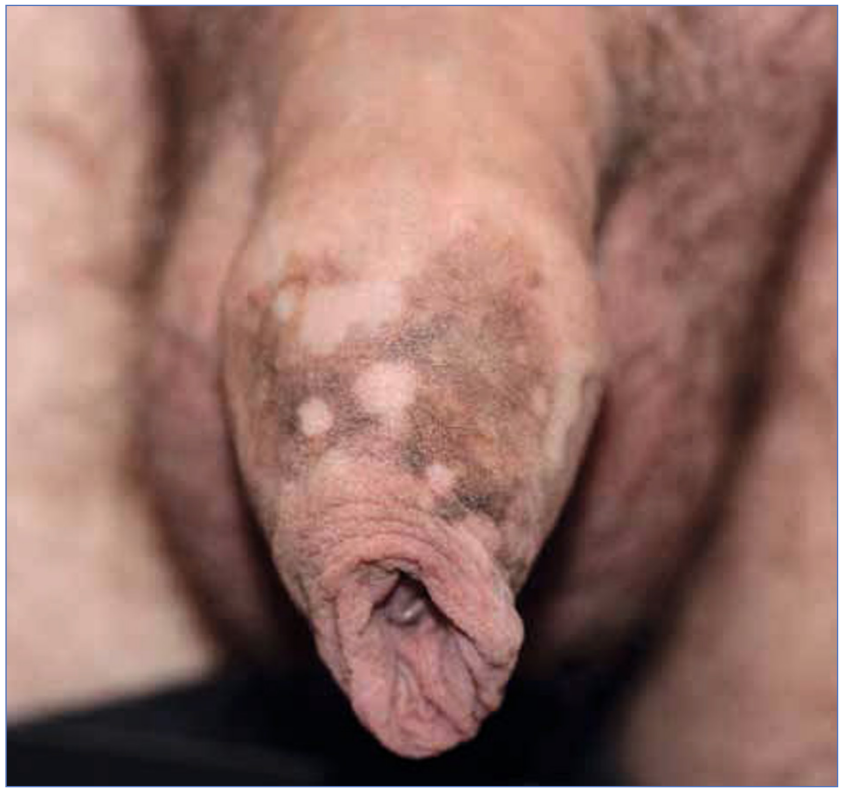
DIFFERENTIAL DIAGNOSIS
- Laugier disease and other genital lentiginosis.
- Genital nevus.
- Melanoma.

TREATMENT
None required. Q-switched lasers are effective.

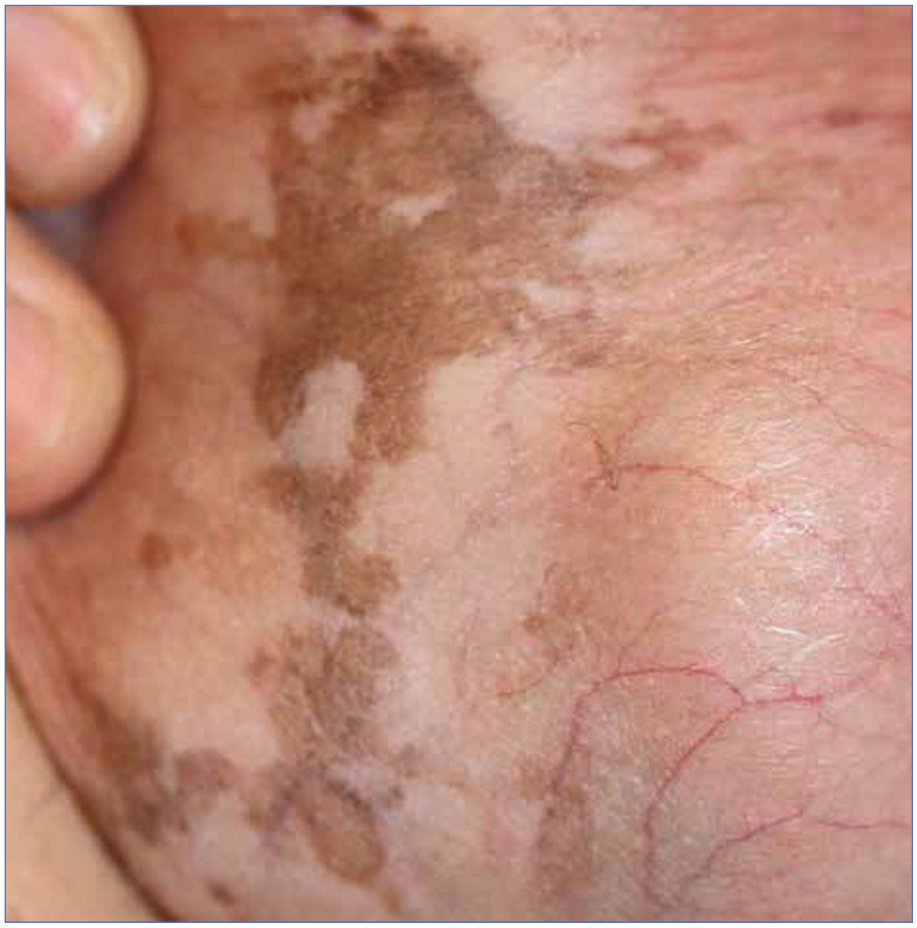
KEY REFERENCES

- Barnhill RL, Albert LS, Shama SK et al. Genital lentiginosis: a clinical and histopathologic study. J Am Acad Dermatol 1990; 22:453-60.
- Breathnach AS, Balus L, Amantea A. Penile lentiginosis. An ultrastructural study. Pigment Cell Res 1992; 5:404-13.

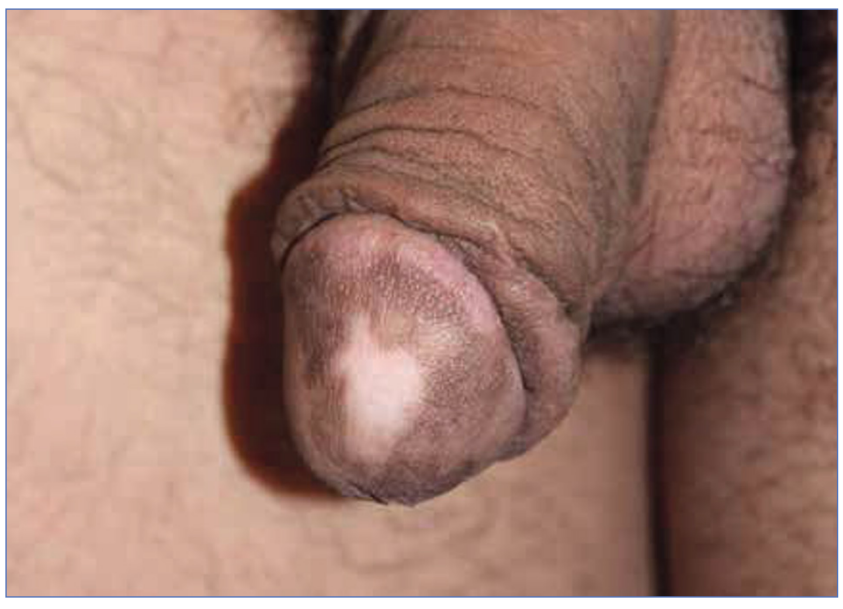
GENITAL MELANOSIS ASSOCIATED WITH LOCALIZED DEPIGMENTATION



Genital melanosis of the penis with white depigmented macules.



Hyperpigmentation of the scrotum with vitiligo-like depigmentation. In fair skin the depigmentation is better visualized with Wood's lamp.



Genital melanosis of the penis associated with localized depigmentation.
Note that some lesions are depigmented while recent ones are only hypopigmented.

EPIDEMIOLOGY

Only a few cases have been reported but the condition is probably not so uncommon.
The condition has been only reported in men so far.
The onset of pigmentation ranges from weeks after birth to 50 years of age. The depigmented areas appear years after the occurrence of the reticulate hyperpigmentation.

PATHOPHYSIOLOGY

Still unclear but the condition appears to be a genital melanosis followed by a depigmentation restricted to the previously hyperpigmented lesions. Although no vitiligo lesions have been reported so far outside the hyperpigmented genital area, this condition appears to be secondary to an autoimmune process restricted to the melanocytes of the genital melanosis. This process appears to be closely related to the one observed in halo nevus.

CLINICAL DERMATOLOGICAL PRESENTATION

Acquired hyperpigmentation with reticular pattern.
Color from light to dark brown.
Depigmented vitiligo-like lesions secondary occur and remain strictly limited to the previously hyperpigmented lesions.
The lesions are asymptomatic.
Localization: penis, scrotum.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Epithelial hyperplasia, elongation of epidermal ridges, and basal keratinocyte hyperpigmentation with few melanophages. No evidence of melanocytic proliferation. Absence of melanocytes in the depigmented area. Localized lymphocytic infiltrate around melanocyte can be observed in early stages of depigmented lesions.

DIFFERENTIAL DIAGNOSIS

- Trichrome vitiligo.
- Melanoma.
- Laugier disease.
- Dowling Degos disease.

TREATMENT

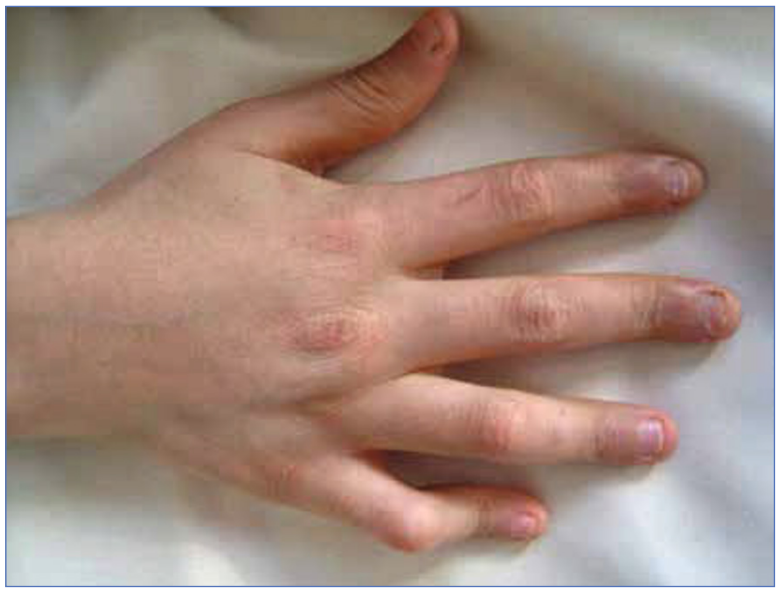
Q-switched laser can be proposed for treating the hyperpigmented lesions.

KEY REFERENCES

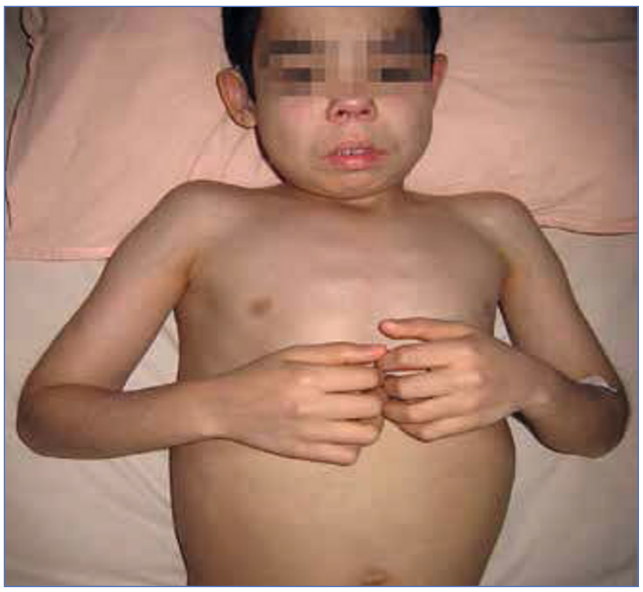
- Harmelin Y, Cardot-Leccia N, Ortonne JP, Bahadoran P, Lacour JP, Passeron T. Localized depigmentation on genital melanosis: a clue for the understanding of vitiligo. Br J Dermatol. 2013;168:663-4.
- Romero-Maté A, Miñano-Medrano R, Nájera-Botello L et al, Reticulate genital pigmentation associated with localized vitiligo, Arch Dermatol. 2010; 146:574-5.

H SYNDROME

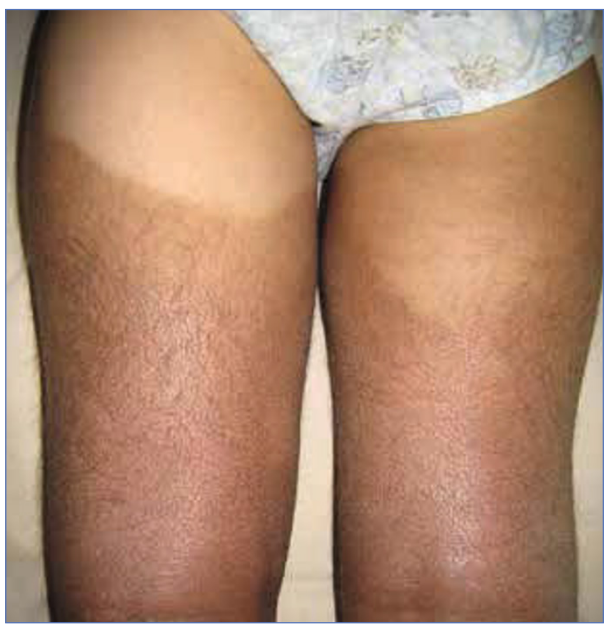
Christine Chiaverini



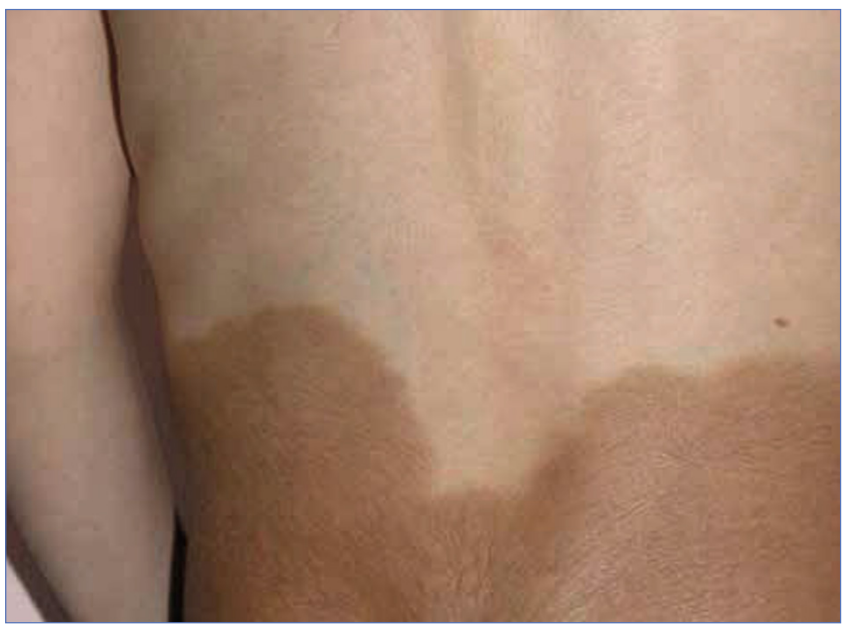
Flexion contracture in H syndrome.



Twenty-year-old man with H syndrome. Note the short stature.



Progressive sclerodermatous thickening of the skin, with overlying hyperpigmentation and hypertrichosis.



Sclerodermatous hyperpigmentation associated with hypertrichosis.

OMIM: #621391

GENETICS

Autosomal recessive inherited disease.

EPIDEMIOLOGY

Extremely rare disease with less than 100 patients reported, mostly of Arab origin.

PATHOPHYSIOLOGY

Mutations in the SLC29A3 gene encoding for the human equilibrative nucleoside transporter (hENT3) which mediates passive sodium-independent transport of nucleoside is responsible for this genodermatosis. Exact role of this protein is unclear. Two allelic disorders with marked clinical overlap with H syndrome: pigmented hypertrichosis with insulin-dependent diabetes mellitus (PHID) syndrome and familial histiocytosis syndrome (FHS) are described.

Recently it has been proposed to include H syndrome in inherited form of histiocyosis.

CLINICAL DERMATOLOGICAL PRESENTATION

Progressive sclerodermatous thickening of the skin, with overlying hyperpigmentation and hypertrichosis.

The onset of the lesions is usually in the first or second decade of life and extend gradually.

Localization: middle and lower parts of the body.

EXTRACUTANEOUS SIGNS

Hepatosplenomegaly or splenomegaly.

Low height (short stature).

Heart abnormalies (atrial septal defect secundum, ventricular septal defect, mitral valve prolapse, or cardiomegaly).

Hearing loss that developed during childhood and deteriorated gradually.

Hypergonadotropic hypogonadism with azoospermia.

Hyperglycemia/diabetes mellitus.

Hallux valgus/flexion contractures.

Various ophthalmologic abnormalities, facial telangiectases and gynecomastia have been also described in some patients.

HISTOPATHOLOGY

Epidermal changes include hyperkeratosis, acanthosis, and increased melanin deposition in basal keratinocyte. Widespread fibrosis in the dermis and subcutis with an interstitial mononuclear infiltrate, composed of small to medium-sized CD68+, S100+ CD1- histiocytes and CD34+ and factor XIIIa+ dendrocytes. Similar findings are observed in enlarged lymph nodes and from nasal mucosa.

DIFFERENTIAL DIAGNOSIS

- Rosai Dorfman disease.
- Scleroderma.
- Panniculitis.

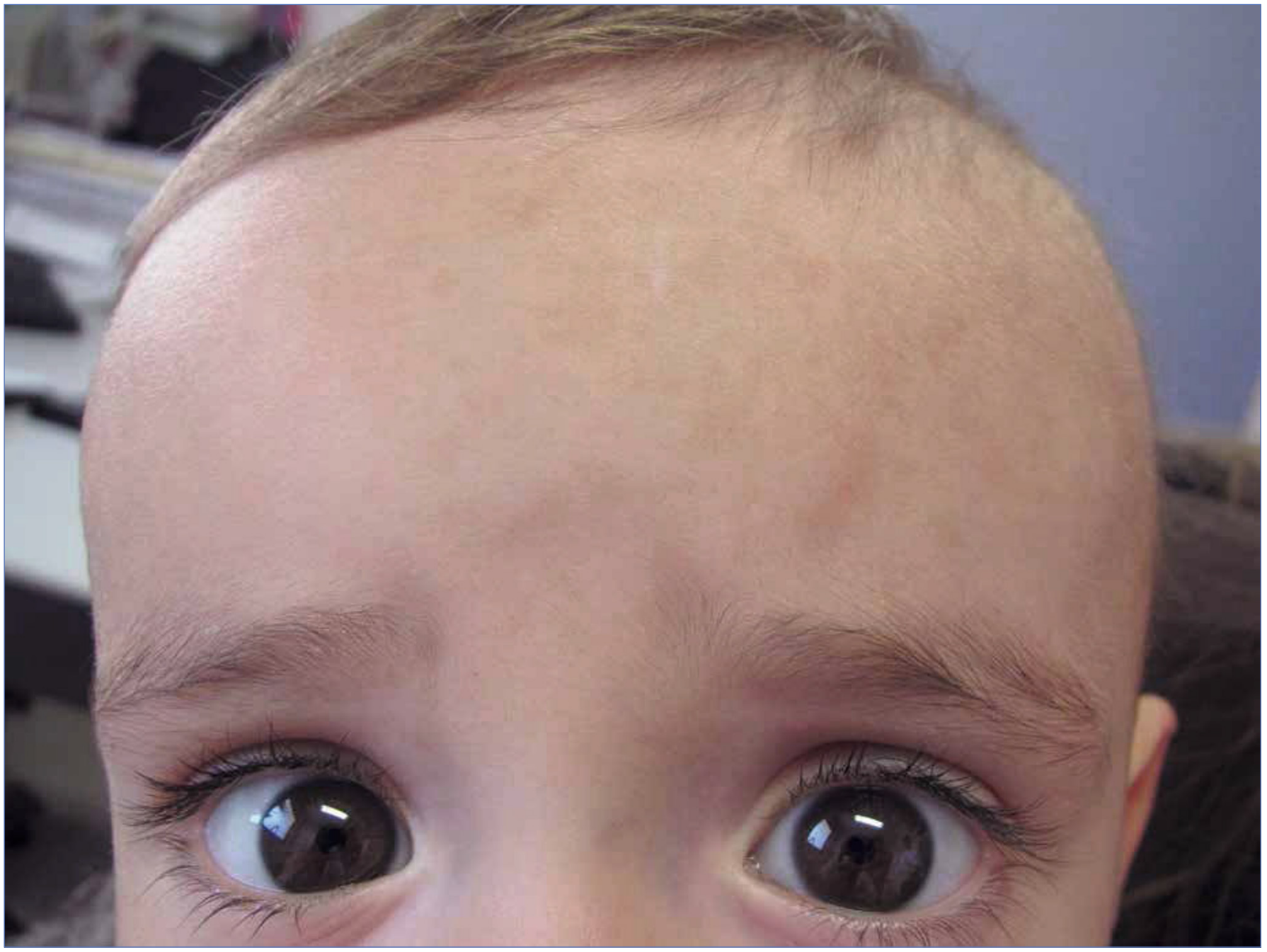
TREATMENT

Various treatments have been used, usually with failure or with only partial response, including: systemic corticosteroids, methotrexate, cyclophosphamide, cyclosporine, 6-mercaptopurine, interferon alfa, colchicine, anakinra, canakinumab, adalimumab, nonsteroidal anti-inflammatory drugs and radiotherapy.

KEY REFERENCES

- Molho-Pessach V, Agha Z, Aamar S, Glaser B, Doviner V, Hiller N, Zangen DH, Raas-Rothschild A, Ben-Neriah Z, Shweiki S, Elpeleg O, Zlotogorski A. The H syndrome: a genodermatosis characterized by indurated, hyperpigmented, and hypertrichotic skin with systemic manifestations. J Am Acad Dermatol. 2008;59:79-85.
- Molho-Pessach V, Ramot Y, Camille F, Doviner V, Babay S, Luis SJ, Broshtilova V, Zlotogorski A. J Am Acad Dermatol. 2014. H syndrome: the first 79 patients. 2014;70:80-8.

HYPERPIGMENTED MACULES ON THE FACE OF YOUNG CHILDREN



Asymptomatic hyperpigmented macules located only on the forehead of this young child.

EPIDEMIOLOGY

This entity has been very recently described and so far only a few cases have been reported. However, it is probably not so rare.
Only in young children between 2 to 24 months of age.
Male and female seem to be equally affected.
No race predilection.

CLINICAL DERMATOLOGICAL PRESENTATION

Hyperpigmented macules of 4 to 15 mm in diameter and light-brown hue and irregular borders.
No preceding erythema, edema or desquamation.
The lesions are asymptomatic.
Localization: only on forehead and temples.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Post-inflammatory hyperpigmentation.
Normal epidermis with mild perivascular dermal inflammatory infiltrate.

DIFFERENTIAL DIAGNOSIS

- Tinea versicolor.
- Flat warts.
- Urticaria pigmentosa.
- Benign cephalic histiocytosis.
- Neonatal lupus erythematosus.

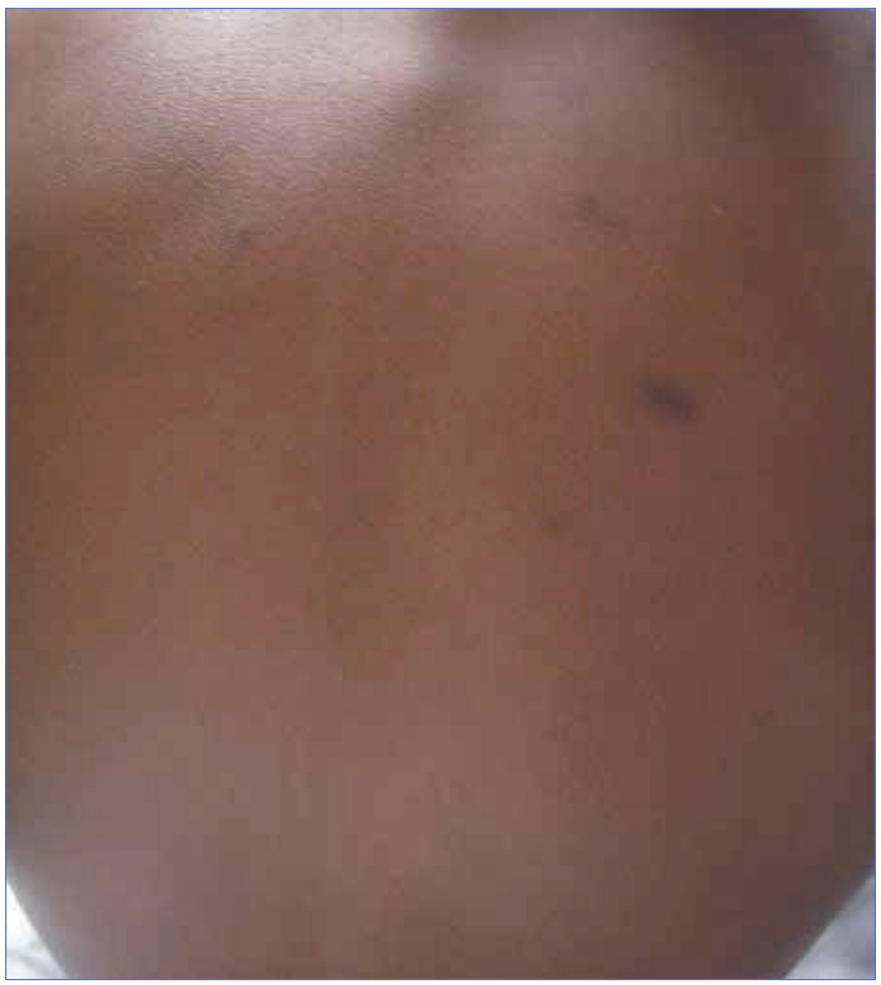
TREATMENT

None reported. Follow-up is still limited but lesions may be stable for months or years or fade progressively.

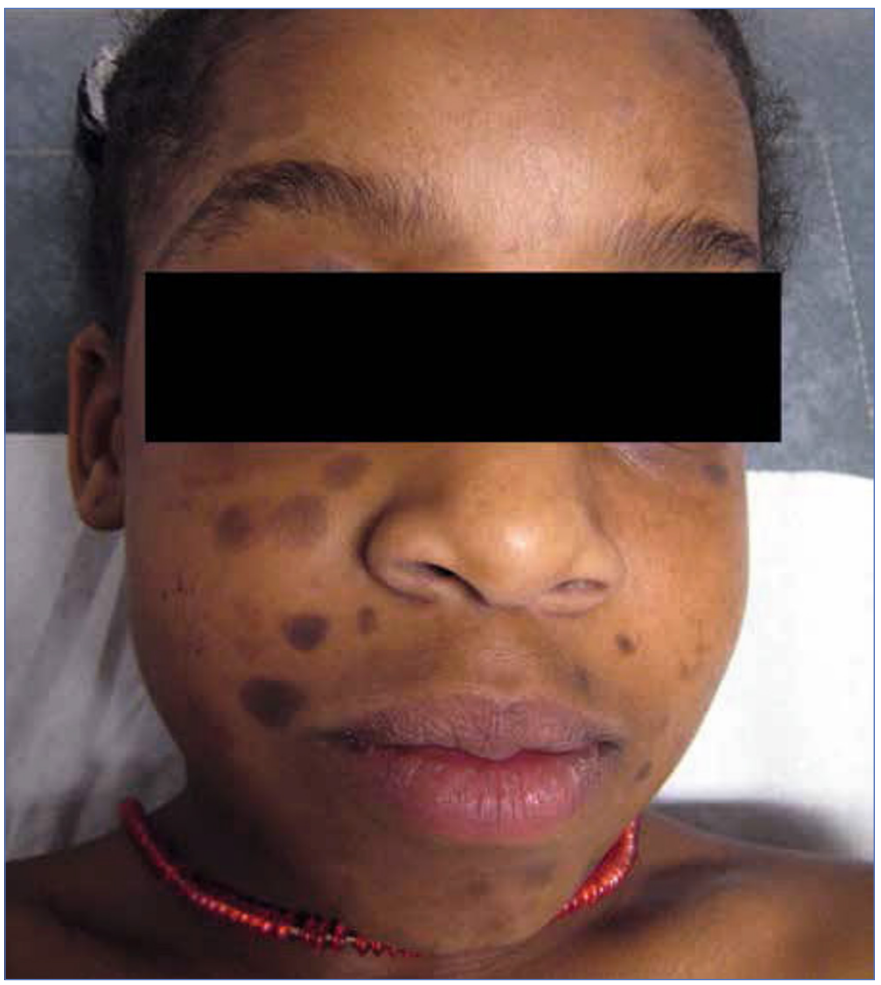
KEY REFERENCE

- Hernández-Martín A, Gilliam AE, Baselga E, Vicente A, Lam J, González-Enseñat M, Azorín D, Torrelo A. Hyperpigmented macules on the face of young children: a series of 25 cases. J Am Acad Dermatol. 2014;70:288-90.

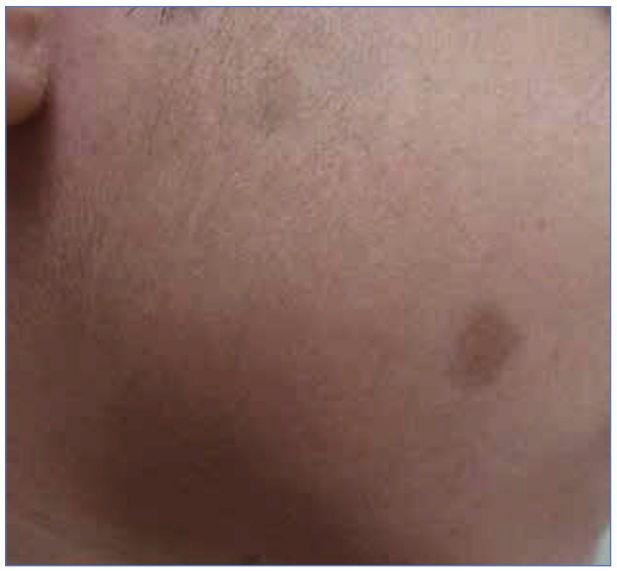
IDIOPATHIC ERUPTIVE MACULAR PIGMENTATION



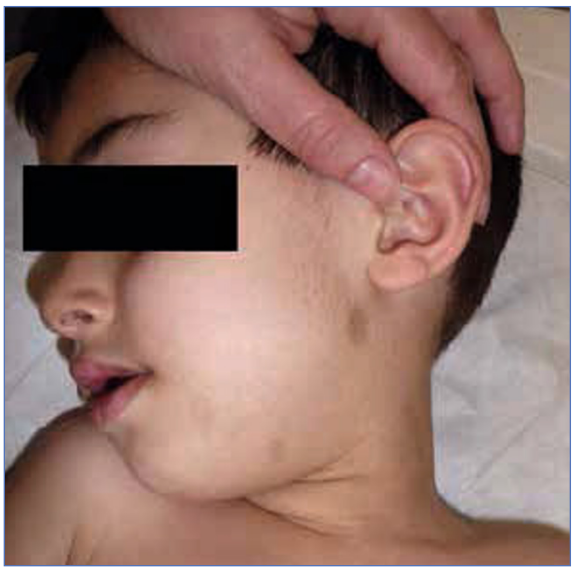
Isolated lesions of the upper part of the back.



Multiple dark brown macules in a widespread form of idiopathic eruptive macular pigmentation.



Idiopathic eruptive macular pigmentation: asymptomatic brown macules of the face.



Idiopathic eruptive macular pigmentation located only on the face.

EPIDEMIOLOGY

Rare. Only a few cases have been reported.
Children and young adults are affected (only one case in a 50-year-old man has been reported so far).

PATHOPHYSIOLOGY

Unknown.
Clinical dermatological presentation.
Multiple brown to dark brown macules.
Asymptomatic without preceding inflammatory process or history of drug exposure.
Localization: neck, face, trunk and proximal limbs.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin in the basal layers of the epidermis and melanophages in the dermis.
No other epidermal changes. No lichenoid or mast cell infiltrate.
Perivascular lymphohistiocytic infiltrate in the papillary dermis.

DIFFERENTIAL DIAGNOSIS

- Erythema dyschromicum perstans.
- Lichen planus pigmentosus.
- Post-inflammatory hyperpigmentation.
- Fixed-drug eruption.
- Mastocytosis.

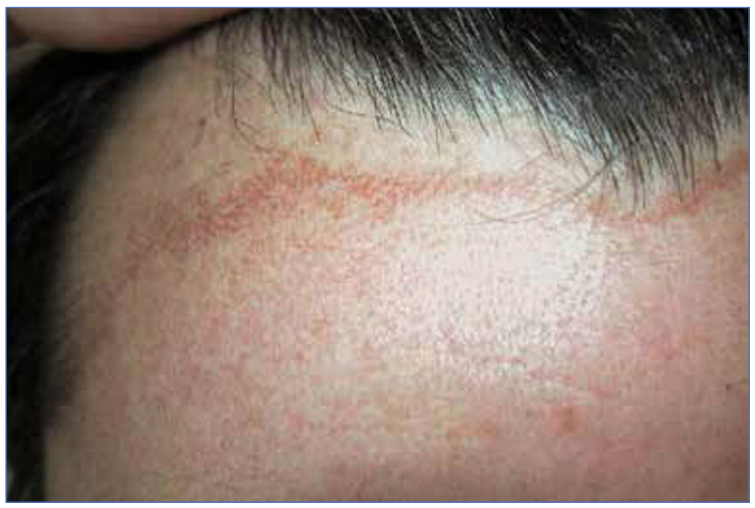
TREATMENT

None is truly effective.
The lesions gradually disappeared during a period of several months to years.

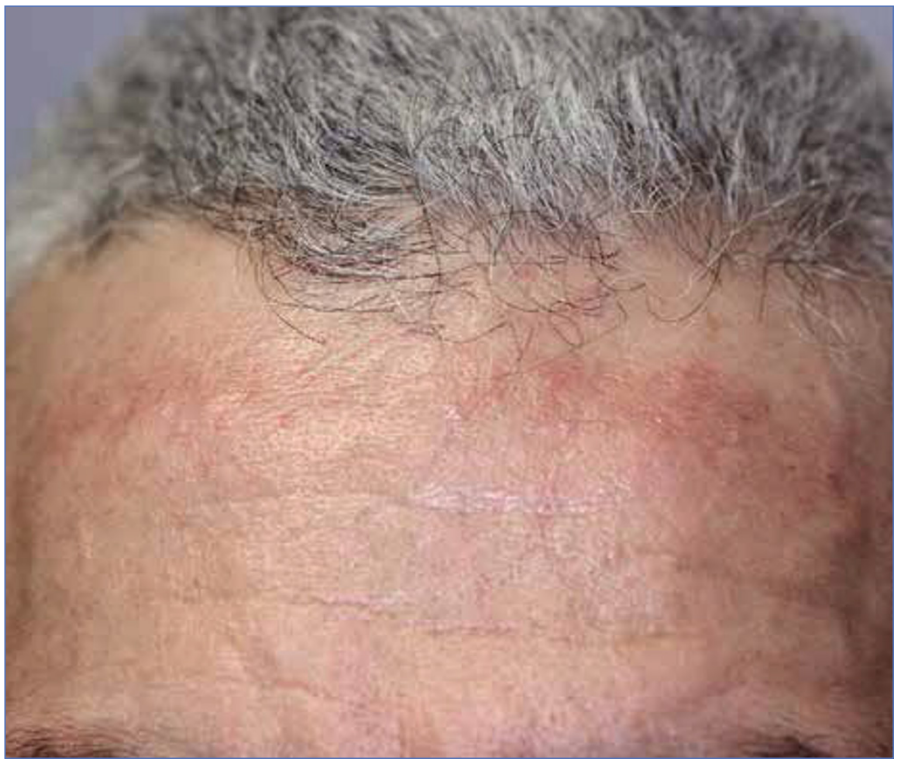
KEY REFERENCES

- Sanz de Galdeano C, Léauté-Labrèze C, Bioulac-Sage P, Nikolic M, Taïeb A. Idiopathic eruptive macular pigmentation: report of five patients. Pediatr Dermatol. 1996;13:274-7.
- Jang KA, Choi JH, Sung KS, Moon KC, Koh JK. Idiopathic eruptive macular pigmentation: report of 10 cases. J Am Acad Dermatol. 2001;44:351-3.

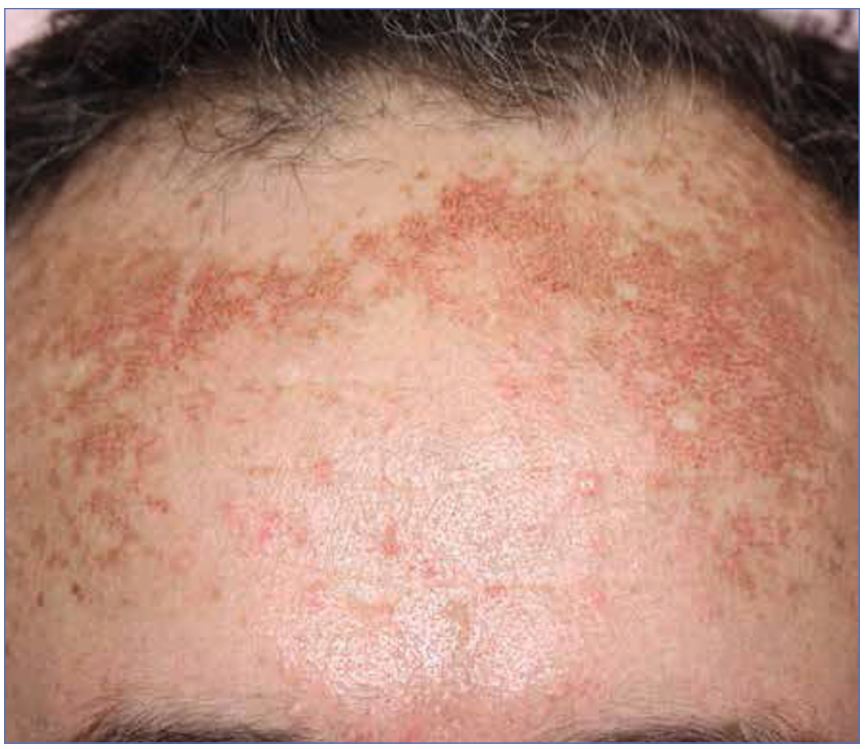
LINEA FUSCA



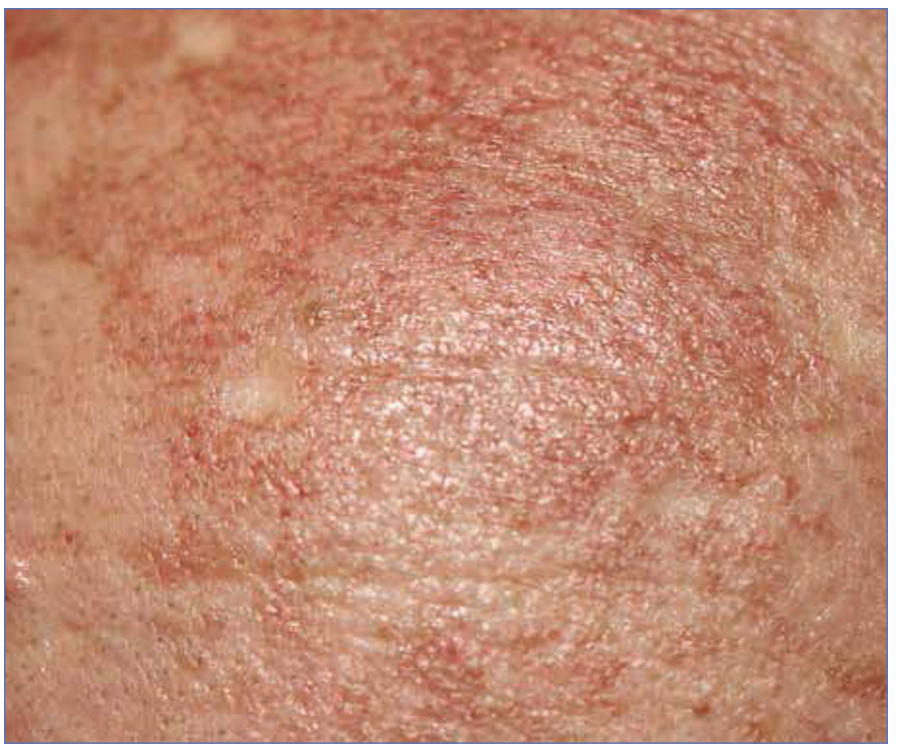
Light-brown hyperpigmented band spreading horizontally across the forehead, sparing the hairline.



Slight form of linea fusca. The clinical pattern remains characteristic of the disorder.



Linea fusca with a larger involvement of the forehead.
Note that the hairline is still spared and lesions remain located on the forehead.



Closer view of the lesion. Note that the hyperpigmentation is associated with an increased superficial vascularization.

SYNONYMS

Brown forehead ring of Andersen, Wernoe and Haxthausen.

EPIDEMIOLOGY

Only few cases have been reported, but it is probably not so rare and frequently misdiagnosed with melasma. Mostly observed in adults. Men and women are affected.

PATHOPHYSIOLOGY

Chemical photosensitizers and excessive sun exposure have been suggested, but the pathophysiology remains poorly understood.

CLINICAL DERMATOLOGICAL PRESENTATION

Light-brown hyperpigmented band.
Asymptomatic.

Localization is very suggestive: horizontally across the forehead, sparing the hairline.
At the contrary of melasma, the lesions are limited only on the forehead.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

None reported. The clinical pattern is highly suggestive of the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Melasma.
- Post inflammatory hyperpigmentation.

TREATMENT

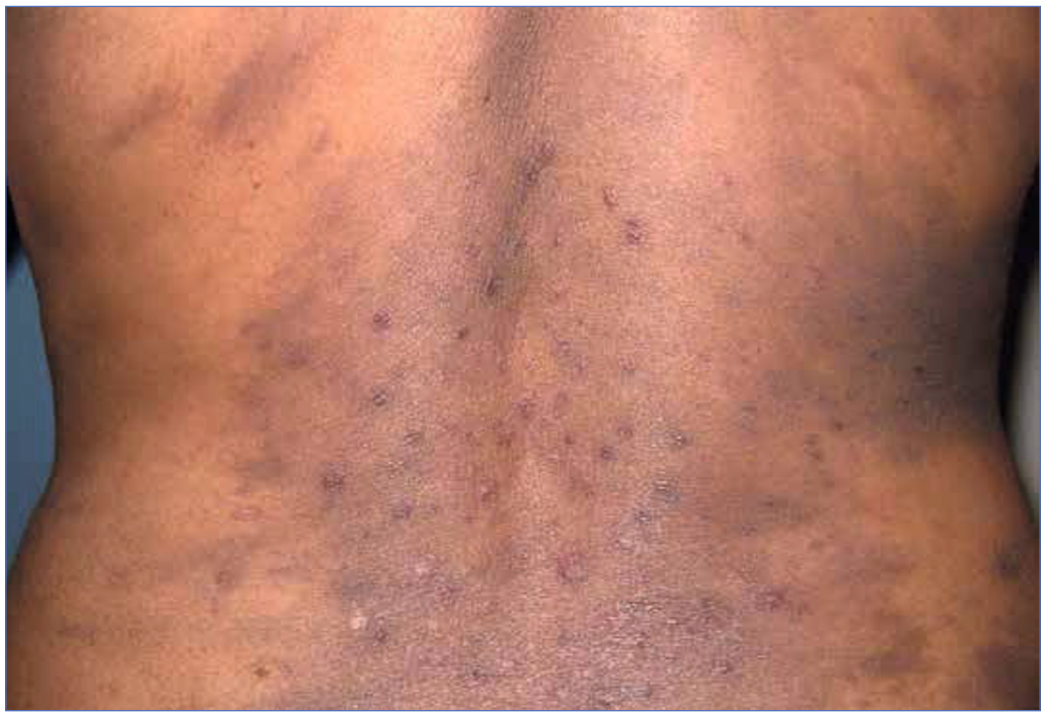
Sun protection is required.
Azelaic acid has been proposed.
In our practice, Kligman's trio with pulse dye laser to treat the vascular component is useful.

KEY REFERENCES

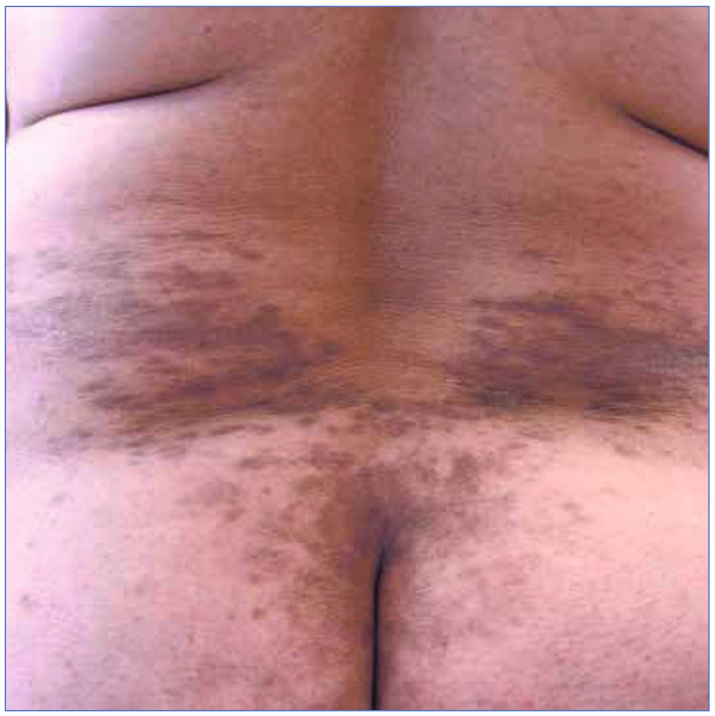
- Michel PJ. Reflexions on the linea fusca; report on 12 cases. Bull Soc Fr Dermatol Syphiligr. 1955;5:510-3.
- Kanitakis J. Linea fusca in a male adolescent successfully treated with azelaic acid. J Eur Acad Dermatol Venereol. 2008;22:1497-8.

LICHEN PLANUS PIGMENTOSUS

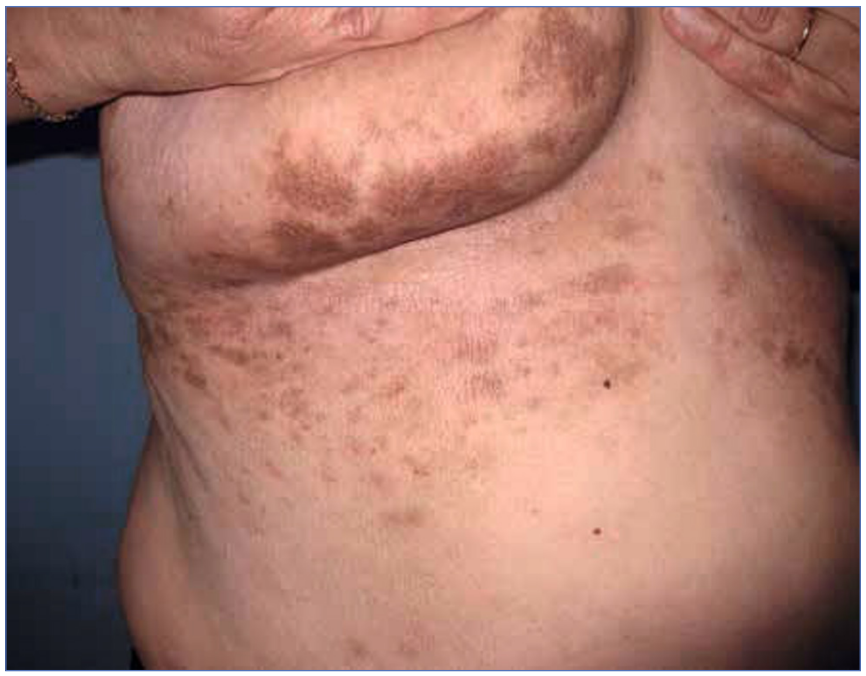
M. Sendhil Kumaran and Davinder Parsad



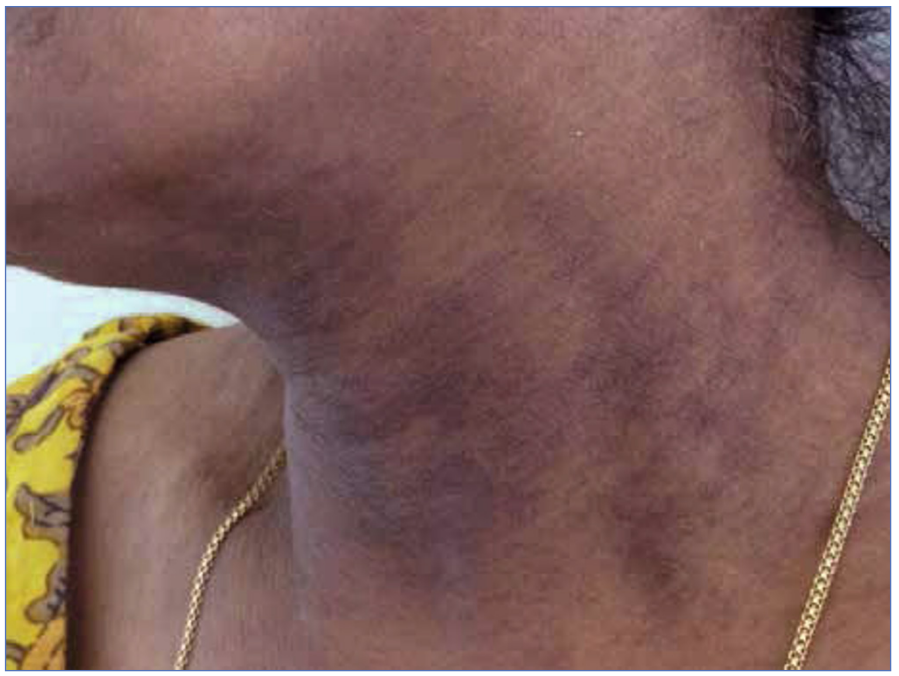
Typical involvement of the lumbar region. Note the association of slate grey macules with the persistence of more inflammatory lichenoid papules.



Lichen planus pigmentosus of the back. Note the predominance of the lesions in the folds.



Lichen planus pigmentosus of the trunk. The hyperpigmented macules affect mostly the infra-mammary folds.



Lichen planus pigmentosus affecting the neck (coll. M. Sendhil Kumaran and Davinder Parsad).

EPIDEMIOLOGY

Worldwide distribution but more common in Indian and Middle East populations.
The disease usually appears in the third and fourth decade of life.

PATHOPHYSIOLOGY

The exact pathogenesis of lichen planus pigmentosus (LPP) still remains elusive. Based on various histopathologic alterations, LPP probably represents a type of lichenoid tissue reaction to an unknown antigen or stimulus. Since LPP demonstrates histopathological features identical to lichen planus (LP), the pathogenesis of LPP could be similar to that of LP.

CLINICAL PRESENTATION

Hyperpigmented, dark-brown to slate gray-coloured macules or patch lesions.
In early stages typical lichenoid papules with pruritus can be observed. In some cases, the preceding lichenoid papules are very slight or absent. In latter stages only the hyperpigmented macules are observed and diagnosis can be more difficult.
Localization: mostly on sun-exposed area and folds.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLGY

Histopathology shows vacuolar degeneration of the basal layer in the epidermis.
In the dermis, a perivascular lymphohistiocytic infiltrate and the presence of melanophages may be seen.

DIFFERENTIAL DIAGNOSIS

- Erythema dyschromicum perstans.
- Reihls melanosis.

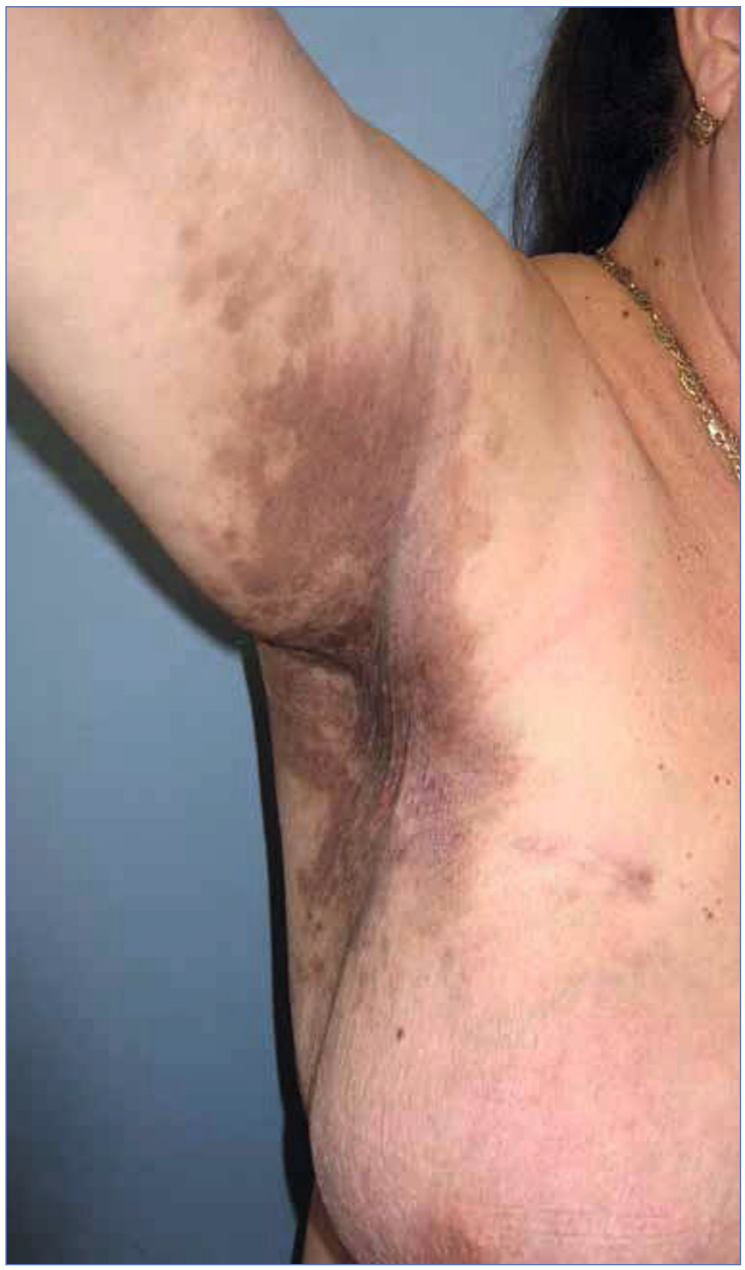
TREATMENT

Large doses of vitamin A, topical corticosteroids and topical calcineurin inhibitors (TCIs) along with photoprotection
Q- switched Nd:YAG laser in combination with topical tacrolimus.

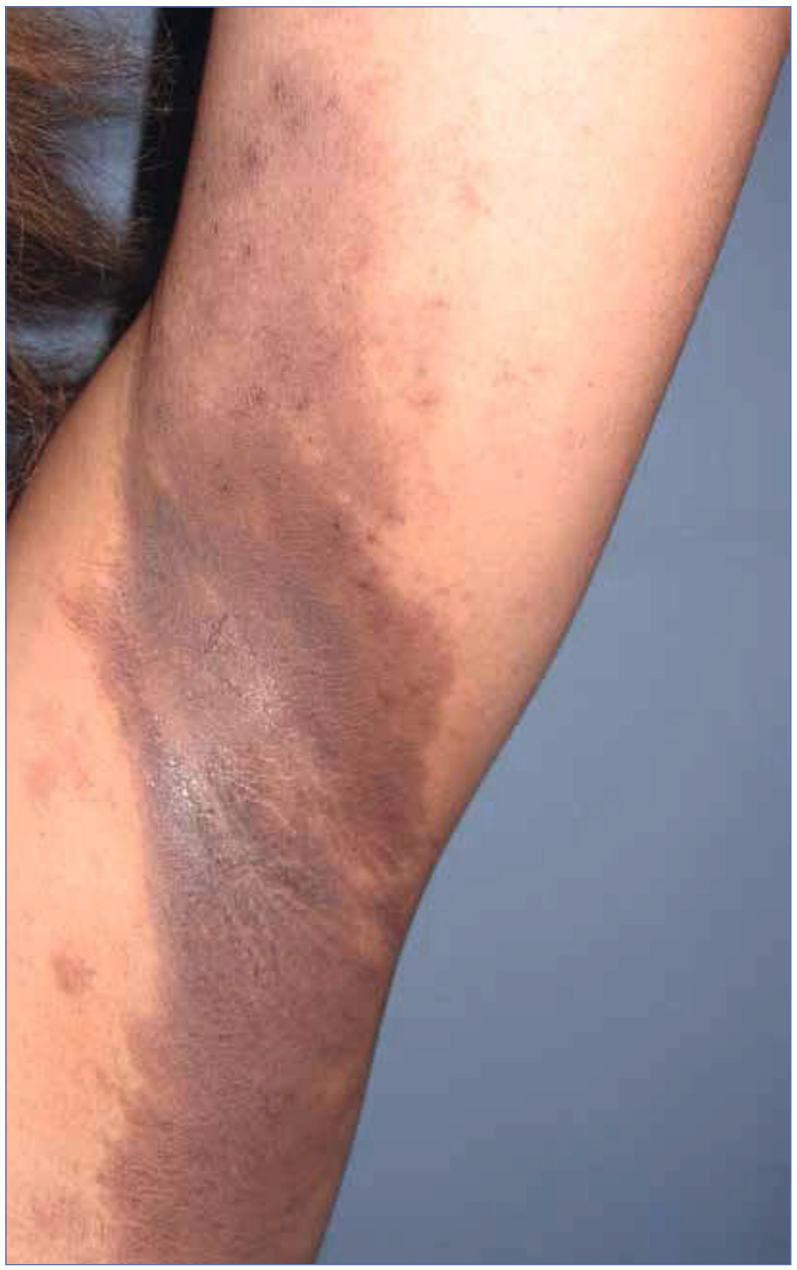
KEY REFERENCES

- Kanwar AJ, Dogra S, Handa S, Parsad D, Radotra BD. A study of 124 Indian patients with lichen planus pigmentosus. Clin Exp Dermatol. 2003;28:481-5.
- Vega ME, Waxtein L, Arenas R, Hojyo T, Dominguez-Soto L. Ashy dermatosis and lichen planus pigmentosus: a clinicopathologic study of 31 cases. Int J Dermatol. 1992;31:90-4.

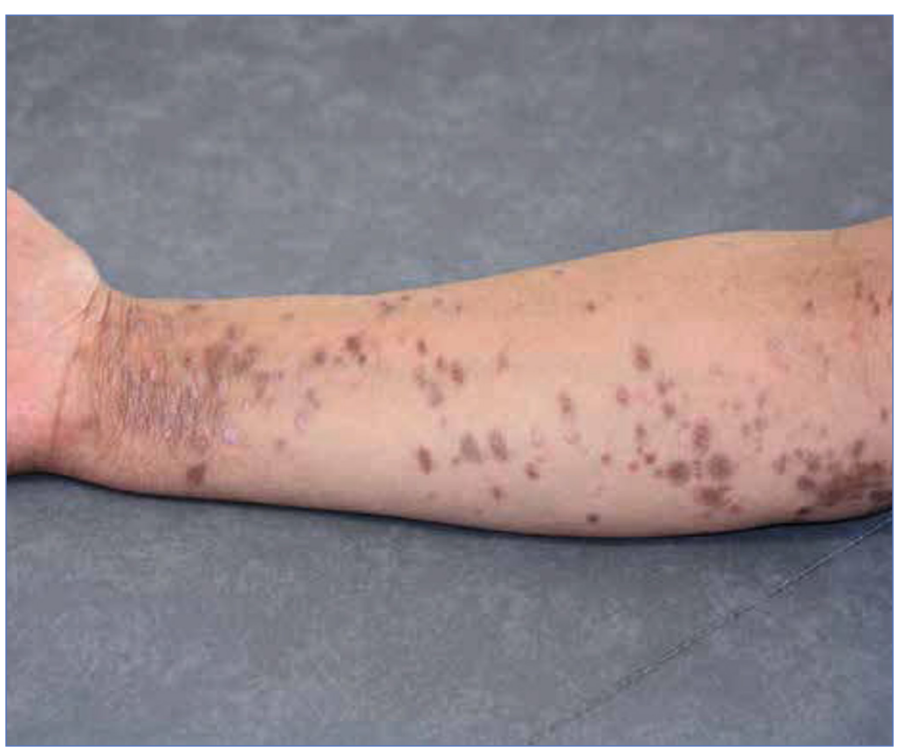
LICHEN PLANUS PIGMENTOSUS



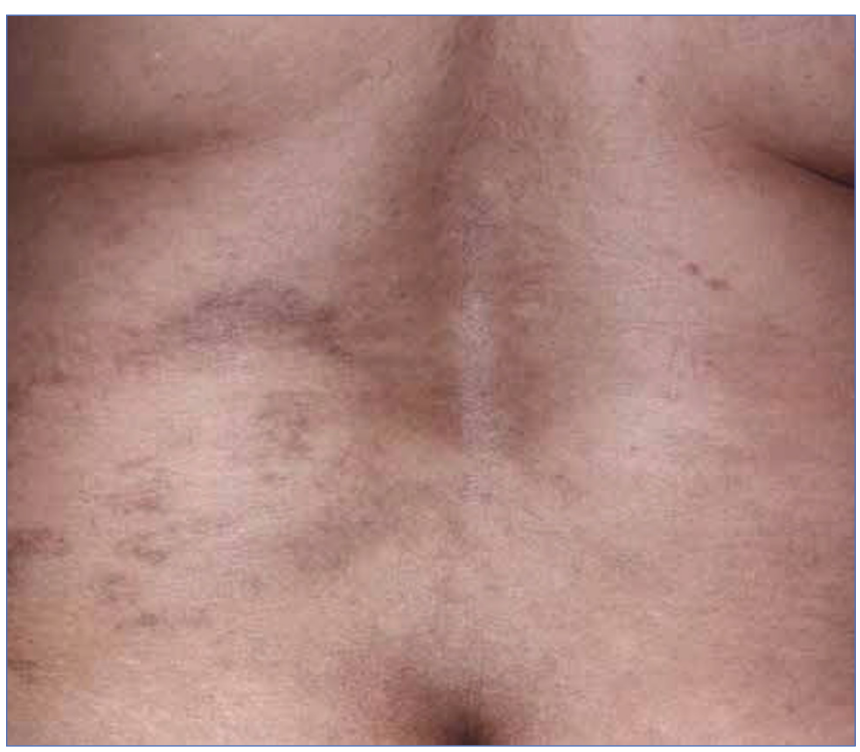
The involvement of the axillary fold is suggestive of the diagnosis.



Lichen planus pigmentosus of the axillary fold.

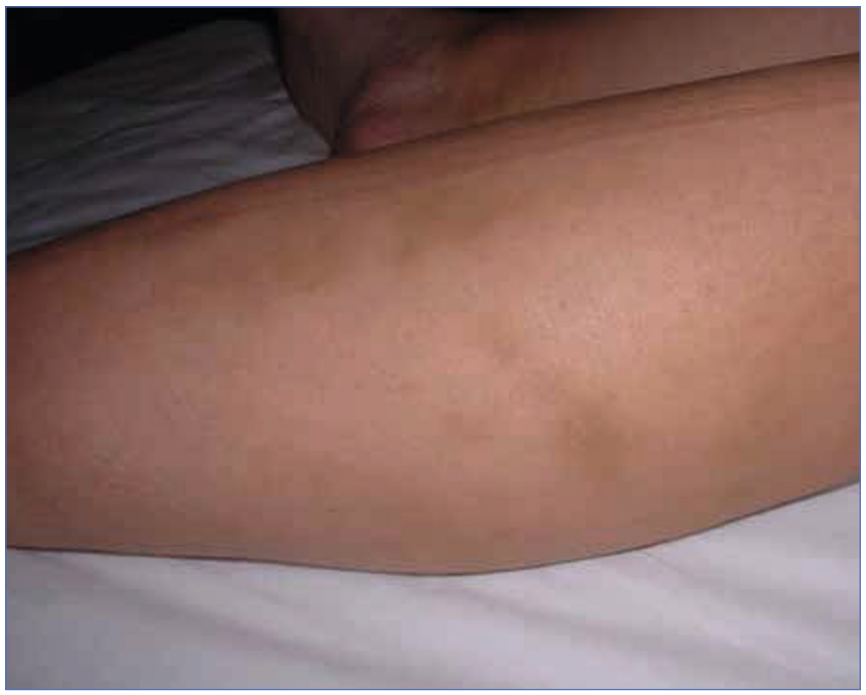


Early stage of lichen planus pigmentosus. Note the typical lichenoid inflammatory and pruritic papules of the arm associated with hyperpigmentation on older lesions.

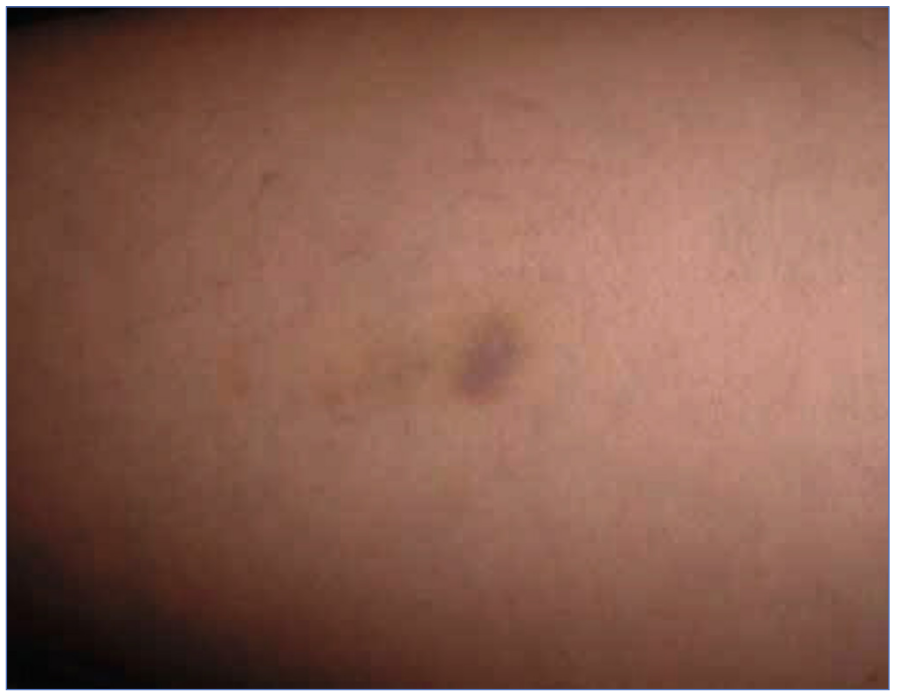


Segmental forms of lichen planus pigmentosus can be observed but they remain quite rare.

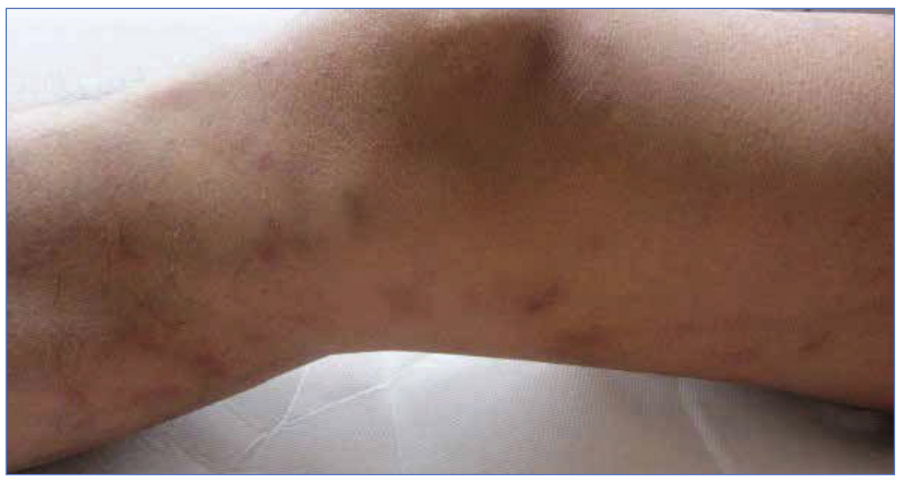
MACULAR ARTERITIS



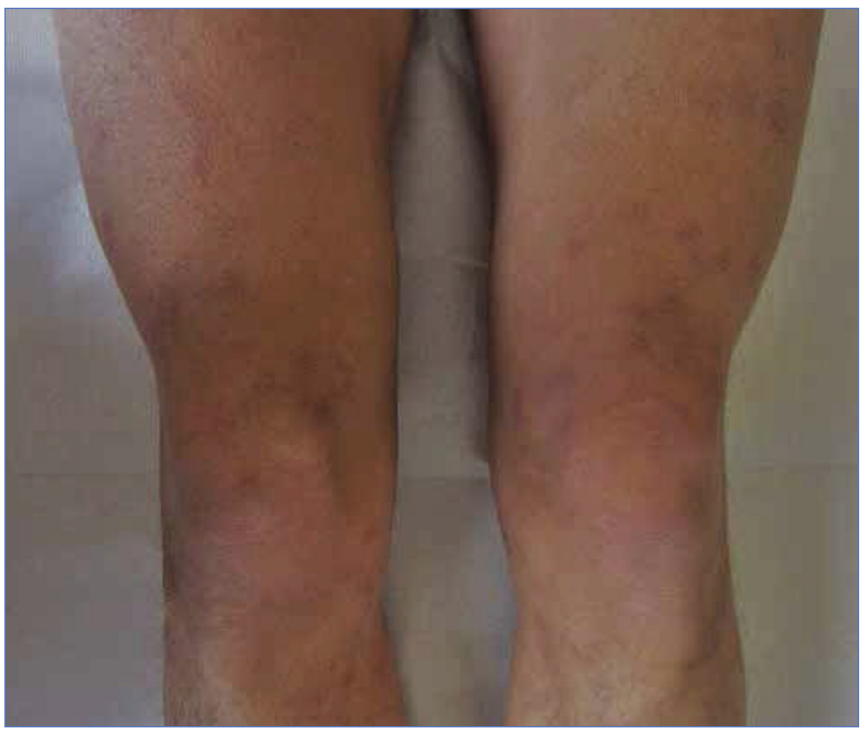
Multiple brownish macules in a woman with macular arteritis.



Close-up on one lesion of macular arteritis.



Linear and round to oval erythematous and brownish macules in a man with macular arteritis.



Macular arteritis: multiple erythematous and brown macules of the lower limbs.

SYNONYMS

Lymphocytic thrombophilic arteritis, macular lymphocytic arteritis.

EPIDEMIOLOGY

Only few cases have been reported so far.
Men and women are affected but seems to be more frequent in women.
Cases from 6 to 73 years of age and in all ethnicities have been reported.

PATHOPHYSIOLOGY

Unknown.

CLINICAL DERMATOLOGICAL PRESENTATION

Round to oval, or linear to reticulated erythematous and brown macules of 0.5 to 3.5 cm in size.
Lesions are asymptomatic without any infiltration.
Localization: lower limbs are constantly affected. Upper limbs are involved in less than half of the cases.

EXTRACUTANEOUS SIGNS

No systemic symptoms have been reported so far.
Increased sedimentation rate, positive antinuclear antibodies and antiphospholipid antibodies can be observed.

HISTOPATHOLOGY

Lymphocytic arteritis with fibrinoid necrosis of the vascular wall and endoluminal thrombus, associated with perivascular lymphocytic infiltrate.
Affects the deep dermis and superficial hypodermis.

DIFFERENTIAL DIAGNOSIS

- Post-inflammatory hyperpigmentation.
- Pigmented purpuric dermatoses.
- Ashy dermatitis.

TREATMENT

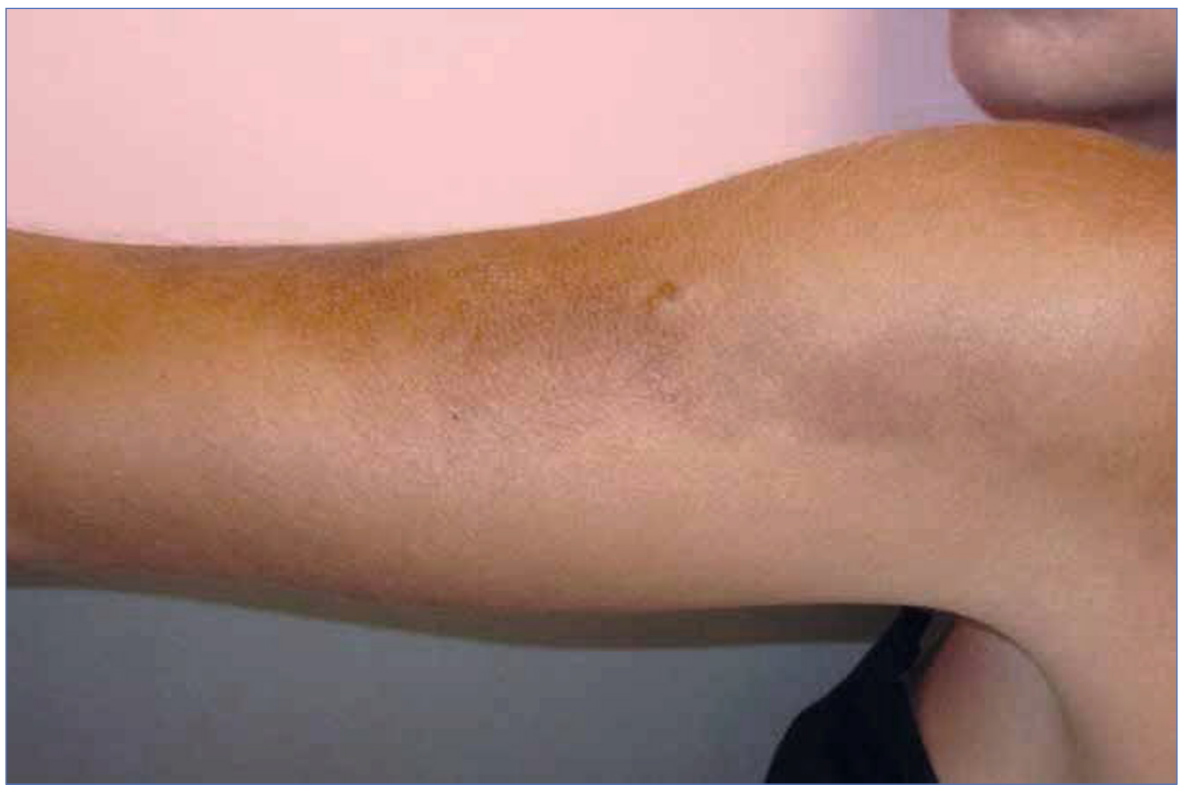
Hydroxychloroquine.
Dapsone.

KEY REFERENCES

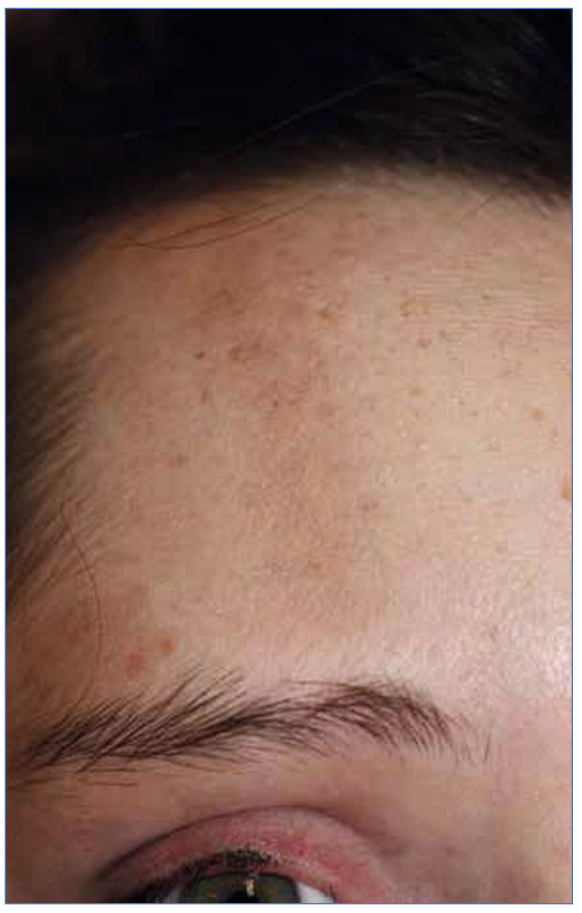
- Fein H, Sheth AP, Mutasim DF. Cutaneous arteritis presenting with hyperpigmented macules: macular arteritis. J Am Acad Dermatol. 2003;49:519-22.
- Saleh Z, Mutasim DF. Macular lymphocytic arteritis: a unique benign cutaneous arteritis, mediated by lymphocytes and appearing as macules. J Cutan Pathol. 2009;36:1269-1274.

MORPHEA AND SCLERODERMA

Chee-Leok Goh and Sai-Yee Chuah



Linear scleroderma affecting the arm and the shoulder.



Early stage of scleroderma (en coup de sable). The hyperpigmentation and the skin atrophy are mild, but note the madarosis (loss of the eyelashes and decrease hair density of the eyebrow) in the extension of the hyperpigmentation.

EPIDEMIOLOGY

Morphea and scleroderma (systemic sclerosis) are relatively uncommon disorders that affects adults and children.
Incidence of morphea is estimated to be approximately 0.4 to 2.7 per 100,000 people in the US. Females are affected approximately three times as often as males.
Epidemiologic studies suggest 0.9 to 5.7% of patients with morphea progress to systemic sclerosis (scleroderma).

PATHOPHYSIOLOGY

Morphea and scleroderma are associated with an overproduction of collagen (particularly types I and III collagen), by fibroblasts and increased extracellular matrix in the dermis. Other proposed pathophysiologic mechanisms include the formation of anti-matrix metalloproteinase antibodies and increase expression of insulin-like growth factor, which enhances collagen production.

CLINICAL DERMATOLOGICAL PRESENTATION

Morphea is classified into several different types according to the appearance of the skin lesions viz, superficial (circumscribed or plaque morphea) and deep variant.

Superficial variant (commonest variant)

Has fewer than three discrete circumscribed, indurated plaques measuring 1 to 20 cm or more in diameter mainly on the trunk.
In active phases, a violaceous border may surround the indurated centre.
As it progresses, sclerosis develops centrally and the surface becomes smooth, shiny, and ivory in color, with loss of hair follicles and sweat glands.
Hyperpigmentation often ensues as lesions evolve and eventually involute.

Deep variant

Involves the subcutaneous fat and underlying structures such as muscle and fascia.
Ill-defined, bound-down, sclerotic plaques with a cobblestone or pseudo-cellulite appearance.
The lesions are frequently hyperpigmented.

Other variants of circumscribed morphea

Guttate morphea, Keloidal morphea, Atrophoderma of Pasini and Pierini, Bullous morphea.
Generalized morphea, Linear morphea (en coup de sabre).

EXTRACUTANEOUS SIGNS

Malaise, fatigue, myalgias, and arthralgias.
Joint contractures, deformity and restricted mobility.
Neurologic manifestations (more common in en coup de sabre or progressive hemifacial atrophy): seizures, headaches, hemipareasis, cranial nerve palsies and visual disturbances.

MORTALITY/MORBIDITY

Morphea typically has a benign, self-limited course.
Survival rates for morphea patients are no different from those of the general population. However, linear and deep morphea subtypes can cause considerable morbidity. Joint contractures, limb-length discrepancy, and prominent facial atrophy result in substantial disability and deformity in a quarter to half of all patients with linear or deep morphea.

HISTOPATHOLOGY

Epidermis is usually normal with flattened rete ridges.
Early inflammatory stage: perivascular and interstitial infiltrate of lymphocytes, plasma cells and occasional eosinophils. Blood vessel walls demonstrate endothelial swelling and edema, and thickening of preexisting collagen bundles.
Late sclerotic stage: inflammatory infiltrate typically disappears. Collagen bundles in the reticular dermis and subcutis become thick, closely packed, and hyalinized.
Adnexal structures appear to be trapped within the middle of the thickened dermis as subcutaneous fat is replaced by collagen.

DIFFERENTIAL DIAGNOSIS

- Primary and systemic amyloidosis.
- Nephrogenic fibrosing dermopathy.
- Graft versus host disease.
- Lichen sclerosus and atrophicus.
- Eosinophilic fasciitis.
- Eosinophilia-myalgia syndrome.
- Scleredema.
- Scleromyxedema.
- Porphyria cutanea tarda.

TREATMENT

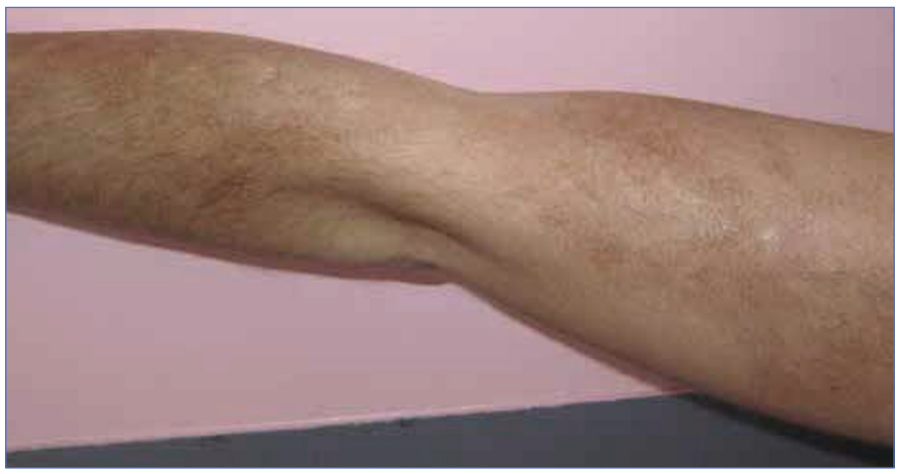
Lesions of superficial circumscribed morphea often undergo gradual spontaneous resolution over a 3- to 5-year period. Limited disease can often be managed with topical therapy (steroids and immunomodulators and calcipotriene) or lesion-limited phototherapy.
Imiquimod 5% cream 3 to 5 times per week has been shown to decrease lesional erythema and induration in small series.
Successful treatment of severe and/or rapidly progressive morphea with systemic corticosteroids in combination with weekly low-dose methotrexate (MTX) has been reported in several case series.
Mycophenolate mofetil is a second-line agent.
Phototherapy may be beneficial as a second-line therapy.
Few cases have shown benefit using extracorporeal photo-pheresis.
Physiotherapy is often recommended to prevent joint contractures when morphea affects the limbs.

KEY REFERENCES

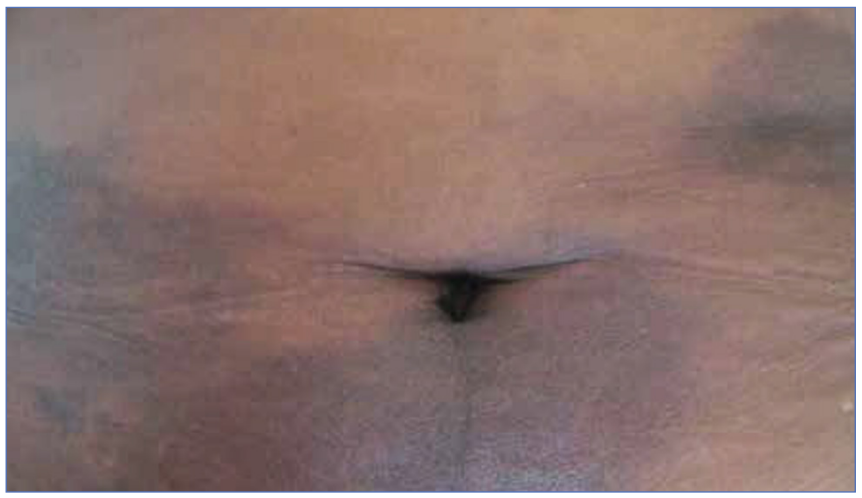
- Sartori-Valinotti JC, Tollefson MM, Reed AM. Updates on morphea: role of vascular injury and advances in treatment. Autoimmune Dis. 2013;2013:467808. doi: 10.1155/2013/467808. Epub 2013 Nov 12.
- Kreuter A. Localized scleroderma. Dermatol Ther. 2012;25:135-47.
- Chung L, Lin J, Furst DE et al. Systemic and localized scleroderma. Clin Dermatol. 2006;24:374-92.

MORPHEA AND SCLERODERMA

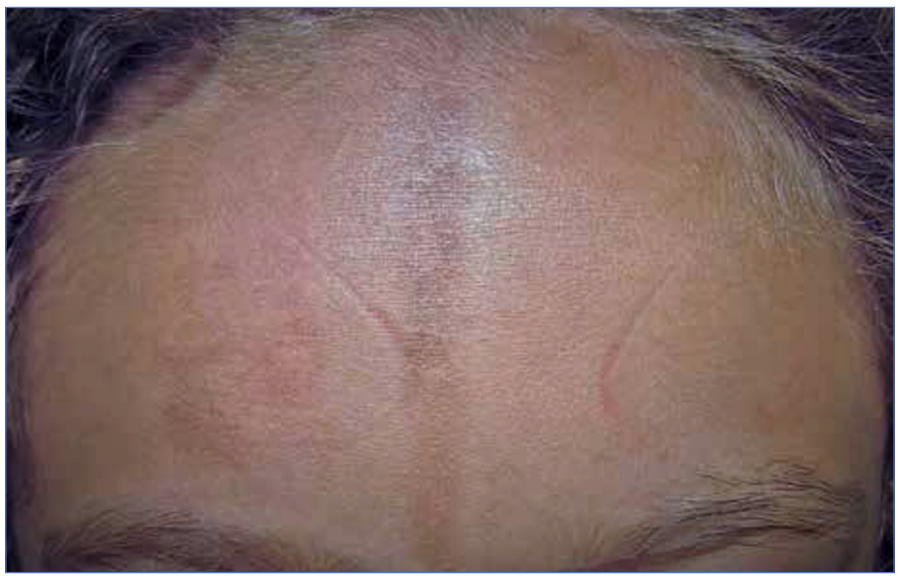
Chee-Leok Goh and Sai-Yee Chuah



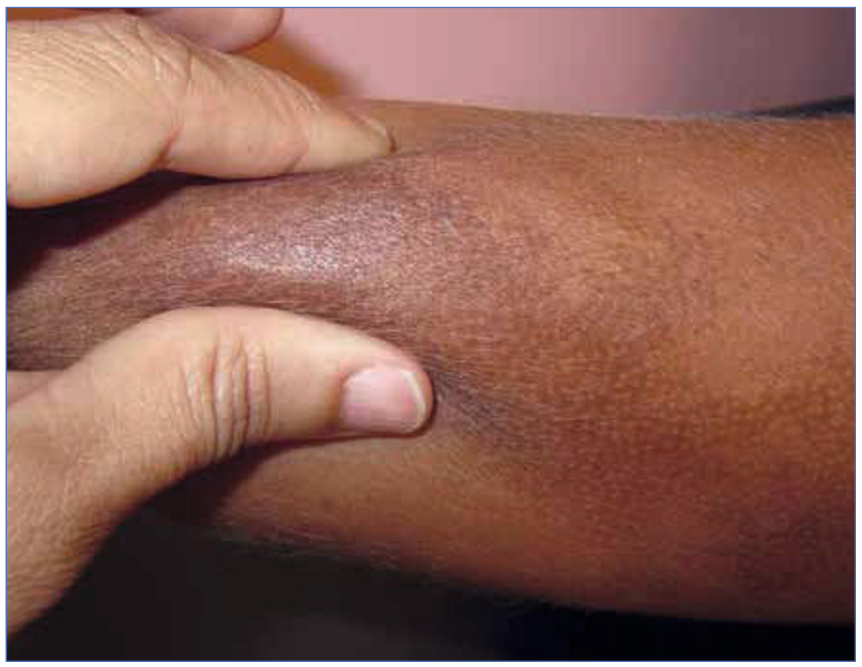
Linear scleroderma of the arm. Note the hypopigmented and atrophic lesions associated with the linear hyperpigmentation.



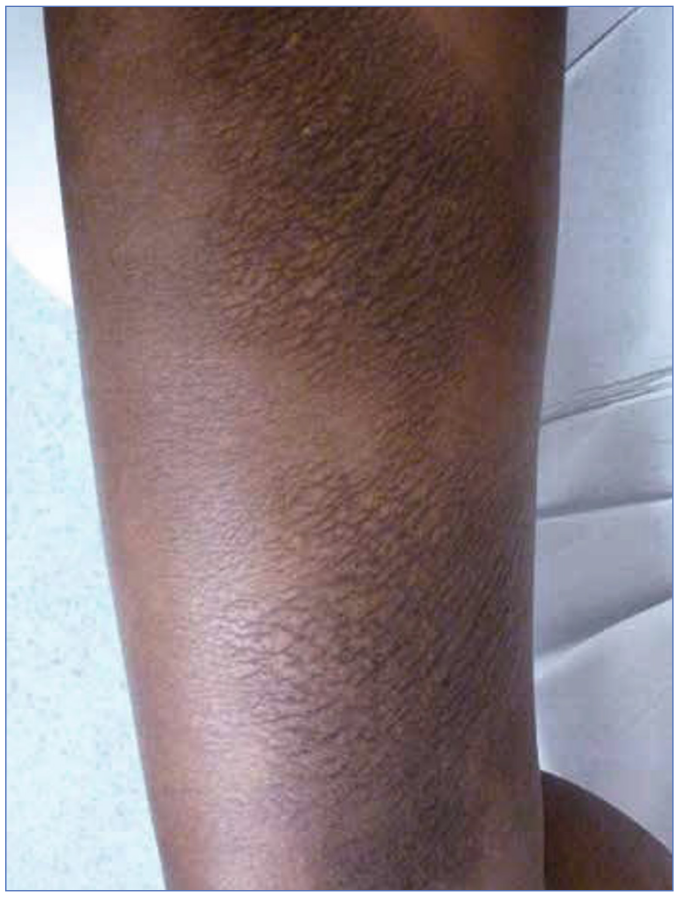
Multiple hyperpigmented lesions of morphea.



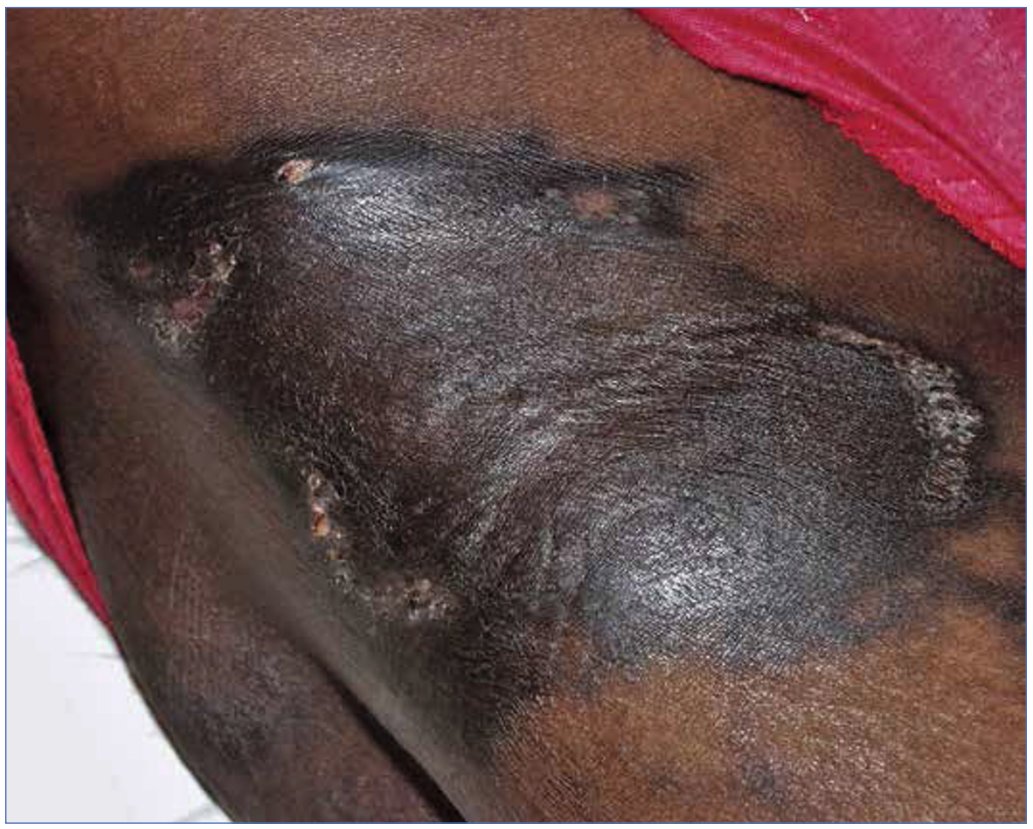
Scleroderma 'en coup de sable' of the forehead. Note the slight atrophy associated with the linear hyperpigmentation.



Skin induration associated with marked hyperpigmentation in linear scleroderma.

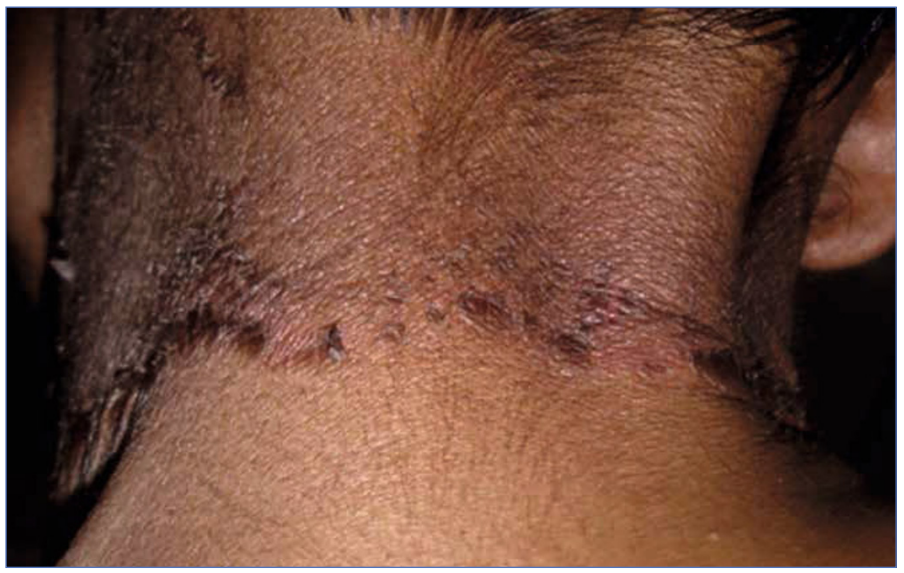


Late stage of linear scleroderma. The hyperpigmentation is associated with skin atrophy.

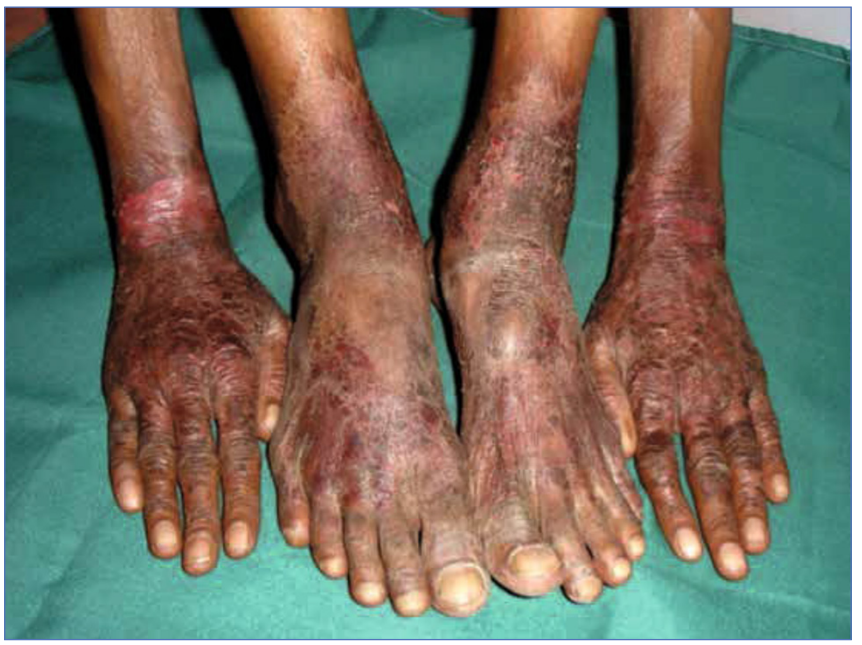


Hyperpigmented and indurated plaque in a woman with systemic scleroderma.

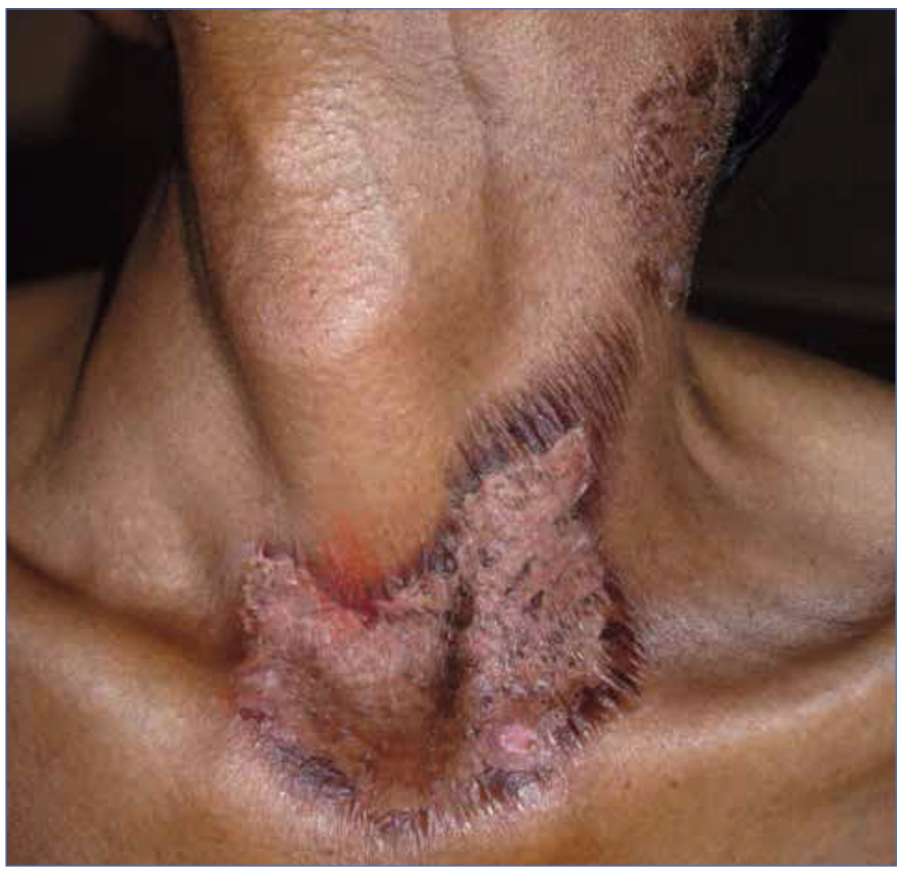
PELLAGRA



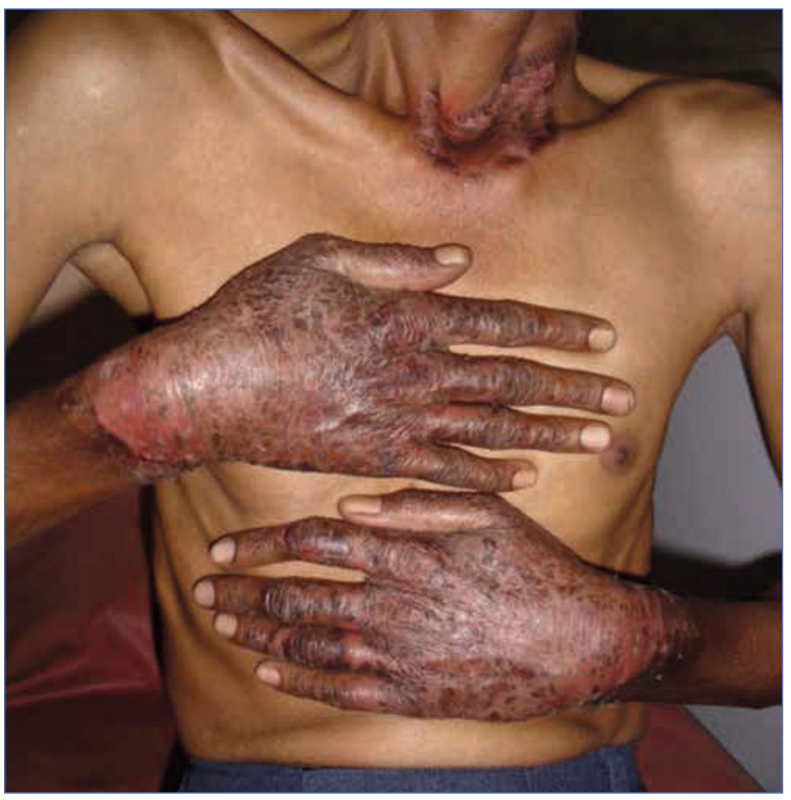
Close-up of pellagra on the neck. Note the brown hyperpigmention associated with scales and crusts (coll. Arun C. Inamadar).



Pellagra lesions of hands and feet (coll. Arun C. Inamadar).



Localized lesion of pellagra on the neck. The hyperpigmentation is more pronounced in the borders. Note some post-vesiculous and bullous erosions (coll. Arun C. Inamadar).



Erythematous and hyperpigmented scaly lesions of pellagra. Note that the lesions are restricted to sun-exposed areas (coll. Arun C. Inamadar).

EPIDEMIOLOGY

Pellagra has become very rare in developed countries but it is still present in areas where malnutrition is observed.
In developed nations, pellagra can affect individuals suffering of chronic alcoholism, malabsorption disorders, eating and psychiatric disorders, and nutrient-drug interactions.
In children the first signs can be seen after breastfeeding ceases. Men and women are equally affected.

PATHOPHYSIOLOGY

Pellagra is caused by a deficit in niacin (vitamin B_3) or its derivatives, nicotinamide.

CLINICAL DERMATOLOGICAL PRESENTATION

Erythema and edema similar to sunburn, in early stages.
Vesicles and bullous can be observed.
Lesions then darkened and erythema becomes a cinnamon-brown hyperpigmentation.
Finally, lesions become hyperpigmented and scaly with hyperkeratosis, fissures and crusts.
Mucusal and anogenital lesions are frequent with glossitis, stomatitis, angular cheilitis, vulvovaginitis and perianal and scrotal involvement ('diaper dermatitis' in children).
Pain and burning sensations are common.
Localization: sun exposed areas.

EXTRACUTANEOUS SIGNS

Diarrhea and Dementia (together with Dermatitis) make the classical triad of the 3 Ds.
Headache, dizziness, anorexia, depression and finally comatose state can complete the neurological symptoms. Abdominal pain, dysphagia, nausea and vomiting are frequently observed.

HISTOPATHOLOGY

Not specific.
Ballooning degeneration and marked papillary dermal edema at early stages. Increased melanin contained in the basal layers of the epidermis with hyperkeratosis, parakeratosis, acanthosis.
Low levels of niacin metabolites in the urine allow the diagnosis to be made.

DIFFERENTIAL DIAGNOSIS

- Photodermatosis.
- Subactute lupus erythematosus.
- Polymorphic ligh eruption.
- Porphyria cutaneous tarda and porphyria variegate.
- Pemphigus.
- Kwashiorkor.
- Atopic dermatitis.
- Drug eruption.

TREATMENT

Oral nicotinamide supplementation.

KEY REFERENCES

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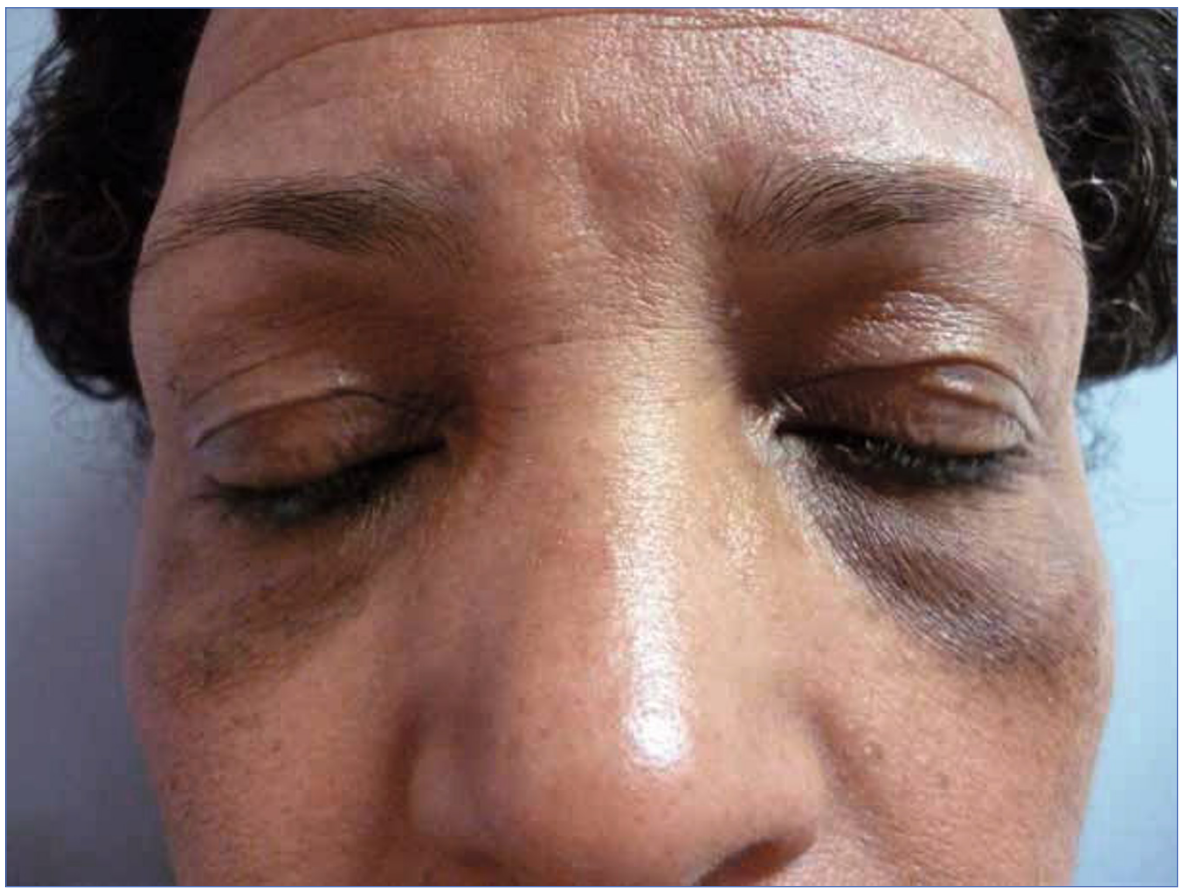
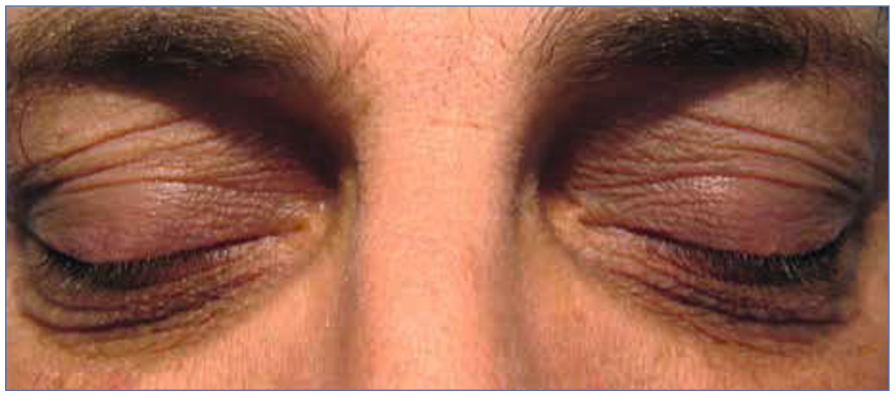
- Wan P, Moat S, Anstey A. Pellagra: a review with emphasis on photosensitivity. Br J Dermatol. 2011;164:1188-200.

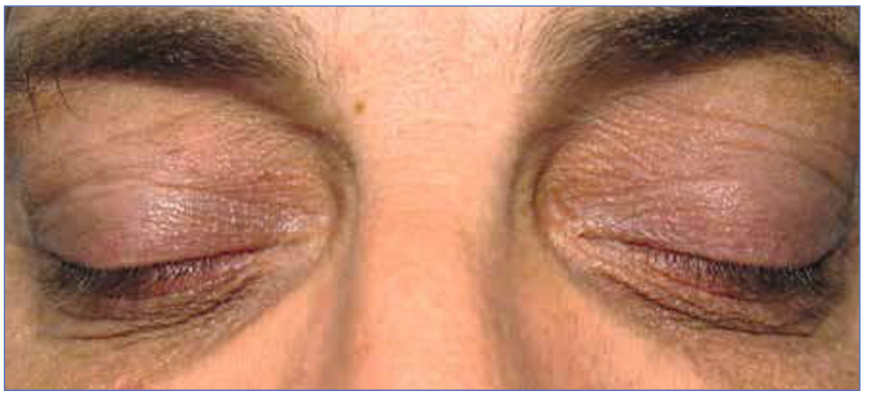
PERIORBITAL HYPERPIGMENTATION



Brownish hyperpigmentation in post-inflammatory hyperpigmentation (PIH) form of dark rings.



A. Constitutional periorbital hyperpigmentation.



B. Mild improvement after one session of 755 nm QS laser.

SYNONYMS

Dark rings, or dark circles.

EPIDEMIOLOGY

Both males and females are equally affected. The condition is more frequent in dark-skinned individuals.
The age of onset is mostly during the second and the third decades of ages.

PATHOPHYSIOLOGY

Periorbital hyperpigmentation is a heterogeneous group.
A recent study in Asians showed that the cause was vascular in 41.8% of cases, a constitutional hyperpigmentation in 38.6%, a post-inflammatory hyperpigmentation (PIH) in 12%, and shadow effects in 11.4%. Skin laxity and skin dryness can cause also periorbital hyperpigmentation.
A vascular origin seems to be more frequent in fair skin patients while constitutional periorbital hyperpigmentation is mostly observed in darker skins types.

CLINICAL DERMATOLOGICAL PRESENTATION

Brownish to black pigmentation in constitutional hyperpigmentations.
A brownish to gray pigmentation with accentuation of skin creases, eczematous lesions and lichenification can be observed in PIH forms.
Erythema or bluish discoloration and visible bluish veins with prominent capillaries or telangiectasia due to a combination of transparency of the overlying skin and dense dermal vascularity are highly suggestive of a vascular origin.
A dark shadow located only on the lower eyelids in shadow effect forms.
Lesions are asymptomatic.
Localization: symmetrical distribution the lower eyelids. Upper eyelids can be affected when in constitutional and PIH forms.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Depends on the cause.
In constitutional hyperpigmentation an orthokeratosis with increased melanin in basal layers of the skin are noted. Melanophages in the upper dermis are frequently observed.

DIFFERENTIAL DIAGNOSIS

- Bilateral nevus of Ota.
- Periorbital ecchymosis.

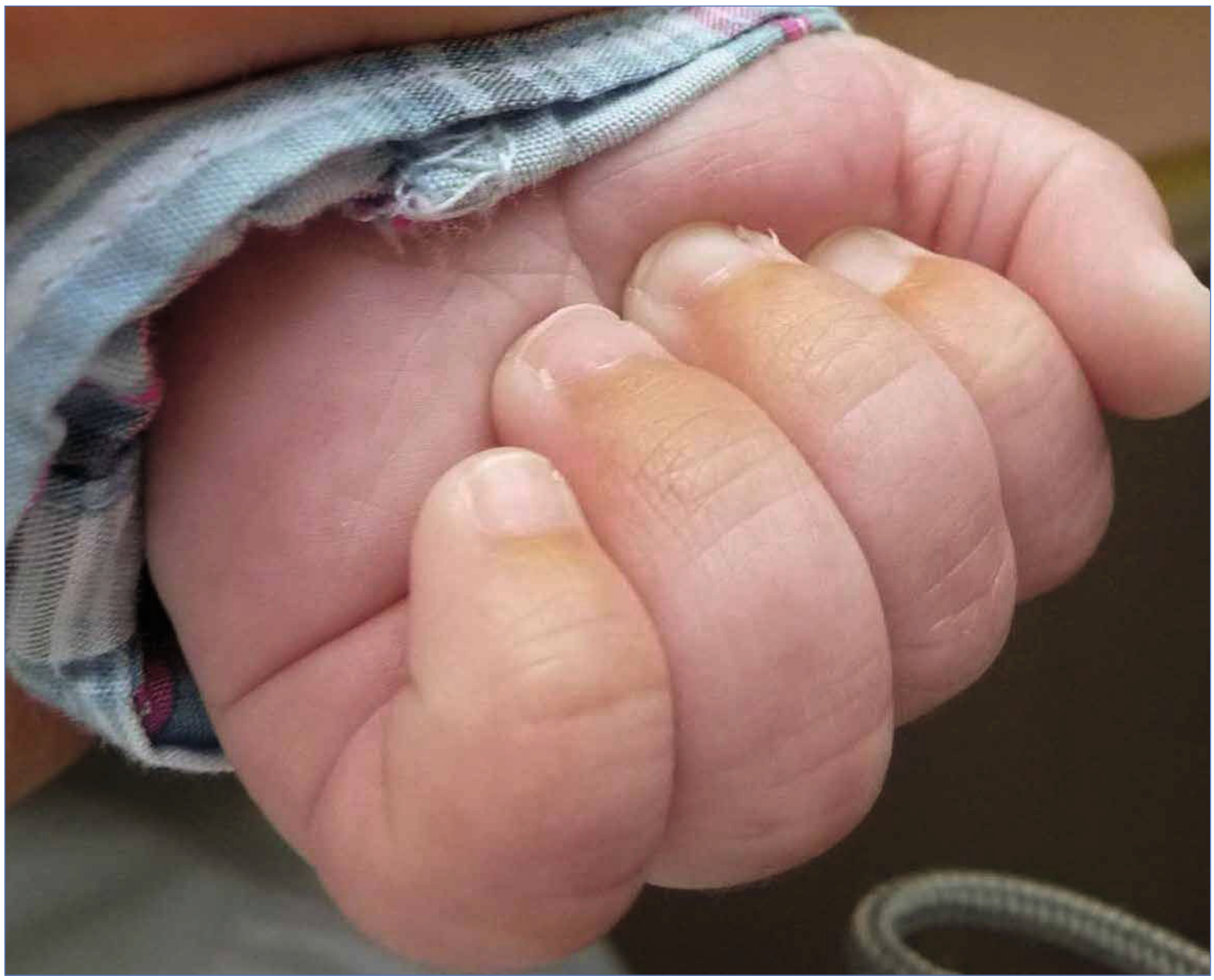
TREATMENT

Many treatments have been proposed but few studies have clearly assessed the type of periorbital hyperpigmentation before treating.
Pulse dye laser can be proposed in some vascular cases.
QS lasers and intense pulsed light (IPL) can be effective in constitutional periorbital hyperpigmentation. Ablative lasers and fractional nonablative lasers have also been proposed.
Autologous fat transplantation, and blepharoplasties can be useful for treating shadow effect.
Treatment of the underlying cause and topical steroids can be proposed for PIH forms.
In all cases photoprotection is required.

KEY REFERENCES

- Goodman RM, Belcher RW. Periorbital hyperpigmentation. An overlooked genetic disorder of pigmentation. Arch Dermatol. 1969;100:169-74.
- Ranu H, Thng S, Goh BK, Burger A, Goh CL. Periorbital Hyperpigmentation in Asians: An Epidemiologic Study and a Proposed Classification. Dermatol Surg 2011;37:1297-1303.

PERIUNGUEAL HYPERPIGMENTATION OF THE NEWBORNS



Periungueal hyperpigmentation in a fair-skinned newborn.

EPIDEMIOLOGY

Benign and transient physiological condition observed during the early months of life.
Not uncommon in dark-skinned newborns but also observed in fair-skinned individuals.

PATHOPHYSIOLOGY

Physiologic melanic pigmentation classified among the transient benign disorders of infancy.

CLINICAL DERMATOLOGICAL PRESENTATION

Light to dark brown hyperpigmentation.
Localization: periungueal, affecting fingers and sparing toes.

Can be observed at birth but more evident between 2 and 6 months and declining before the age of 2 years.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Not performed.

DIFFERENTIAL DIAGNOSIS

- Acromelanosis progressiva.
- The rare forms of Cushing syndrome observed in newborns (mostly in the context of McCune-Albright syndrome) can be discussed.

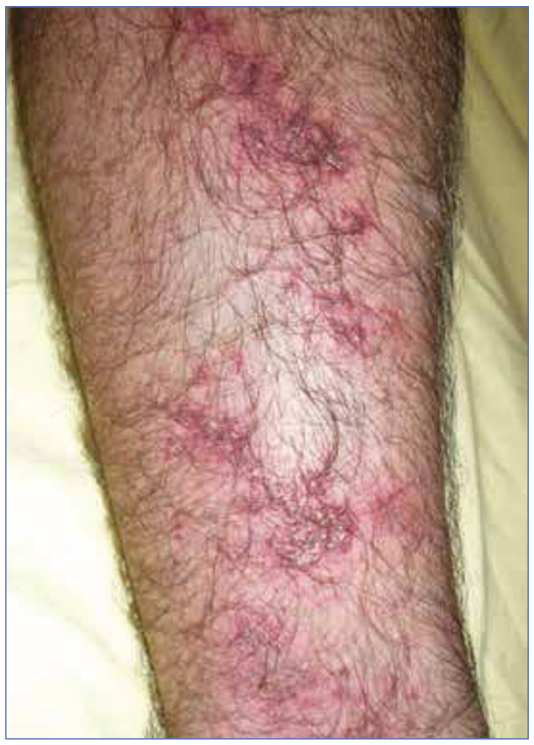
TREATMENT

None required. The hyperpigmentation always regresses in the first years of life.

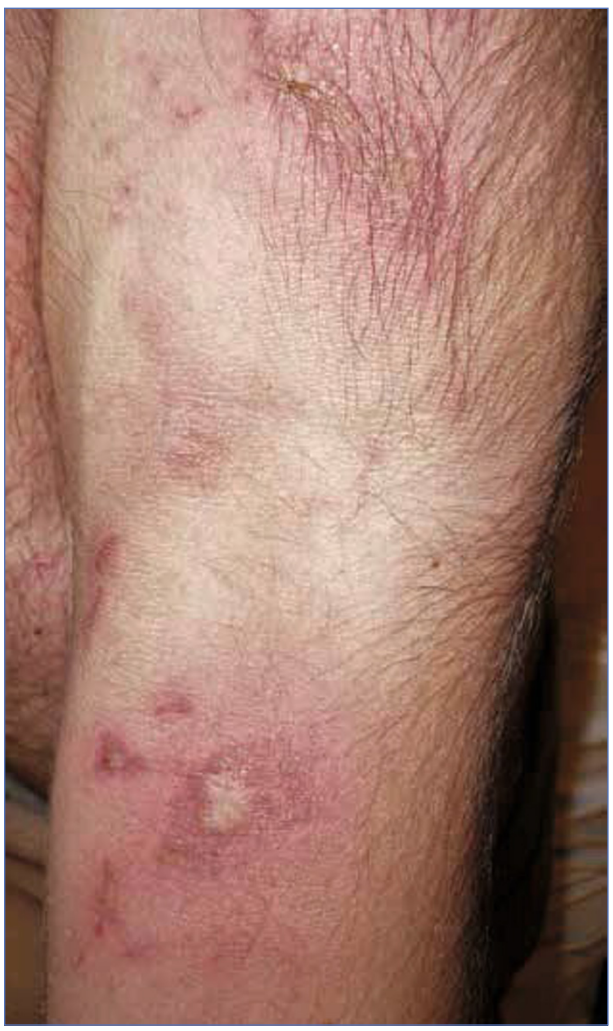
KEY REFERENCES

- Prigent F, Vige P, Martinet C. Lésions cutanées de la première semaine de vie chez 306 nouveau-nés consécutifs. Ann Dermatol Venereol 1991;118:697-9.
- Iorizzo M, Oranje AP, Tosti A. Periungual hyperpigmentation in newborns. Pediatr Dermatol. 2008;25:25-7.

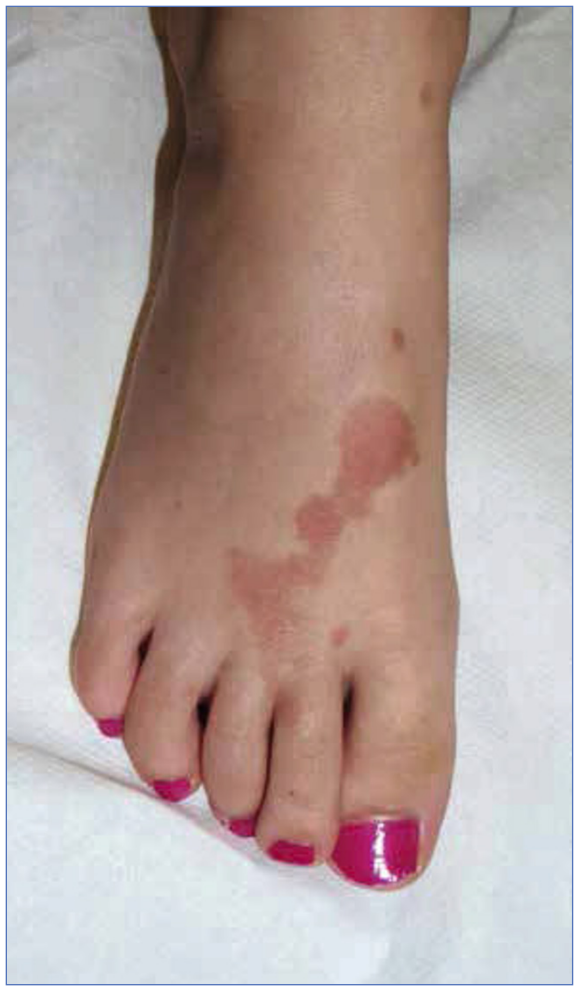
PHYTOPHOTODERMATOSIS



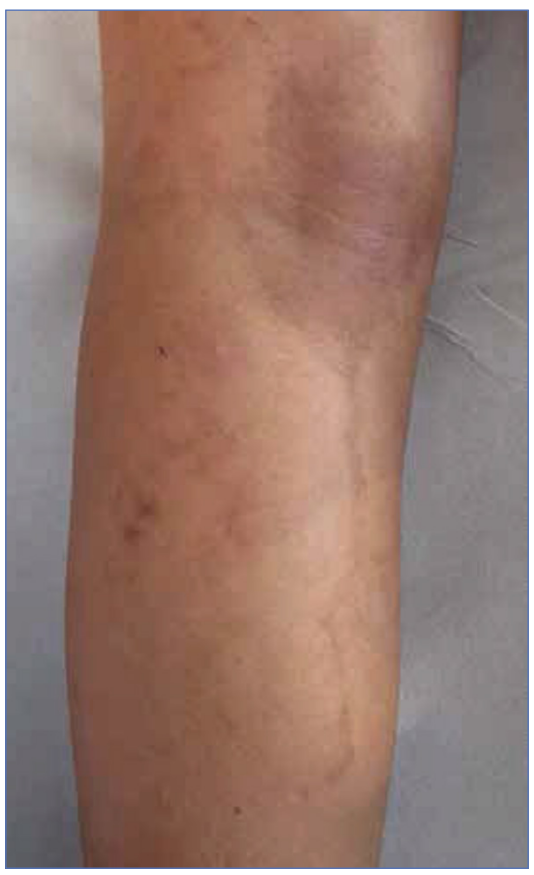
Acute phase of phytophotodermatitis on the leg with erythematous and bullous lesions. Note the figurate pattern of the lesions.



Phytophotodermatitis on the arm. The acute lesions progressively disappear here, with vesicles and erythema starting to be replaced by crusts and hyperpigmentation.



Phytophotodermatitis on the dorsum of the foot. Mild erythema persists associated with hyperpigmentation on lesional skin.



Late stage of phytophotodermatitis. Only the hyperpigmentation is observed but the pattern is highly suggestive of the diagnosis. This child played under a fig tree and was exposed concomitantly to sun exposure. Some drops of fig milk ran down his leg leading to this linear disposition of the hyperpigmentation.

SYNONYMS

Phototoxic dermatitis, Berloque dermatitis, dermatitis bullosa striata pretensis.

EPIDEMIOLOGY

Frequent condition all around the world.

PATHOPHYSIOLOGY

The mechanism is a post-inflammatory hyperpigmentation secondary to the association of the marked inflammation due to the exposure to the plant phototoxic chemicals and the ultraviolet light.

CLINICAL DERMATOLOGICAL PRESENTATION

Sharply demarcated brown hyperpigmentation macules or patches with typical figurate pattern.
In the acute phase erythematous and edematous lesions are observed. Vesicles coalescing into bullae are frequent. Within the following days desquamation followed by the hyperpigmentation are observed.
Localization: only on sun-exposed areas.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin in the epidermis associated with pigmentary incontinence in the dermis both extracellularly and within melanophages.
Aspect of contact dermatitis is observed in the early phase.

DIFFERENTIAL DIAGNOSIS

- Drug-induced photosensitivity.
- Polymorphous light eruption.
- Lupus erythematosus.
- Porphyria cutaneous tarda.
- Pellagra.

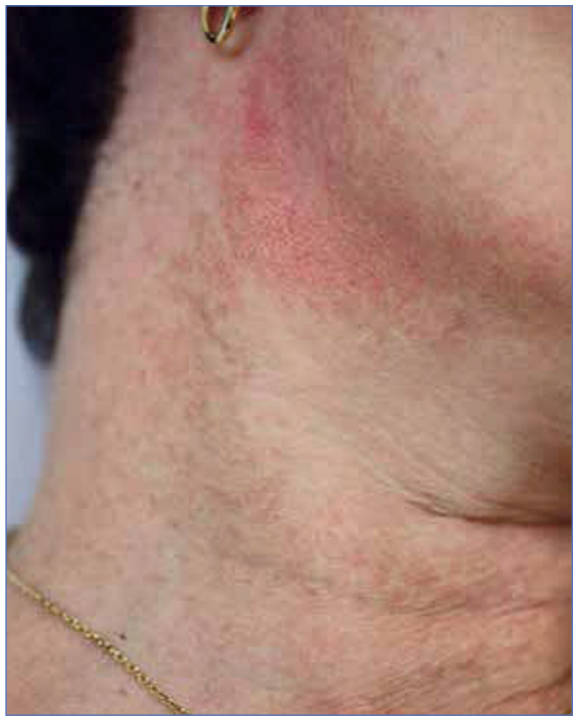
TREATMENT

High potent topical steroid are effective in the acute phase.
Protection against sun exposure is crucial.
The hyperpigmentation gradually fades over weeks and more often months. Kligman's duo (topical steroids and 4 to 5% of hydroquinone) can be proposed but the efficacy is limited at the stage of the hyperpigmented sequelae.

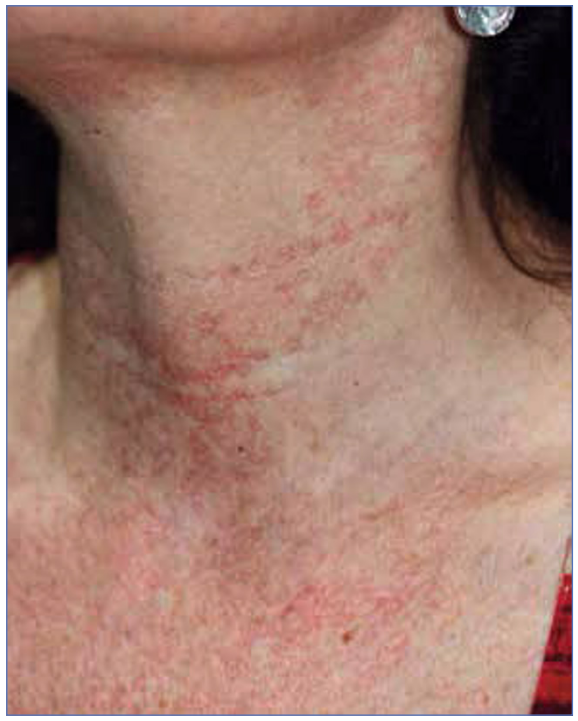
KEY REFERENCES

- Sasseville D. Clinical patterns of phytodermatitis. Dermatol Clin. 2009;27:299-308.

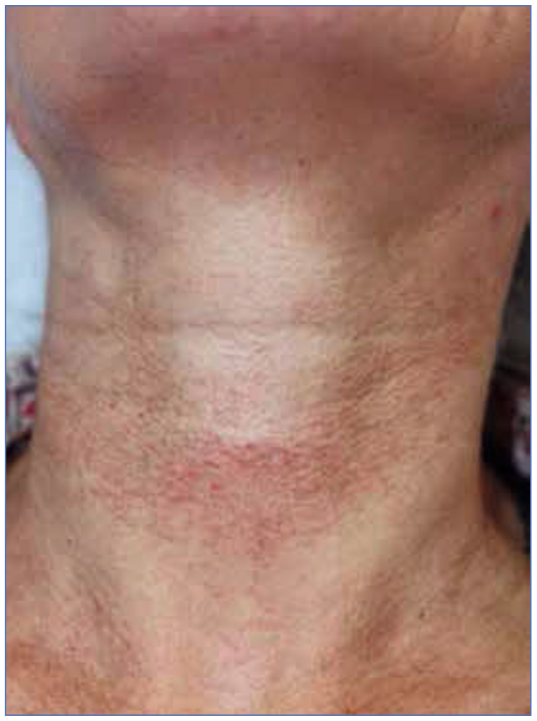
POIKILODERMA OF CIVATTE



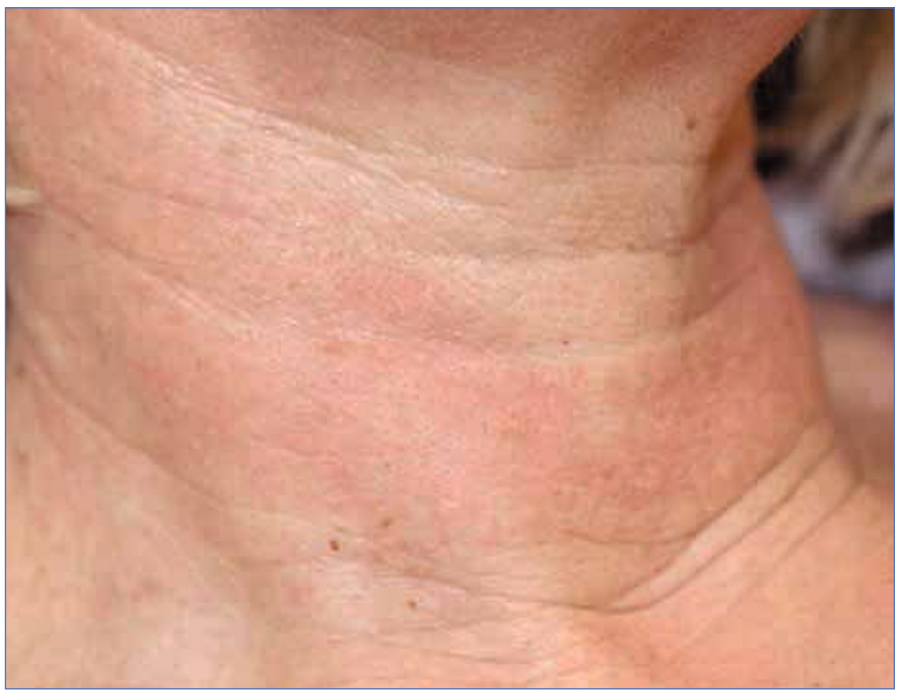
Poikiloderma of civatte. In this patient, the upper part of the lesion associates telangieactasia and hyperpigmentation, while in the lower part there is almost only reticulated hyperpigmentation.



Typical presentation of poikiloderma of civatte.



Poikiloderma of civatte. Note the respect of the submental triangle area.



Early stage of poikiloderma of civatte. The hyperpigmentation and atrophia are very mild.

SYNONYMS

Atrophic degenerative pigmentary dermatitis, menopausal solar dermatitis.

EPIDEMIOLOGY

The condition is quite common, but mostly observed in fair-skinned patients.
More frequently observed in middle-aged and elderly women, and in outdoor workers.

PATHOPHYSIOLOGY

Chronic sun exposure in combination with hormonal changes and genetic predisposition.
Photosensitizing chemicals in fragrances and cosmetics could also play a role.

CLINICAL DERMATOLOGICAL PRESENTATION

Reticulate brown hyperpigmentation.
Association with epidermal atrophy and telangiectasia.
Asymptomatic in half of cases. Mild itching, burning sensation and flushing.
Localization: lateral face of the neck and upper chest.
The submental triangle area is spared.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Irregular hyperpigmentation of the basal layers of the epidermis with frequent pigmentary incontinence.
Atrophic and flattened epidermis hyperkeratosis and occasional follicular plugging.
Elastosis of papillary dermis.
Vascular ectasia.
Mild perivascular lymphohistiocytic infiltrate and edema of the upper dermis can also be observed.

DIFFERENTIAL DIAGNOSIS

- Riehl melanosis.
- Erythromelanosis facei and colli melasma.
- Berloque dermatitis.
- Dermatopolymyositis and lupus erythematosus.

TREATMENT

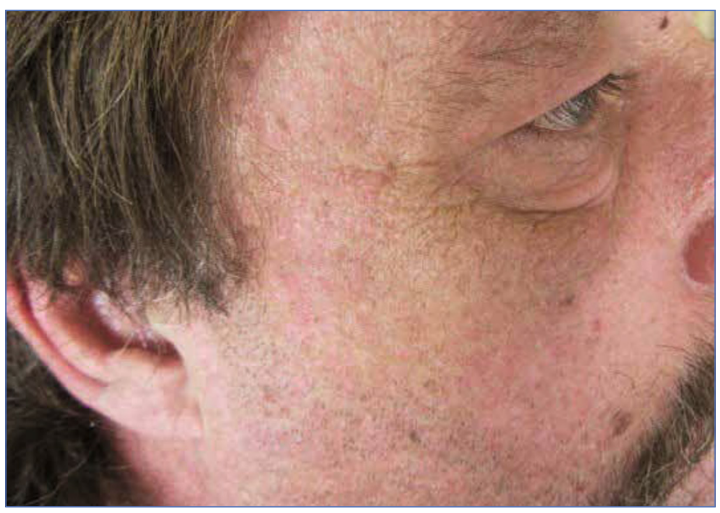
Photoprotection.
Intense pulse light and pulsed dye laser.
Ablative fractional laser.

KEY REFERENCES

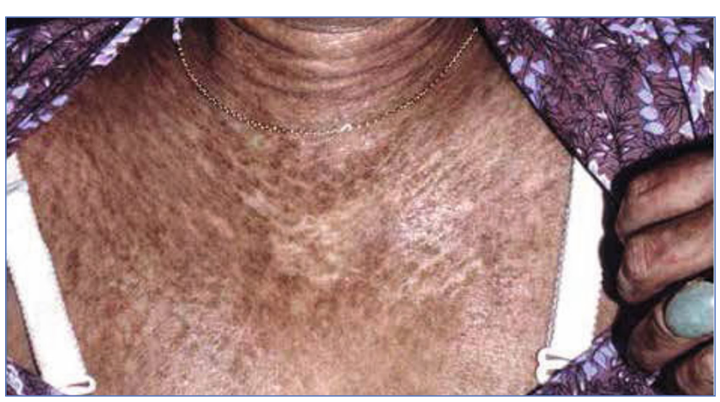
- Katoulis AC, Stavrianeas NG, Georgala S, Bozi E, Kalogeromitros D, Koumantaki E, Katsambas AD. Poikiloderma of Civatte: a clinical and epidemiological study. J Eur Acad Dermatol Venereol. 2005;19:444-8.
- Katoulis AC, Stavrianeas NG, Panayiotides JG, Bozi E, Vamvasakis E, Kalogeromitros D, Georgala S. Poikiloderma of Civatte: a histopathological and ultrastructural study. Dermatology. 2007;214:177-82.

PORPHYRIA CUTANEA TARDA

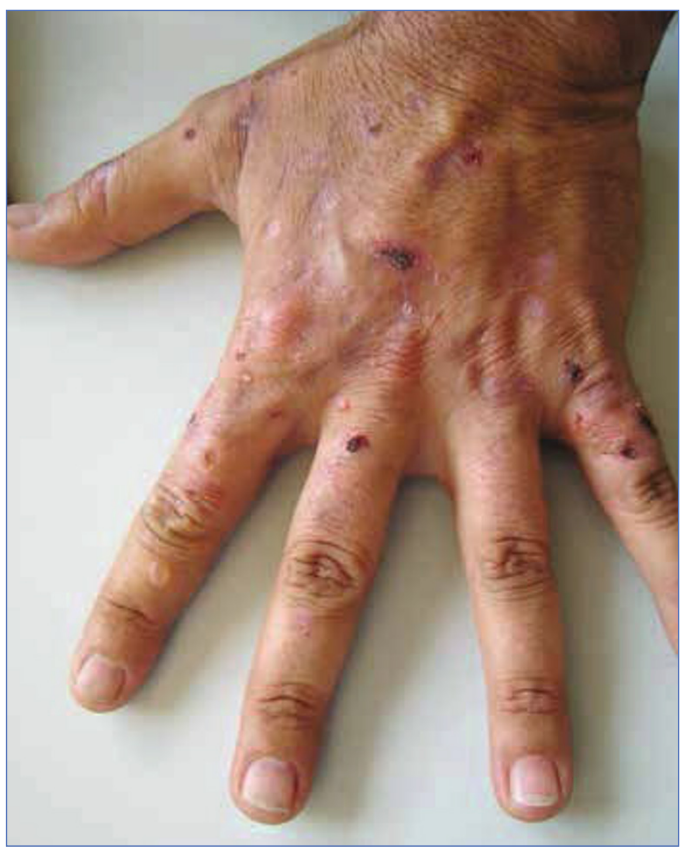
Chee-Leok Goh and Sai-Yee Chuah



Mild hyperpigmentation on the face of a patient with porphyria cutanea tarda.



Association of hyperpigmentation and hypopigmentation along with pseudoscleroderma changes in a woman with porphyria cutanea tarda (coll. Chee-Leok Goh).



Blisters, erosions and crusts on the dorsum of the hand of a man with porphyria cutanea tarda.

OMIM: #176100

GENETICS

Porphyria cutanea tarda (PCT) is a metabolic disorder caused by deficiency/dysfunction of enzymes involved in the biosynthesis of the heme pathways.
Familial porphyria cutanea tarda arises from an autosomal dominant inheritance.
The non-familial disease is due to heterozygous mutation in the gene encoding for uroporphyrinogen decarboxylase (UROD) (1p34.1)

MOUSE MODEL

URO-D +/-

EPIDEMIOLOGY

PCT is the commonest type of porphyria.
Approximately 80% of all cases of PCT are acquired or sporadic (type 1) and 20% are familial (type 2).
Type 1 PCT generally begins in mid-life adult and type 2 patients are younger at onset.
PCT occurs in all races and both sexes.

PATHOPHYSIOLOGY

The disease arises from decreased catalytic activity of UROD, the fifth enzyme in heme biosynthesis.
Exposure to certain chemicals that suppress or overwhelm the activities of UROD in the liver which result in increase in the accumulation of uroporphyrins may exacerbate the condition.
These include:

- Alcohol.
- Estrogen, eg, oral contraceptive, hormone replacement or liver disease.
- Environmental exposure to polyhalogenated aromatic hydrocarbons (eg, dioxins).
- Iron overload, due to excessive intake (orally or by blood transfusion).
- Viral infections (hepatitis, especially hepatitis C).
- Chronic blood disorders such as thalassaemia, haemochromatosis.
- Hepatitis (eg, viral hepatitis), chronic liver disease.

CLINICAL DERMATOLOGICAL PRESENTATION

PCT usually affects adults in the 3rd or 4th decade of life. Its manifestations are predominantly cutaneous including:

- Photosensitivity.
- Increased mechanical fragility after sunlight exposure with blisters, erosions, crusts and milia.
- Scars in sun-exposed site.
- Hypertrichosis.
- Scarring alopecia.

Morpheaform and sclerodermoid changes may be observed.
Brown hyperpigmentation, mostly on photoexposed areas.
Hypopigmentation may be seen along with sclerodermoid changes.

EXTRACUTANEOUS SIGNS

Urine is darker than usual, with a reddish or tea-colored hue (due to increased concentration of uroporphyrin I).
Chronic liver problems are common in patients with the type 1 sporadic form of PCT. These include liver cirrhosis and inflammation. Cutaneous signs of chronic liver disease may be seen, eg, spider telangiectasia, palmar erythema, jaundice, etc.
Hepatoma may develop.

HISTOPATHOLOGY

Subepidermal bullae with minimal dermal inflammatory infiltrate is commonly seen. There is festooning of dermal papillae. There is thickening and hyalinization of upper dermal capillary walls with scanty perivascular infiltrates. The dermoepidermal basement membrane zone is accentuated with the periodic acid-Schiff (PAS) stain. Sclerosis of dermal collagen and hyaline deposits may be seen in the dermis.
Direct immunofluorescence examination shows deposition of immunoglobulins and complement in and around the dermal capillaries and at the basement membrane zone.
These deposits are believed to be immunoproteins leaked from the damaged vasculature.

DIFFERENTIAL DIAGNOSIS

- Other types of cutaneous porphyria that manifest with blistering including congenital erythropoietic porphyria, hepatoerythropoietic porphyria, variegate porphyria, hereditary coproporphyria and pseudoporphyria.
- Epidermolysis bullosa acquisita.
- Polymorphous light eruption.
- Phototoxic and bullous drug eruptions.
- Hydroa vacciniforme.
- Bullous lupus erythematosus.

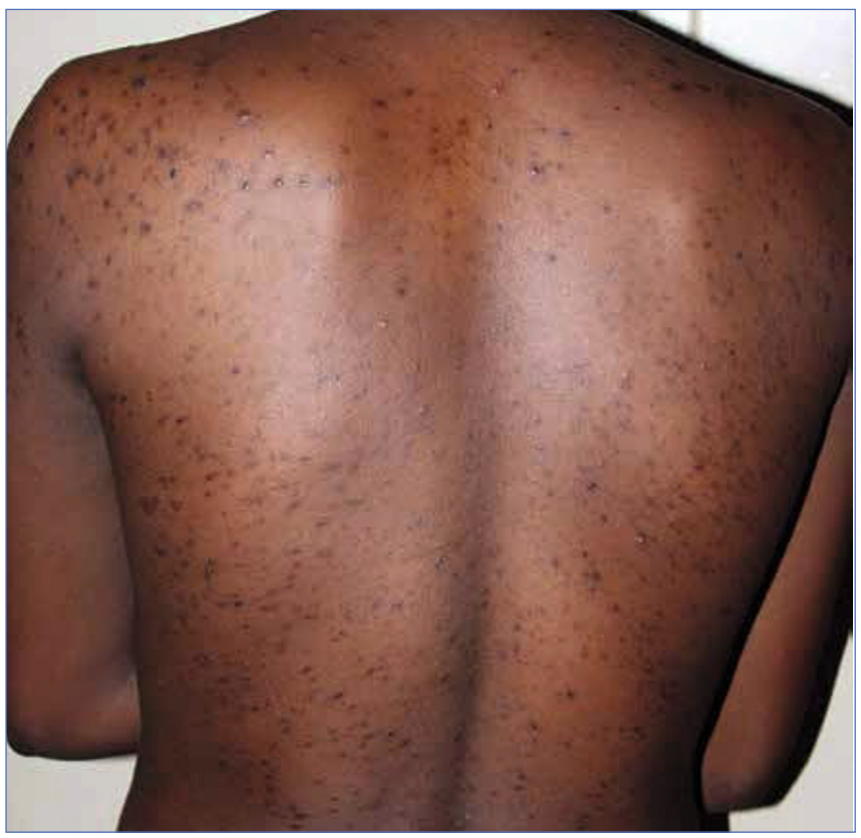
TREATMENT

Sunlight avoidance, the responsible light is the Soret band at 400 nm, which is unfortunately not blocked by most sun-screens.
Avoid alcohol, estrogen, and iron.
Phlebotomy – up to 500 mL blood is removed every one to two weeks until the hemoglobin and iron levels drop to low normal levels. It may take 3 to 6 months to improve. Venesection may need to be repeated after a year or more.
Antimalarial tablets, ie, low-dose chloroquine or hydroxychloroquine may be recommended, but must be used cautiously. This medication makes the porphyrins more soluble so more are excreted in the urine.
Autologous red cell transfusion.

KEY REFERENCES

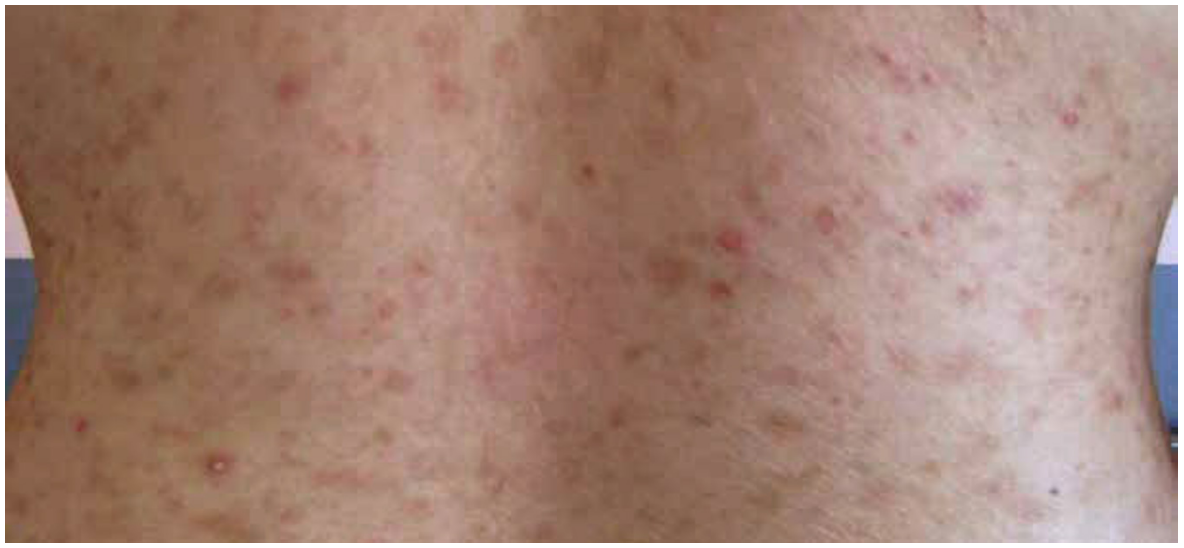
- Phillips JD, Jackson LK, Bunting M et al. A mouse model of familial porphyria cutanea tarda. Proc Natl Acad Sci USA. 2001;2;98:259-64.
- Bleasel NR, Varigos GA. Porphyria cutanea tarda. Australas J Dermatol. 2000;41:197-206; 207-8.
- Köstler E, Wollina U. Therapy of porphyria cutanea tarda. Expert Opin Pharmacother. 2005:6:377-83.

POSTINFLAMMATORY PIGMENTATION SECONDARY TO ACNE



Severe post-inflammatory hyperpigmentation secondary to acne spreading in the entire back. Note that the pigmentation remains localized on the back and that the limbs are spared.

Post-inflammatory hyperpigmentation secondary to acne. Note the hyperpigmented macules associated with inflammatory lesions of acne.



Post-inflammatory hyperpigmentation secondary to acne of the back in a fair skinned patient.

EPIDEMIOLOGY

Post-inflammatory hyperpigmentation (PIH) secondary to acne is mainly observed in dark phototypes (IV, V and VI). It is observed in two-thirds of acne in the African American population.

PATHOPHYSIOLOGY

The hyperpigmentation occurs secondary to the inflammation, but also concomitantly in active lesions. The pigmentation can regress with the inflammatory lesions or can persist for several months.

CLINICAL DERMATOLOGICAL PRESENTATION

Brown pigmented macules from 3 to 10 mm in diameter. Often associated with inflammatory or retentional lesions of acne.
Localization: face, upper back. Sometimes more widespread involvement of the trunk.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin pigment in the basal cell layer of the epidermis sometimes associated with pigment incontinence with melanophages in the papillary dermis. Dilated follicle with a plug of dense keratin and inflammatory infiltrate of the dermis with bacteria proliferation are associated if active lesions of acne are associated with the hyperpigmentation.

DIFFERENTIAL DIAGNOSIS

- Urticaria pigmentosa (especially when the trunk is involved).
- Other post-inflammatory processes.

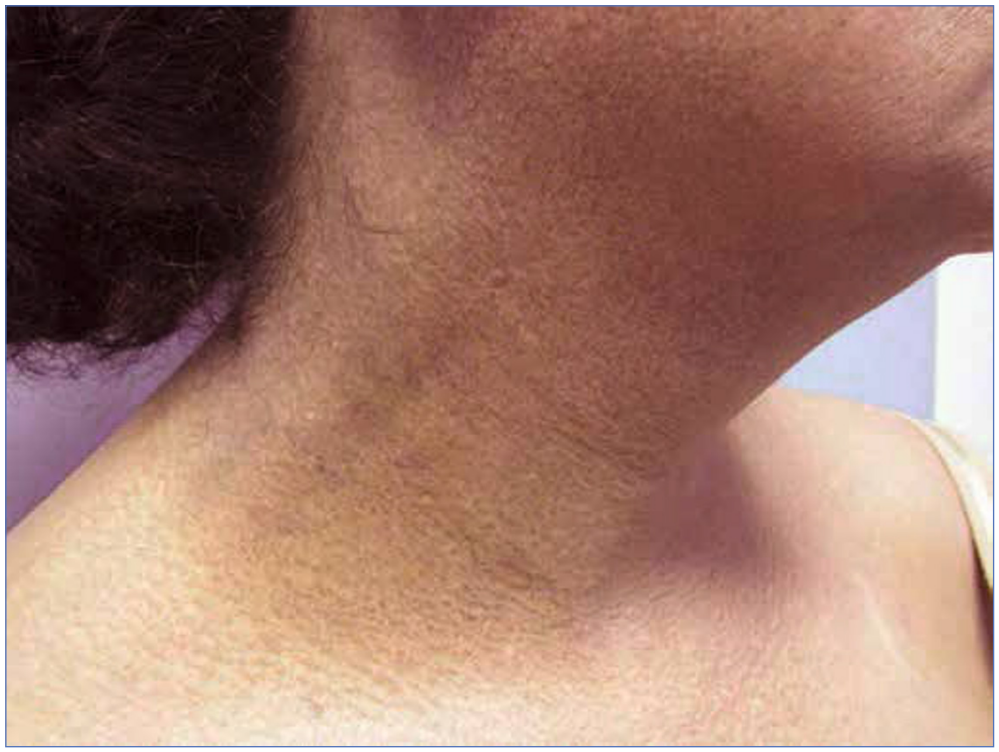
TREATMENT

Topical tretinoin or topical adapalene if acne is still active. Oral isotretinoin can be discussed in severe forms. Topical hydroquinone 4 or 5%, alone or associated with tretinoin and topical steroid (Kligman trio) when active lesions of acne have been treated and only PIH remains. Stable fixed dose triple combination therapy can be useful in these forms

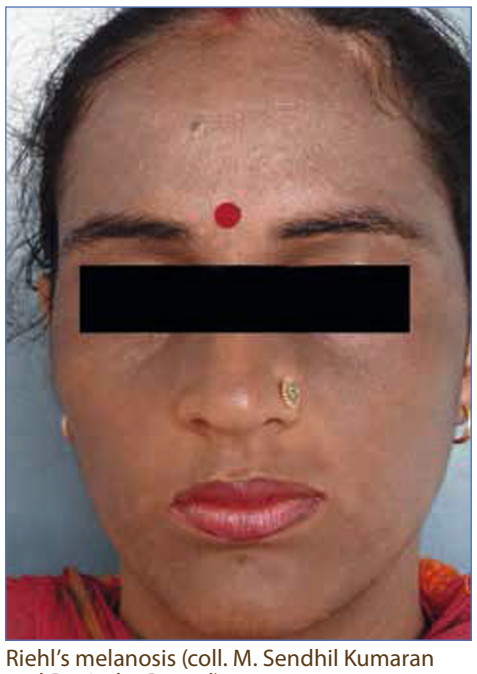
KEY REFERENCES

- Bulengo-Ransby SM, Griffiths C, Kimbrough-Green CK, et al. Topical tretinoin (retinoic acid) therapy for hyperpigmented lesions caused by inflammation of the skin in black patients. N Engl J Med. 1993;328:1438-43.
- Taylor SC. Acne vulgaris in skin of color. J Am Acad Dermatol. 2002;46:S98-106.
- Ho SG, Yeung CK, Chan NP, Shek SY, Kono T, Chan HH. A retrospective analysis of the management of acne post-inflammatory hyperpigmentation using topical treatment, laser treatment, or combination topical and laser treatments in oriental patients. Lasers Surg Med. 2011;43:1-7.

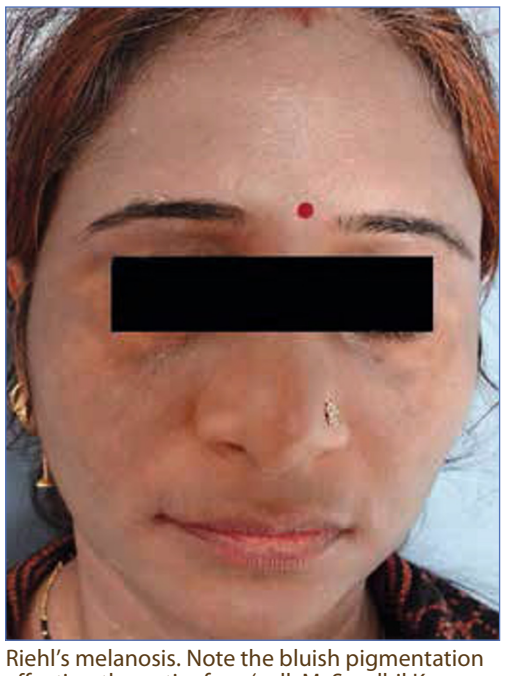
RIEHL'S MELANOSIS



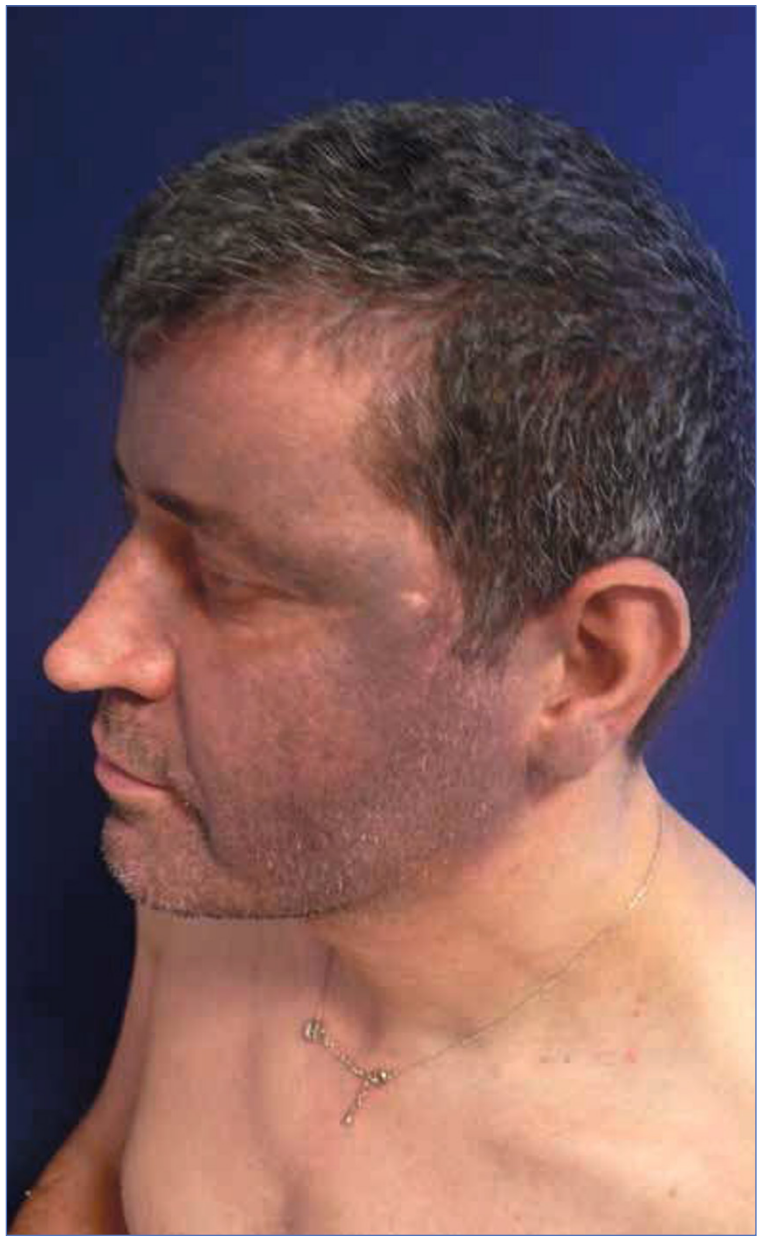
Gray-brown reticulate pigmentation of the neck in Riehl's melanosis.



Riehl's melanosis (coll. M. Sendhil Kumaran and Davinder Parsad).



Riehl's melanosis. Note the bluish pigmentation affecting the entire face (coll. M. Sendhil Kumaran and Davinder Parsad).



Severe form of Riehl's melanosis affecting the entire face (coll. Liliane Laroche).

SYNONYMS

Pigmented contact dermatitis, female facial melanosis.

EPIDEMIOLOGY

Only a few cases have been reported but the dermatosis is not so uncommon.
Mostly observed in middle-aged women.

PATHOPHYSIOLOGY

Lichenoid reaction to intrinsic or extrinsic (cosmetics and fragrances) factors.

CLINICAL DERMATOLOGICAL PRESENTATION.

Brown or bluish reticulate hyperpigmentation.
Mild erythema or scaling can be observed at early stages.
Localization: face and neck.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Melanophages in the dermis.
Interface dermatitis with vacuolar basal degeneration.
Mild to moderate histiolymphocytic infiltrate of the upper dermis.

DIFFERENTIAL DIAGNOSIS

- Poikiloderma of Civatte.
- Erythromelanosis follicularis faciei et colli.
- Erythrose péribuccale pigmentaire de Brocq.
- Post-inflammatory hyperpigmentation.
- Melasma.
- Acquired bilateral nevus of Ota-like macules.

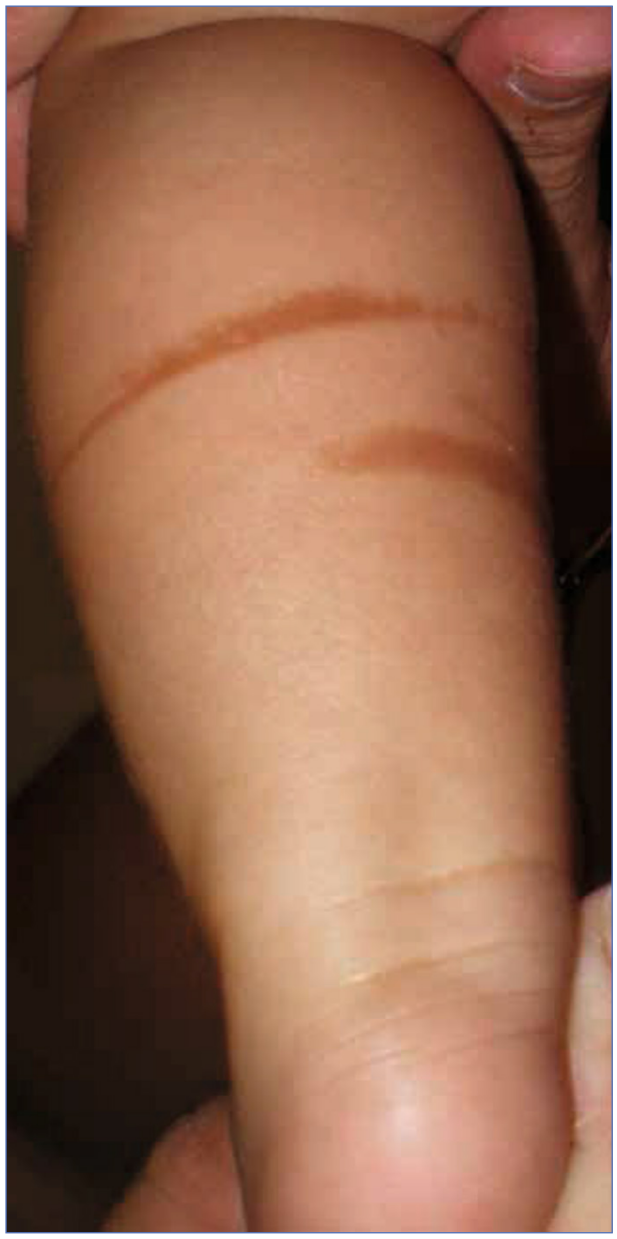
TREATMENT

Sun protection and avoidance of cosmetics and fragrances.
Blanching creams are rarely effective.
Intense pulsed light has shown promising results in a pilot study.

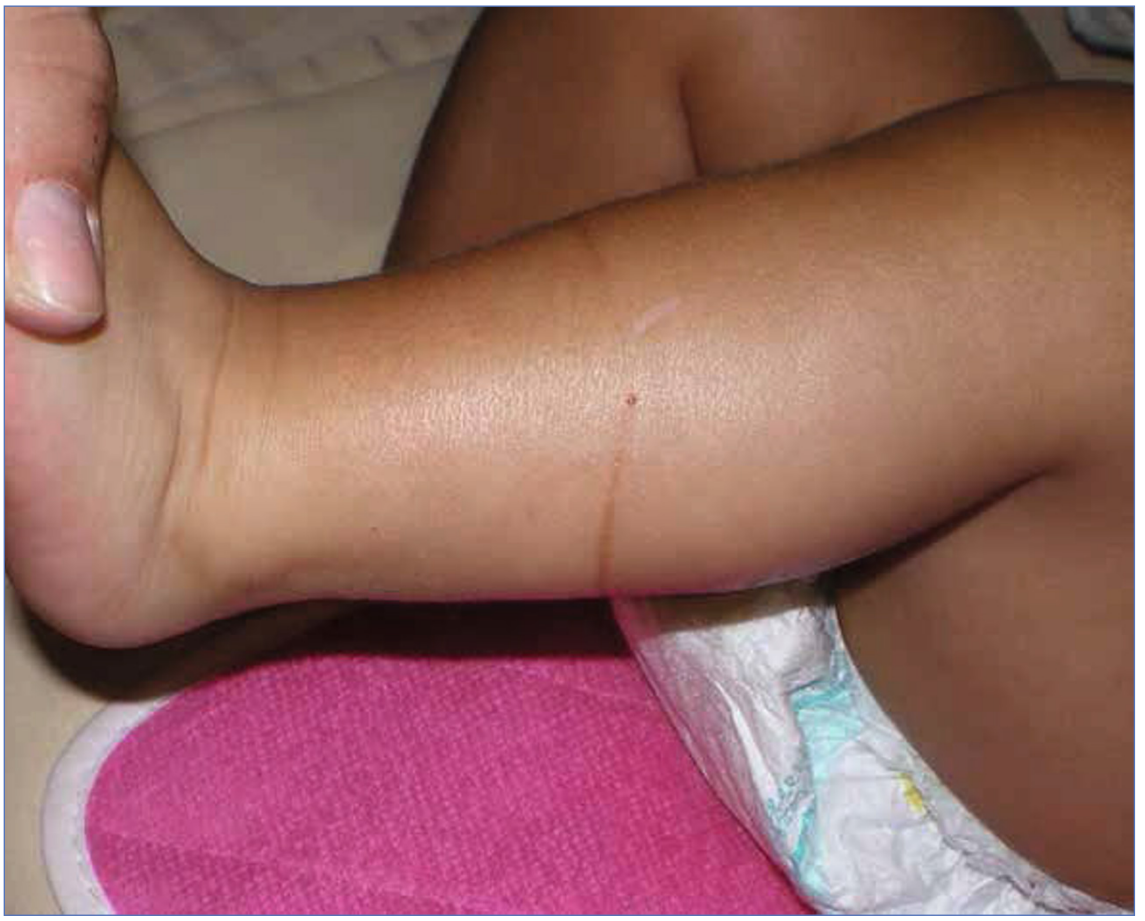
KEY REFERENCES

- Li YH, Liu J, Chen JZ, Wu Y, Xu TH, Zhu X, Liu W, Wei HC, Gao XH, Chen HD. A pilot study of intense pulsed light in the treatment of Riehl's melanosis. Dermatol Surg. 2011;37:119-22.
- Serrano G, Pujol C, Cuadra J, Gallo S, Aliaga A. Riehl's melanosis: pigmented contact dermatitis caused by fragrances. J Am Acad Dermatol. 1989;21(5 Pt 2):1057-60.

SOCKS LINE PIGMENTATION



Acquired horizontal hyperpigmented lesions that do not follow Blaschko lines.



Isolated linear hyperpigmented line of the calf that appeared at 2 months of age.

EPIDEMIOLOGY
Entity recently described but probably not uncommon.

PATHOPHYSIOLOGY
Post-inflammatory hyperpigmentation due to the elastic contention of socks or pants.

CLINICAL DERMATOLOGICAL PRESENTATION
Slight to dark brown linear pigmentation.
Horizontal position.
Do not follow Blaschko lines.
Absents at birth and appears in the first months of life.
Always located on ankles or calves.

EXTRACUTANEOUS SIGNS
None.

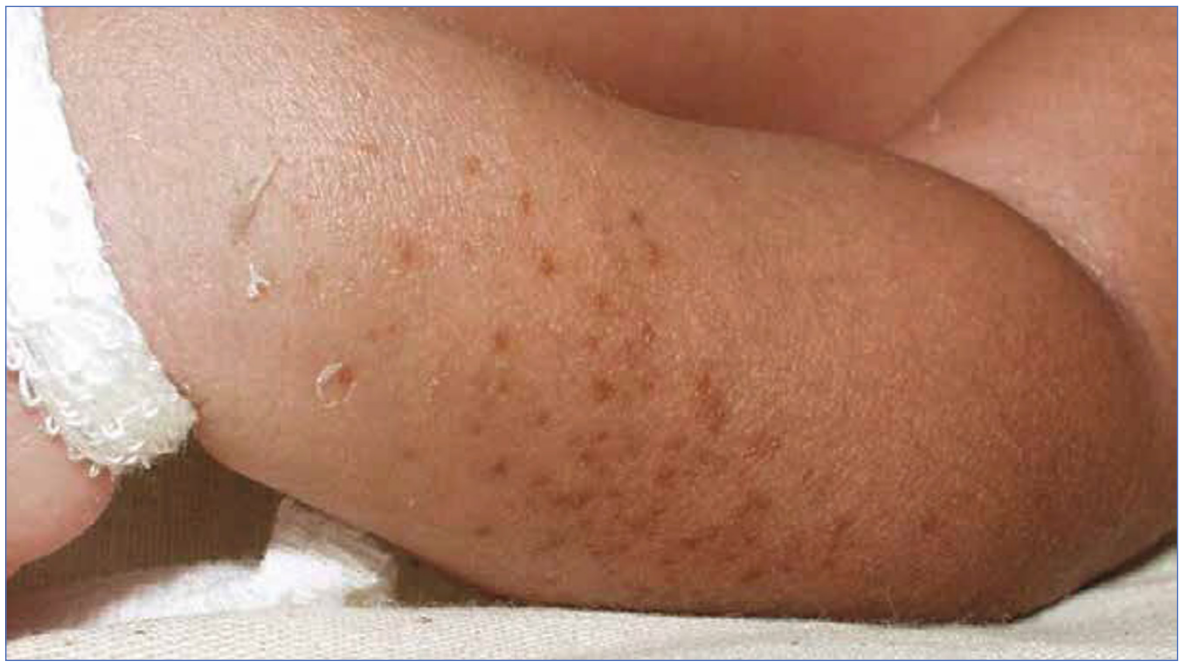
HISTOPATHOLOGY
Increased melanin pigment in the basal cell layer of the epidermis associated with pigment incontinence and melanophages in the papillary dermis.

DIFFERENTIAL DIAGNOSIS
- Pigmentary mosaicisms.
- Other post-inflammatory hyperpigmentation.

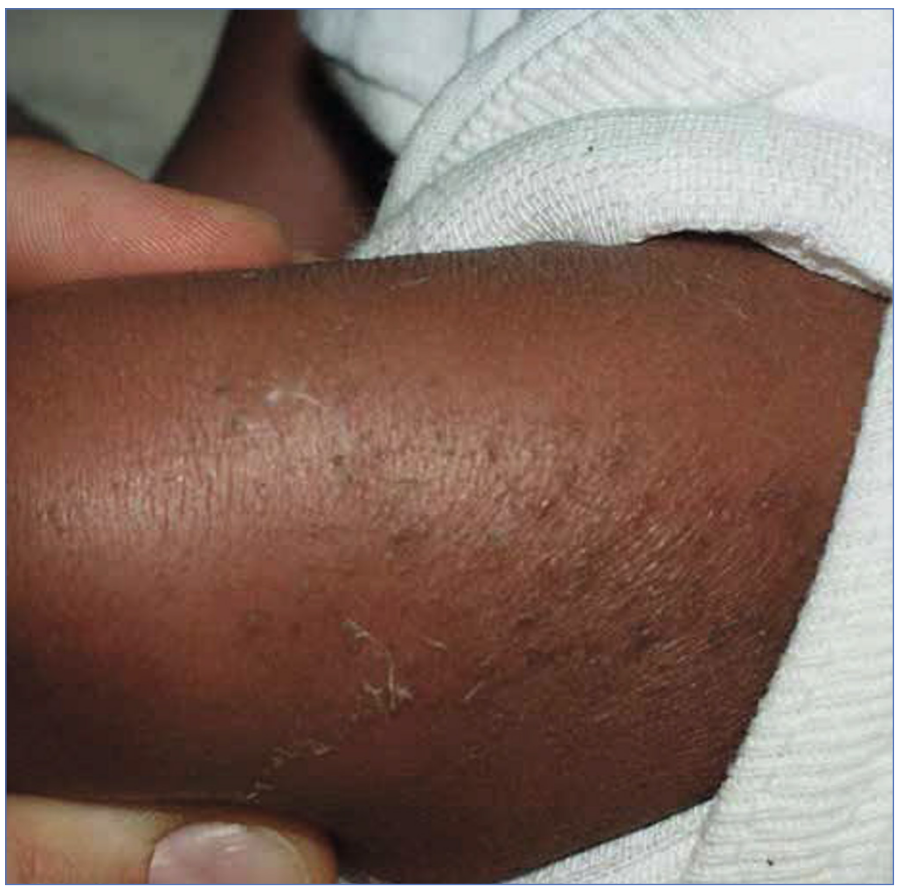
TREATMENT
Spontaneous regression of the pigmentation after the withdrawal of elastic contention.

KEY REFERENCE
Berk DR, Tapia B, Lind A, Bayliss SJ. Sock-line hyperpigmentation: case series and literature review. Arch Dermatol. 2007;143:428-30.

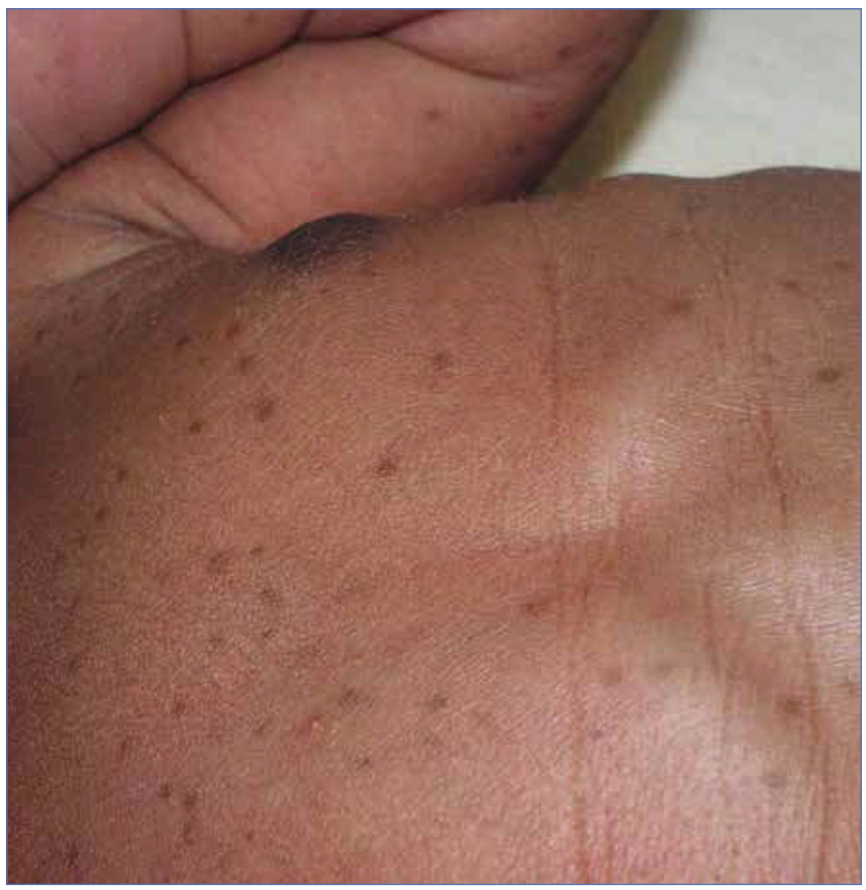
TRANSIENT NEONATAL PUSTULAR MELANOSIS



Hyperpigmented macules of the forearm. Note the slight desquamation.



Hyperpigmented macules, pustules and slight desquamation on the thigh of a newborn.



Multiple macular hyperpigmentations of the trunk and proximal limbs in a newborn. Note the association with sparse pustules

EPIDEMIOLOGY

Observed in about 4% of Black newborns as compared to less than 1% in White newborns.

PATHOPHYSIOLOGY

The mechanism of the hyperpigmentation is pre- and post-inflammatory. Close relation with the erythema toxicum neonatorum.

CLINICAL DERMATOLOGICAL PRESENTATION

Brown pigmented macules from 2 to 5 mm in diameter.
Present at birth or maximum at the first day of life.
Often associated with transient pustules (but pustules may be lacking).
Slight desquamation in the periphery of the lesions can be observed.
Localization: the entire body can be involved but trunk, proximal part of the limbs, chin and forehead are more frequently affected.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin pigment in the basal cell layer of the epidermis sometimes.
Intracorneal eosinophilic or neutrophilic pustules can be associated with the hyperpigmentation.

DIFFERENTIAL DIAGNOSIS

Lentiginosis.

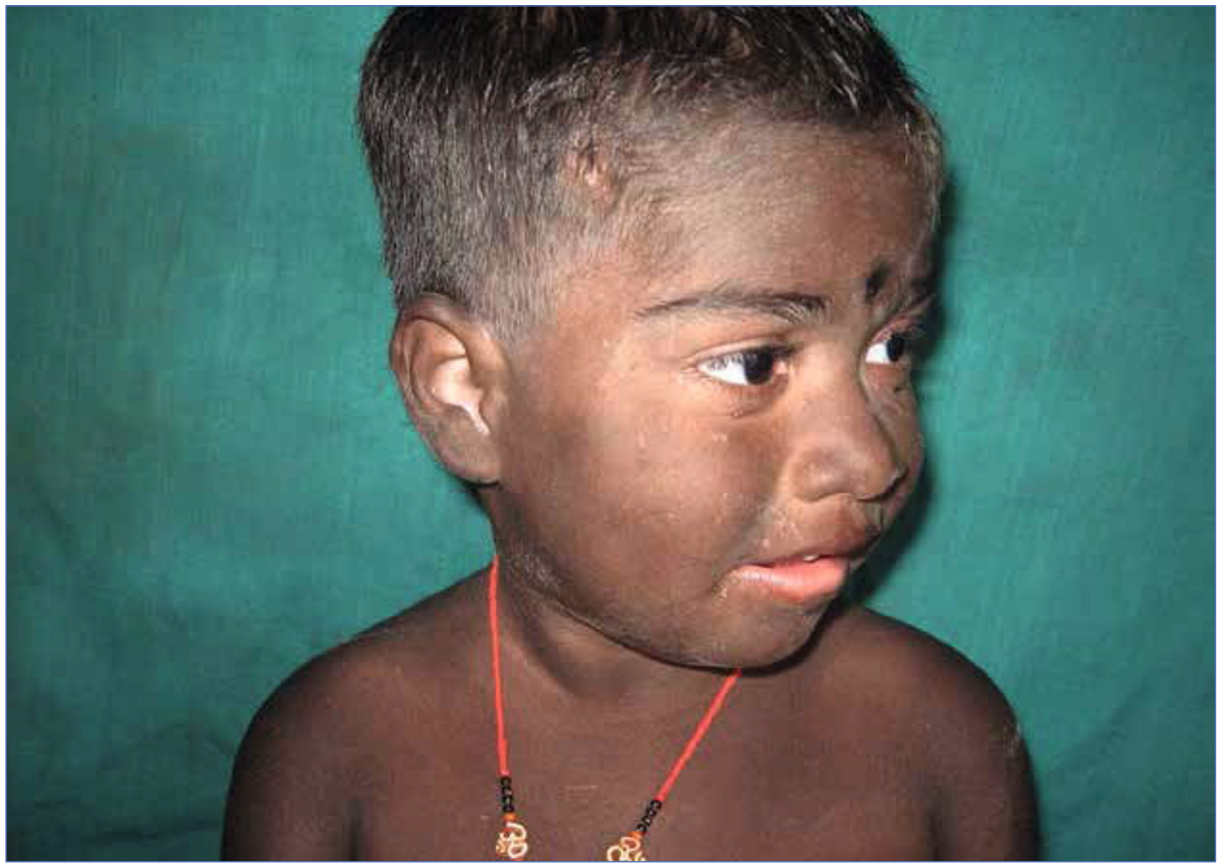
TREATMENT

None required. Spontaneous regression is constant.

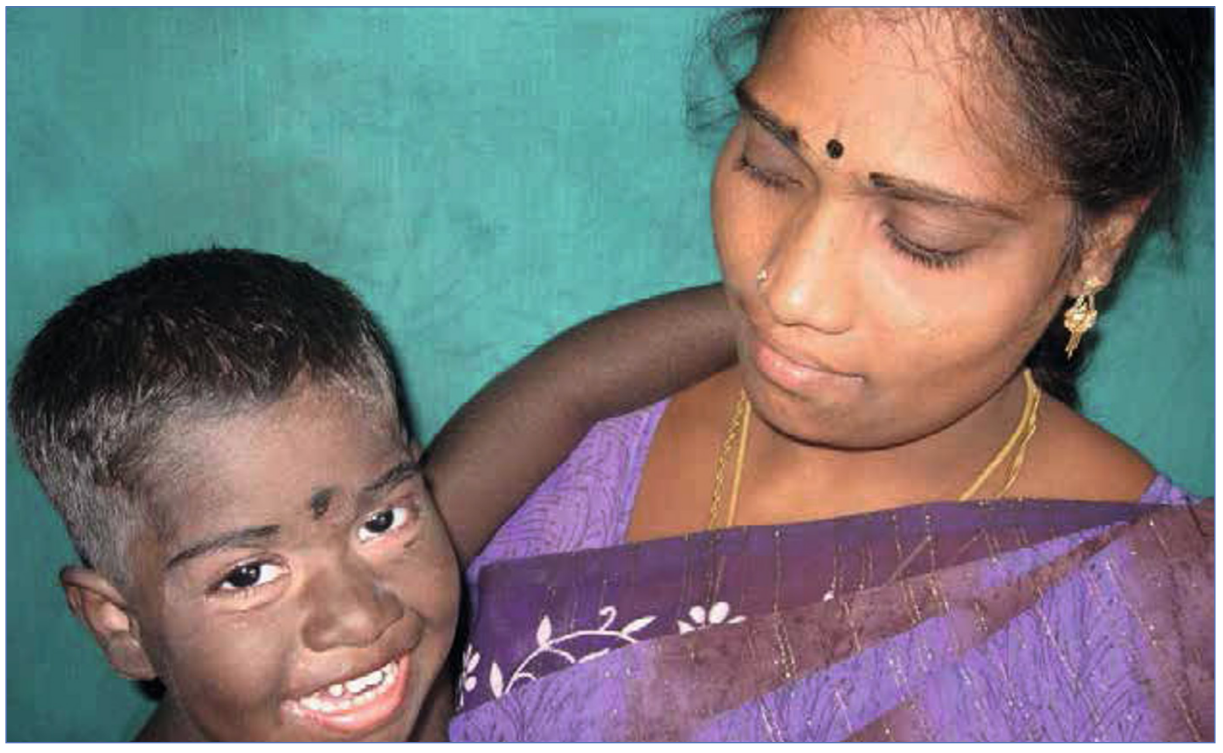
KEY REFERENCES

- Ramamurthy RS, Reveri M, Esterly NB, Fretzin DF, Pildes RS. Transient neonatal pustular melanosis. J Pediatr. 1976;88:831-5.
- Ferrándiz C, Coroleu W, Ribera M, Lorenzo JC, Natal A. Sterile transient neonatal pustulosis is a precocious form of erythema toxicum neonatorum. Dermatology. 1992;185:18-22.

UNIVERSAL ACQUIRED MELANOSIS



Universal acquired melanosis in a young Indian boy (coll. P. V. S. Prasad and P. K. Kaviarasan).



Universal acquired melanosis. Note the difference in skin color with his mother (coll. P. V. S. Prasad and P. K. Kaviarasan).

SYNONYMS
Carbon baby syndrome.

EPIDEMIOLOGY
Only a few cases have been described (none in Caucasian population so far).

PATHOPHYSIOLOGY
Unknown.

CLINICAL DERMATOLOGICAL PRESENTATION
Progressive generalized blue-black hyperpigmentation.
Mucous membranes and conjunctiva can be involved.
Onset in the first months of age often on the face and limbs with progressive extension over the entire body after several years of evolution.
Asymptomatic.
Localization: the entire body is affected but palms and soles are usually spared.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Increase of melanin content in the epidermis.
Melanophages in the upper dermis.
Orthohyperkeratosis has been reported.

DIFFERENTIAL DIAGNOSIS
- Congenital diffuse melanosis.
- Dyschromatosis symmetrica hereditaria.
- Erythema dyschromicum perstans.

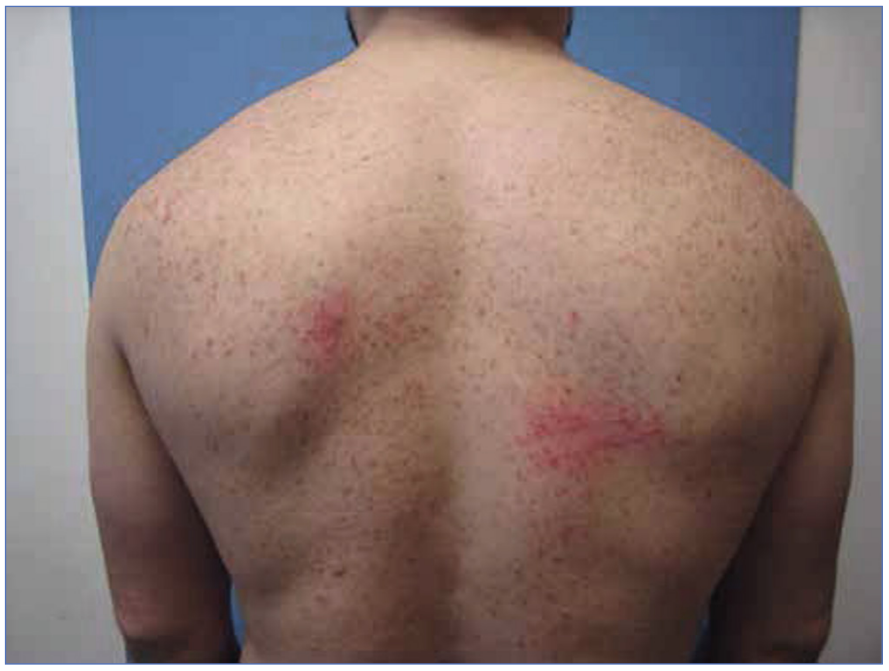
TREATMENT
None reported.
Sun protection is advised to limit the hyperpigmentation.

KEY REFERENCES

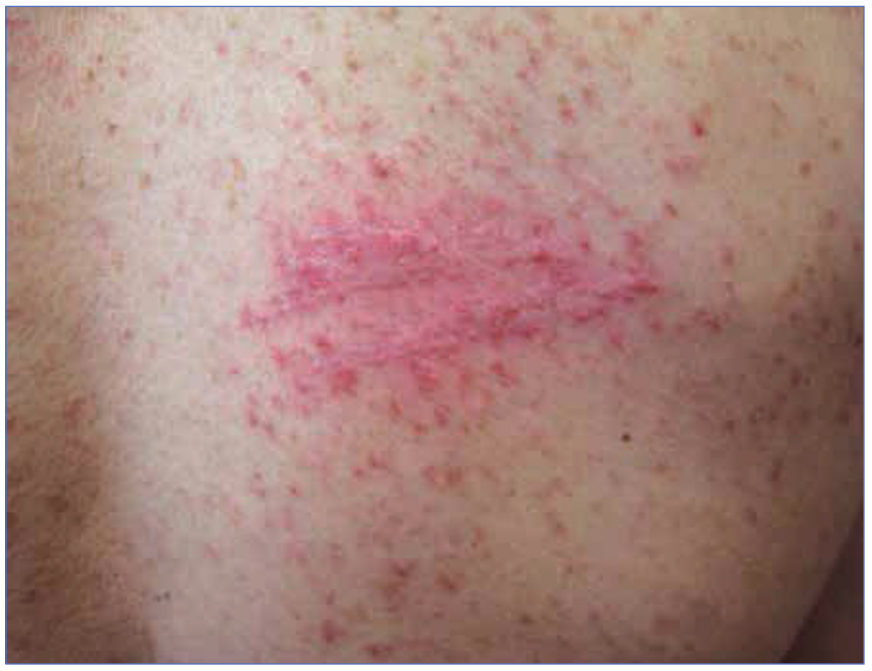
- Ruiz-Maldonado R, Tamayo L, Fernández-Diez J. Universal acquired melanosis. The carbon baby. Arch Dermatol. 1978;114:775-8.
- Kaviarasan PK, Prasad PV, Joe JM, Nandana N, Viswanathan P. Universal acquired melanosis (Carbon baby). Indian J Dermatol Venereol Leprol. 2008;74:38-40.

URTICARIA PIGMENTOSA

Chee-Leok Goh and Sai-Yee Chuah



Urticaria pigmentosa. Note the Darier's sign.



Close-up on Darier's sign. The lesions become erythematous and edematous.

OMIM: #154800

GENETICS

Urticaria pigmentosa (UP) is the most common form of cutaneous mastocytosis.
Both dominant and recessive inheritance had been postulated.
Sporadic non-familial cases had been reported to be related to mutations in the KIT gene (4q12).

MOUSE MODEL

Transgenic mouse model– expressing human KIT gene with an activating mutation at codon 816.

EPIDEMIOLOGY

Urticaria pigmentosa is an uncommon disorder affecting males and females equally.
It commonly affects children but may occur in infants or young children. It usually resolves by puberty.
It may also present in late adulthood.

PATHOPHYSIOLOGY

KIT is a protein product of the proto-oncogene c-kit and belongs to the type III receptor tyrosine kinase subfamily. It is expressed on mast cells, melanocytes, primitive hematopoietic stem cells and primordial germ cells. Activation of KIT induces cellular growth, extends cell survival by preventing apoptosis.

Increased local concentrations of soluble mast cell growth factor in lesions of cutaneous mastocytosis are believed to stimulate mast cell proliferation, melanocyte proliferation, and melanin pigment production. The induction of melanocytes explains the hyperpigmentation that commonly is associated with cutaneous mast cell lesions.

CLINICAL DERMATOLOGICAL PRESENTATION

Oval or round red-brown macules, papules, or plaques ranging in number from a few to thousands.
Darier's sign - when an urticaria pigmentosa is stroked, it typically urticates, becoming pruritic, edematous, and erythematous.
Localization: most commonly on the trunk but it can involve any anatomical site.

EXTRACUTANEOUS SIGNS

Involvement of the skeletal system may manifested as bone pain. Fracture may occur due to long-term exposure to heparin and stem cell factor released from degranulated mast cells putting patients at risk for osteoporosis.
Neuropsychiatric symptoms with non-specific changes such as irritability, malaise and headache may occur.
Gastrointestinal symptoms include abdominal pain, diarrhea, nausea and vomiting and weight loss.
Cardiovascular effects include chest pain, dyspnea, palpitations and syncope (resulting from vasodilation).

MORTALITY/MORBIDITY

Urticaria pigmentosa in children usually resolve spontaneously but acute and extensive degranulation rarely can cause life-threatening shock. Increased serum baseline tryptase levels and extensive skin involvement are predictors for the severity of mast cell activation episodes in children with mastocytosis.

Patients with adult- or adolescent-onset urticaria pigmentosa are more likely to have persistent disease and are at greater risk for systemic involvement. Juvenile-onset systemic mastocytosis has a malignant transformation rate as high as 7%, whereas adult-onset systemic mastocytosis has a malignant transformation rate of up to 30%.

HISTOPATHOLOGY

Increased melanin in the basal cell layer and melanophages in the upper dermis.
Infiltration of mast cells in the dermis and around blood vessels.
Mast cell granules can be demonstrated with Leder, Giemsa or toluidine blue stain.

DIFFERENTIAL DIAGNOSIS

- Arthropod bites.
- Urticaria.
- Café-au-lait macules.
- Spitz nevi.
- Juvenile xanthogranuloma.
- Pseudolymphoma.

For patients presenting with bullae: bullous impetigo, bullous arthropod bites, herpes simplex virus infection, linear IgA bullous dermatoses and other autoimmune bullous dermatoses.

TREATMENT

Treatment of UP is directed primarily at alleviating symptoms. Most cases do not require any treatment.
Avoid potential mast cell degranulating activities and agents: excessive exercise, aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs), codeine and morphine (narcotics), alcohol, anticholinergics, polymyxin B sulfate.
Systemic anesthetic (lidocaine, d-tubocutarine, metocurine, etomidate, thiopental, succinylcholine hydrochloride (suxamethonium chloride), enflurane, isoflurane.
Local and systemic therapy for symptom control include:
Potent and super-potent topical corticosteroids or intralesional or oral corticosteroids.
Oral antihistamines.
Mast cell stabilizers: oral disodium cromoglicate may help in some cases.

Psoralen + UVA (PUVA): Two or three treatments each week for a few months may lessen itch and improve the appearance.

Interferon α-2b: An expensive treatment appropriate only for those severely affected.
Imatinib: an expensive treatment for systemic mastocystosis.

KEY REFERENCES

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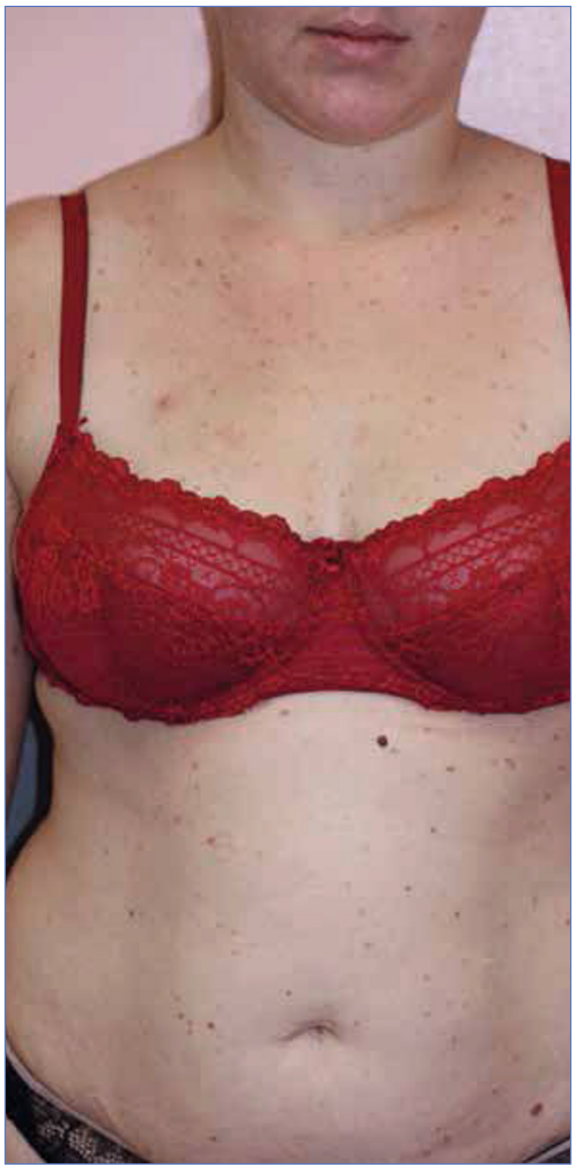
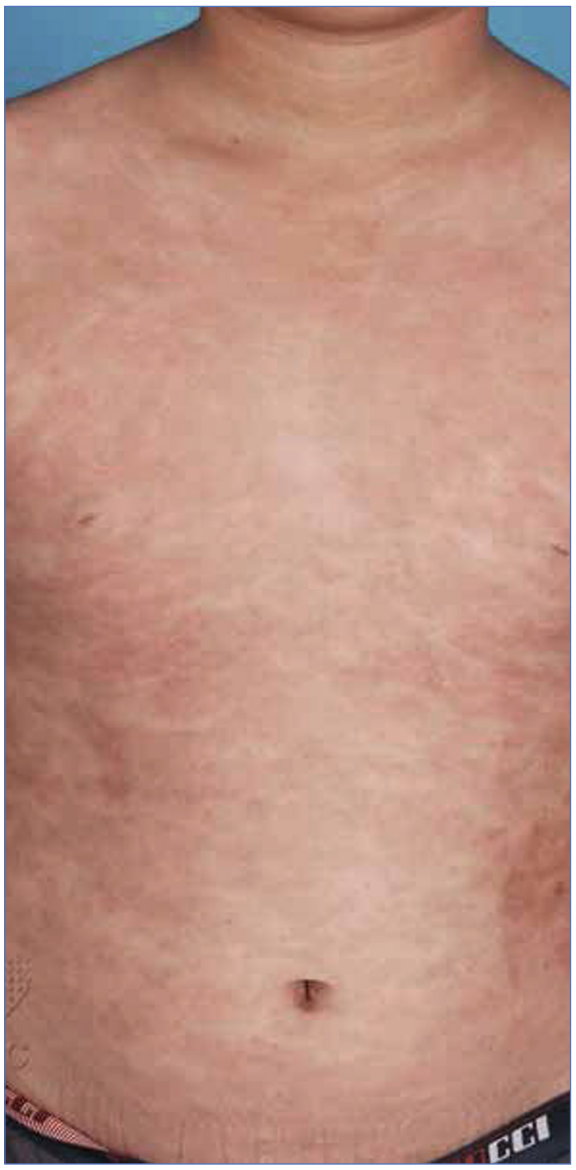
- Fett NM, Teng J, Longley BJ. Familial urticaria pigmentosa: report of a family and review of the role of KIT mutations. Am J Dermatopathol. 2013;35:113-6.
- Valent P, Horny HP, Escribano L et al. Diagnostic criteria and classification of mastocytosis: a consensus proposal. Leuk Res. 2001;25:603-25.

URTICARIA PIGMENTOSA

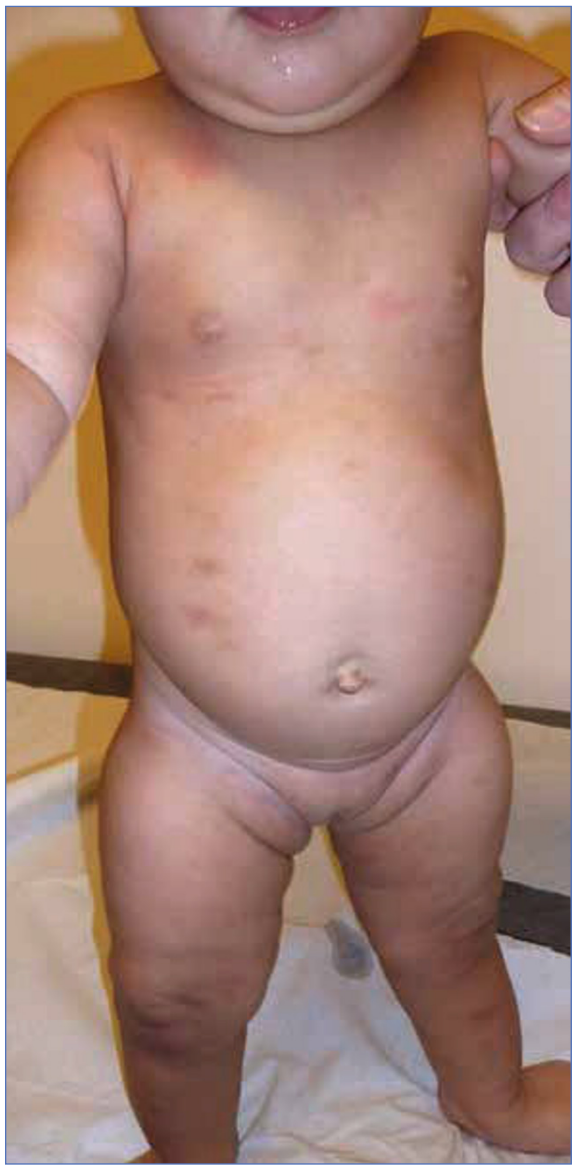
Chee-Leok Goh and Sai-Yee Chuah



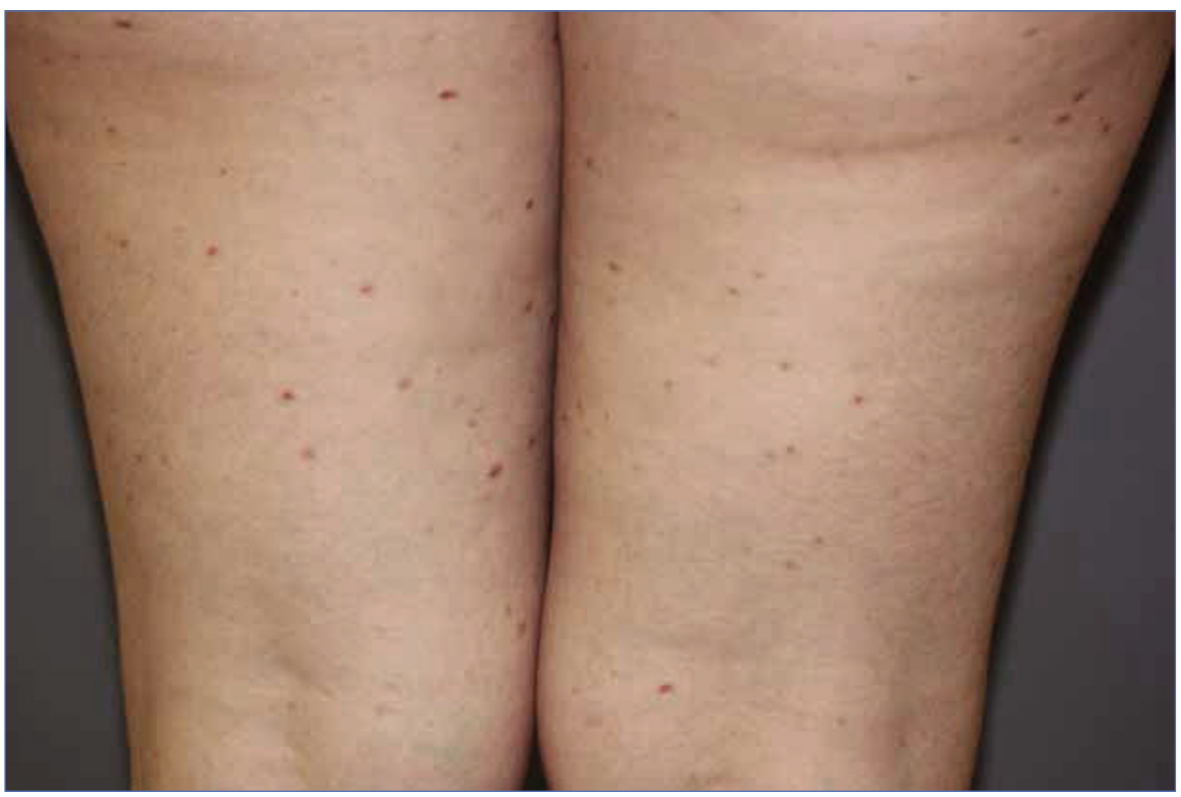
Hundreds hyperpigmented macules in a woman with urticaria pigmentosa.



Urticaria pigmentosa (coll. Chee-Leok Goh).



Urticaria pigmentosa in a young child.



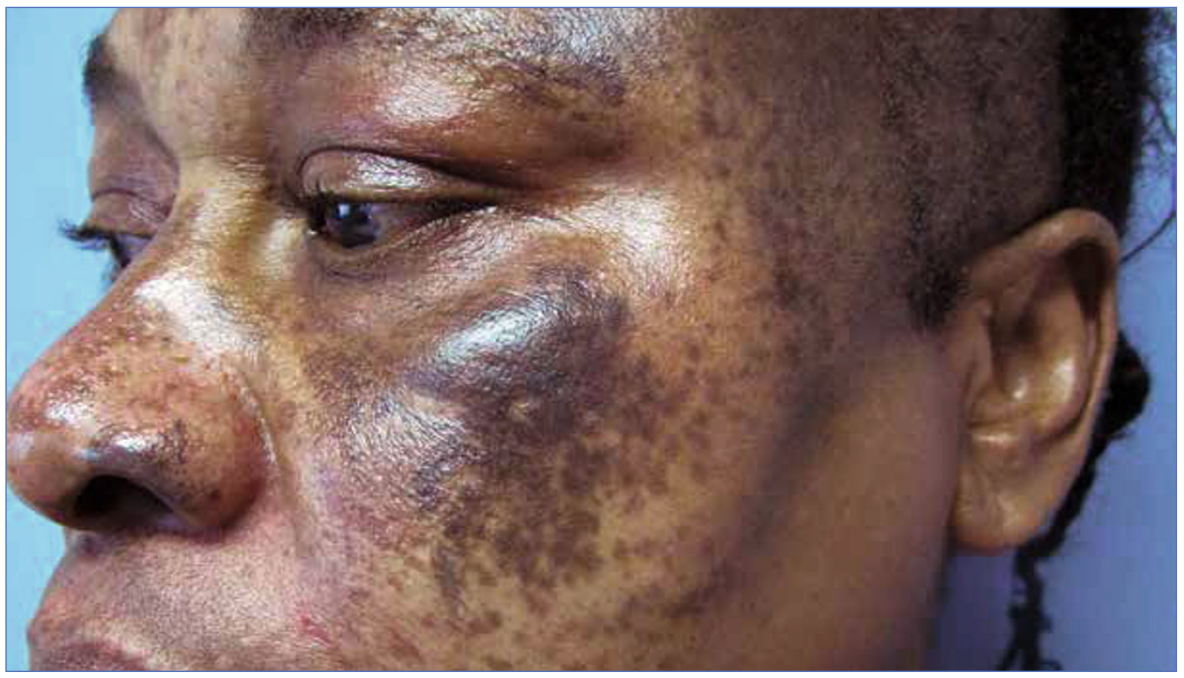
Red-brown macules of urticaria pigmentosa.

ACQUIRED HYPERMELANOSIS

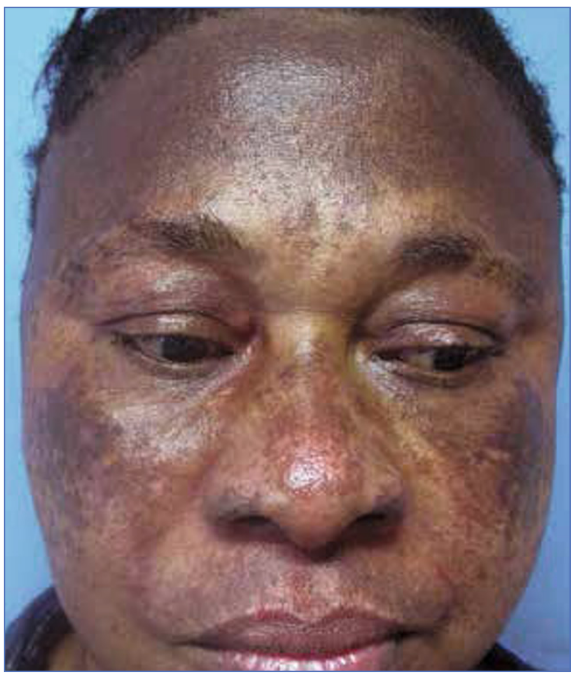
Dermal hypermelanosis

ACQUIRED BILATERAL NEVUS OF OTA-LIKE MACULES (ABNOM)

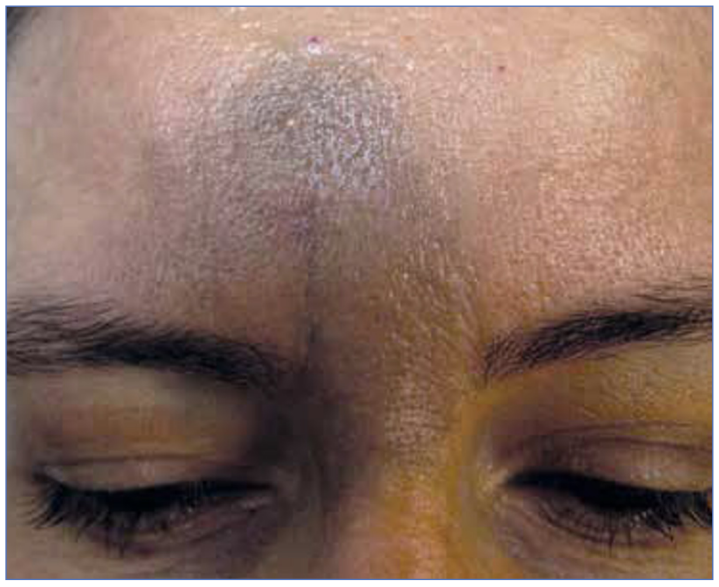
Sai-Yee Chuah



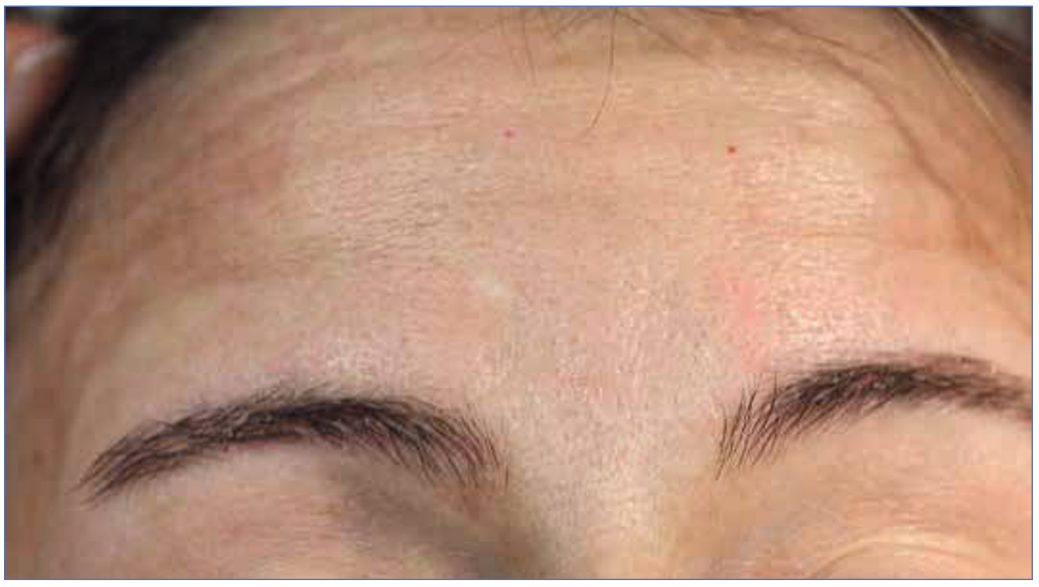
Acquired bilateral nevus of ota-like macules. The aspect may look like melasma but the presence of lesions on the nasal alae and the absence of worsening during summer are highly suggestive of the diagnosis.



Acquired bilateral nevus of ota-like macules. Symmetrically distributed slate-gray macules that appeared at the age of 33 years.



A. Acquired asymmetrical dermal melanocytosis that appeared at the age of 25 years.



B. Almost complete regression after three sessions of Alexandrite Q-switched laser.

EPIDEMIOLOGY

Most commonly found in Asian populations.
More frequent in females.
The onset is usually between the second and the fourth decade of life.

PATHOPHYSIOLOGY

Remains unclear.
Several possible mechanisms with regards to the origin of dermal melanocytes:

- dropping off of epidermal melanocytes;
- migration of hair bulb melanocytes;
- activation of pre-existing latent or immature melanocytes.

Studies on Japanese patients have demonstrated the presence of immature or non-pigmented melanocytes not only in the lesions of acquired, bilateral nevus of Ota-like macules (ABNOM) but also in uninvolved skin and even in normal skin from healthy individuals, which suggest that the activation of pre-existing immature dermal melanocytes is the most probable mechanism for the development of ABNOM.

More common in Asians than in Caucasians, suggesting that the presence of dermal melanocytes in Asians may not always be pathological but is sometimes physiological.
Thus it is considered that the activation of latent dermal melanocytes may occur frequently in Asians leading to the appearance of ABNOM.
Factors aggravating or inducing ABNOM:

- Exposure to ultraviolet (UV) light (more frequently located on the zygomatic region).
- Sex hormones: estrogen and progesterone (more common in females and frequent darkening during pregnancy).

CLINICAL DERMATOLOGICAL PRESENTATION

Symmetrically as blue-brown or slate-gray macules.
Localization: malar/zygomatic region, lateral temples, nasal alae, eyelids, forehead.
Rare forms of acquired dermal hypermelanocytosis can be asymmetrical and may affect extrafacial region such as the upper and lower extremities.

EXTRA CUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Irregularly shaped, bipolar melanocytes in the upper and middle dermis without disturbance of the normal skin architecture.

DIFFERENTIAL DIAGNOSIS

- Melasma.
- Blue nevus.
- Riehl's melanosis.
- Post-inflammatory hyperpigmentation.
- Vascular malformation.

TREATMENT

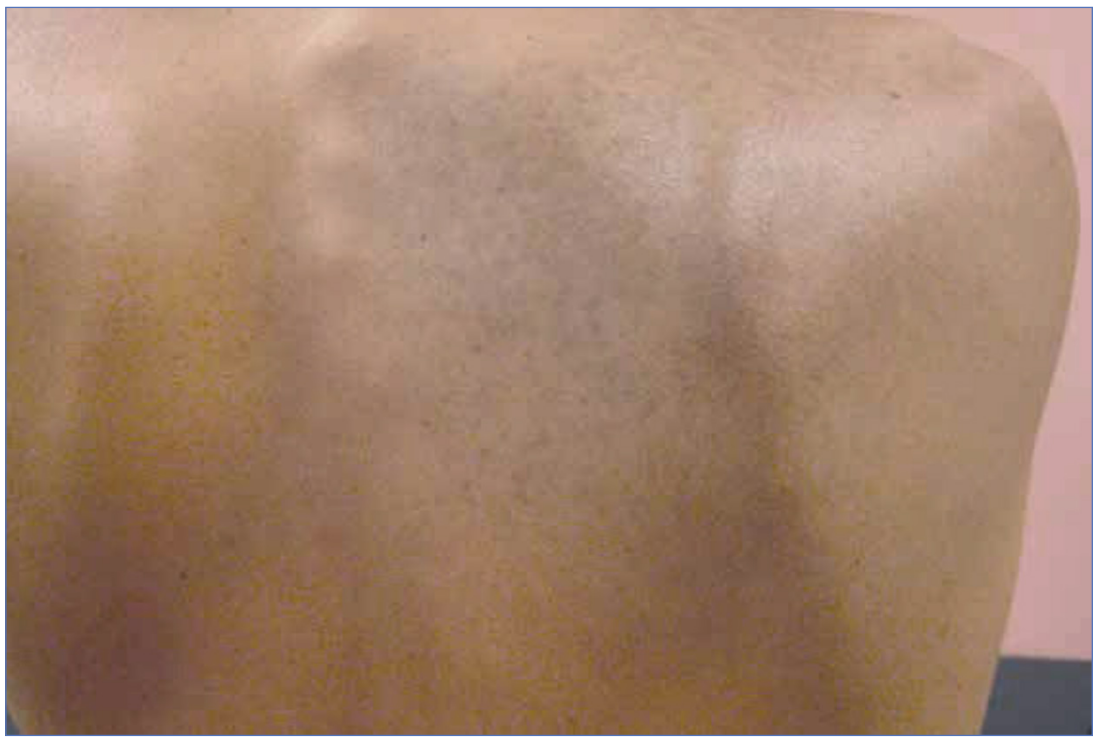
Cosmetic camouflage.
Q-switched lasers (Nd:YAG is the best laser, but Alexandrite and Ruby are usually very effective).

KEY REFERENCES

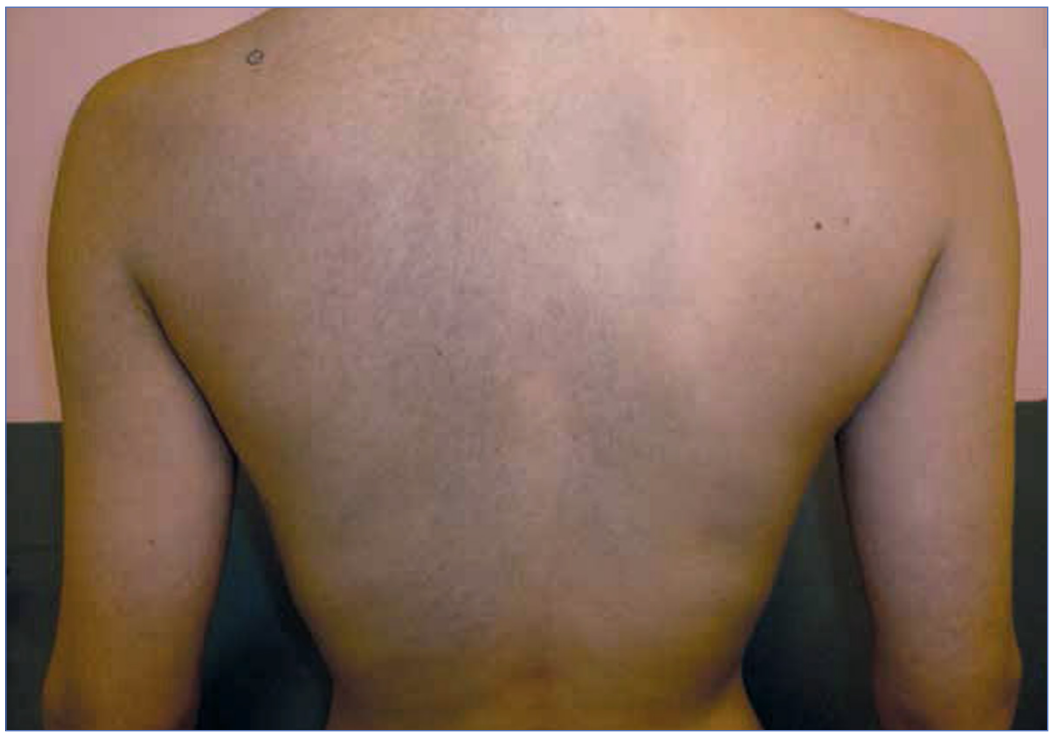
- Murakami F, Soma Y, Mizoguchi M. Acquired symmetrical dermal melanocytosis (naevus of Hori) developing after aggravated atopic dermatitis. Br J Dermatol. 2005;152:903-8.
- Hidano A, Kaneko K. Acquired dermal melanocytosis of the face and extremities. Br J Dermatol. 1991;124:96-9.
- Park JM, Tsao H, Tsao S. Acquired bilateral nevus of Ota-like macules (Hori nevus): etiologic and therapeutic considerations. J Am Acad Dermatol. 2009;61:88-93.

OTHER ACQUIRED DERMAL HYPERMELANOCYTOSIS

Sai-Yee Chuah



Acquired dermal melanocytosis of the back that occurred at the age of 25 years during pregnancy.



Extensive acquired dermal melanocytosis of the back.
The onset was at the age of 20 years, the only triggered factor that may be involved was a severe sunburn.

EPIDEMIOLOGY

Uncommon condition.
Occurs in adult life. More common in females.

PATHOPHYSIOLOGY

Still unclear.
Proposed to be due to the reactivation of pre-existing dermal melanocytes or the manifestation of latent dermal melanocytosis triggered by dermal inflammation, atrophy or degeneration of the epidermis or dermis.
Has been reported following trauma, atopic dermatitis, lichen planus and systemic sclerosis.
Ultraviolet irradiation may increase melanocyte-stimulating hormone (MSH) or endothelins, increasing tyrosinase activity and thus inducing melanogenesis, especially when the lesions are photodistributed.
Female hormones (estrogen and progesterone) may play a role as acquired dermal melanocytosis is more common in females and has been reported to occur during pregnancy.

CLINICAL DERMATOLOGICAL PRESENTATION

Blue-gray or brown macules or patches appearing at the puberty or adulthood.
Asymptomatic.
Localization: any site of the body can be affected; can be generalized.

EXTRACUTANEOUS SIGNS

May involved the oral mucosa and the ocular region.

HISTOPATHOLOGY

Presence of dendritic dermal melanocytes and melanophages in the dermis.
Normal epidermis.

DIFFERENTIAL DIAGNOSIS

- Melanoma.
- Post-inflammatory hyperpigmentation.
- Carleton-Biggs syndrome.
- Blue macules associated with progressive systemic sclerosis.
- Lichen planus pigmentosus.
- Drug-induced pigmentation.

TREATMENT

Q-switched laser may be effective for the hyperpigmented lesions.

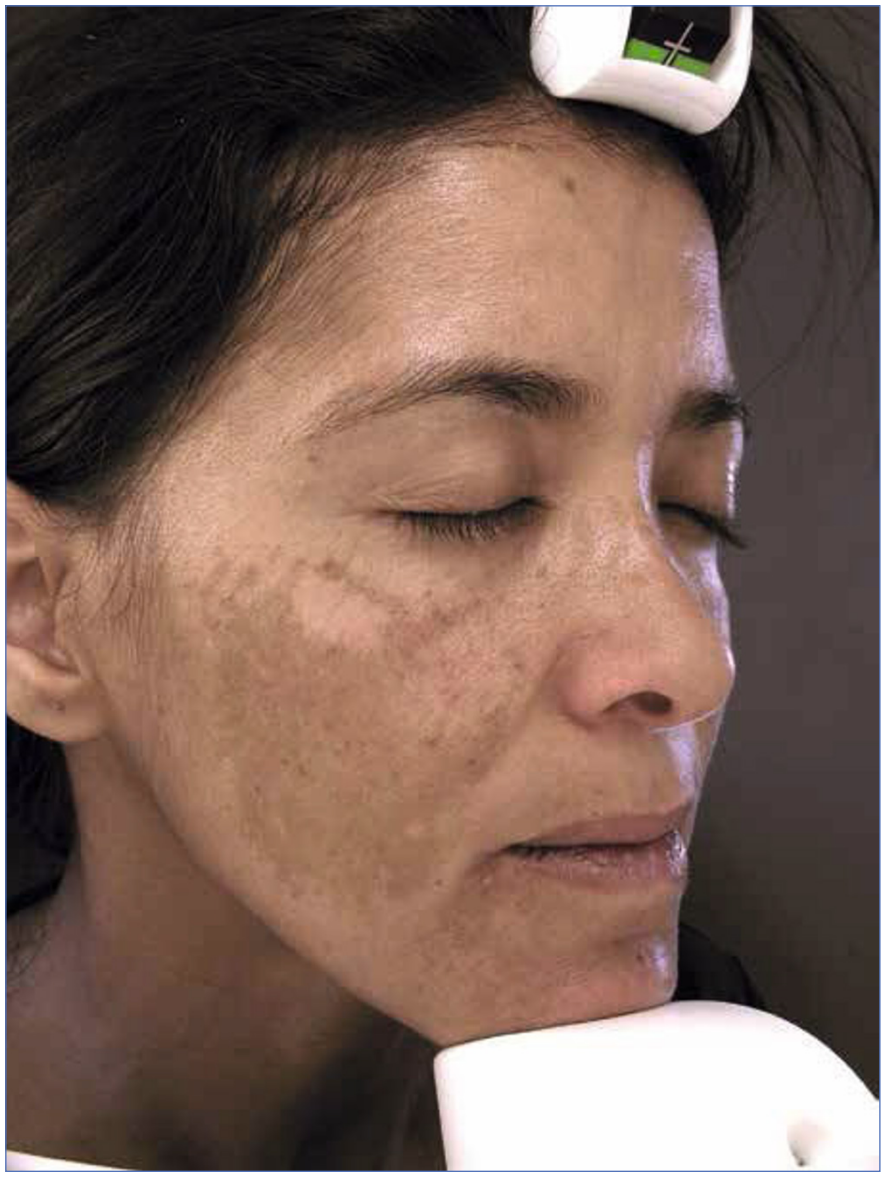
KEY REFERENCES

- Permatasari F, Zhou BR, Luo D. Late-onset acquired dermal melanocytosis on the hand of a Chinese woman. Indian J Dermatol Venereol Leprol. 2013;79:269.
- Rubin AI, Laborde SV, Stiller MJ. Acquired dermal melanocytosis: Appearance during pregnancy. J Am Acad Dermatol. 2001;45:609-13.

ACQUIRED HYPERMELANOSIS

Melasma

MELASMA



A. Marked melasma.

B. The ultra-violet (UV) light shows an increased contrast between lesional and healthy skin suggestive of a mostly epidermal form of melasma.

SYNONYMS

Chloasma, pregnancy mask.

EPIDEMIOLOGY

The condition is common (up to 30% of women of child-bearing age in some populations).
All skin types can be affected but more frequent in Asian and Hispanic population.
Sex ratio 1:10. Most patients are affected during the third or the fourth decade of life, but onset of the lesions after 40- or 50-years of age is observed in 14% and 6% of cases, respectively.
The onset of the disease is found to be earlier in light skin types, while dark skin types (V and VI) are usually associated with a late onset of melasma (even post-menopausal).
Recent studies have shown that only 20% of melasma occurred in the peri-pregnancy period. Moreover the contraceptive pills appear to have a weak impact on the evolution of melasma and the impact of the hormonal treatment is even weaker in cases of familial history of melasma.

PATHOPHYSIOLOGY

Genetic background, exposure to ultraviolet radiation, and female sex hormones are classical influencing factors.
Recent studies have emphasized the role of other players such as vascularization, keratinocyte and fibroblast secreted factors, and visible light.

CLINICAL DERMATOLOGICAL PRESENTATION

Light to dark brown hyperpigmentation.
Symmetrical distribution with irregular border.
Worsening in summer period.
Wood's lamp examination allows to assess if the melasma is mostly epidermal or dermal. However, recent studies using laser confocal microscopy showed that all melasmas are mixed with a strong heterogeneity within the same lesion.
Asymptomatic.
Localization: Central pattern (forehead, nose, medial part of the cheeks, upper lip, chin) (accounts for more than 60% of cases)/Malar pattern (cheeks and nose)/ Mandibular pattern
Chronic evolution for 10 to 20 years.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Hyperpigmentation of the basal and supra basal layers of the epidermis sometimes associated with pendulous melanocytes
Pigmentary incontinence.
Elastosis and vascular ectasia.

DIFFERENTIAL DIAGNOSIS

- Acquired bilateral nevus of Ota-like macules.
- Post-inflammatory hyperpigmentation.
- Linea fusca.
- Riehl's melanosis.
- Erythrose péribuccale pigmentaire de Brocq.

TREATMENT

Strict avoidance of sunlight.
Avoid friction and irritative procedures.
The Kligman's formulation remains the gold standard treatment.
Peeling can be proposed in secondary intention.
Cosmetic depigmenting agents can be proposed for maintenance treatment.
Q-switched lasers are not a good option for melasma.

KEY REFERENCES

- Kang HY, Suzuki I, Lee DJ, Ha J, Reiniche P, Aubert J, et al. Transcriptional profiling shows altered expression of wnt pathway- and lipid metabolism-related genes as well as melanogenesis-related genes in melasma. J Invest Dermatol. 131;1692-1700.
- Kang HY, Bahadoran P, Suzuki I, Zugaj D, Khemis A, Passeron T, Andres P, Ortonne JP. In vivo reflectance confocal microscopy detects pigmentary changes in melasma at a cellular level resolution. Exp Dermatol. 2010;19:e228-33.
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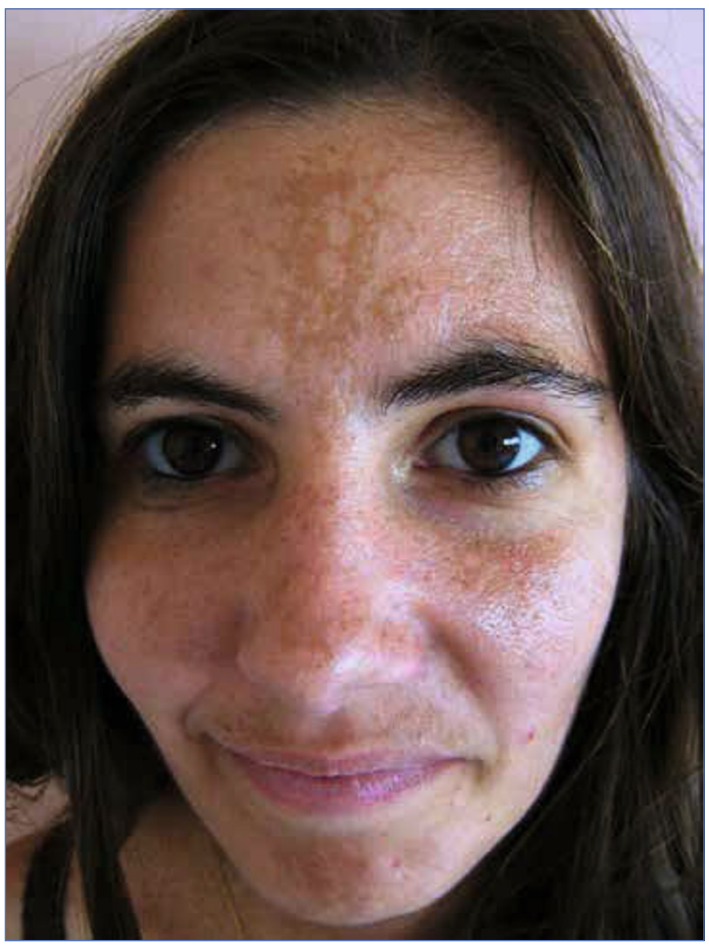
- Taylor SC, Torok H, Jones T, et al. Efficacy and safety of a new triple-combination agent for the treatment of facial melasma. Cutis. 2003;72:67-72.

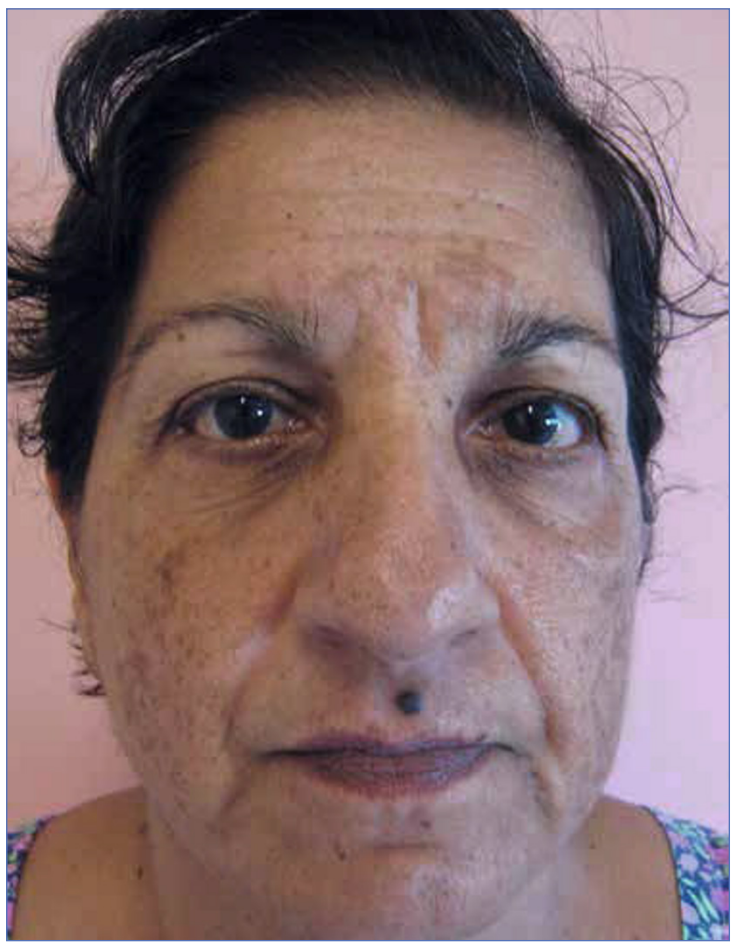
MELASMA

Melasma affecting only the malar area.

Melasma in a man.



Mild melasma with a central pattern.



Melasma with a post-menopausal onset.

SMOKER'S MELANOSIS

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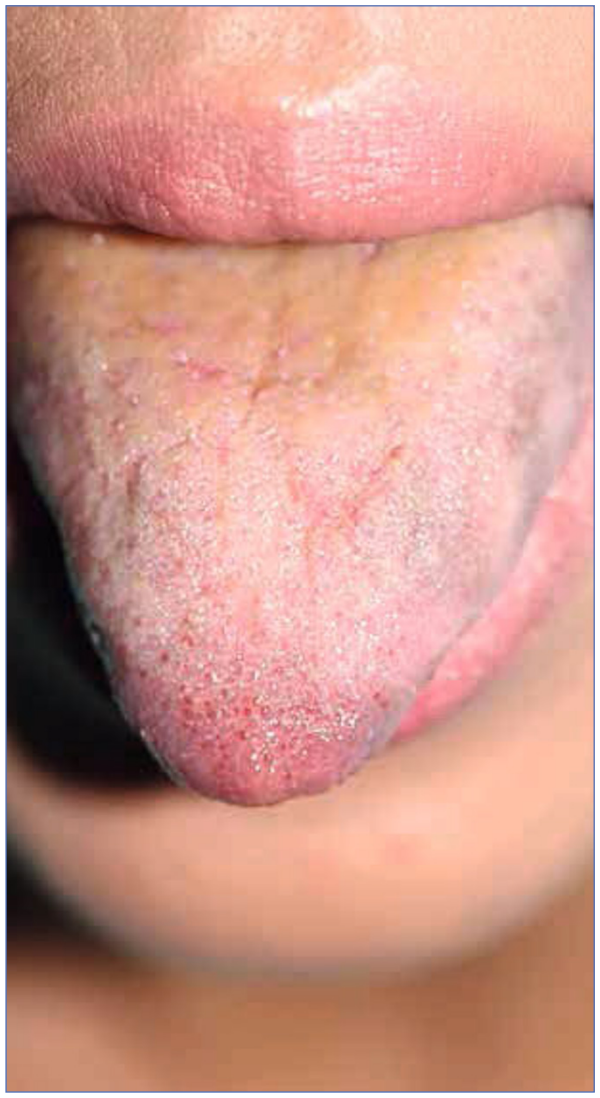
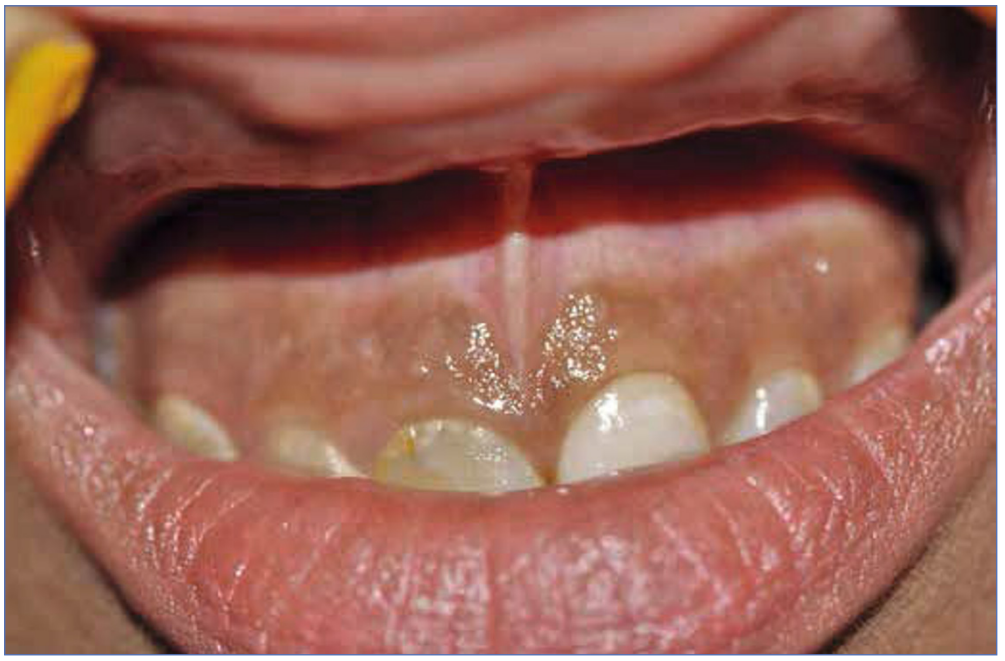
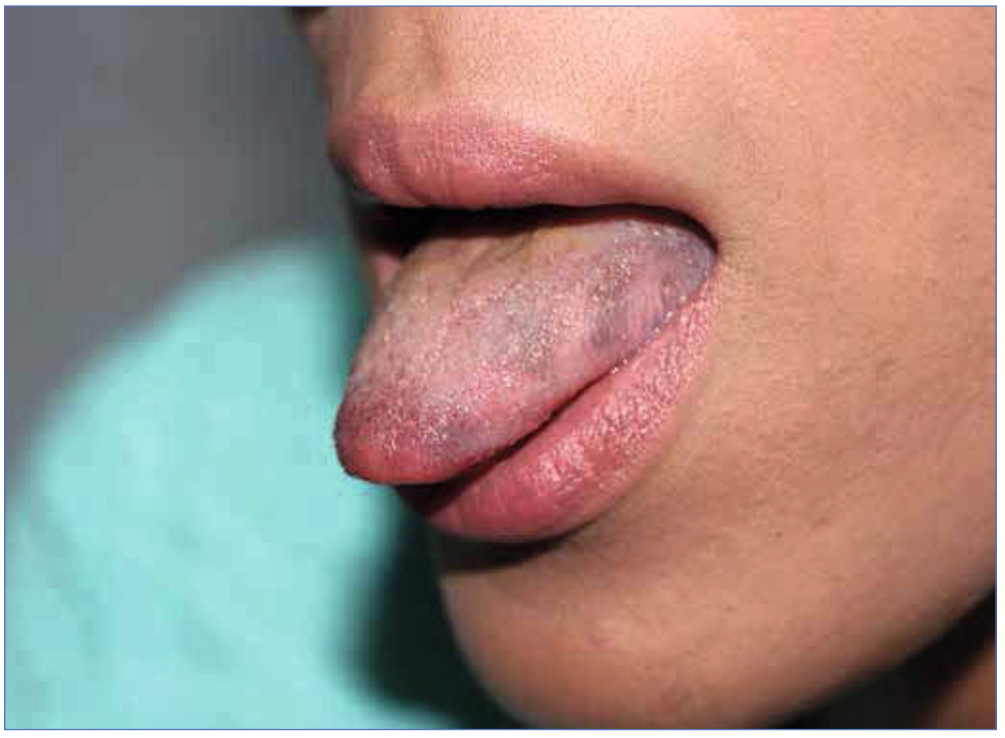


Yellow-brown discoloration of the tongue due to an early stage of black hairy tongue (lingua villosa nigra) in the same patient.



Smoker's melanosis: brown hyperpigmentation of the anterior gingiva.



Acquired brown macules on the tongue due to regular tobacco consumption.

EPIDEMIOLOGY

The prevalence of smoker's melanosis is not well-known. Some series report up to 30% of cases in tobacco smokers.

All races are affected but smoker's melanosis is easier to observe in fair skinned people as they lack the physiological pigmentation of the oral mucosa.

A female predominance is observed (role of estrogens?).

PATHOPHYSIOLOGY

A stimulation of melanogenesis by nicotine is suspected.

CLINICAL DERMATOLOGICAL PRESENTATION

Brown hyperpigmentation of the oral mucosa.

Asymptomatic.

Localization: anterior gingiva, hard palate, tongue.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Increased melanin contained in the basal layers of the epidermis.

Melanin incontinence may be observed.

DIFFERENTIAL DIAGNOSIS

- Physiological pigmentation in dark skin individuals.
- Drug-induced hyperpigmentation.
- Laugier disease.

TREATMENT

Progressive decrease of the hyperpigmentation is observed after discontinuation of smoking. However, the disappearance of the melanosis can take years.

KEY REFERENCES

- Hedin CA. Smokers' melanosis. Occurrence and localization in the attached gingiva. Arch Dermatol. 1977;113:1533-8.
- Hedin CA, Axéll T. Oral melanin pigmentation in 467 Thai and Malaysian people with special emphasis on smoker's melanosis. J Oral Pathol Med. 1991;20:8-12.