NON-MELANIC PIGMENTARY DISORDERS

Hemoglobinopathies and vascular disorders

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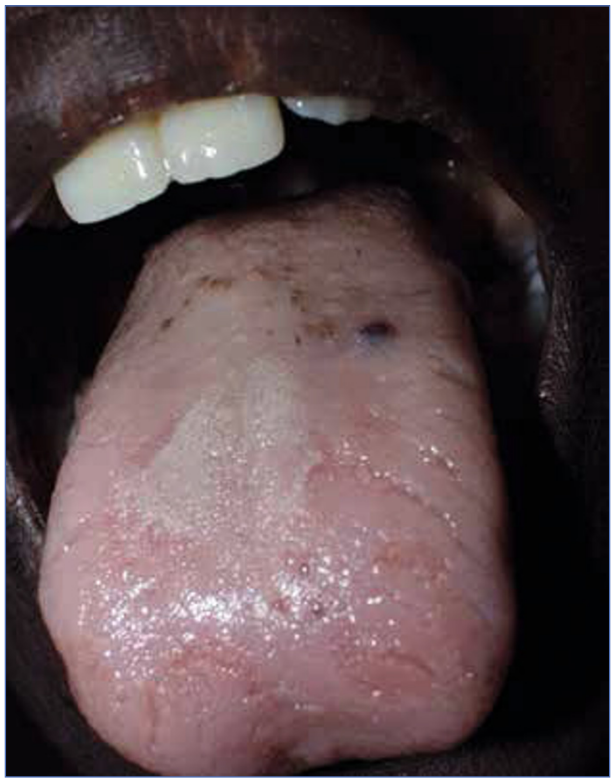
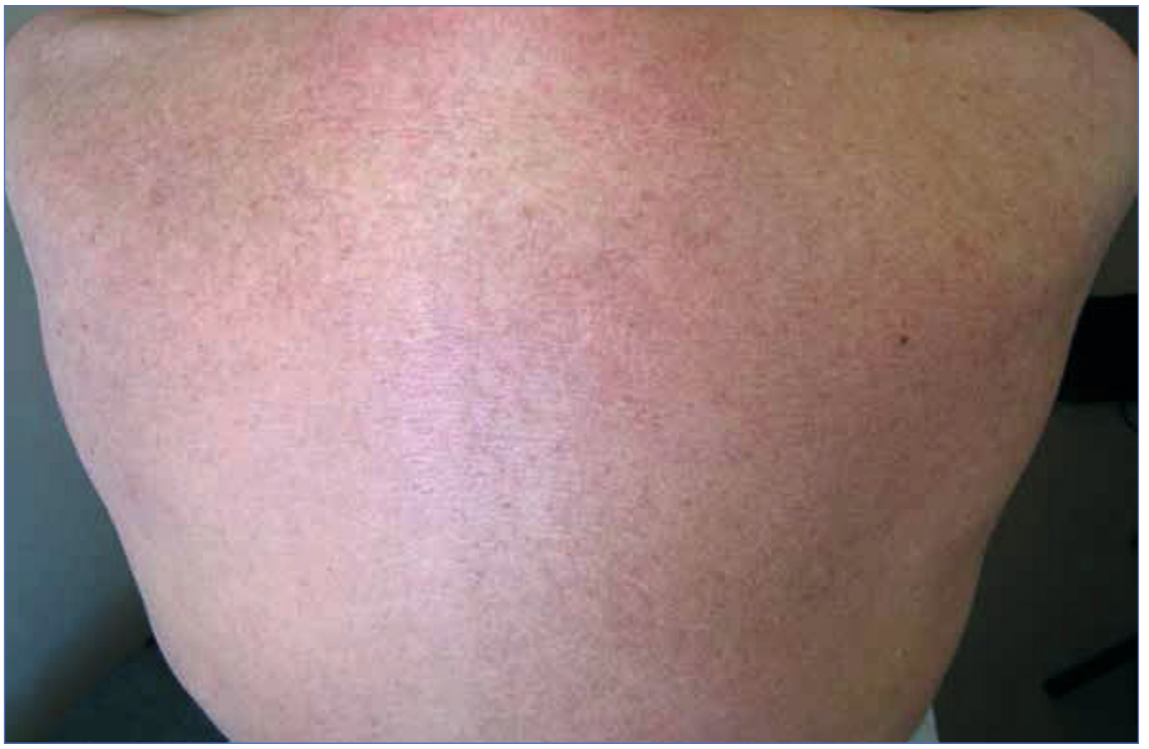
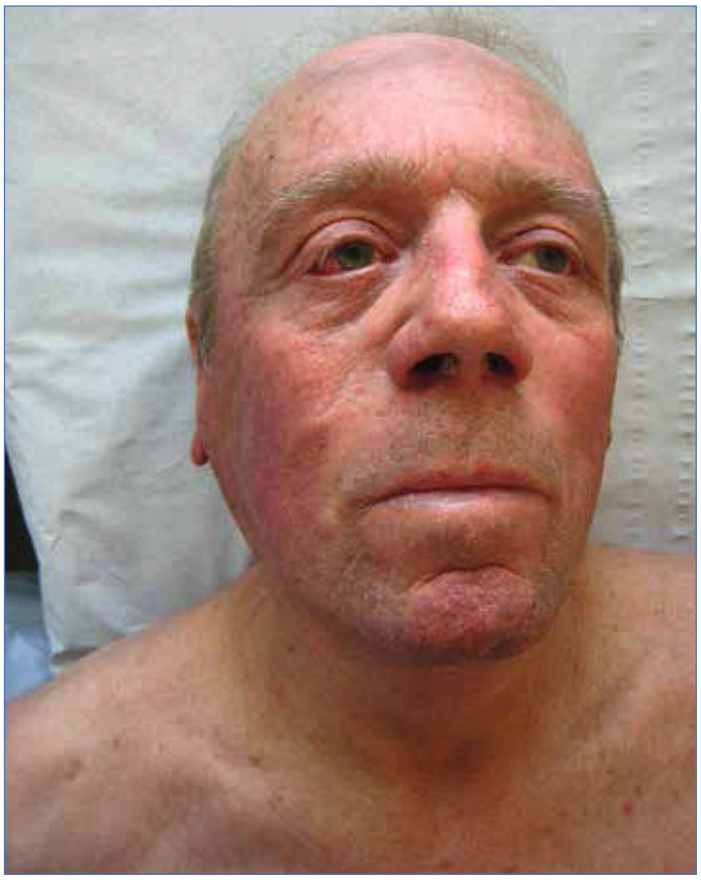
ANEMIA AND POLYCYTEMIA



Pale tongue with glossitis due to severe anemia in blue rubber bleb nevus syndrome. Note the venous malformation on the left side rear area of the tongue.



Skin redness due to polycytemia vera.



Polycytemia vera with redness of the skin and conjunctiva.

EPIDEMIOLOGY

Anemia is quite common and has multiple causes. Polycythemia can be primitive (polycythemia vera) or secondary. Polycythemia vera occurs in 0.6 to 1.6 persons per million.

PATHOPHYSIOLOGY

Hemoglobin is, after melanins, one of the most important pigment of the skin. The decrease or the increase of hemoglobin induces on the skin and mucous membranes a pallor or a redness, respectively.

CLINICAL DERMATOLOGICAL PRESENTATION

Anemia: pallor of the skin and mucous membrane.
Polycythemia: redness of the skin and conjunctivas.
Pruritus and ecchymosis may be observed.
Localization: generalized. The conjunctival pallor is a good clinical sign of anemia. Face, palms, mucous membrane and conjunctiva are more frequently affected in polycythemia.

EXTRACUTANEOUS SIGNS

Anemia: weakness, tachycardia, dyspnea, dizziness, head-ache, chest pain.
Polycythemia: hyperviscosity syndrome (including headache, dizziness, vertigo, intermittent claudication, visual disturbances, chest pain, erythromelalgia).
Other clinical manifestations can be observed depending on the cause of the anemia or of the polycythemia.

HISTOPATHOLOGY

Normal.

DIFFERENTIAL DIAGNOSIS

None.

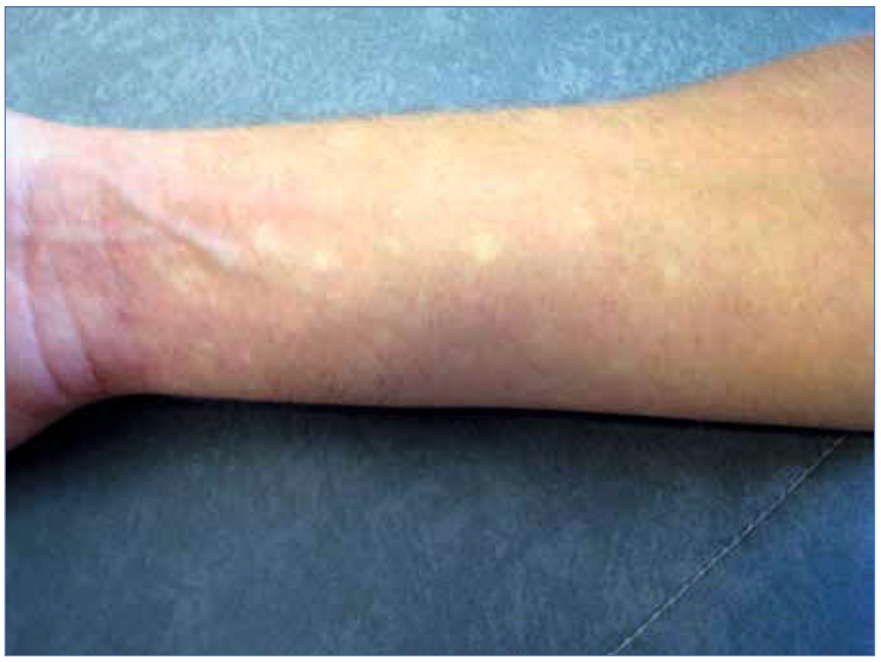
TREATMENT

Anemia: depends on the cause. Blood transfusions; iron, vitamin B12, or folic acid supplementation can be required.
Polycythemia: depends on the cause. Phlebothomy. Hydroxy-urea and more recently Janus kinase-1 and -2 inhibitors have been proposed for treating polycythemia vera.

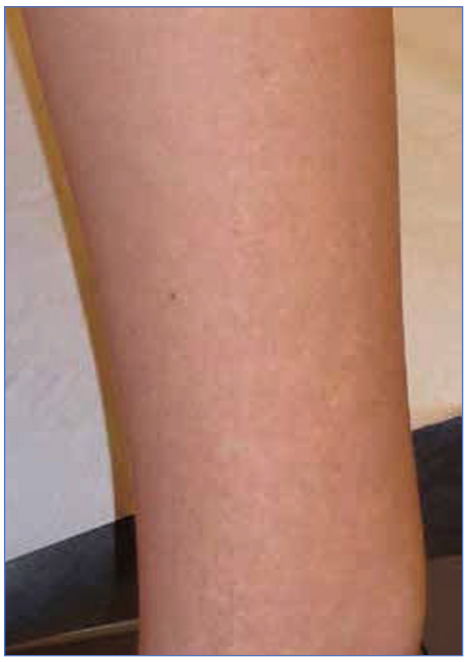
KEY REFERENCES

- Sheth TN, Choudhry NK, Bowes M, Detsky AS. The relation of conjunctival pallor to the presence of anemia. J Gen Intern Med. 1997;12:102-6.
- Keohane C, McMullin MF, Harrison C. The diagnosis and management of erythrocytosis. BMJ. 2013;347:f6667.

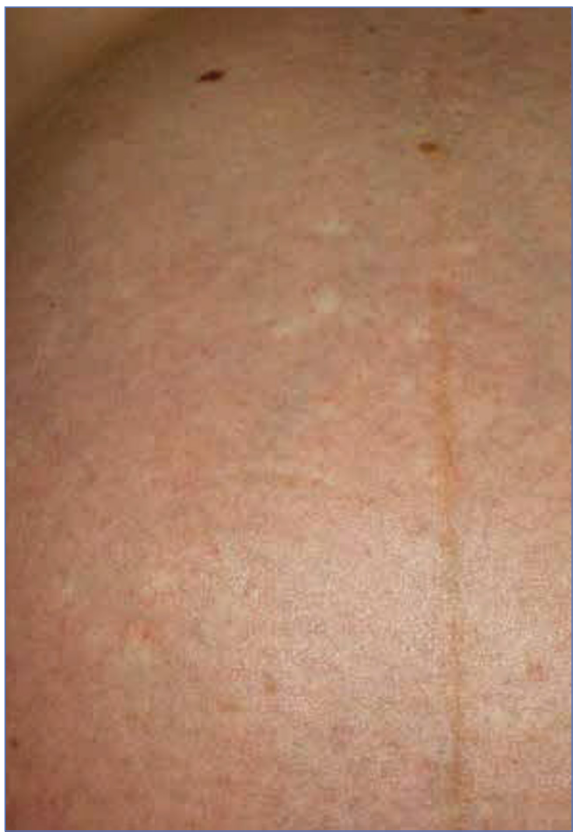
BIER SPOTS



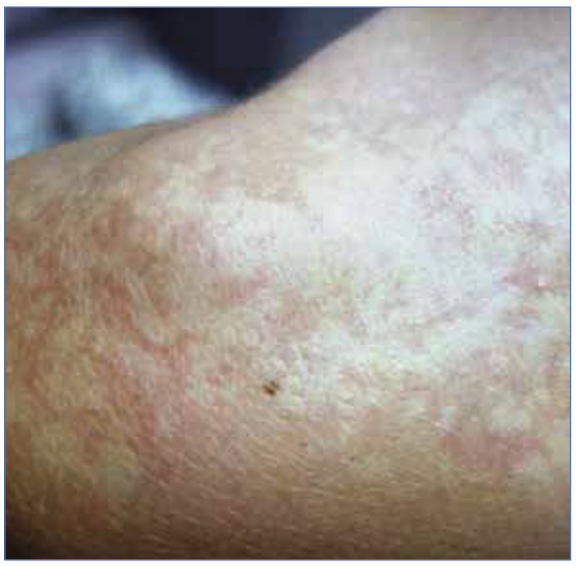
Bier spots on the arm. The white macules disappear if pressure is applied confirming the vascular cause of the discoloration.



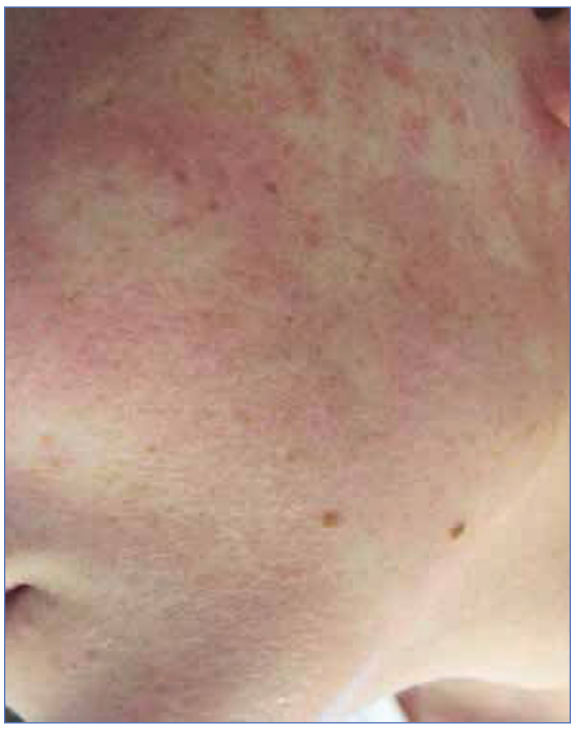
Multiple hypochromic Bier macules of the arm in a 10-year-old boy.



Bier spots on the belly that appeared during the third term of pregnancy.



Vasoplegic hypochromic spots of the upper back.



Vasoplegic hypochromic spots on the face mostly visible on dependency, or after emotional stress or physical activity.

EPIDEMIOLOGY

Not uncommon in young adults. Can be commonly observed on the belly in the third term of pregnancy.

PATHOPHYSIOLOGY

Benign physiologic vascular anomaly corresponding to a vasoconstriction of small vessels.

CLINICAL DERMATOLOGICAL PRESENTATION

Hypochromic irregularly shaped macules from 3 to 15 mm, disappearing when pressure is applied or when the limb is elevated.
Can be more visible after emotional stress or after physical activities.
Localization: can affect any part of the body but arms (sometimes named multiple anemic macules of the arms) and legs, face (mostly the forehead), and belly for pregnant women, who are more commonly affected.

EXTRACUTANEOUS SIGNS

None.
Diffuse Bier spots can reveal cryoglobulinemia, scleroderma renal crisis and aortic hypoplasia.

HISTOPATHOLOGY

Normal.

DIFFERENTIAL DIAGNOSIS

- Achromic nevus.
- Pityriasis versicolor.
- Post-inflammatory hypopigmentation.
- Vitiligo.

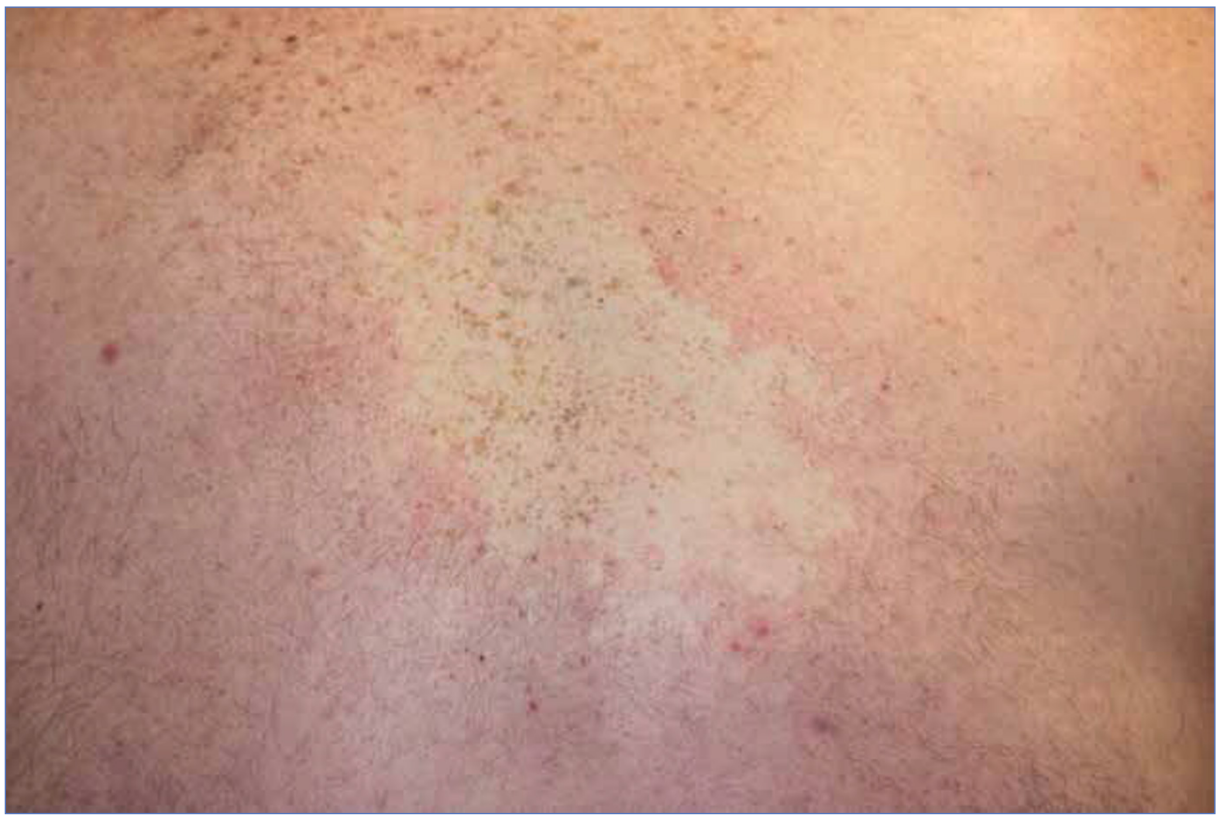
TREATMENT

Etiologic if associated with a systemic disorder.

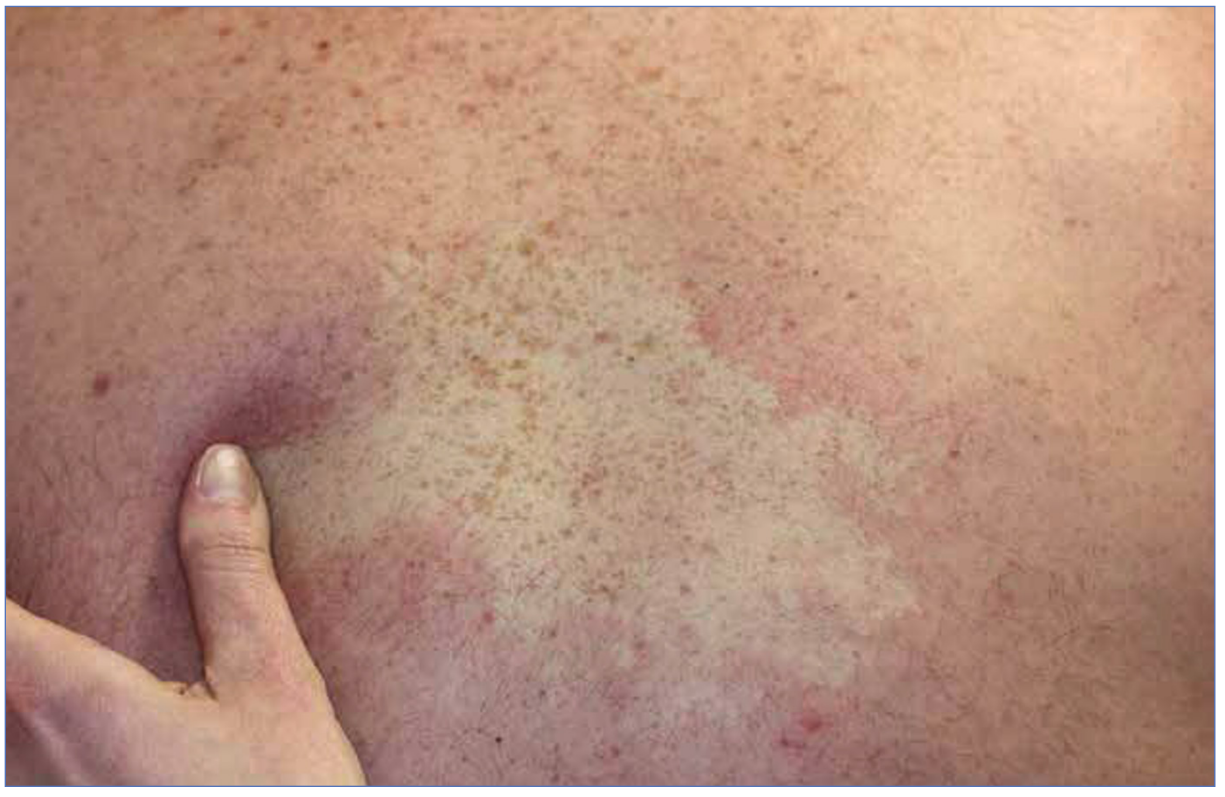
KEY REFERENCES

- Schoenlaub P, Dupré D, Redon JY, Plantin P. Numerous and large Bier's spot associated with pregnancy. Eur J Dermatol 1999;9:230-1.
- Bessis D, Dereure O, Rivire S, Ravi N, Le Quellec A, Guilhou JJ. Diffuse Bier white spots revealing cryoglobulinaemia. Br J Dermatol. 2002;146:921-2.
- Fan YM, Yang YP, Li W, Li SF. Bier spots: six case reports. J Am Acad Dermatol. 2009;61:e11-2.

NEVUS ANEMICUS



Nevus anemicus of the back.



Note that the contrast with the surrounding non-lesional skin disappears when pressure is applied.

EPIDEMIOLOGY

Prevalence unknown, but it is relatively rare.

PATHOPHYSIOLOGY

Vasoconstriction of small vessels probably due to an increased sensitivity of α-adrenergic receptors of the endothelial cells of the affected area. A decrease of E-selectine expression has also been reported.

CLINICAL DERMATOLOGICAL PRESENTATION

Present at birth.
Hypochromic irregularly shaped macule from 1 to several cm in diameter.
The contrast with the surrounding non-lesional skin disappears when pressure is applied. More visible after emotional stress or after physical activities.
Localization: mostly on the trunk but face and limbs can be affected.
Sometimes associated with port wine stains.
Nevus anemicus and juvenile xantogranuloma have been found in higher frequency in patients with type 1 neurofibromatosis, and can be useful for early diagnosis of this genetic disorder.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Normal.

DIFFERENTIAL DIAGNOSIS

- Achromic nevus.
- Bier spots.
- Post-inflammatory hypopigmentation.
- Vitiligo.

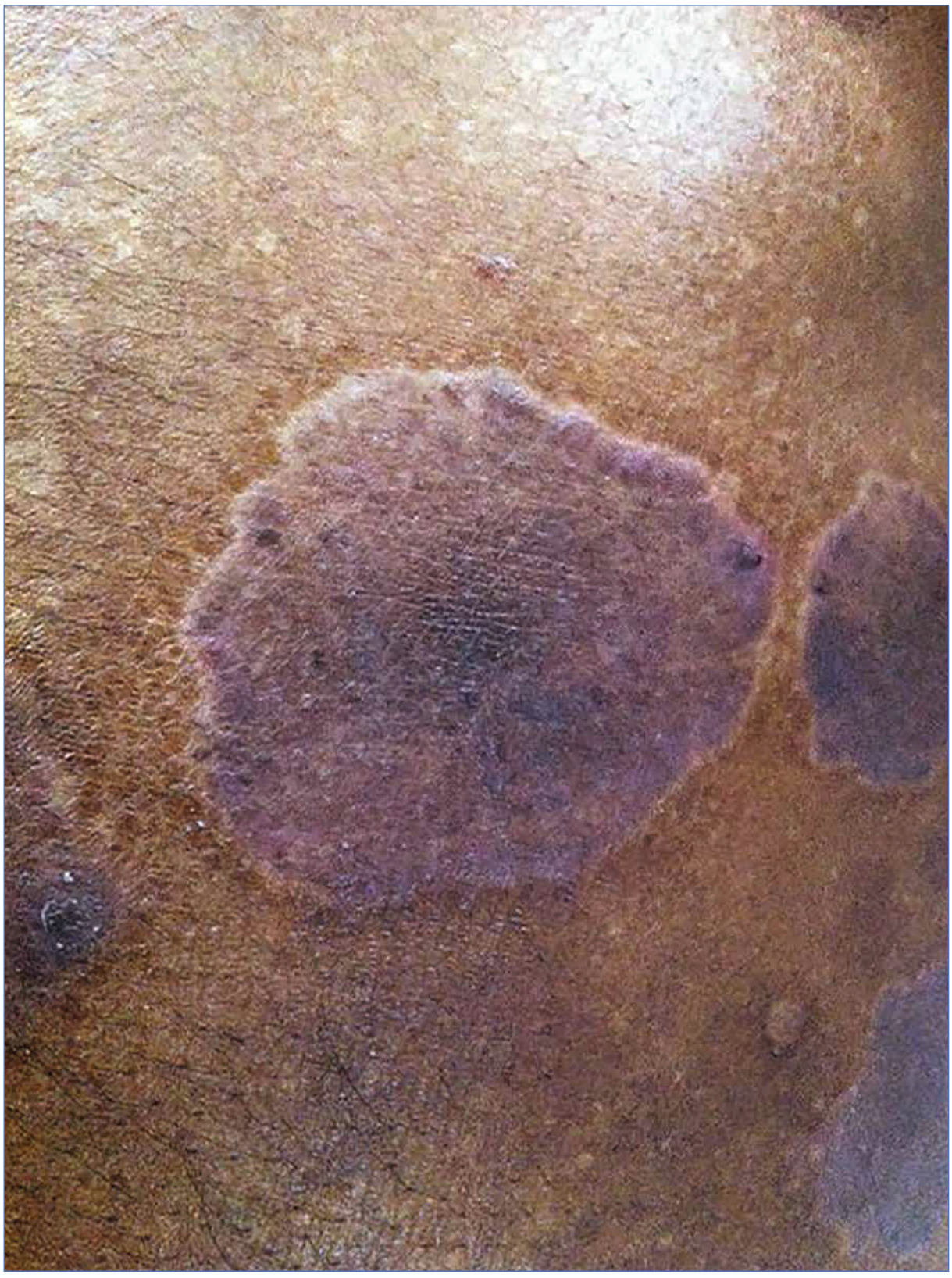
TREATMENT

None.
When associated with a port wine stain, the laser treatment of the port wine stain usually significantly improves the cosmetic appearance by decreasing the contrast.

KEY REFERENCES

- Ferrari F, Masurel A, Olivier-Faivre L, Vabres P. Juvenile xanthogranuloma and nevus anemicus in the diagnosis of neurofibromatosis type 1. JAMA Dermatol. 2013;150:42-6.
- Mizutani H, Ohyanagi S, Umeda Y, Shimizu M, Kupper TS. Loss of cutaneous delayed hypersensitivity reactions in nevus anemicus. Evidence for close concordance of cutaneous delayed hypersensitivity and endothelial E-selectin expression. Arch Dermatol. 1997;133:617-20.

WORONOFF RING



Haloes of hypochromic non-reddened skin around psoriatic plaques (coll. Arun C Inamadar).

EPIDEMIOLOGY

Rare phenomenom occurring in psoriatic lesions after phototherapy or topical treatment. It can also be observed without any treatment.

PATHOPHYSIOLOGY

Woronoff rings may result from inhibition of prostaglandin synthesis, but the hypochromic halo can't be ascribed to vasoconstriction. A decreased endoglin expression was found in the border of psoriatic lesions and could lead to reduced inflammation and thus explain this white ring.

CLINICAL DERMATOLOGICAL PRESENTATION

Hypochromic halo of non-reddened skin surrounding an erythematous plaque of psoriasis.
Localization: can affect any part of the body.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Normal.

DIFFERENTIAL DIAGNOSIS

- Post-inflammatory hypopigmentation.
- Vitiligo associated with psoriasis.

TREATMENT

Treatment of the psoriatic lesions.

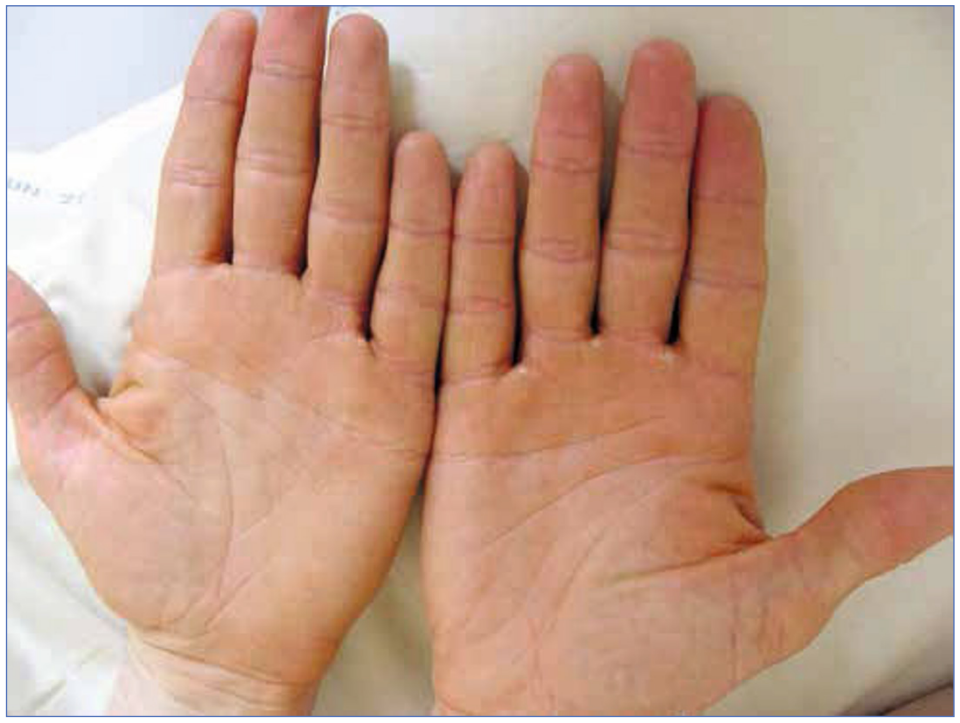
KEY REFERENCES

- Penneys NS, Ziboh V, Simon P, Lord J. Pathogenesis of Woronoff ring in psoriasis. Arch Dermatol. 1976;112:955-7.
- Van de Kerkhof PCM. The Woronoff zone surrounding the psoriatic plaque. Br J Dermatol. 1998;139:167-8.

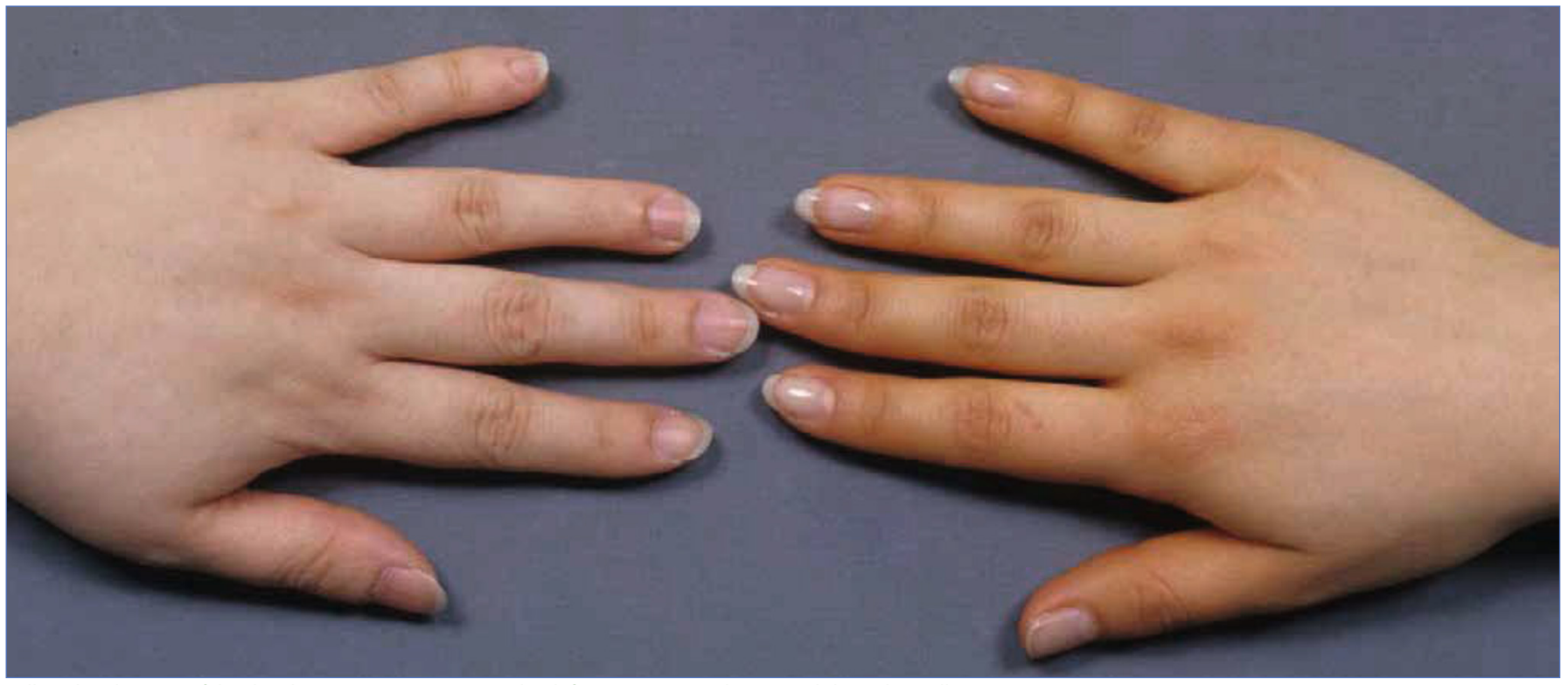
NON-MELANIC PIGMENTARY DISORDERS

Xanthodermia

CAROTENEMIA



Yellow discoloration of the palms due to the daily ingestion of more than a liter of carrot juice.



Yellow discoloration of the skin due to carotenemia. Note the difference compared to normal skin color (coll. Hee Young Kang).

PATHOPHYSIOLOGY

Deposits of excess serum carotene in the skin (mainly in stratum corneum and subcutaneous fat).
Carotene is the precursor of vitamin A. Most forms of carotenemia are due to the ingestion of excess carotene-bearing foods (carrots).
β-Lipoproteins are the major carriers of serum carotene. Elevated levels of β-lipoproteins associated with hypothyroidism, hyperlipidemias, diabetes, anorexia nervosa, or nephrotic syndrome may induce carotenemia.
Rare cases of congenital errors of metabolism that interfere with conversion of carotene to vitamin A can also induce carotenemia.

CLINICAL DERMATOLOGICAL PRESENTATION

Yellow discoloration of the skin that is more pronounced under artificial light.
Localization: palms and soles, nasolabial folds, tip of the nose and forehead are involved first. Then the yellow pigmentation spreads to the entire body.
Sclerae are always spared (allows the distinction from jaundice).

EXTRACUTANEOUS SIGNS

None at beginning.
Then, weakness, weight loss, amenorrhea, hypotension, hepatomegaly and neutropenia can be observed.

HISTOPATHOLOGY

Auto-fluorescence in the superficial horny layer can be observed.

DIFFERENTIAL DIAGNOSIS

- Jaundice.
- Lycopenemia (lycopene is an isomer of β-carotene and its accumulation due to ingestion of high amounts of tomatoes and yellow vegetables induces a similar discoloration of the skin with a more orangey color).
- Sorafenib, quinacrine, mepacrine, dinitrophenol, saffron, tetryl, picric acid and canthaxanthins intake can also induce a yellow discoloration of the skin.

TREATMENT

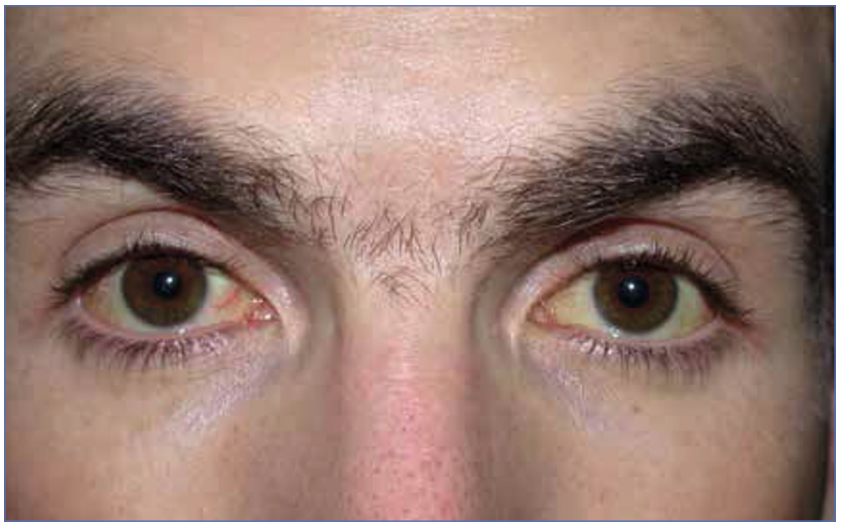
The discoloration progressively fades when the diet is adapted or the underlying disorder is treated.

KEY REFERENCES

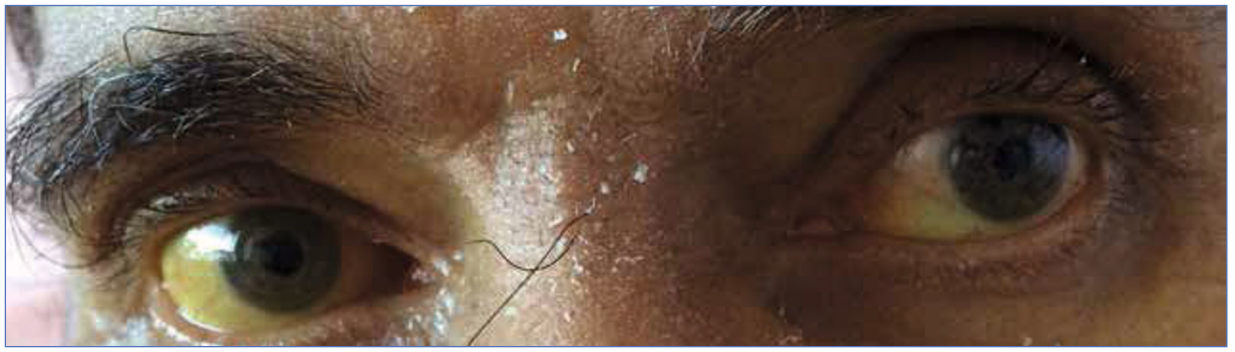
- Dasanu CA, Alexandrescu DT, Dutcher J. Yellow skin discoloration associated with sorafenib use for treatment of metastatic renal cell carcinoma. South Med J. 2007;100:328-30.
- Svensson A, Vahlquist A. Metabolic carotenemia and carotenoderma in a child. Acta Derm Venereol. 1995;75:70-1.

JAUNDICE

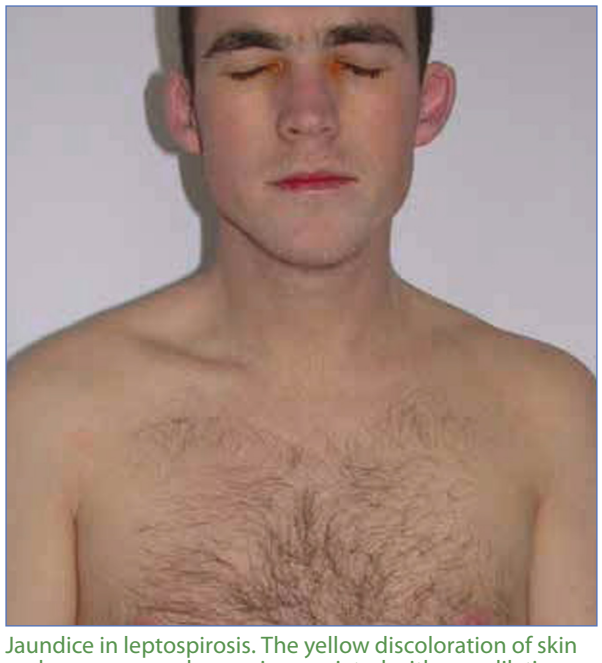
Yellow discoloration of the skin in a patient with jaundice secondary to hepatocarcinoma. Note the difference compared to normal skin.



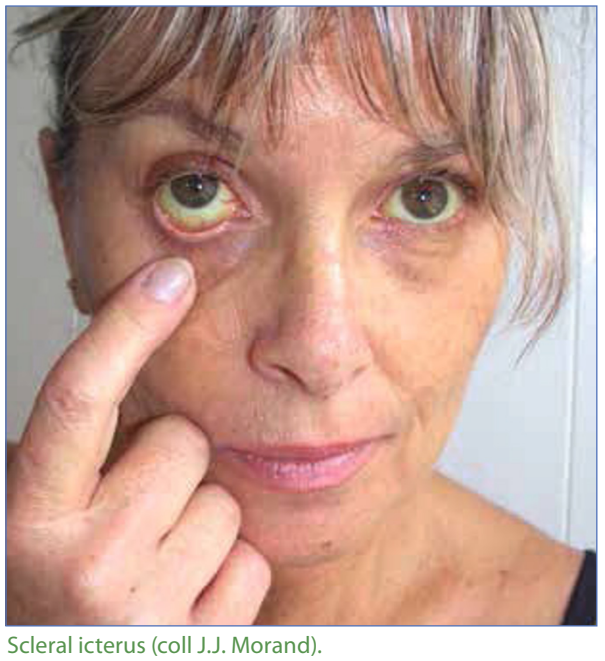
Association of yellow discoloration and redness of conjunctiva in a patient with leptospirosis (coll J.J. Morand).



Scleral icterus in a patient with hepatocarcinoma.



Jaundice in leptospirosis. The yellow discoloration of skin and mucous membranes is associated with vasodilation: flamboyant icterus (coll J.J. Morand).



Scleral icterus (coll J.J. Morand).

EPIDEMIOLOGY

Neonatal jaundice is a very common condition. Depending on gestational age, ethnicity, geographic localization (altitude) the incidence varies from 3% to more than 50% of newborns.
The condition is also quite common in adulthood.
A large number of disease states, including hepatitis and cirrhosis, biliary obstruction, hemolysis, and Gilbert syndrome, lead to an increased level of bilirubin in plasma.

PATHOPHYSIOLOGY

Deposits of excess of bilirubin in the skin, mucous membranes and sclerae.

CLINICAL DERMATOLOGICAL PRESENTATION

Yellow discoloration of the skin and mucous membranes.
Localization: generalized.
Scleral icterus is frequent (allows the distinction from carotenemia).
Pruritus can be severe if a cholestasis is associated.

EXTRACUTANEOUS SIGNS

Brownish discoloration of the urine.
Other signs depend on the underlying disorder.

DIFFERENTIAL DIAGNOSIS

- Carotenemia.
- Lycopenemia (lycopene is an isomer of β-carotene and its accumulation, due to ingestion of high amounts of tomatoes and yellow vegetables, induces a similar discoloration of the skin with a more orangey color).
- Sorafenib, quinacrine, mepacrine, dinitrophenol, saffron, tetryl, picric acid and canthaxanthins intake can also induce a yellow discoloration of the skin.

TREATMENT

The discoloration progressively fades when the levels of serum bilirubin are normalized.
Therapy of the underlying disorder.
Blue light therapy is useful in neonatal jaundice.
Ursodeoxycholic acid is useful in chronic liver diseases.

KEY REFERENCES

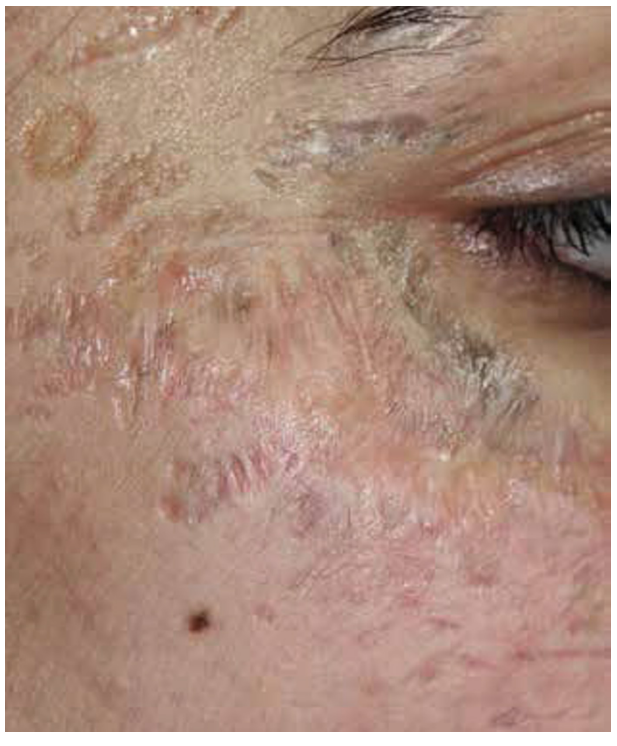
- Haught JM, Patel S, English JC 3rd. Xanthoderma: a clinical review. J Am Acad Dermatol. 2007;57:1051-8.
- Stack KM, Churchwell MA, Skinner RB Jr. Xanthoderma: case report and differential diagnosis. Cutis. 1988;41:100-2.

NON-MELANIC PIGMENTARY DISORDERS

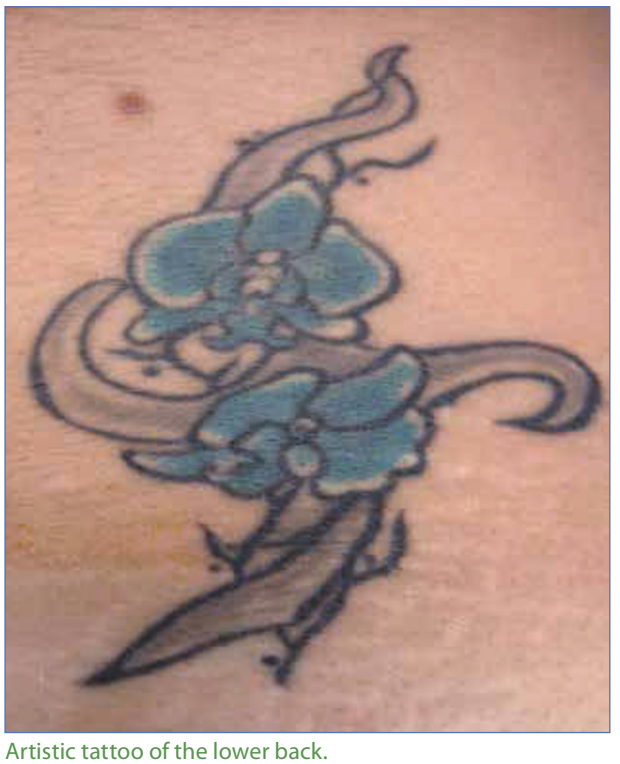
Tattoos

TATTOOS

Cosmetic tattoo of the eyebrow. The first tattoo has been treated once with a Q-switched laser and turned green. Such reaction is common with cosmetic tattoos and needs further additional sessions to be removed. Patients have to be clearly informed of this risk.



Scar of the face after a car accident. The asphalt left a traumatic tattoo.



Artistic tattoo of the lower back.

EPIDEMIOLOGY

The prevalence of tattoos is highly variable depending on age and country. Almost one-fourth of the people aged from 18 to 50 years of age and living in the US are reported to have an artistic tattoo.

PATHOPHYSIOLOGY

Implantation of pigmented particles into the dermis. Most tattoos are intentional and made for artistic or ethnic purposes. Some tattoos are performed to locate an area (eg, for radiotherapy). Traumatic tattoos result after a fall on the asphalt or are due to gunpowder.

CLINICAL DERMATOLOGICAL PRESENTATION

Most amateur tattoos are black (carbon) but a vast variety of color and patterns can be observed especially with professional tattoos.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Exogenous pigment of various origins (carbon, iron, mercuric and cadmium sulfite, titanium oxide, etc) located into the dermis.

DIFFERENTIAL DIAGNOSIS

None.

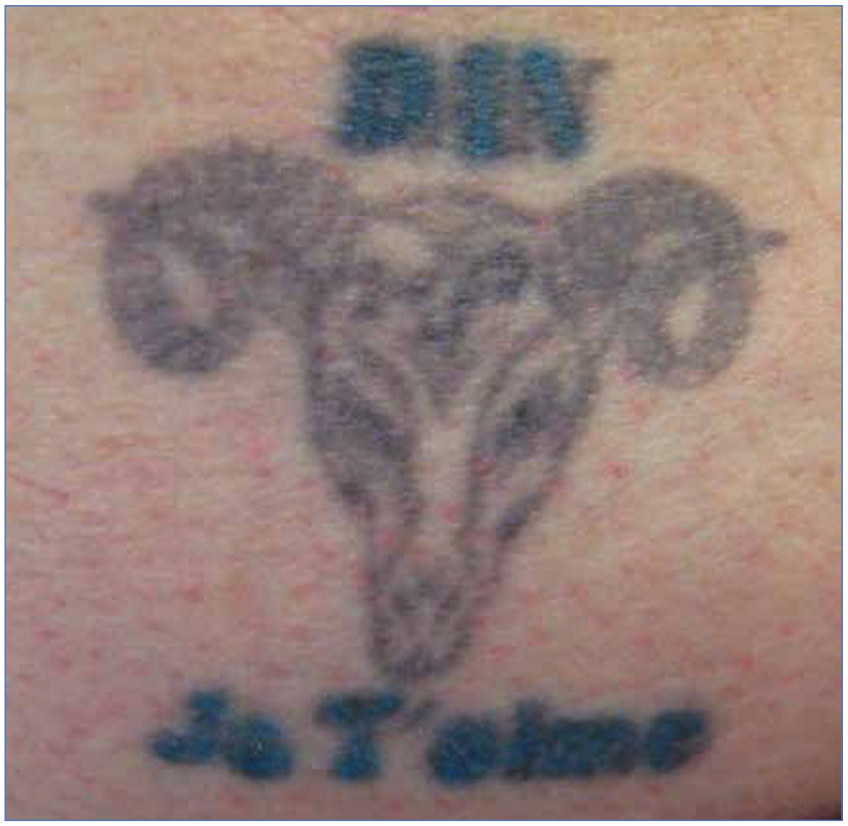
TREATMENT

Q-switched lasers are the gold standard treatment. Picosecond lasers have recently developed for this indication.
Small localized tattoos can be easily removed surgically. Due to the risk of local explosion, gun powder tattoos should not be treated by Q-switched lasers.

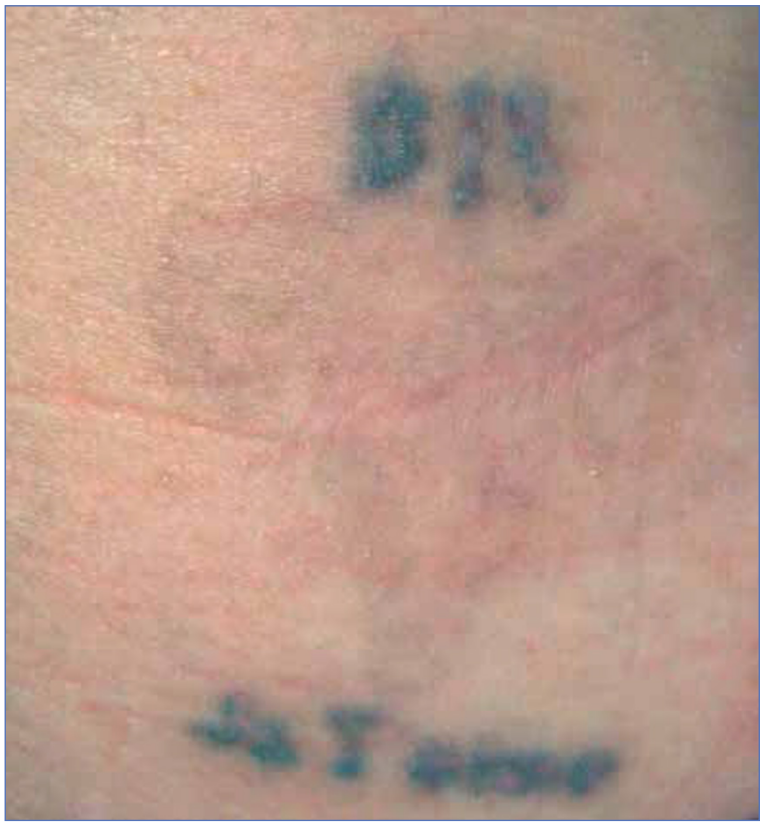
KEY REFERENCES

- Laumann AE, Derick AJ. Tattoos and body piercings in the United States: a national data set. J Am Acad Dermatol. 2006;55:413-21.
- Goyal S, Arndt KA, Stern RS, O'Hare D, Dover JS. Laser treatment of tattoos: a prospective, paired, comparison study of the Q-switched Nd:YAG (1064 nm), frequency-doubled Q-switched Nd:YAG (532 nm), and Q-switched ruby lasers. J Am Acad Dermatol. 1997;36:122-5.

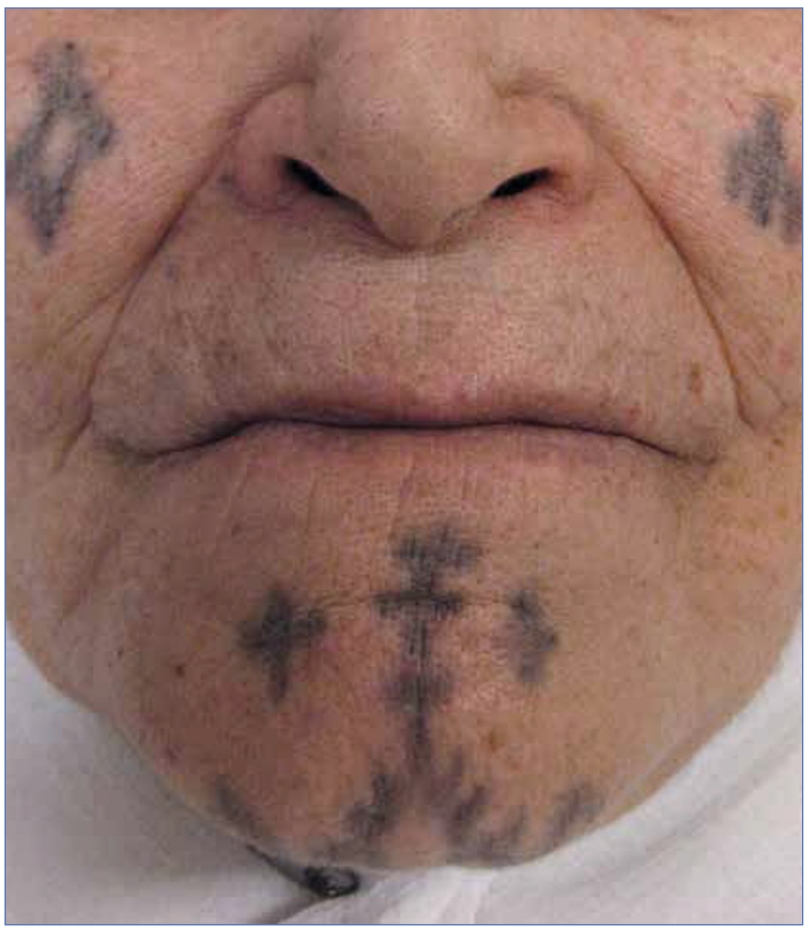
TATTOOS



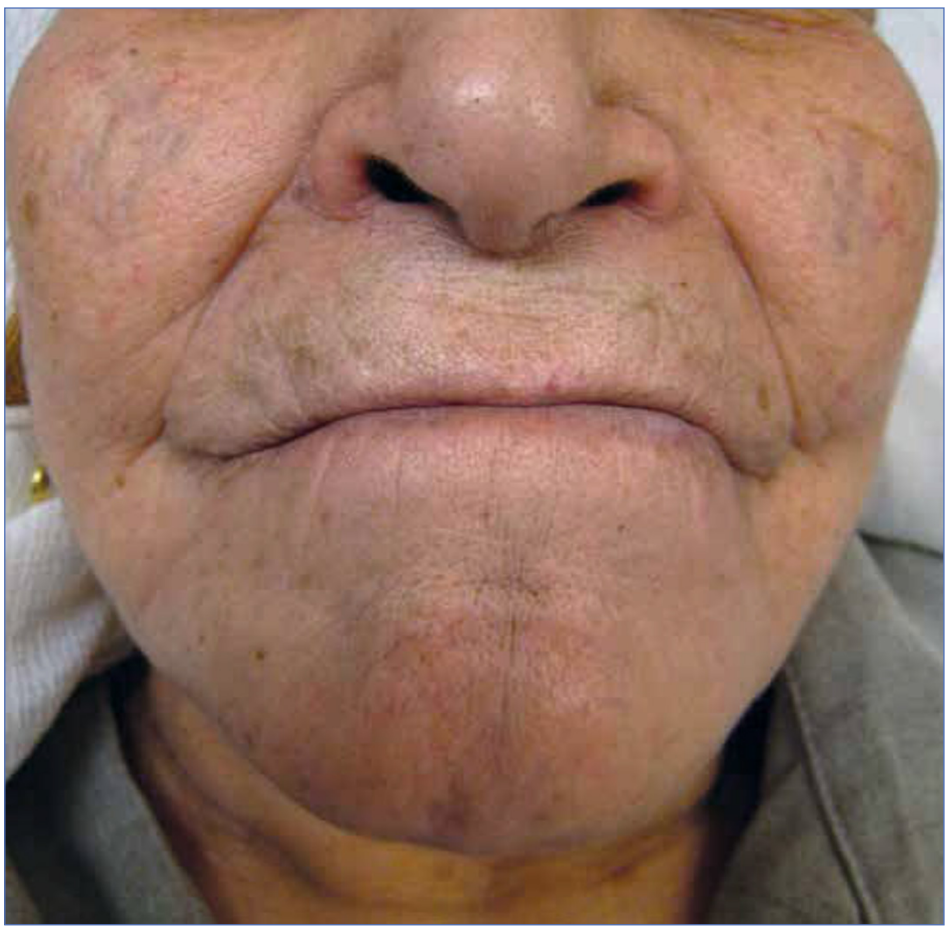
A. Professional tattoo.



B. After three sessions of Q-switched alexandrite 755 nm laser. The black pigment of the center of the cartoon is almost gone but the green letters still need additional sessions.



A. Ethnic tattoo.

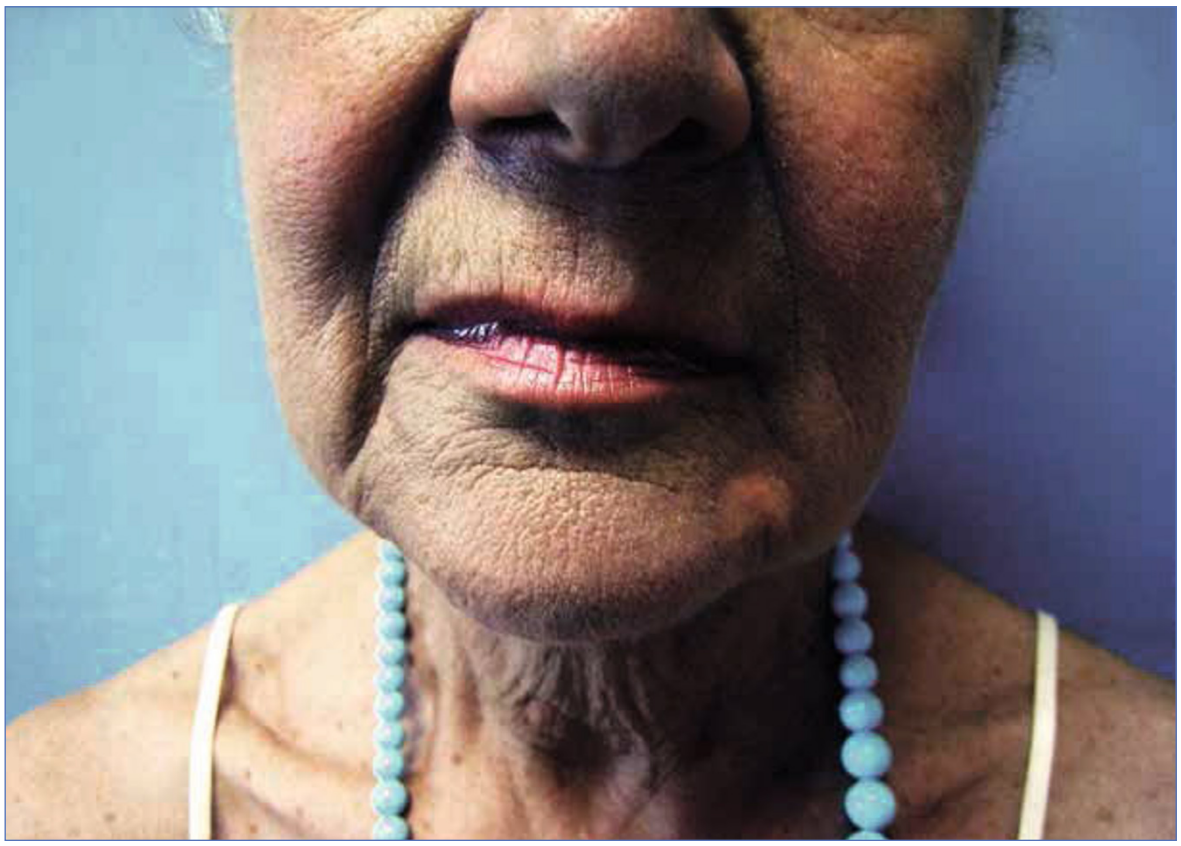


B. Almost all the pigment has been removed after only two sessions of Q-switched alexandrite 755 nm laser.

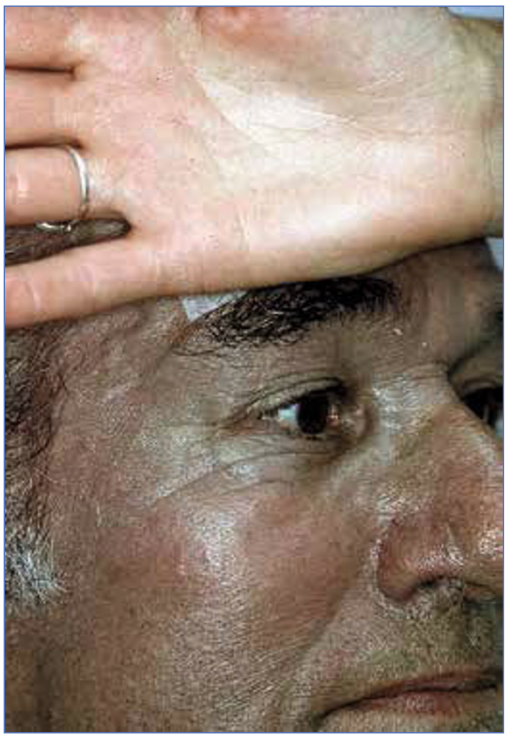
NON-MELANIC PIGMENTARY DISORDERS

Heavy metal depositions

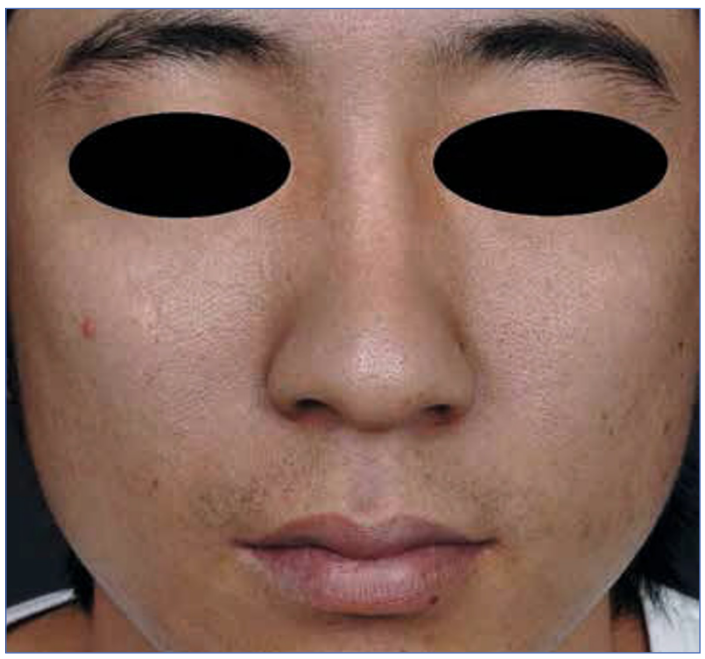
ARGYRIA



Blue discoloration of the skin due to prolonged use of silver salts. Note the white patch on the left side of the skin corresponding to the normal color of the skin achieved after a test session with 1064 nm q-switched laser.



Diffuse blue-gray pigmentation in a patient with argyria. Note for comparison the color of normal skin of the hand.



Mild form of argyria (coll. Hee Young Kang).

EPIDEMIOLOGY

Silver compounds were taken orally and also applied on mucosal areas (nasal spray, eye drops) for treating infections.
Professional exposure is also reported (photographers working with silver-containing solutions). Cases of argyria have been reported after acupuncture.
Nowadays most agents containing silver compounds have been withdrawn and argyria has become rare and is mostly observed in the older population.

PATHOPHYSIOLOGY

Abnormal accumulation of silver in the skin and mucous membranes.

CLINICAL DERMATOLOGICAL PRESENTATION

Asymptomatic progressive slate-gray pigmentation.
Localization: generalized but more pronounced in nails and sun exposed areas. Localized forms can be observed after long-term topical application of silver-containing compounds.

EXTRACUTANEOUS SIGNS

Pigmentation of the viscera can be observed but it remains asymptomatic.

HISTOPATHOLOGY

Routine hematoxylin-eosin sections show granular brown-black pigments in the dermis mostly aggregated around eccrine glands. Dark-field illumination reveals the strikingly refractile silver granules.

DIFFERENTIAL DIAGNOSIS

- Drug induced pigmentation.
- Ochronosis.

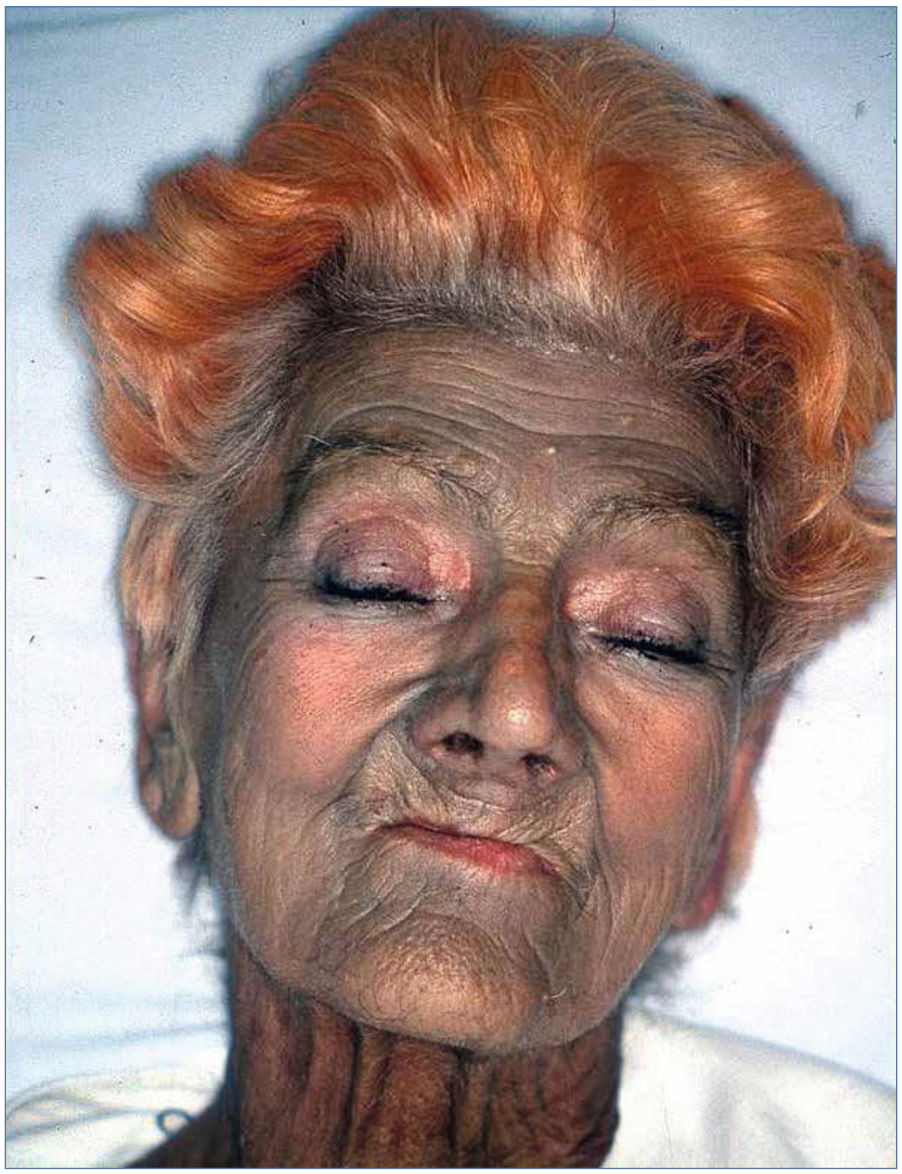
TREATMENT

Discontinuation of exposure to silver-compounds if it is still used by the patient.
Successful treatments with 1064 nm Q-switched laser have been reported.

KEY REFERENCES

- Tanita Y, Kato T, Hanada K, Tagami H. Blue macules of localized argyria caused by implanted acupuncture needles. Electron microscopy and roentgenographic microanalysis of deposited metal. Arch Dermatol. 1985;121:1550-2.
- Rhee DY, Chang SE, Lee MW, Choi JH, Moon KC, Koh JK. Treatment of argyria after colloidal silver ingestion using Q-switched 1,064-nm Nd:YAG laser. Dermatol Surg. 2008;34:1427-30.

CHRYSIASIS



Blue-gray hyperpigmentation of the face due to chrysiasis in a woman treated for years with gold sodium thiosulfate for rheumatoid arthritis.

EPIDEMIOLOGY

Gold sodium thiosulfate was used for rheumatoid arthritis, psoriatic arthritis and pemphigus. Nowadays many alternatives are available and this treatment is rarely prescribed.

PATHOPHYSIOLOGY

Abnormal accumulation of gold in the skin.
The sun-exposed localization is not fully understood. UV light may induce preferential uptake of gold by the skin. Dermal gold may increase melanogenesis by indirectly increasing tyrosinase activity. When ultraviolet light is added, the result is a synergistic induction of hyperpigmentation.

CLINICAL DERMATOLOGICAL PRESENTATION

Asymptomatic progressive blue-gray hyperpigmentation.
Localization: sun-exposed areas. Nails and mucous membranes are spared. A yellow discoloration of the nails was reported once in a patient with a high cumulative dose of gold intake.
NB. Q-switched lasers have been reported to enhance localized chrysiasis.

EXTRACUTANEOUS SIGNS

Corneal chrysiasis (most often asymptomatic).

HISTOPATHOLOGY

Granular black pigments in the dermis mostly within dermal macrophages and aggregated around appendages, vessels and nerves. No particles within appendages, epidermis or basement membranes. Epipolarized light enhances the detection of gold particles.

DIFFERENTIAL DIAGNOSIS

- Drug-induced pigmentation.
- Ochronosis.
- Hemochromatosis.
- Argyria.

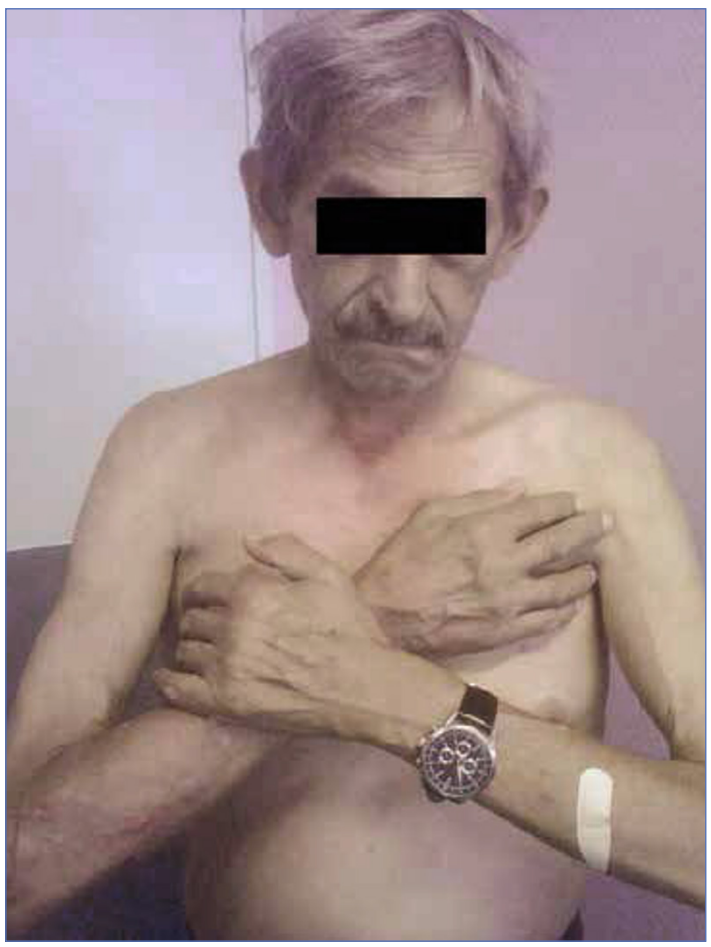
TREATMENT

Discontinuation of gold intake.
Sun avoidance.
While Q-switched lasers might enhance chrysiasis, long pulsed laser (such as pulsed dye lasers) might be beneficial.

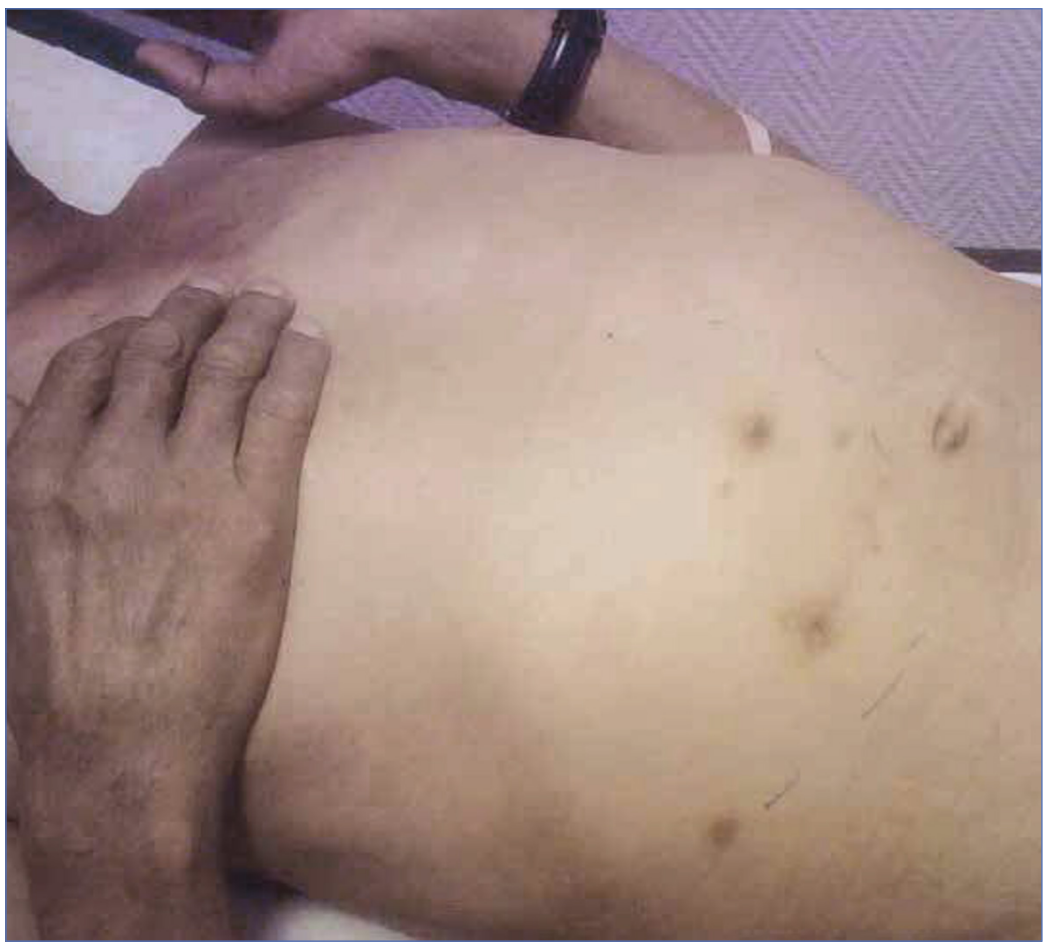
KEY REFERENCES

- Leonard PA, Moatamed F, Ward JR, Piepkorn MW, Adams EJ, Knibbe WP. Chrysiasis: the role of sun exposure in dermal hyperpigmentation secondary to gold therapy. J Rheumatol. 1986;13:58-64.
- Yun PL, Arndt KA, Anderson RR. Q-switched laser-induced chrysiasis treated with long-pulsed laser. Arch Dermatol. 2002;138:1012-4.

HEMOCHROMATOSIS



Slate gray hyperpigmentation on sun-exposed areas in a patient with hemochromatosis (coll. Rodolphe Anty).



Hemochromatosis. Cirrhosis (note the hepatomegaly), diabetes and hyperpigmentation (bronze diabetes) (coll. Rodolphe Anty).

OMIM #235200

(for the hereditary form of hemochromatosis)

EPIDEMIOLOGY

The world wide frequency of mutations in hemochromatosis gene is about 10%. Prevalence of homozygous hemochromatosis is 0.4% in northern European ancestry, with only half presenting clinical signs. Prevalence is lower among Africans and Asians.
Higher incidence of serious complications (cirrhosis, diabetes mellitus) is observed in men but skin hyperpigmentation is more frequently observed in women.

PATHOPHYSIOLOGY

Hereditary hemochromatosis is an autosomal recessive disorder most often caused by mutations in HFE gene.
Secondary hemochromatosis is caused by disorders of erythropoiesis and disorders requiring recurrent blood transfusions. Increased intestinal iron absorption and iatrogenic iron overload are rarely observed.
This leads to an abnormal accumulation of iron in liver, heart, pancreas, pituitary, joints, and skin.
The hyperpigmentation of hemochromatosis results in a combination of melanin and hemosiderin. Iron stimulates melanin production by melanocytes but the exact mechanism is still unknown.

CLINICAL DERMATOLOGICAL PRESENTATION

Various degrees of cutaneous hyperpigmentation are observed in more than 90% of patients with hemochromatosis. This is one of the earliest signs of the disease but the intensity is mild and the hyperpigmentation is usually not the sign allowing the diagnosis.
Color: brownish-bronze (can be taken for a suntan), sometimes slate gray.
Localization: generalized but more pronounced on sun-exposed areas (face).

EXTRACUTANEOUS SIGNS

Excess iron is deposited in a variety of organs leading to their failure.
Cirrhosis, hepatocarcinomas, diabetes mellitus ('bronze diabetes'), cardiomyopathy, arthritis and hypogonadotropic hypogonadism are the most frequent manifestations.

HISTOPATHOLOGY

Increased melanin in basal and supra basal layers.
Perls coloration reveals free homosiderin in upper dermis, eccrine sweat glands and vessels, and hemosiderin within macrophages.

DIFFERENTIAL DIAGNOSIS

- Drug induced pigmentation.
- Ochronosis.
- Argyria.

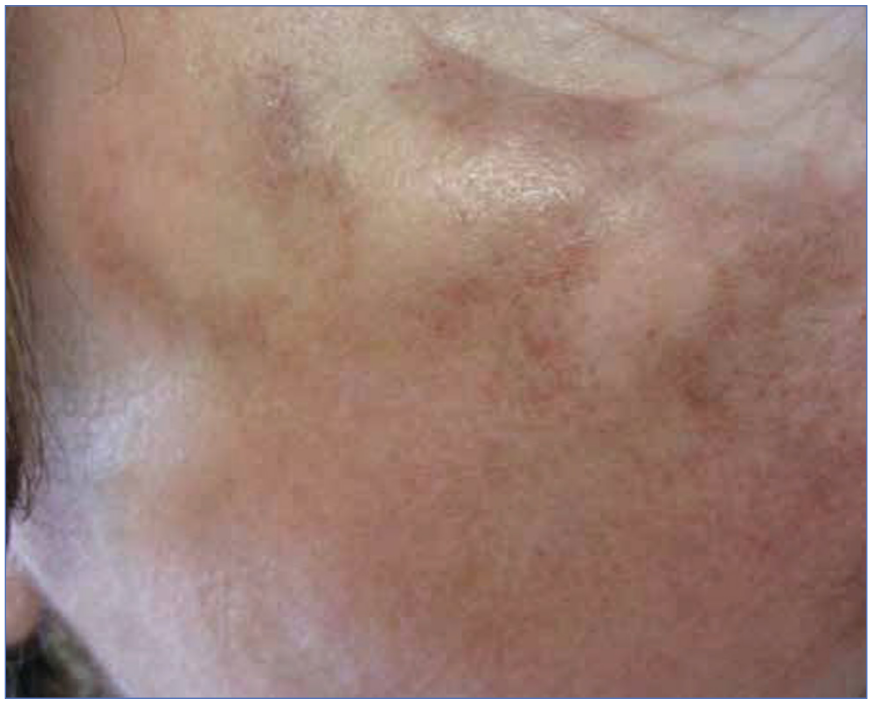
TREATMENT

Phlebotomy is the gold standard treatment.
Deferoxamine is mostly used in secondary hemochromatosis.

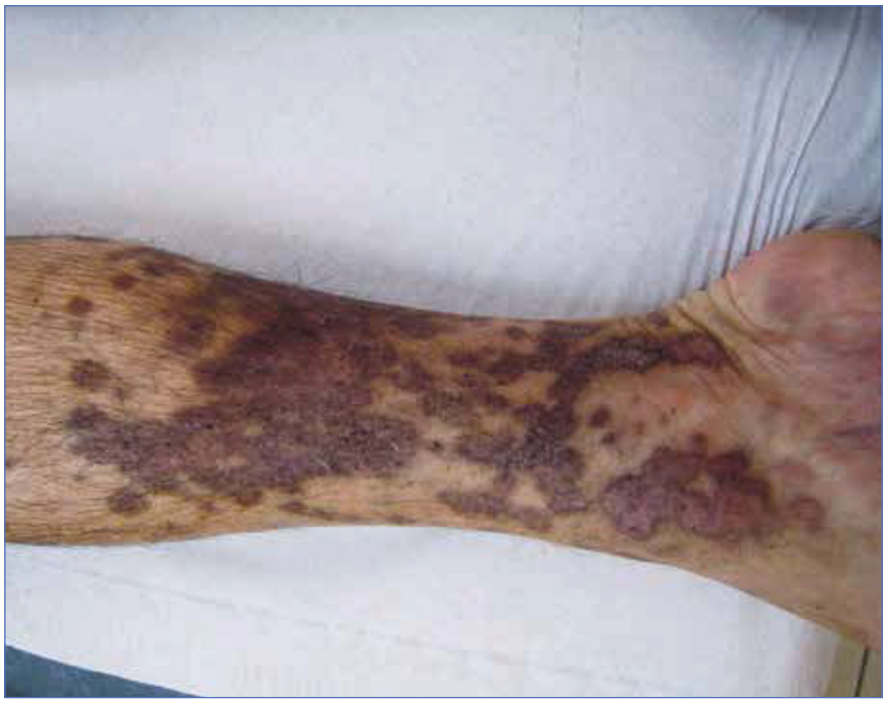
KEY REFERENCES

- Moirand R, Adams PC, Bicheler V, Brissot P, Deugnier Y. Clinical features of genetic hemochromatosis in women compared with men. Ann Intern Med. 1997;127:105-10.
- Chevrant-Breton J, Simon M, Bourel M, Ferrand B. Cutaneous manifestations of idiopathic hemochromatosis. Study of 100 cases. Arch Dermatol. 1977;113:161-5.

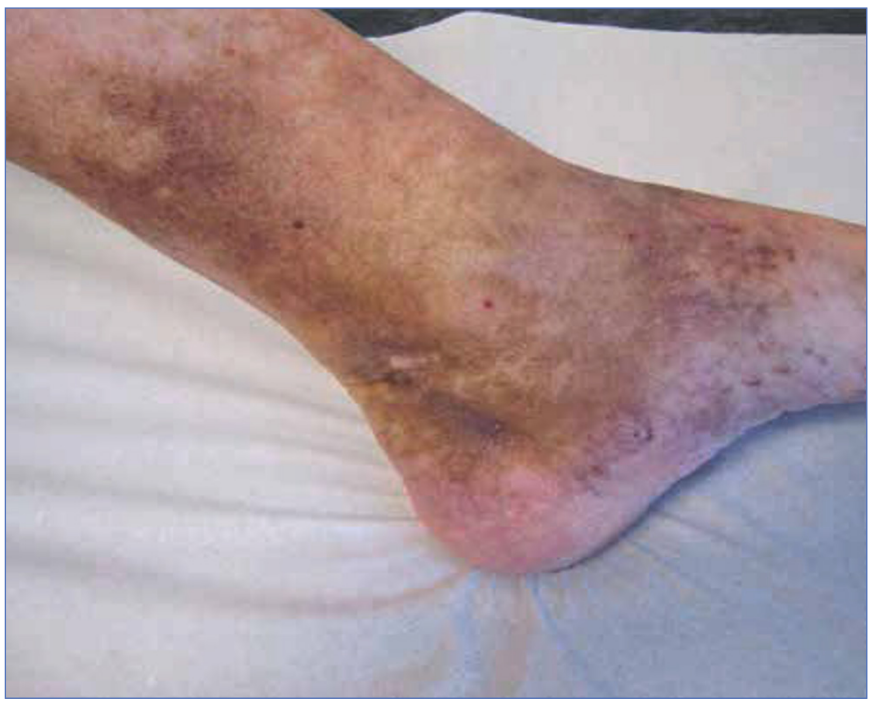
HEMOSIDEROSIS AND SIDEROSIS



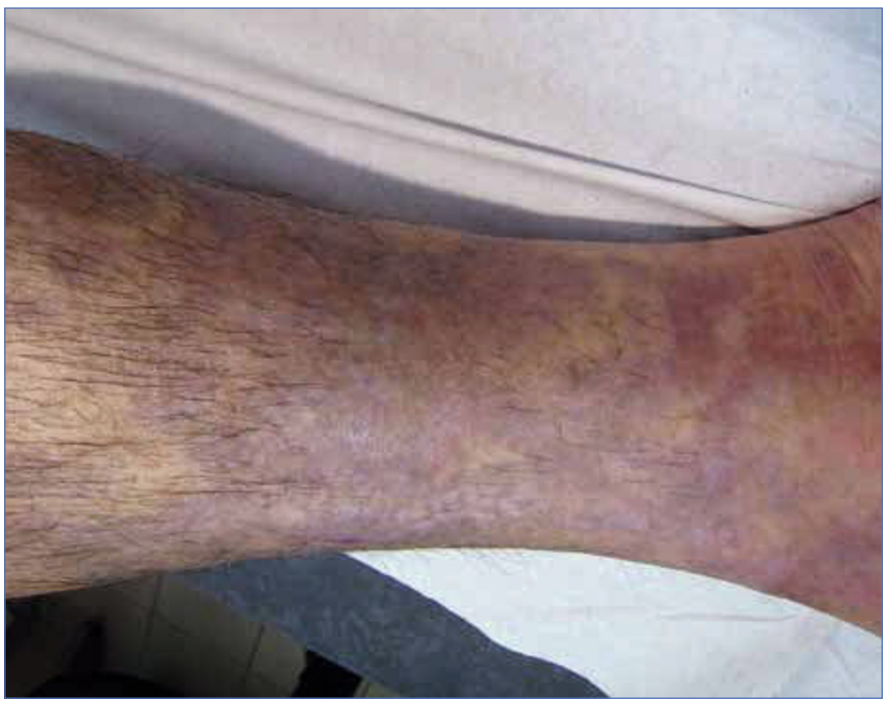
Light brown irregular pigmentation of the face due to hemosiderosis that occurred after intense pulsed light treatment of actinic lentigos. The histological examination showed the absence of melanin increase at Fontana Masson staining but the Perls staining revealed an iron accumulation in the macrophages of the dermis.



A. Brown discoloration of the leg due to hemosiderosis as sequelae of treated Kaposi's sarcoma.



Stasis dermatitis with irregular brownish-bronze pigmentation of the lower leg.



B. Marked improvement 6 months after five sessions of 532 and 755 nm Q-switched lasers.

EPIDEMIOLOGY

Hemosiderosis and siderosis are frequently observed in clinical practice but the incidence and prevalence are unknown due to the multiplicity of causes.

PATHOPHYSIOLOGY

Hemosiderosis is caused by erythrocyte extravasation. Many conditions can induce hemosiderosis. Stasis dermatitis in relation with varicose veins and venous ulcer, and Bateman purpura (actinic purpura) are the most frequent causes of hemosiderosis. Vasculitis, vascular malformation or tumors are other causes of hemosiderosis.
Siderosis is due to intramuscular injection or extravasation of iron solutions.

CLINICAL DERMATOLOGICAL PRESENTATION

Highly variable clinical presentation due to the variety of causes.
Color: brownish-bronze to blue gray color is usually observed (stasis dermatitis). Purple to brown coloration in senile purpura or vasculitis.
Localization: dorsum of the hands and arms for senile purpura, legs for stasis dermatitis and vasculatis, but all the teguments can be affected depending on the etiology.

EXTRACUTANEOUS SIGNS

Other organs than skin can be affected by hemosiderosis such as lungs after pulmonary hemorrhage. Liver (porphyria cutanea tarda) and kidney can also be involved.

HISTOPATHOLOGY

Deposition of iron (mostly in its ferric state) revealed with Perls coloration in affected organs. Other histological signs can be associated depending on the cause of the hemosiderosis (eg, Vasculitis, targetoid hemosiderotic hemangioma, etc).

DIFFERENTIAL DIAGNOSIS

- Drug-induced pigmentation.

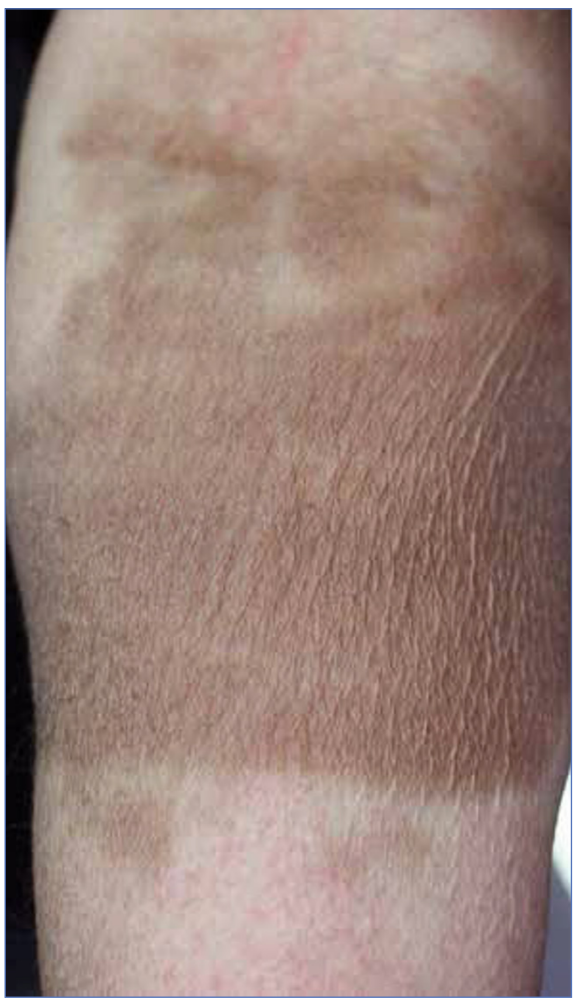
TREATMENT

Treatment of the underlying condition.
Photoprotection in senile purpura.
Surgery for tumors.
Q-switched lasers and intense pulsed light are effective treatments.

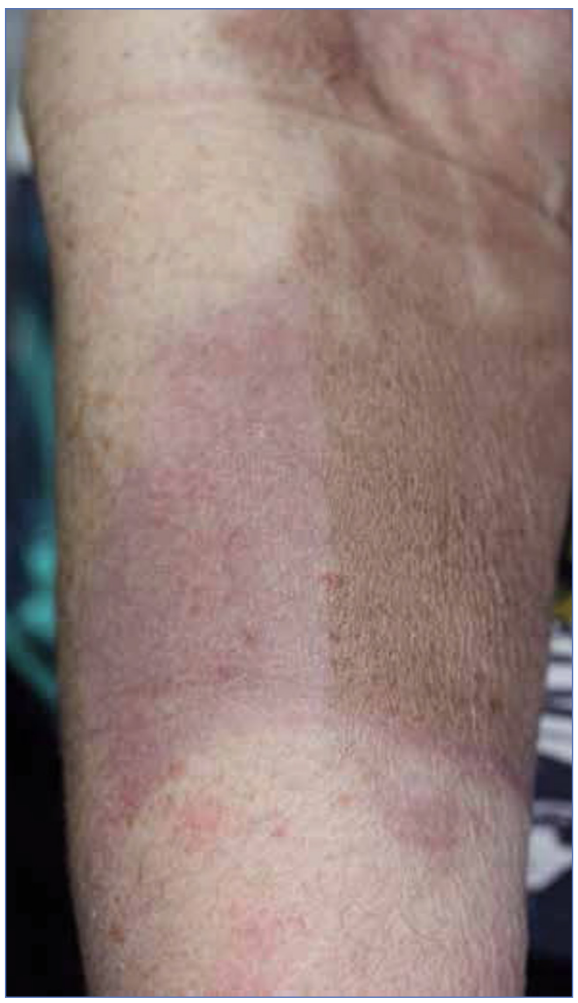
KEY REFERENCES

- Tsuji T. Experimental hemosiderosis: relationship between skin pigmentation and hemosiderin. Acta Derm Venereol. 1980;60:109-14.
- Pimentel CL, Rodriguez-Salido MJ. Pigmentation due to stasis dermatitis treated successfully with a noncoherent intense pulsed light source. Dermatol Surg. 2008;34:950-1.
- Hughes R, Lacour JP, Passeron T. Pigmentary sequelae of AIDS-related cutaneous Kaposi sarcoma: successful treatment by Q-switched 755-nm alexandrite and 532-nm Nd:YAG lasers. Arch Dermatol. 2011;147:779-81.

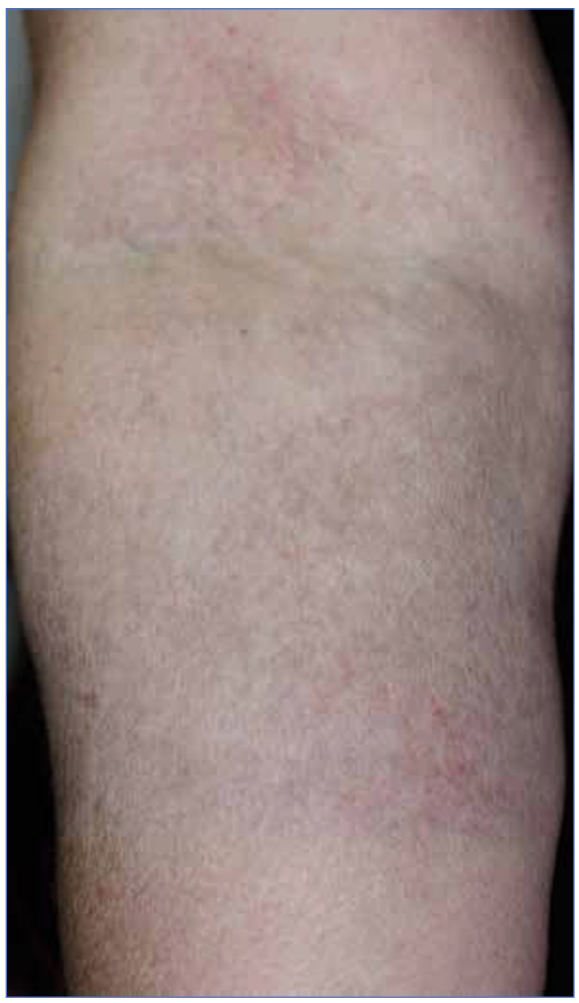
HEMOSIDEROSIS AND SIDEROSIS



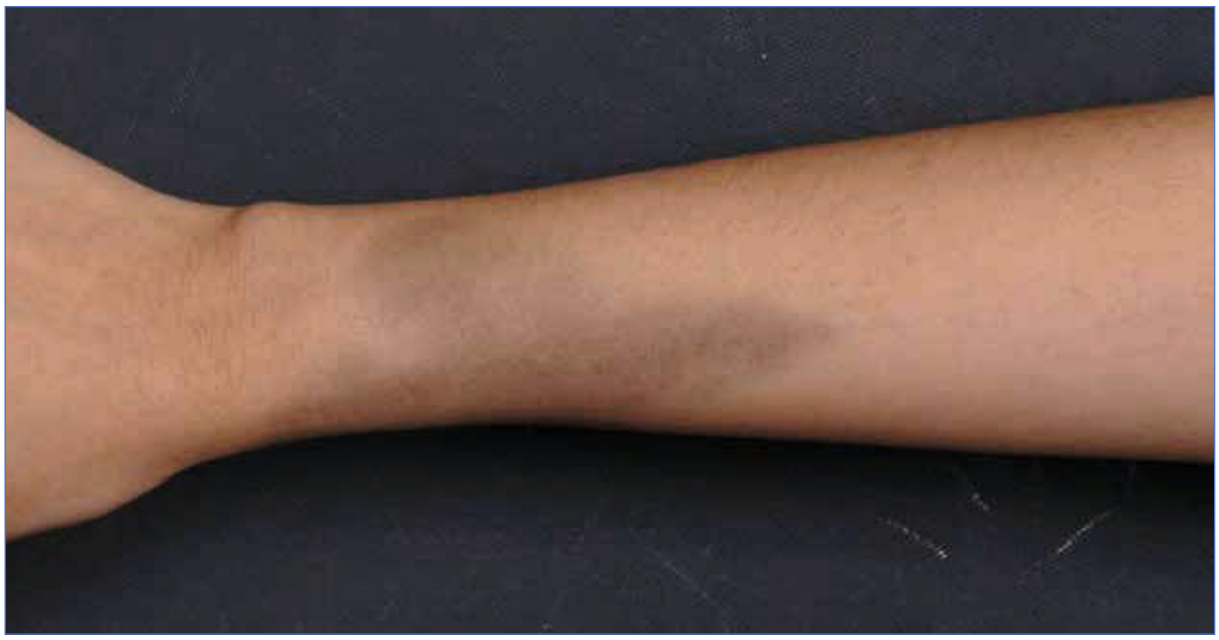
A. Brownish plaque of siderosis after intravenous iron extravasation.



B. Clinical aspect two months after one session of 532 nm QS NdYAG laser as compared to the part of the lesion untreated.

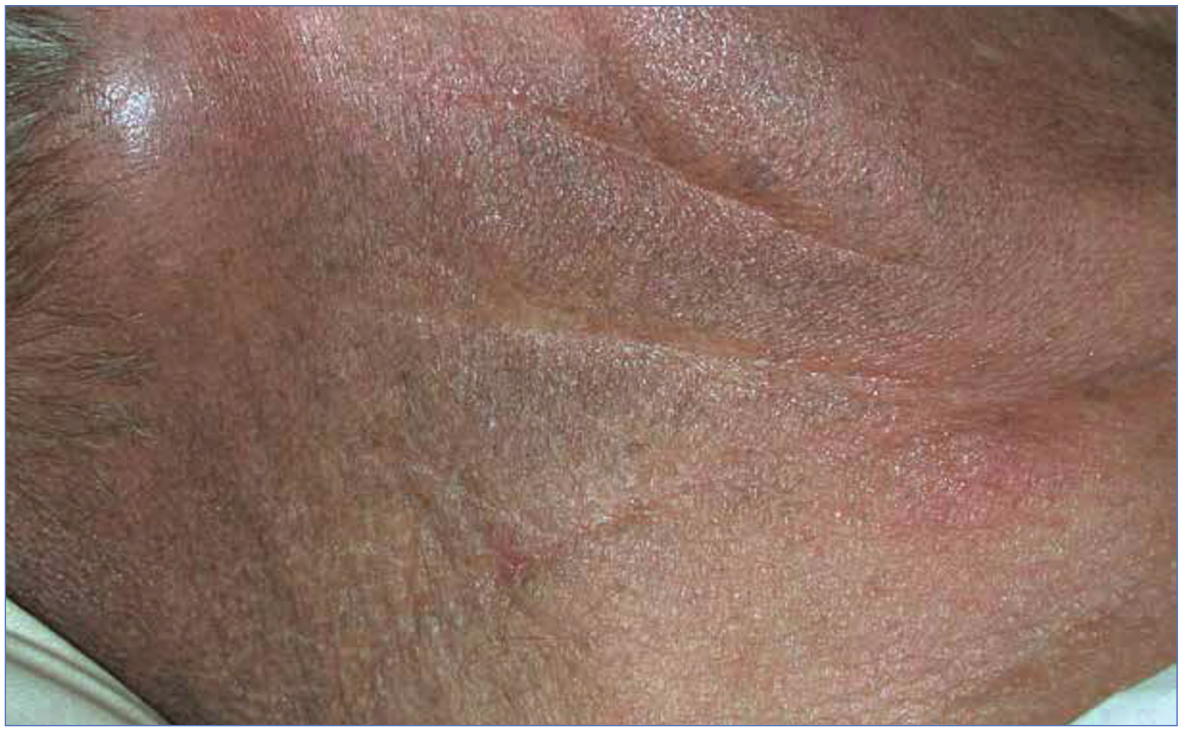


C. Marked bleaching 6 months after four laser sessions.

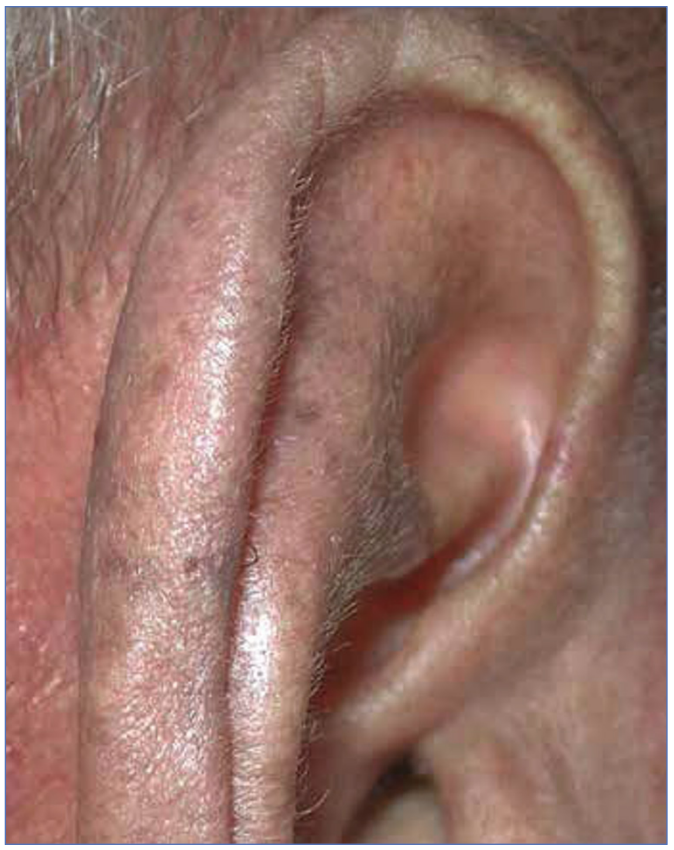


Siderosis after iron injection for anemia (coll. Hee Young Kang).

PIGMENTATION TO AMIODARONE



Slate-gray pigmentation of the neck in a patient taking amiodarone for almost 3 years.



Onset of discoloration due to amiodarone with slate-gray macules of the ear.

EPIDEMIOLOGY

1 to 10% of patients on prolonged therapy with amiodarone will develop a discoloration of the skin.

PATHOPHYSIOLOGY

The mechanism involved is a drug-induced phospholipodosis; when it accumulates within the cells, amiodarone impairs the cholesterol transport and induces lipid accumulation.

The preferentially involvement of sun-exposed areas suggests a phototoxic reaction. UV radiation may promote the deposit of amiodarone itself or a metabolite (desethylamiodarone) in the dermis.

CLINICAL DERMATOLOGICAL PRESENTATION

Asymptomatic and progressive slate-gray pigmentation.

Localization: mostly located in sun-exposed areas.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Routine hematoxylin-eosin sections reveal yellow-brown granules in the reticular dermis, both in the cytoplasm of macrophages and between the collagen bundles. The histochemical stainings of the granules show a lipofuscin pigment rather than melanin.

DIFFERENTIAL DIAGNOSIS

- Other drug induced pigmentation.
- Argyria.

TREATMENT

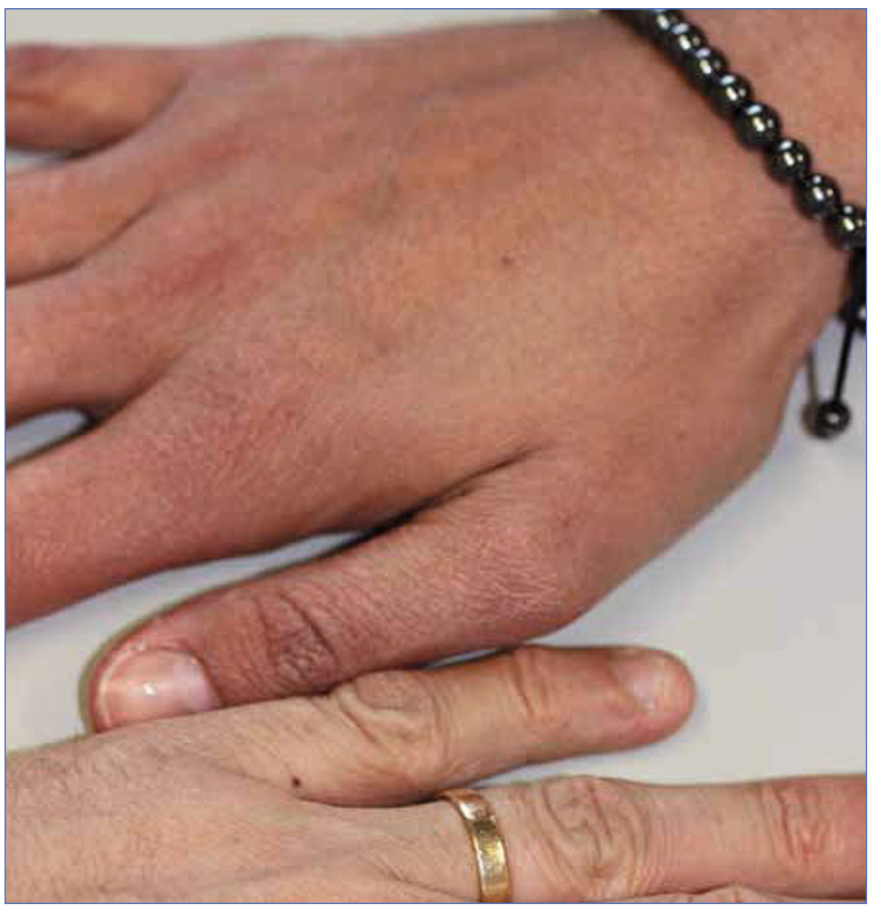
Progressive but delayed and inconstant resolution of the blue-gray discoloration can be observed after discontinuation of amiodarone.

Successful treatments with Q-switched lasers have been reported.

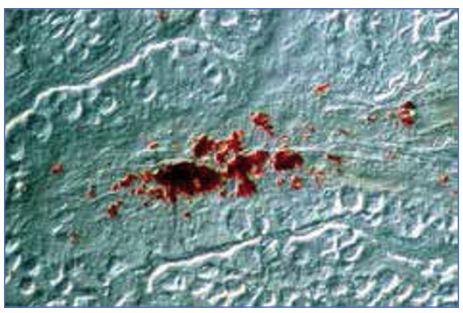
KEY REFERENCES

- Palmeri S, Battisti C, Malandrini A, Federico A. Amiodarone induced lipidosis similar to Niemann-Pick C disease. Biochemical and morphological study. Life Sci. 1995;57:1963-71.
- Blackshear JL, Randle HW. Reversibility of blue-gray cutaneous discoloration from amiodarone. Mayo Clin Proc. 1991;66:721-6.
- Karrer S, Hohenleutner U, Szeimies RM, Landthaler M. Amiodarone-induced pigmentation resolves after treatment with the Q-switched ruby laser. Arch Dermatol. 1999;135:251-3.

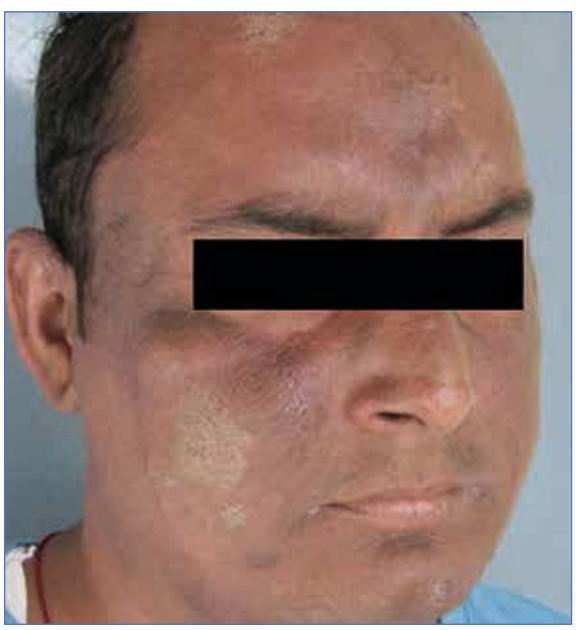
PIGMENTATION TO CLOFAZIMINE



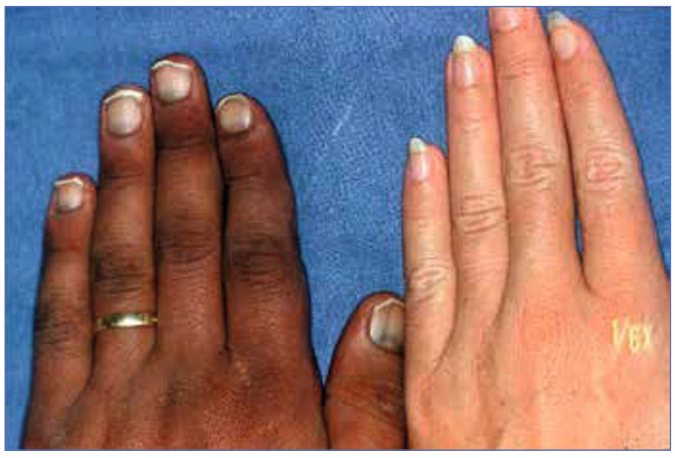
Mild form of discoloration of the hand (as compared to normal hand) due to the chronic absorption of clofazimine.



Red crystals in the bowel biopsy of the same patient.



Reddish hyperpigmentation of the face due to clofazimine treatment (coll. M. Sendhil Kumaran and Davinder Parsad).



Discoloration of the hand (as compared to normal hand) due to the chronic absorption of clofazimine.

EPIDEMIOLOGY

Clofazimine is used for treating leprosy, and other mycobacterial infections. It is also used in dermatology to treat neutrophilic, granulomatous and infectious diseases.

PATHOPHYSIOLOGY

Abnormal deposition of clofazimine into the skin. Clofazimine is highly absorbed by macrophages and thus, inflammatory lesions can present a stronger discoloration.

CLINICAL DERMATOLOGICAL PRESENTATION

Asymptomatic progressive reddish cutaneous and conjunctival discoloration within the first two weeks of use. Active inflammatory lesions can display a deep red-blue coloration.
If the treatment is prolonged the coloration of the skin becomes violet-brown or bluish .
Ichthyosis is observed in 66% of cases.
Localization: generalized. A darkening of hair can be observed.

EXTRACUTANEOUS SIGNS

Corneal changes with fine and brownish lines have been reported.
Enteropathy with diarrhea, abdominal pain, edema and hypoalbuminaemia can be observed.

HISTOPATHOLOGY

The drug deposition is difficult to see in routine colorations. Frozen section can better show the deposition of red crystals around vessels in the reticular dermis. Ceroid-lipofuscin pigment was demonstrated inside macrophages that contained numerous phagolysosomes.

DIFFERENTIAL DIAGNOSIS

- Drug-induced pigmentation.
- Ochronosis.

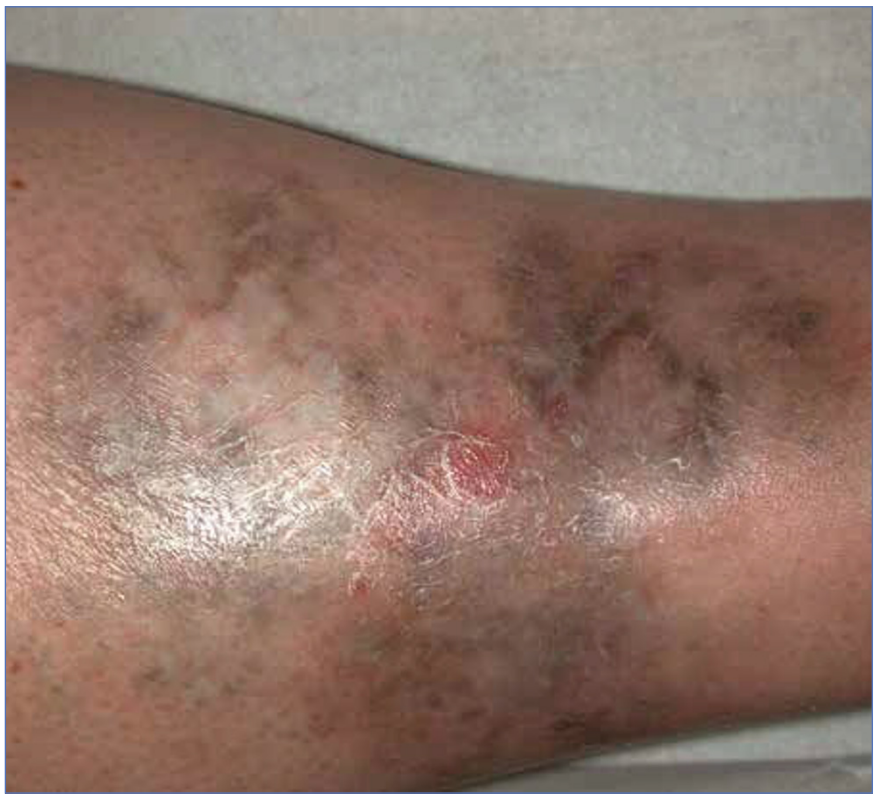
TREATMENT

Discontinuation of exposure to clofazimine leads to a progressive fading of pigmentary changes.

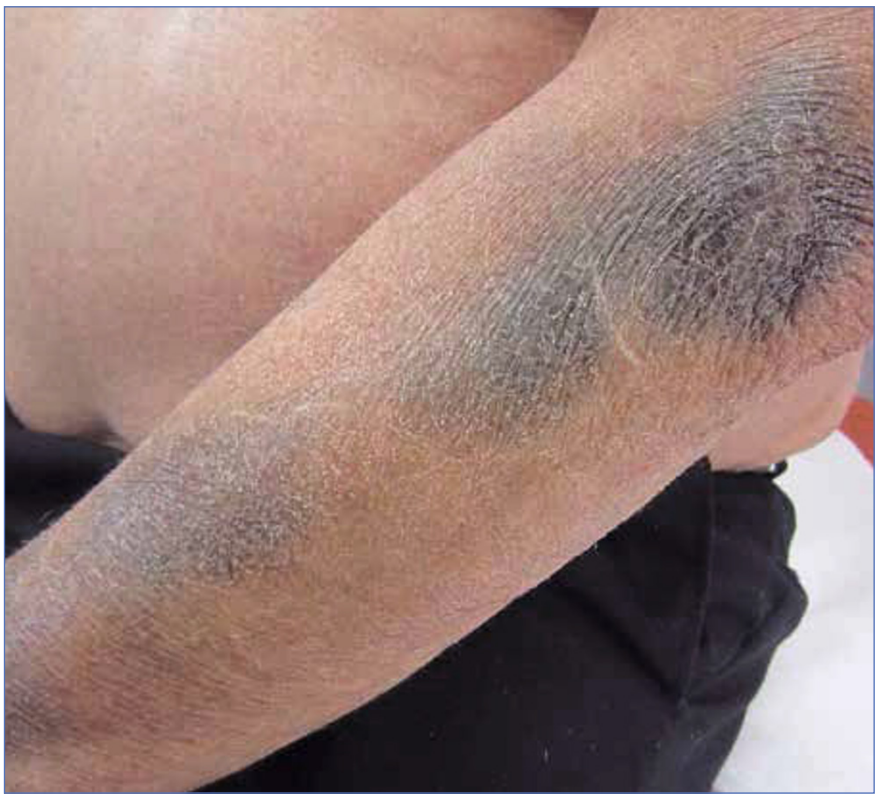
KEY REFERENCES

- Philip M, Samson JF, Simi PS. Clofazimine-induced Hair Pigmentation. Int J Trichology. 2012;4:174-5.
- Job CK, Yoder L, Jacobson RR, Hastings RC. Skin pigmentation from clofazimine therapy in leprosy patients: a reappraisal. J Am Acad Dermatol. 1990;23:236-41.
- Ramu G, Iyer GG. Side effects of clofazimine therapy. Lepr India. 1976;48:722-31.

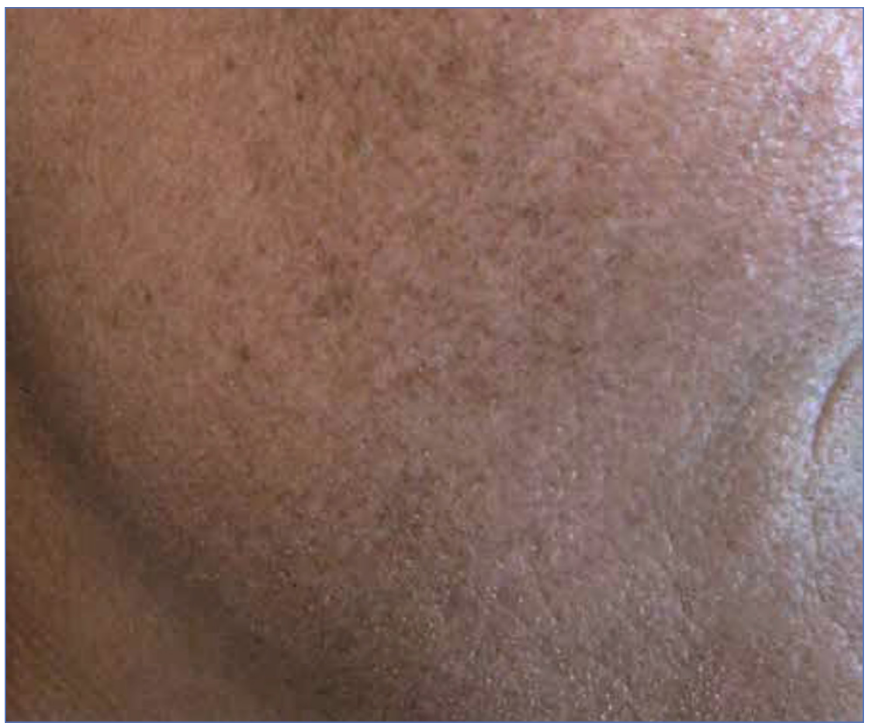
PIGMENTATION TO MINOCYCLINE



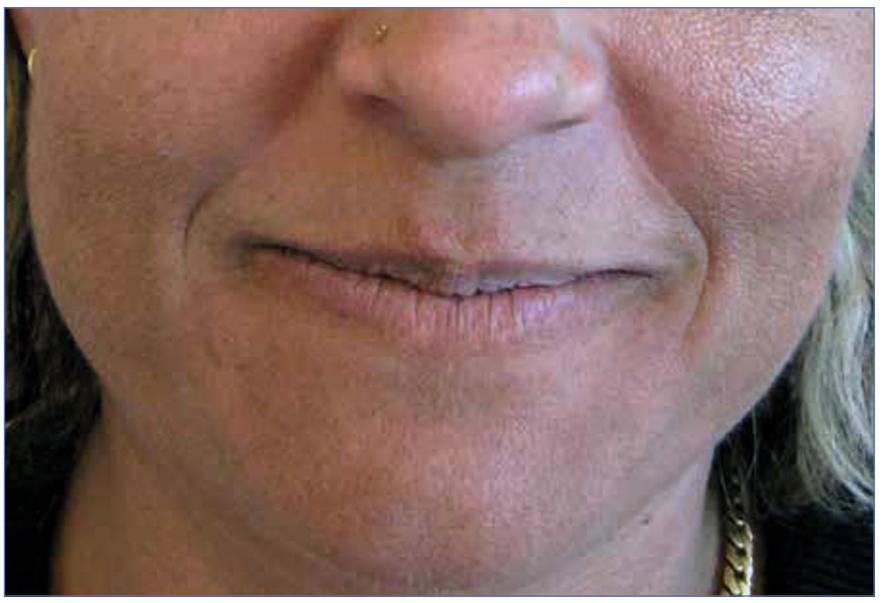
Blue-gray pigmentation of the lower leg due to minocycline. Note that the pigmentation is confined to the sequela of a leg ulcer (type I).



Blue-gray circumscribed pigmentation of normal skin of the forearms (type II).



Type III pigmentation on the face due to the prolonged use of minocycline.



Type III pigmentation on the face due to the prolonged use of minocycline.

EPIDEMIOLOGY

Hyperpigmentation to minocycline results from long-term administration of the drug but a discoloration has been reported as early as 9 weeks after 200 mg/d of treatment.

PATHOPHYSIOLOGY

Oxidized minocycline metabolite can chelate iron leading to the presence of siderosomes that color the skin. Minocycline can also increase the production of melanin by promoting the transcription of tyrosinase, TRP1 and DCT enzymes.

CLINICAL DERMATOLOGICAL PRESENTATION

Asymptomatic and progressive pigmentation of the skin, mucous membranes, sclera, teeth and nails.
Three distinct types of minocycline-induced cutaneous pigmentation have been described.

Type I: blue-black pigmentation confined to sites of scarring or inflammation.
Type II: blue-gray circumscribed pigmentation of normal skin of the lower legs and forearms.
Type III: diffuse muddy brown pigmentation of normal skin accentuated in sun-exposed areas.

EXTRACUTANEOUS SIGNS

Pigmentation of viscera has been reported but it remains asymptomatic.

HISTOPATHOLOGY

Perls staining reveals iron deposition in type I and II while an increased melanization in the basal layer and in the upper dermis is found in type III.

DIFFERENTIAL DIAGNOSIS

- Other drug induced pigmentation.
- Argyria.

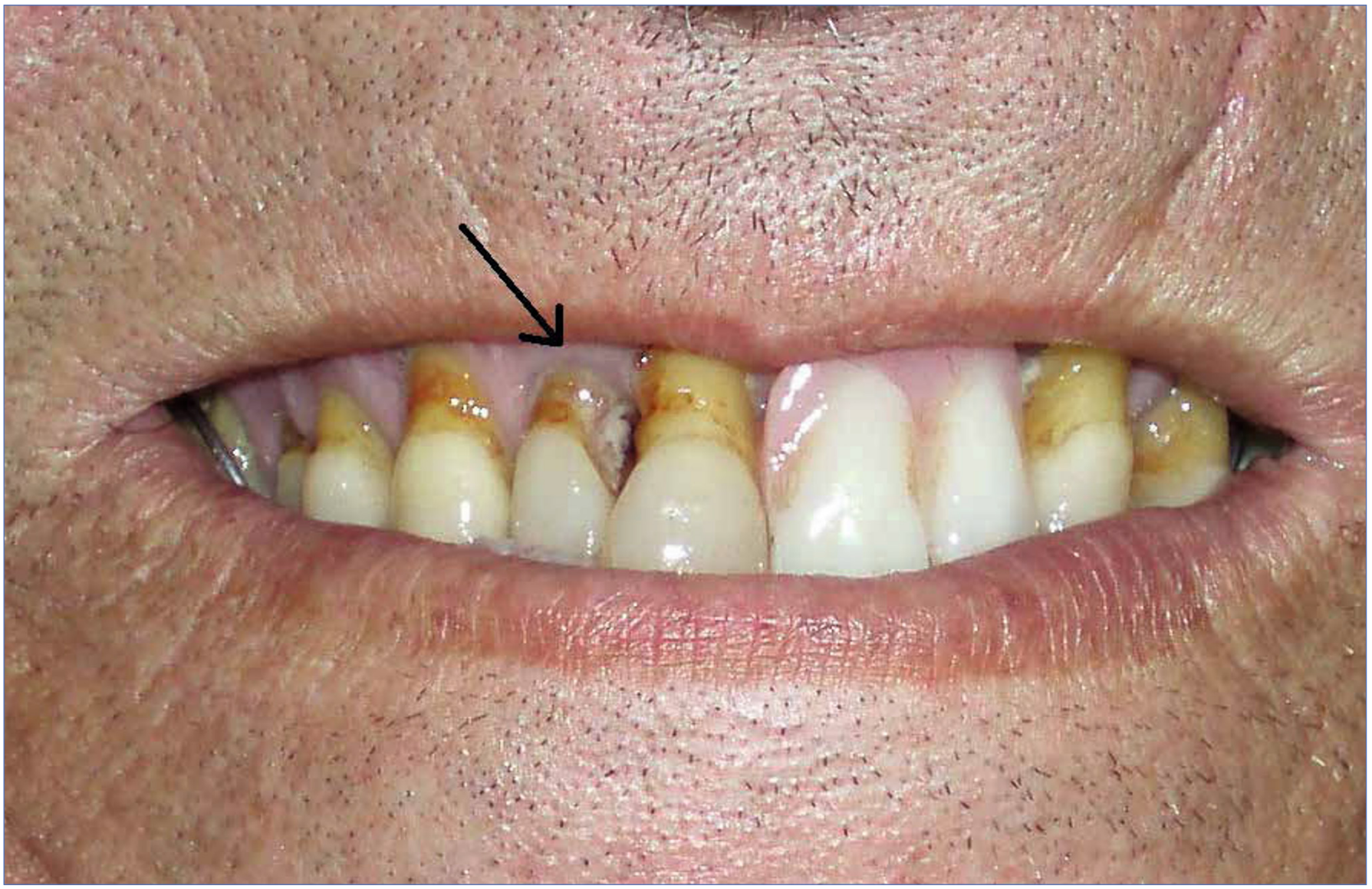
TREATMENT

Progressive slow resolution of the discoloration is observed after discontinuation of minocycline.
Successful treatments with Q-switched lasers and after fractional photothermolysis have been reported.

KEY REFERENCES

- Sato E, Tsukimoto M, Shimura N, Awaya A, Kojima S. Mechanism of pigmentation by minocycline in murine B16 melanoma cells. Yakugaku Zasshi. 2011;131:731-8.
- Green D, Friedman KJ. Treatment of minocycline-induced cutaneous pigmentation with the Q-switched Alexandrite laser and a review of the literature. J Am Acad Dermatol. 2001;44 (2 Suppl):342-7.

PLUMBISM



Asymptomatic blue-gray Burton line on the marginal gingivae in a patient with lead poisoning (coll. Jayne Camuglia, with permission of the Medical Journal of Australia).

EPIDEMIOLOGY

Lead poisoning has been reported in almost every country. It is more frequently observed in low socioeconomic populations. The incidence has decreased with the discontinuation of use of lead in paints and plumbing.
Young children are at the greatest risk for lead poisoning, because they are most likely to put things containing lead into their mouths.
80% of patients with chronic lead intoxication will present Burton lines.

PATHOPHYSIOLOGY

Abnormal accumulation of lead in the tissues.

CLINICAL DERMATOLOGICAL PRESENTATION.

Asymptomatic blue-gray Burton line (lead line) on the marginal gingivae.
Localization: only the gingivae. Skin is never involved.
Nail discoloration has been reported once.

EXTRACUTANEOUS SIGNS

Chronic lead-induced nephropathy.
Acute lead poisoning causes colic, encephalopathy, peripheral neuritis and anemia.
High blood pressure is also a common complication.
NB. The Burton line may be the sole clue of plumbism in some patients.

HISTOPATHOLOGY

Dark brown pigment within subepithelial connective tissue.

DIFFERENTIAL DIAGNOSIS

- Drug-induced pigmentation.
- Ethnic mucosal pigmentation.

TREATMENT

Discontinuation of exposure to lead.
Chelating agents (succimer, D-penicillamine, dimercaprol, EDTA). Symptomatic treatment of related symptoms. Calcium, zinc, and iron supplementation.

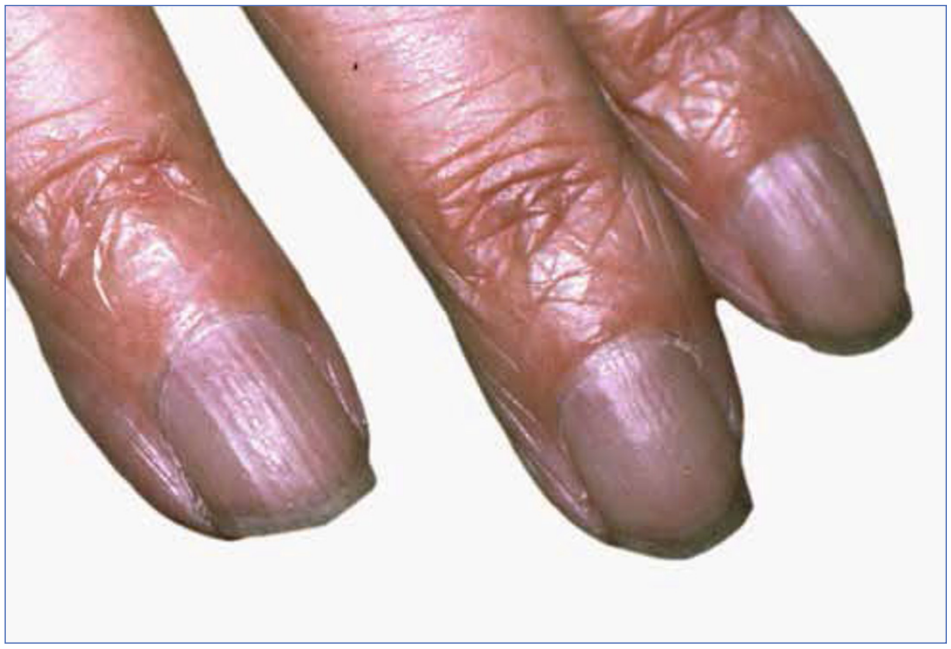
KEY REFERENCES

- Lockhart PB. Gingival pigmentation as the sole presenting sign of chronic lead poisoning in a mentally retarded adult. Oral Surg Oral Med Oral Pathol. 1981;52:143-9.
- ten Bruggenkate CM, Lopes Cardozo E, Maaskant P, van der Waal I. Lead poisoning with pigmentation of the oral mucosa. Review of the literature and report of a case. Oral Surg Oral Med Oral Pathol. 1975;39:747-53.
- Camuglia JE, Grigoriadis G, Gilfillan CP. Lead poisoning and Burton's line. Med J Aust. 2008;189:339.

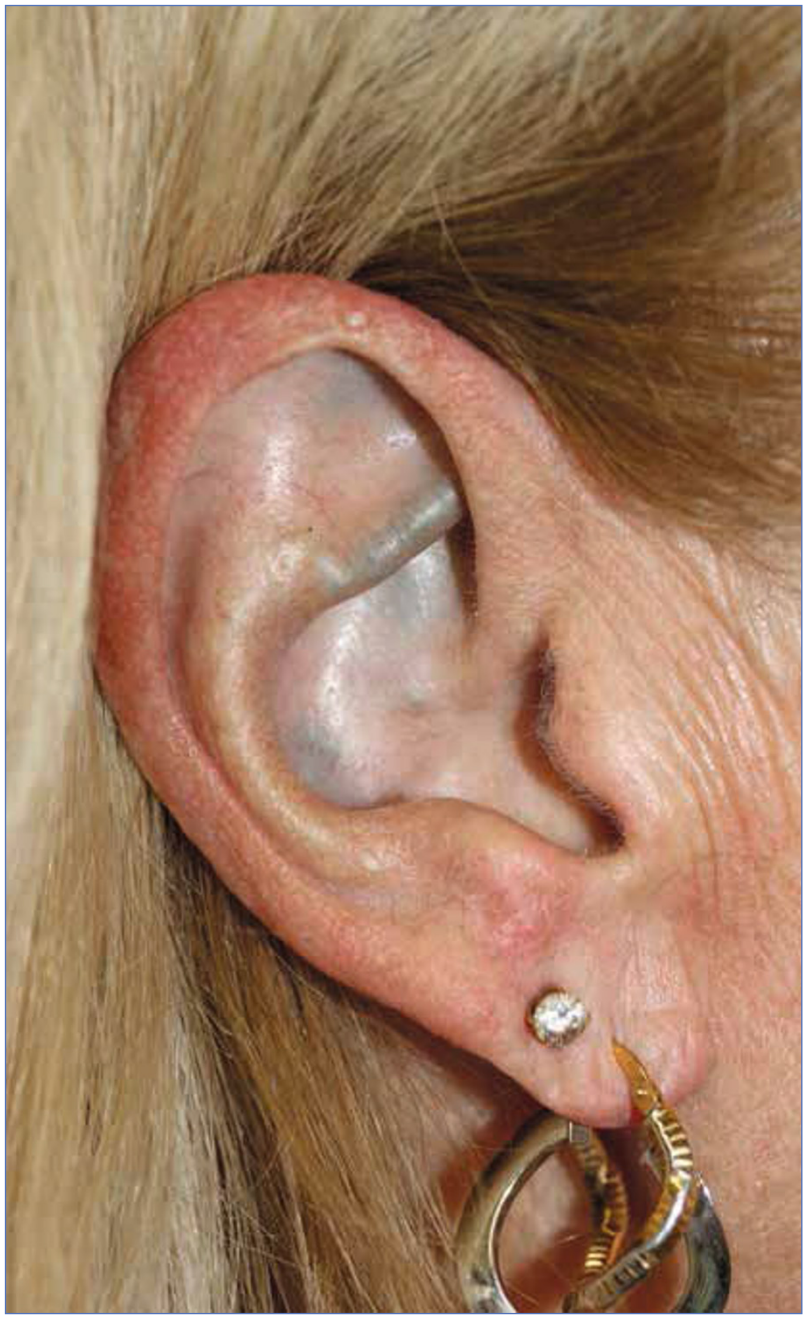
NON-MELANIC PIGMENTARY DISORDERS

Ochronosis

ALKAPTONURIA



Nail discoloration in a patient with alkaptonuria (coll. R. Baran).



Blue pigmentation of the sclera of the ears.

OMIM: #203500

SYNONYMS

Endogenous ochronosis.

EPIDEMIOLOGY

Alkaptonuria shows a very low prevalence (1:100,000 to 250,000) in most ethnic groups, but it was found to be unusually frequent in the Dominican Republic and in Slovakia (1:19,000).
Sex ratio = 1.

PATHOPHYSIOLOGY

Autosomal recessive (rare cases with autosomal dominant trait have been reported) metabolic disorder due to mutations in the homogentisic acid (HGA) oxidase gene (3q21-q23) leading to an altered catabolic pathway of tyrosine and phenylalanine.
The deficiency in the HGA oxidase gene results in accumulation and deposition of HGA.

CLINICAL DERMATOLOGICAL PRESENTATION

The clinical symptoms can be observed in early infancy but begin in most cases after the third decade of life.
The eruption begins with asymptomatic macules with dark brown or black color.
Progressively, the lesions infiltrate to become papules and sometimes nodules with a reticular pattern.
Localization: sun-exposed areas such as face, neck, shoulders and arms are mostly affected.
Progressive pigmentation of the sclera of the eyes and the ears.

EXTRACUTANEOUS SIGNS

Joint pains are the main symptoms.
Kidney stones.
Valvular heart disease.
Urine turns red or black when left exposed to the air.

HISTOPATHOLOGY

Routine hematoxylin-eosin sections show deposition of yellow-brown pigment globules in the papillary dermis. Ochronotic pigments are positive with Fontana-Mason staining and negative with Pearls reagents. Degeneration of collagen and elastic fibers are also observed and emphasizes the promoting role of the solar irradiation in ochronosis. The same histological aspects are observed with endogenous and exogenous ochronosis.

DIFFERENTIAL DIAGNOSIS

- Exogenous ochronosis and argyria for the skin manifestations.
- Rheumatoid arthritis and ankylosing spondylarthritis for the joint symptoms.
- Porphyria cutanea tarda can be discussed in the front of black urine.

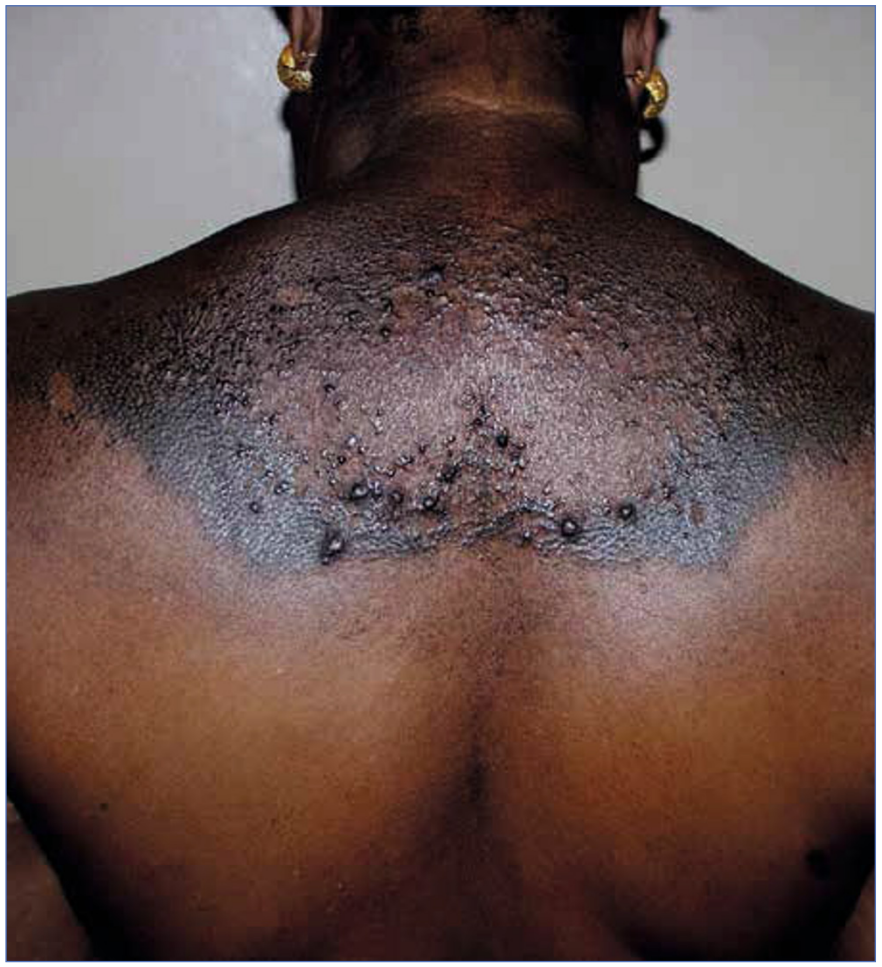
TREATMENT

Mild dietary restriction in tyrosine and phenylanine.
Vitamin C 1 g/day (weak efficacy in controlled trials).
Nitisinone, a potent inhibitor of the second enzyme in the tyrosine catabolic pathway, shows a 95% reduction of HGA in urine and plasma but a recent prospective trial did not prove the clinical benefit.

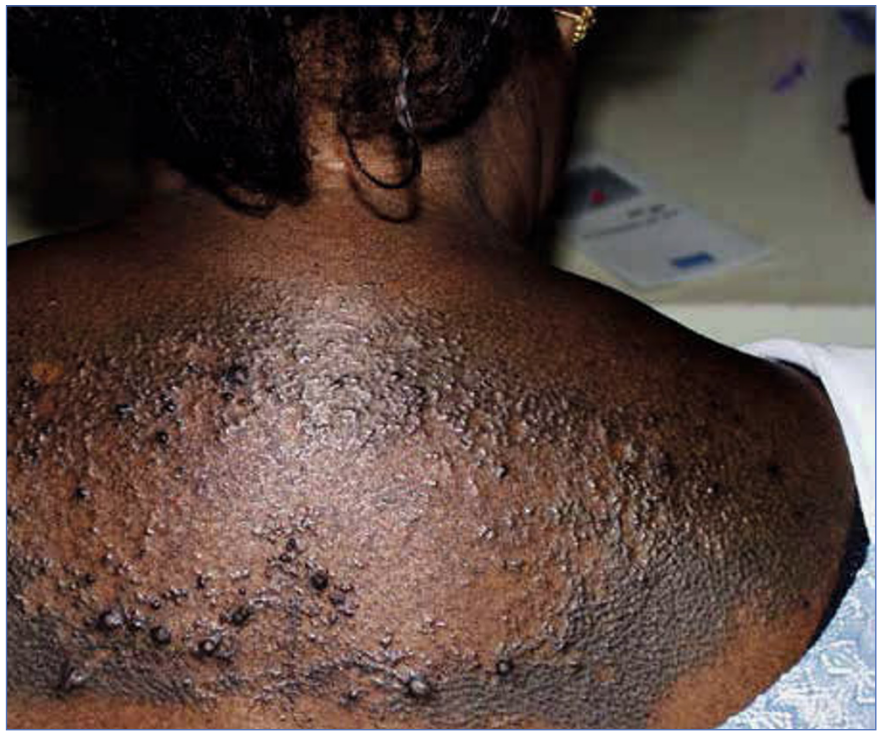
KEY REFERENCES

- Fernandez-Canon JM, Granadino B, Beltran-Valero de Bernabe D, et al. The molecular basis of alkaptonuria. Nature Genet. 1996;14:19-24.
- Introne WJ, Perry MB, Troendle J, et al. A 3-year randomized therapeutic trial of nitisinone in alkaptonuria. Mol Genet Metab. 2011;103:307-14.

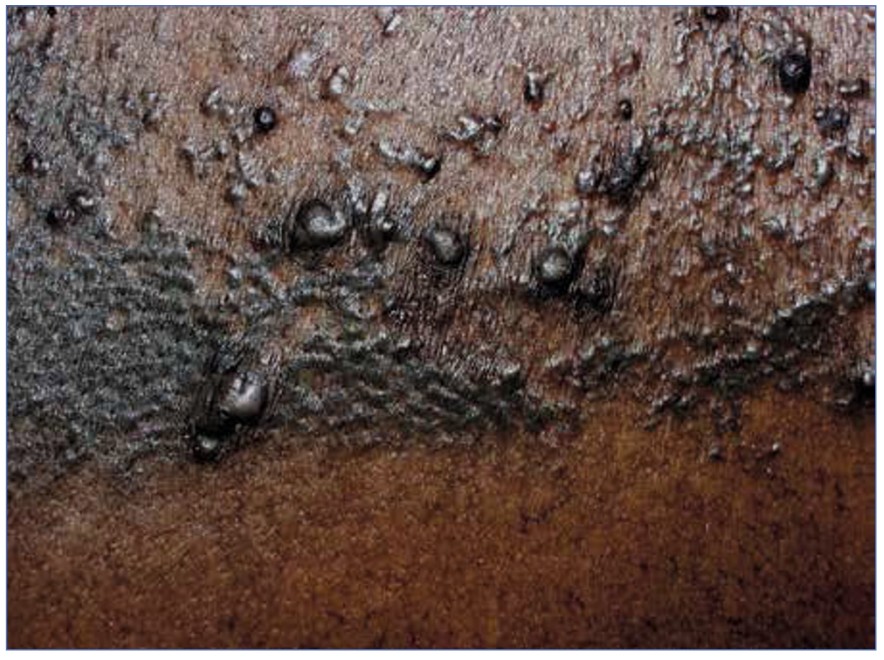
EXOGENOUS OCHRONOSIS



Marked hyperpigmentation of the upper back due to the chronic applications of hydroquinone.



Exogenous ochronosis in the same woman. Note that the lesions are located on sun-exposed areas while the hydroquinone was applied on the entire body.



Close up showing some nodular and granulomatous ochronosis lesions.

EPIDEMIOLOGY

Exogenous ochronosis is due to the prolonged exposure to topical applications of hydroquinone preparation. In most cases it results from daily applications of hydroquinone for blanching the skin. The frequency of exogenous ochronosis appears quite rare in America, Europe and Asia. However, in some African countries about half of the women confess to using blanching products, leading to a substantial increase in frequency of exogenous ochronosis in those countries.
Other substances such as phenol, trinitrophenol, benzene, resorcinol and anti-malarials have been reported to induce exogenous ochronosis.

PATHOPHYSIOLOGY

Genetic deficiency in homogentisic acid oxidase leads to alcaptonuric ochronosis (endogenous ochronosis). Hydroquinone might induce ochronosis by inhibiting this enzyme.

CLINICAL DERMATOLOGICAL PRESENTATION

The eruption begins with asymptomatic macules with dark brown or black color.
Progressively the lesions infiltrate and become papules and sometimes nodules with a reticular pattern.
Localization: sun-exposed areas such as face, arms, neck and shoulders are mostly affected.

EXTRACUTANEOUS SIGNS

None.
Signs of hypercorticism must be searched for, as chronic applications of highly potent topical steroids are frequently used concomitantly with hydroquinone for whitening the skin.

HISTOPATHOLOGY

Routine hematoxylin-eosin sections show deposition of yellow-brown pigment globules in the papillary dermis. Ochronotic pigments are positive with Fontana-Mason staining and negative with Pearls reagents. Granulomatous lesions can be observed. Degeneration of collagen and elastic fibers are also observed and emphasize the promoting role of the solar irradiation in ochronosis. The same histological aspects are observed with endogenous and exogenous ochronosis.

DIFFERENTIAL DIAGNOSIS

- Acanthosis nigricans.
- Post-inflammatory hyperpigmentation.

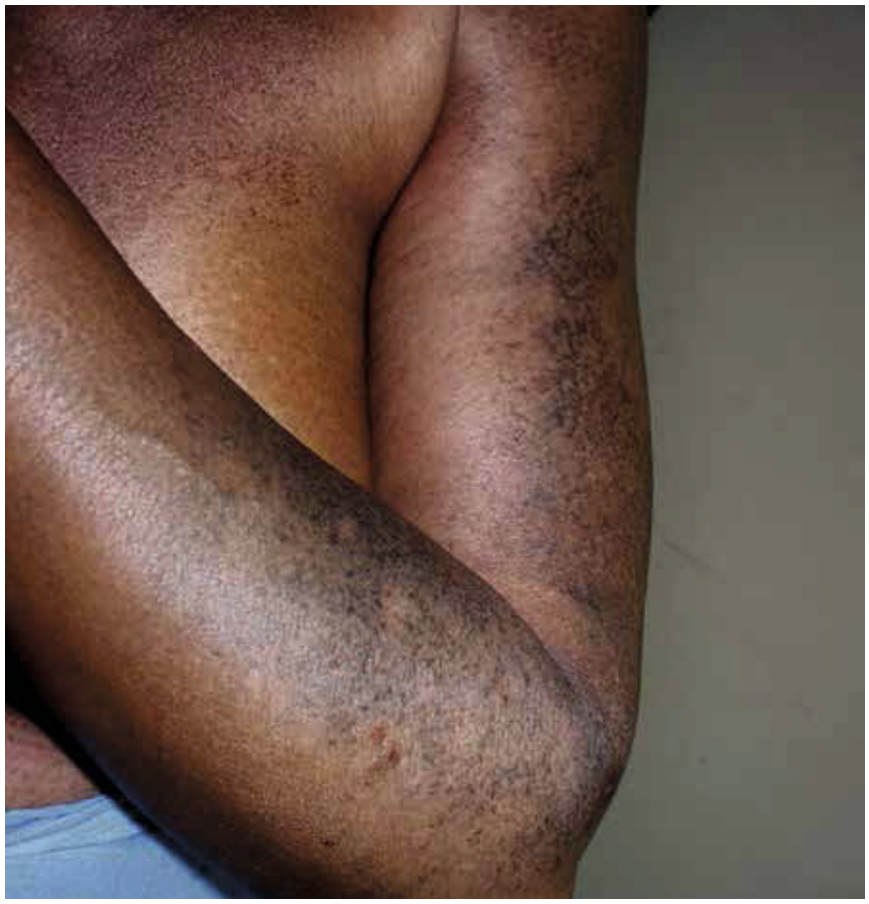
TREATMENT

Discontinuation of the application of hydroquinone.
CO2 laser assisted dermabrasion and Q-switched lasers have been proposed.

KEY REFERENCES

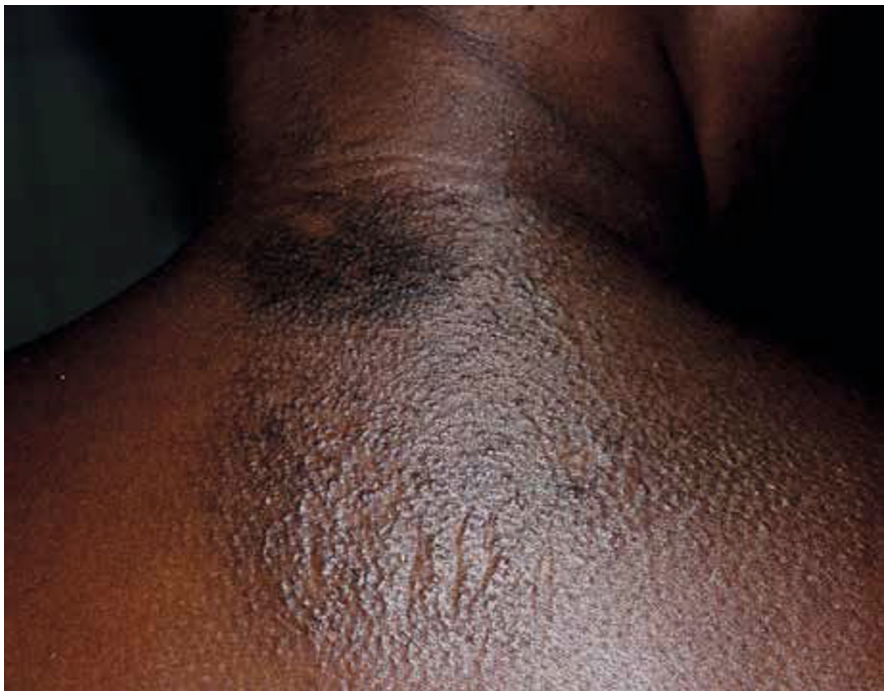
- Levin CY, Maibach H. Exogenous ochronosis. An update on clinical features, causative agents and treatment options. Am J Clin Dermatol. 2001;2:213-7.
- Mahé A, Ly F, Aymard G, Dangou JM. Skin diseases associated with the cosmetic use of bleaching products in women from Dakar, Senegal. Br J Dermatol. 2003;148:493-500.
- Findlay GH, Morrison JG, Simson IW. Exogenous ochronosis and pigmented colloid milium from hydroquinone bleaching creams. Br J Dermatol. 1975;93:613-22.

EXOGENOUS OCHRONOSIS

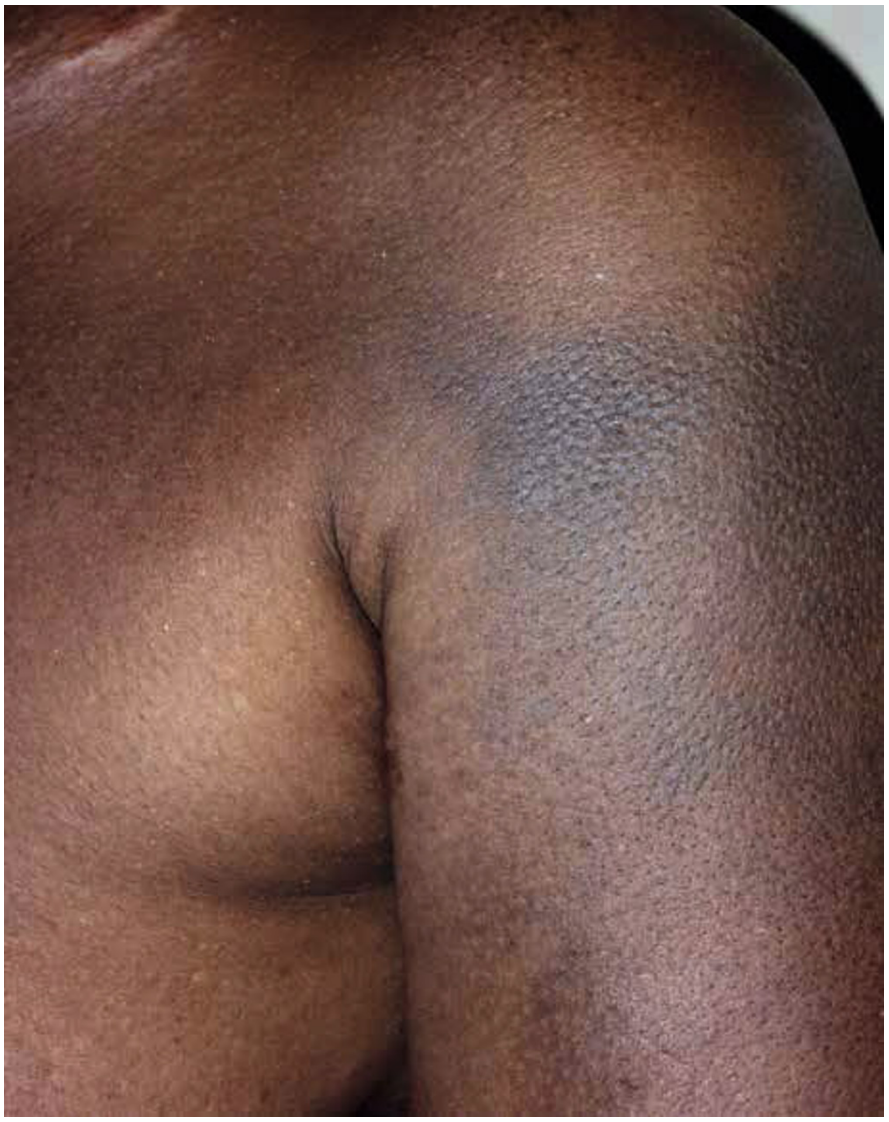


Exogenous ochronosis of the arms and trunk. Note that lesions are located predominantly on sun-exposed areas.

Periorbital hyperpigmentation due to the chronic applications of hydroquinone.



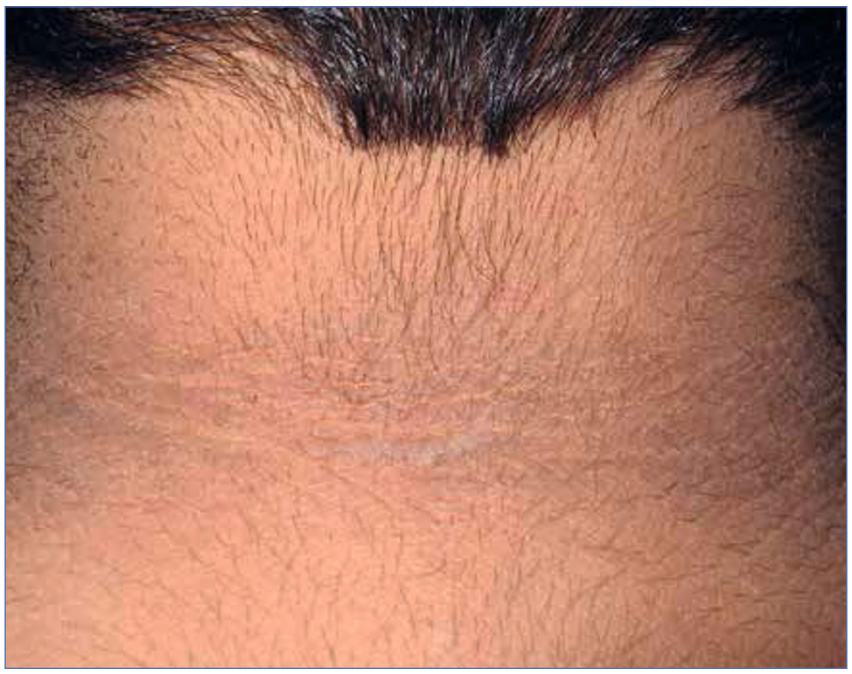
Black hyperpigmentation with reticular pattern of the neck and upper back.



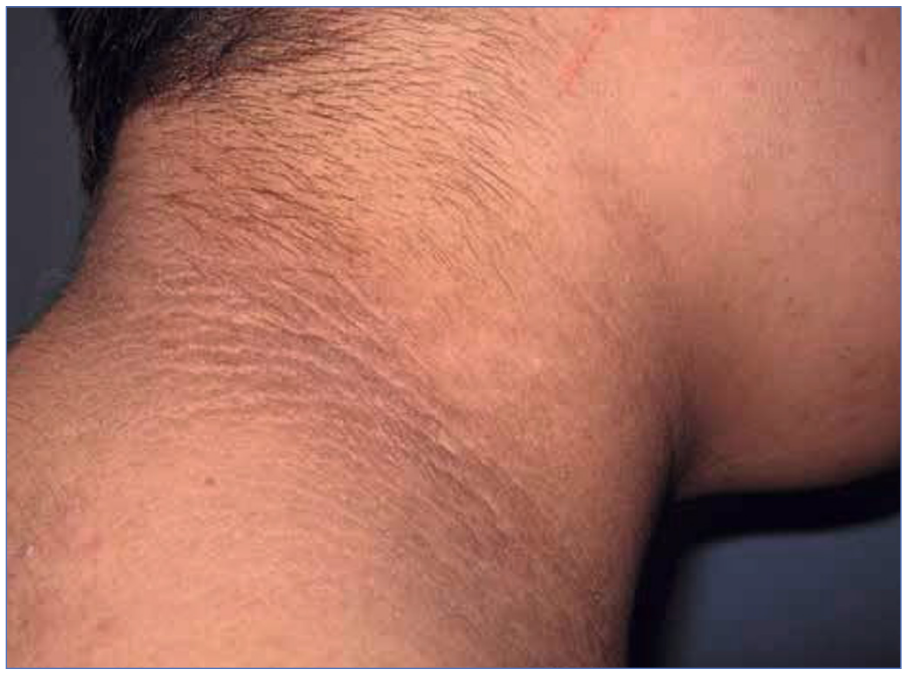
Exogenous ochronosis of arm at early stage.

Dyskeratosis

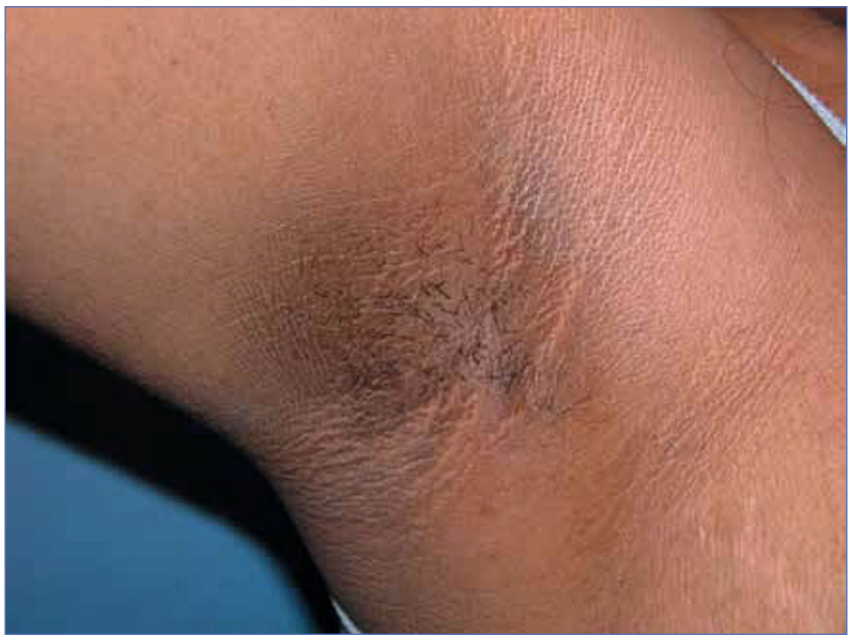
ACANTHOSIS NIGRICANS



Velvety hyperpigmented plaques of acanthosis nigricans on the neck.



Velvety hyperpigmented plaques of acanthosis nigricans on the neck.



Slight acanthosis nigricans of the axillae fold with hyperpigmented velvety plaques with poorly demarcated margins.

EPIDEMIOLOGY

Increased incidence in darker phototypes; less than 1% in Caucasians, compared to more than 10% in African-Americans. Clear correlation with obesity and insulin resistance (observed in almost all the people who weigh greater than 250% of their ideal body weight).
Sex ratio = 1.
Familial forms of acanthosis nigricans with autosomal dominant inheritance have been described.
Malignant forms of acanthosis nigricans are far less common and mostly observed in patients with gastro-intestinal adenocarcinomas.

PATHOPHYSIOLOGY

Dysregulation of growth factors that stimulate keratinocytes and fibroblasts. In high concentrations insulin binds insulin-like growth factor 1 (IGF-1) receptors and stimulates the epidermal proliferation.
Malignant acanthosis nigricans seem to be related to the abnormal production of IGF-1 and tumor growth factor alpha (TGF-α) by the tumors and their binding to IGF-1 and epidermal growth factor (EGF) receptors.

CLINICAL DERMATOLOGICAL PRESENTATION

Symmetrical hyperpigmented velvety plaques with poorly demarcated margins.
Color from light to dark brown.
Localization: axillae, neck, groin (less frequently popliteal and antecubital folds, umbilicus).
Acrochordons are frequently associated.

EXTRACUTANEOUS SIGNS

Type A syndromic acanthosis nigricans: HAIR-AN syndrome (hyperandrogenemia, insulin resistance, acanthosis nigricans).
Type B syndromic acanthosis nigricans: diabetes mellitus, ovarian hyperandrogenism, autoimmunity with anti-insulin receptor antibodies (lupus erythematosus, scleroderma, Sjögren syndrome, Hashimoto thyroiditis, etc).
Malignant acanthosis nigricans: gastro-intestinal adenocarcinomas (gastric), Wilms tumor, kidney cancer, ovarian and testicular cancer, lymphomas, etc.
Drug-induced acanthosis nigricans: nicotinic acid, insulin, diethylstilbestrol, oral contraceptive, methyl-testosterone, pituitary extract, systemic corticosteroids, triazinate and palifermin (modified human keratinocyte growth factor [KGF]).

HISTOPATHOLOGY

Marked hyperkeratosis with finger-like papillomatosis and mild acanthosis. Slight hyperpigmentation and minimal melanocytic hyperplasia can be observed but the clinical hyperpigmentation is due to the hyperkeratosis.

DIFFERENTIAL DIAGNOSIS

- Pityriasis versicolor.

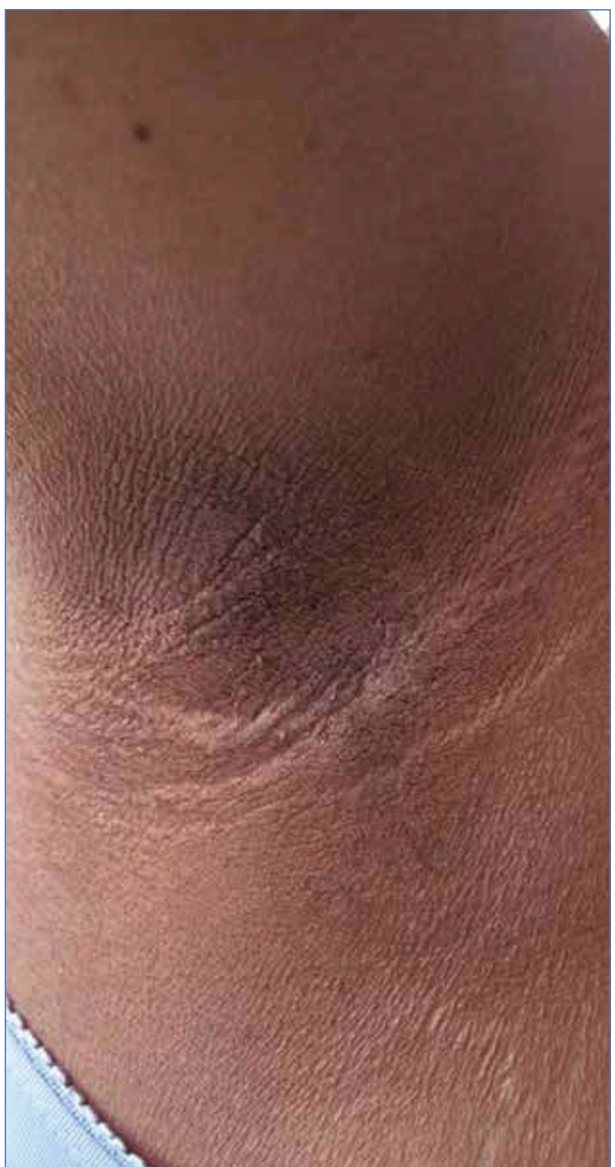
TREATMENT

Treatment of the hyperinsulinism, treatment of the underlying disorder or discontinuation of the medication.
Topical keratolytics, topical tretinoin, Kligman's trio.
Metformin, isotretinoin.
CO_2 ablative laser.

KEY REFERENCES

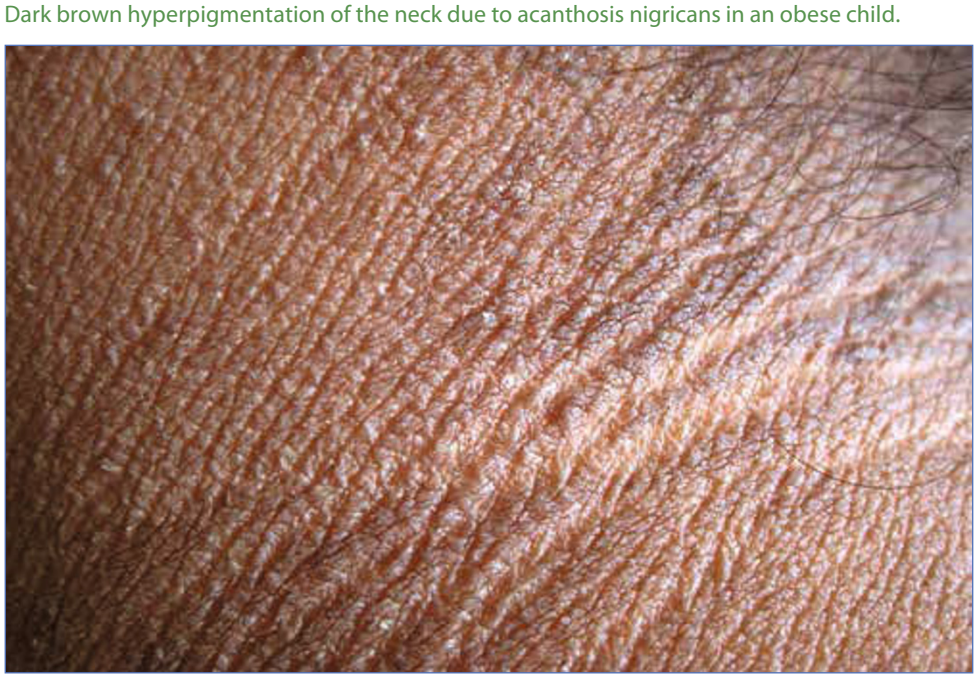
- Hud JA Jr, Cohen JB, Wagner JM, Cruz PD Jr. Prevalence and significance of acanthosis nigricans in an adult obese population. Arch Dermatol. 1992;128:941-4.
- Wilgenbus K, Lentner A, Kuckelkorn R, Handt S, Mittermayer C. Further evidence that acanthosis nigricans maligna is linked to enhanced secretion by the tumour of transforming growth factor alpha. Arch Dermatol Res. 1992;284:266-70.

ACANTHOSIS NIGRICANS

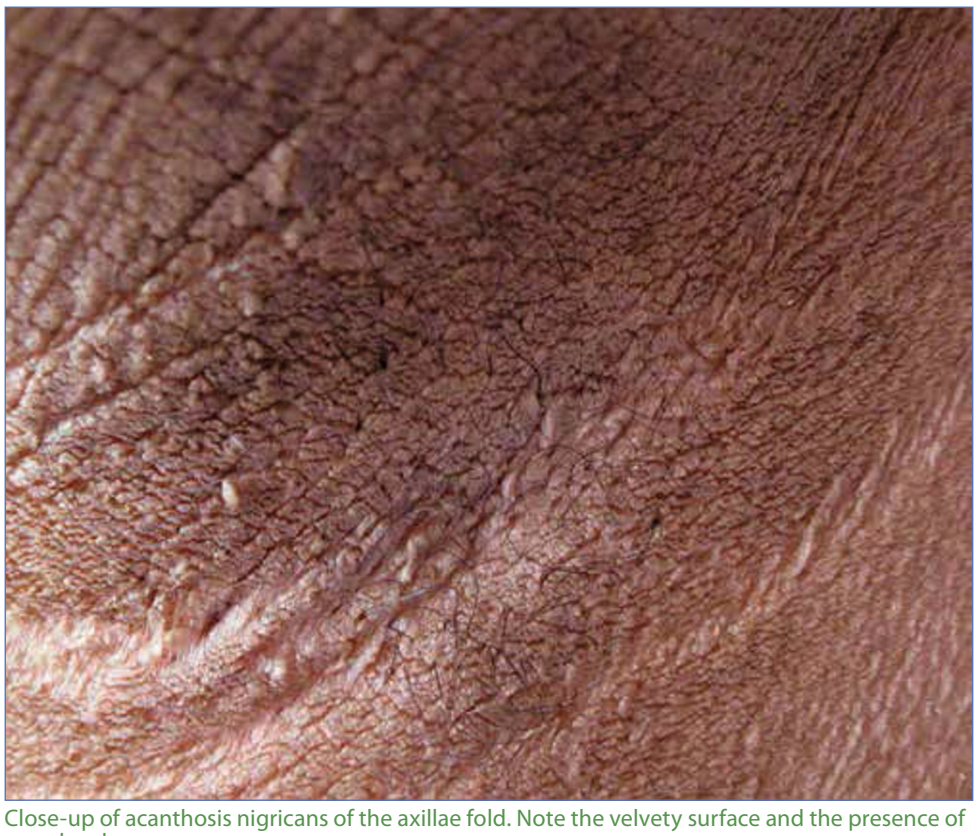


Acanthosis nigricans of the axillae fold.

Dark brown hyperpigmentation of the neck due to acanthosis nigricans in an obese child.

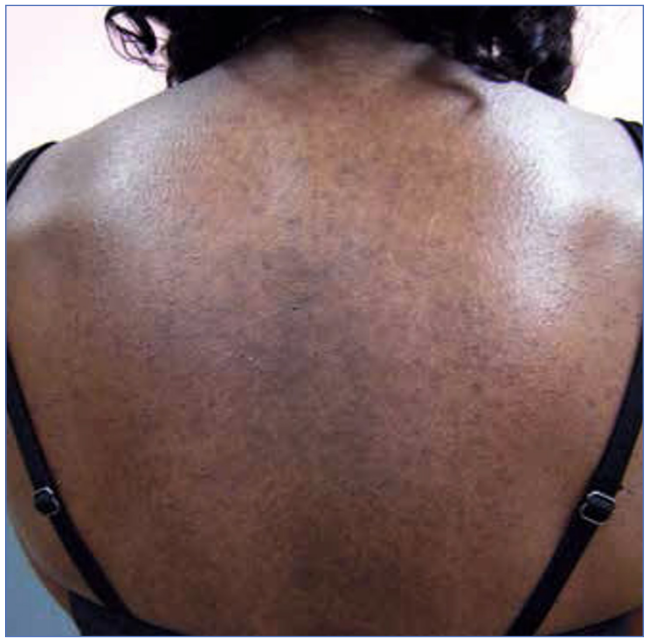


Acanthosis nigricans of the neck.

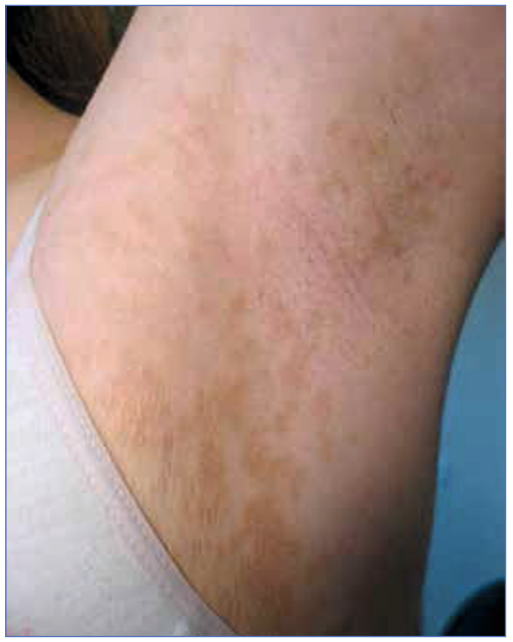


Close-up of acanthosis nigricans of the axillae fold. Note the velvety surface and the presence of acrochordons.

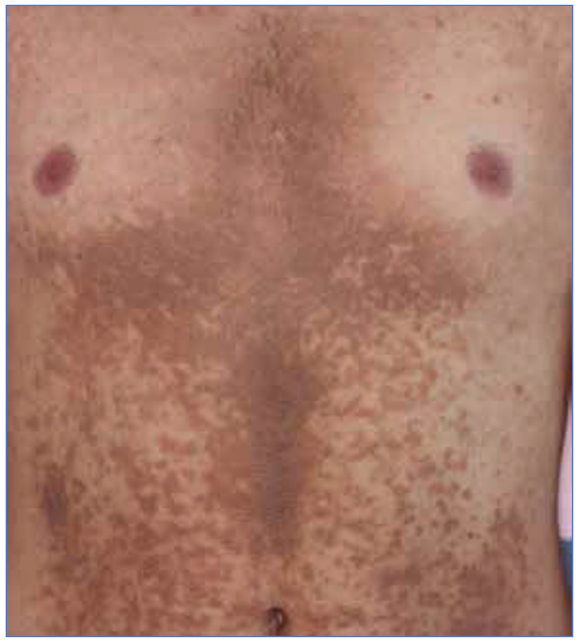
CONFLUENT AND RETICULATED PAPILLOMATOSUS



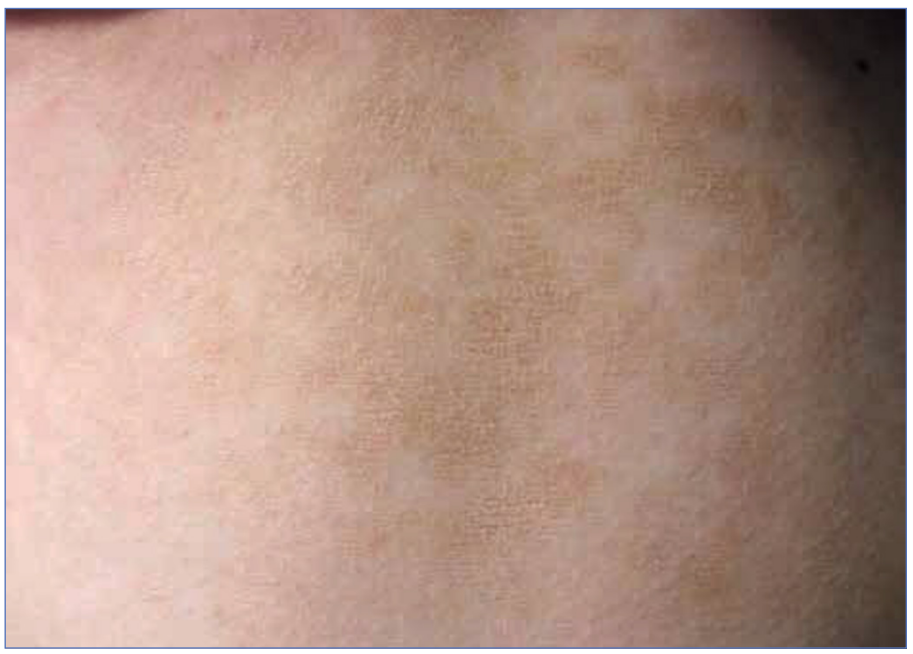
Grayish blue hyperkeratotic papules that began on the interscapular region and progressively spread over the entire back.



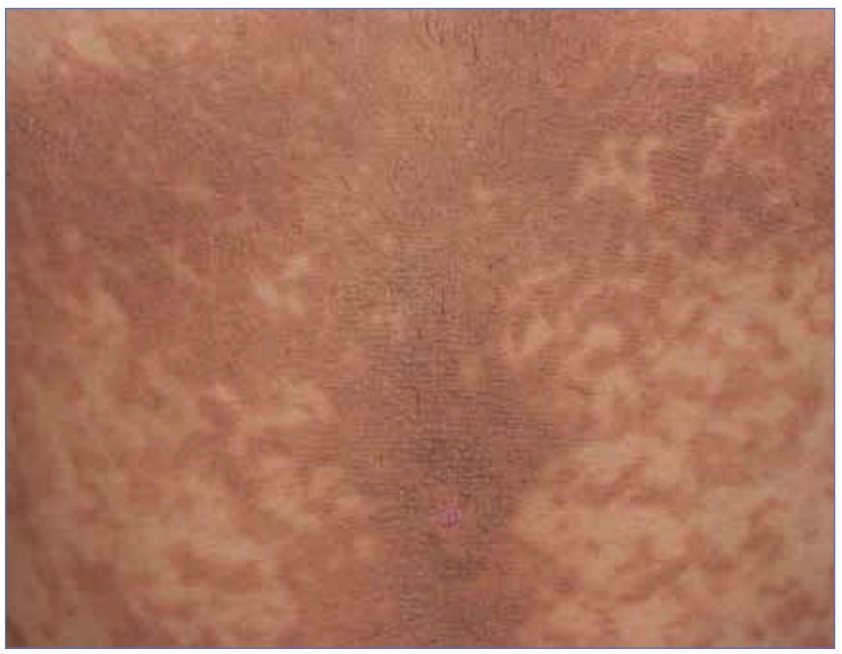
Confluent and reticulated papillomatosis spreading in the axillae fold.



Diffuse confluent and reticulated papillomatosis.



Onset of the confluent and reticulated papillomatosis on the interscapular region. Note the slightly pigmented and keratotic lesions that have not yet coalesced in plaques.



The lesions had begun in the intermammary region and had coalesced in a confluent plaque while in the periphery a typical reticular pattern is observed.

SYNONYMS

Gougerot Carteaud disease.

EPIDEMIOLOGY

Relatively rare disorder but the exact frequency is unknown.
Usually occurs shortly after puberty.

PATHOPHYSIOLOGY

Gougerot Carteaud is defined by an abnormal keratinocyte differentiation and maturation. Some authors suggest that it could be a reaction pattern to bacterial or mycosal infection in susceptible individuals.
Several hormonal disturbances can be associated (Cushing disease, obesity, abnormal glucose tolerance or diabetes mellitus, thyroid disease, pituitary dysfunction, menstrual irregularities). However, in many of the cases, no abnormality exists at all.
Familial cases are reported.

CLINICAL DERMATOLOGICAL PRESENTATION

Grayish blue to brown hyperkeratotic papules, usually located on the trunk. The lesions begin at 1 to 2 mm in diameter then progressively enlarge and coalesce to form confluent plaques centrally and a reticular pattern peripherally.
Localization: usually begins in the intermammary or inter-scapular regions then progressively spread over the entire trunk.
Mild pruritus is observed in less than one half of the cases.

EXTRACUTANEOUS SIGNS

The disorder is limited to the skin but signs of hormonal abnormalities have to be searched.

HISTOPATHOLOGY

Hyperkeratosis with focal parakeratosis, inconstant papillomatosis with mild and irregular acanthosis. Slight hyperpigmentation of the basal layers.

DIFFERENTIAL DIAGNOSIS

- Pityriasis versicolor.
- Dowling-Degos disease.
- Galli-Galli disease.

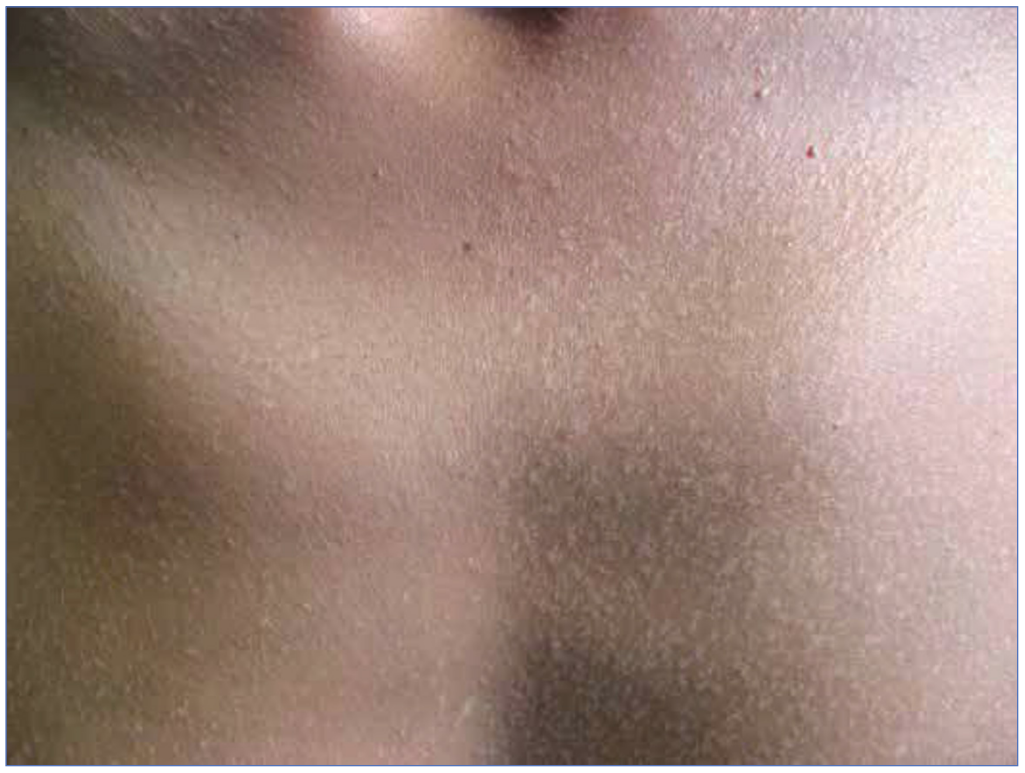
TREATMENT

Systemic use of erythromycin or minocycline can improve the condition. Oral isotretinoin for at least 4 months is also effective.
Topical vitamin D analog or topical tretinoin can be useful.

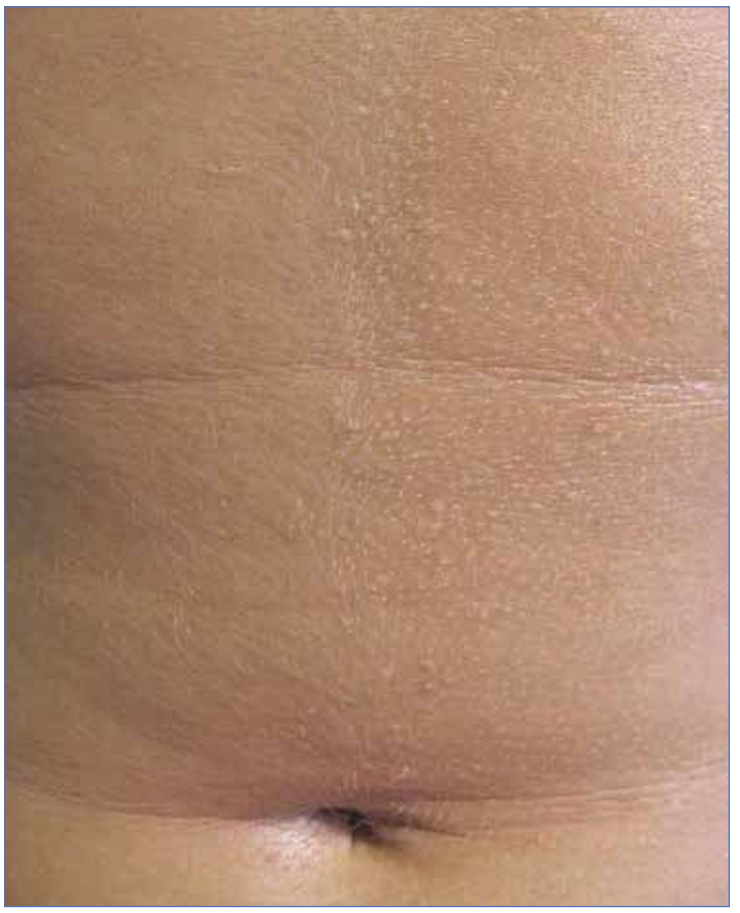
KEY REFERENCES

- Davis MD, Weenig RH, Camilleri MJ. Confluent and reticulate papillomatosis (Gougerot-Carteaud syndrome): a minocycline-responsive dermatosis without evidence for yeast in pathogenesis. A study of 39 patients and a proposal of diagnostic criteria. Br J Dermatol. 2006;154:287-93.
- Lee MP, Stiller MJ, Mc Clain SA et al. Confluent and reticulated papillomatosis: response to high dose oral isotretinoin therapy and reassessment of epidemiologic data. J Am Acad Dermato. 1994,31:327-31.

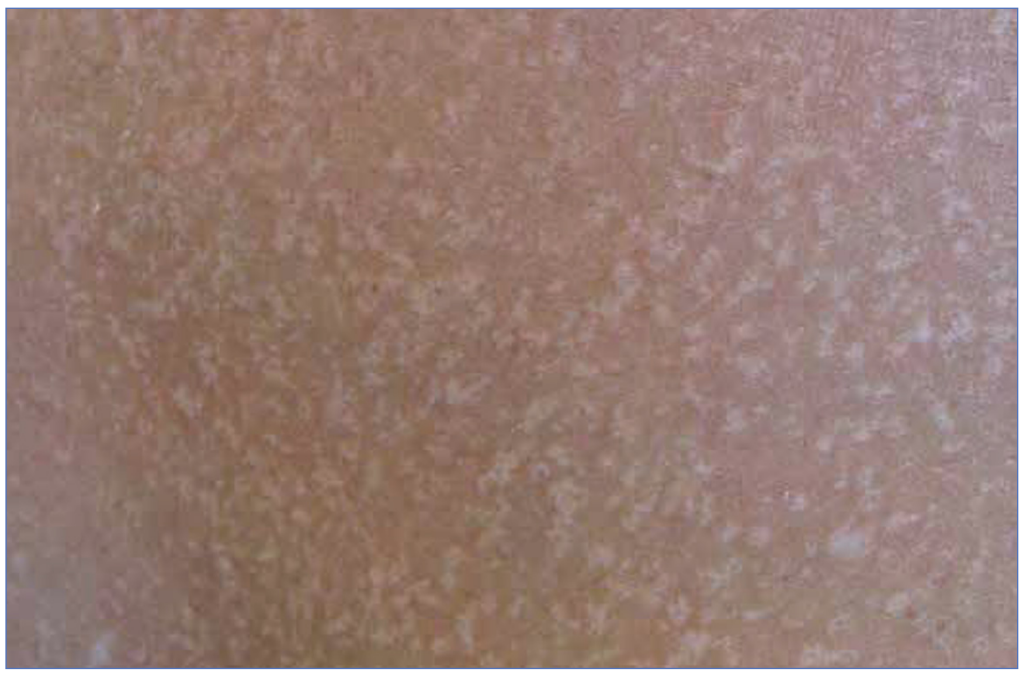
DARIER-WHITE DISEASE



Hypopigmented macules and papules of the trunk in darier disease. Lesions are visible on both sides but a marked segmental increase is observed on the left part of the thorax.



Segmental Darier disease presenting only with hypopigmented macules and papules.



Hypochromic warty papules of Darier disease.

SYNONYMS
Darier disease, keratosis follicularis.

OMIM: #124200

GENETICS
Autosomal dominant disorder. Results from mutations in the ATP2A2 gene (12q23-q24.1).

EPIDEMIOLOGY
Prevalence 1 out of 55,000.
Males and females are equally affected.
The onset of the disease is usually before the third decade of life but cases from 4 to 70 years of age have been reported.
Leukoderma is not rare in Darier disease and is mostly observed in dark-skinned individuals.

PATHOPHYSIOLOGY
The ATP2A2 gene encodes the sarco/endoplasmic reticulum Ca^{2+}-ATPase type 2 isoform (SERCA2) . The protein is highly expressed in keratinocytes and regulates cell-to-cell adhesion and differentiation of the epidermis.

CLINICAL DERMATOLOGICAL PRESENTATION
Warty papules of 2 to 5 mm in diameter that can coalesce into plaque. The color is usually red-brown, but hypopigmented macules or papules can be observed (alone or associated with red-brown papules).
Pruritus is common but the intensity is variable.
Localization: mostly on seborrheic areas such as central trunk, flexures, scalp, and forehead.
Segmental forms of Darier disease have been described.
Bullous lesions can be observed.
Palmo-plantar punctate keratosis and palmar pits.
Nail involvement with red and white longitudinal bands, often with a V-shaped nick at the free margin of the nail.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Decreased melanin contained in the epidermis. The number of melanocytes can be reduced.
Acantholytic dyskeratosis.

DIFFERENTIAL DIAGNOSIS
- Lichen sclerosus.
- Vitiligo punctata.
- Grover's disease.
- Leukoderma punctata.
- Idiopathic guttate hypomelanosis.
- Focal dermal hypoplasia.

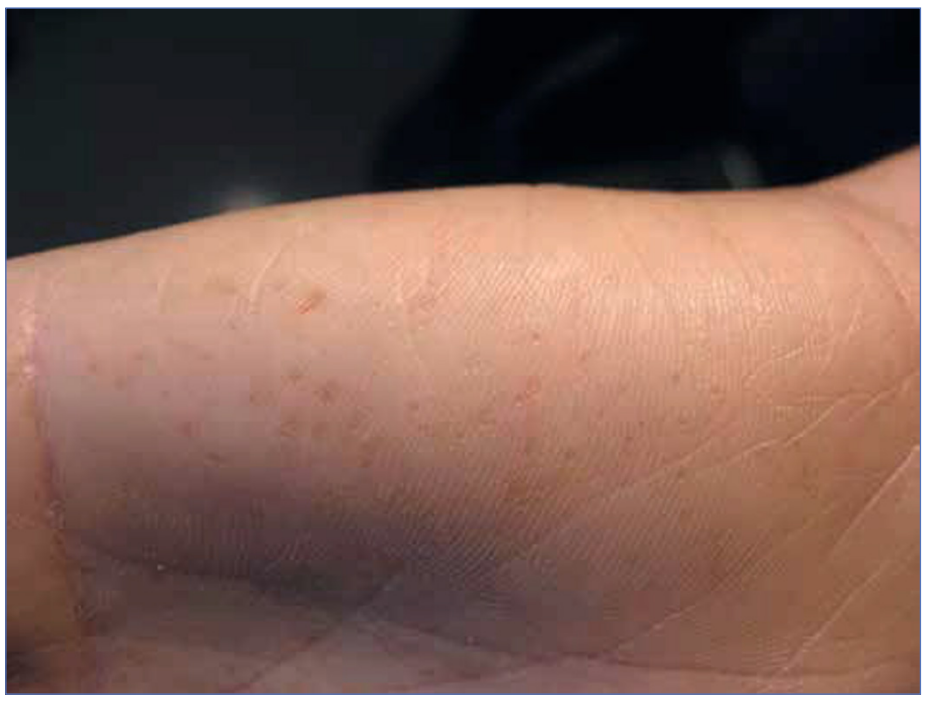
TREATMENT
Emollients and keratolytics.
Topical and oral retinoids.
UV and sun exposures should not be used to attempt to repigment the hypochromic lesions as they can induce flares of the disease.

KEY REFERENCES

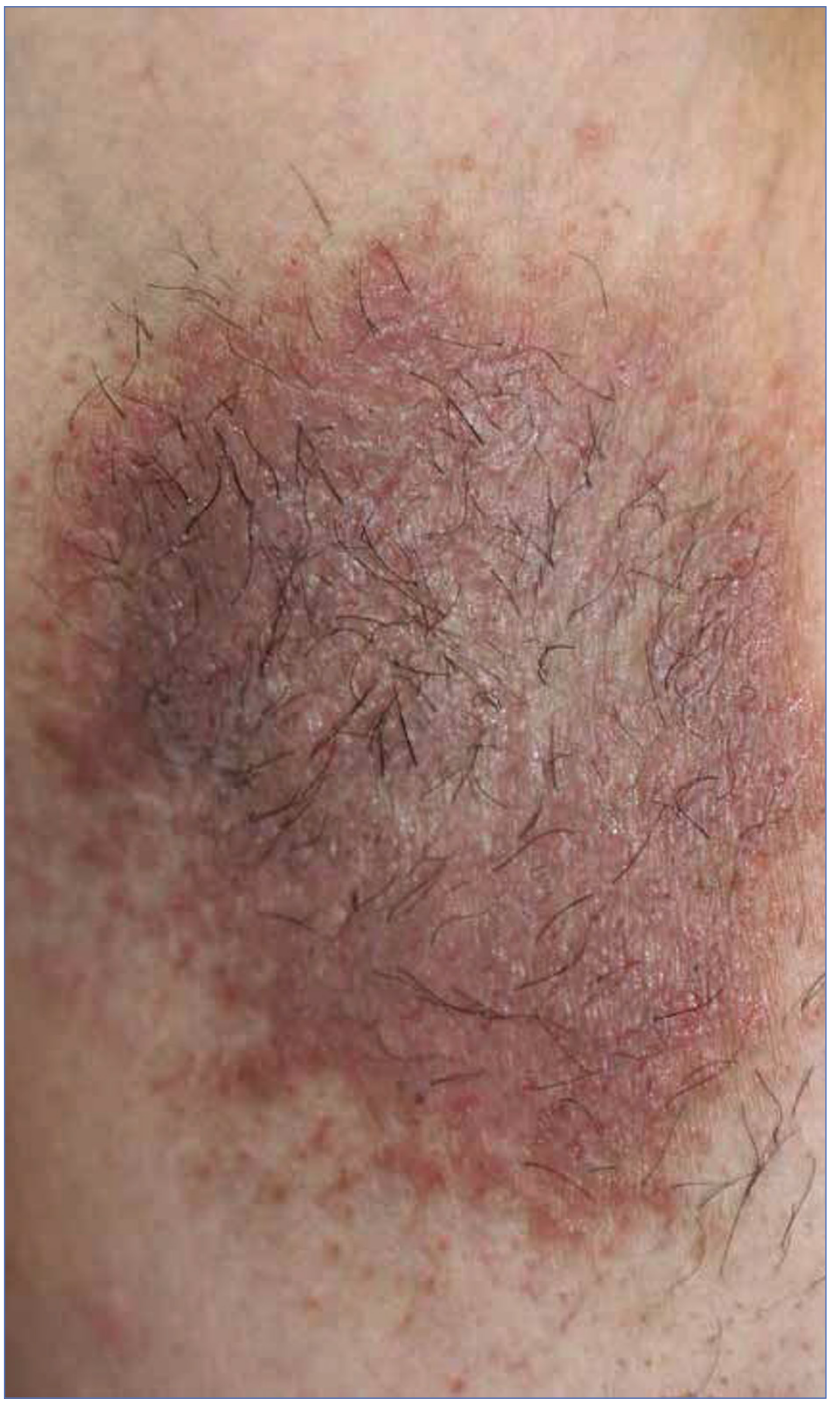
- Gupta S, Shaw JC. Unilateral Darier's disease with unilateral guttate leukoderma. J Am Acad Dermatol. 2003;48:955-7.
- Cornelison RL, Smith EB, Knox JM. Guttate leukoderma in Darier's disease. Arch Dermatol. 1970;102:447-50.

DARIER-WHITE DISEASE

V-shaped nick at the free margin of the nail in a patient with Darier disease.

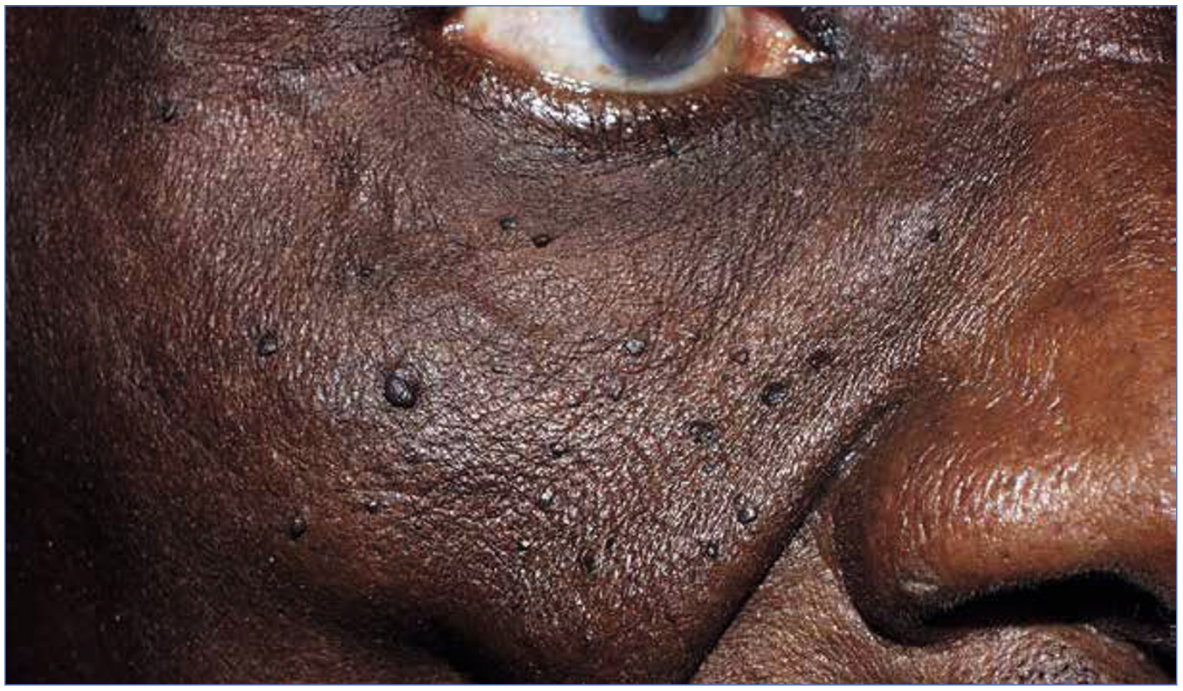


Palmar pits.

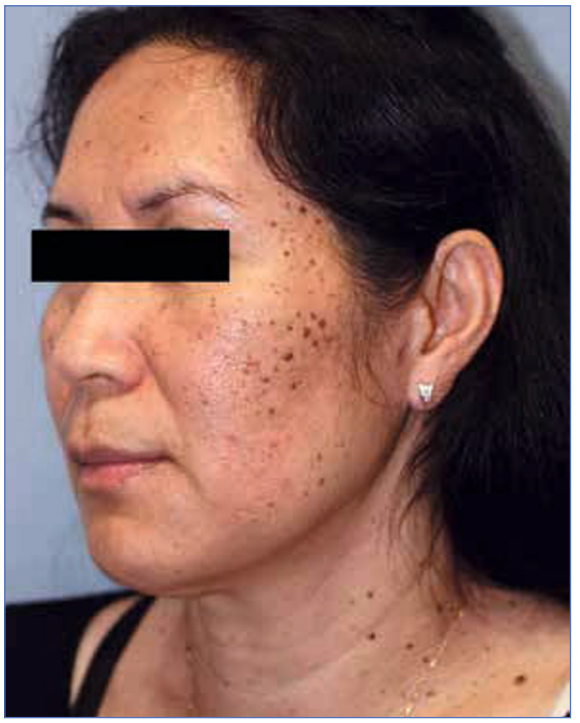


Classical presentation of Darier disease, with red-brown papules coalescing into plaques in flexural areas.

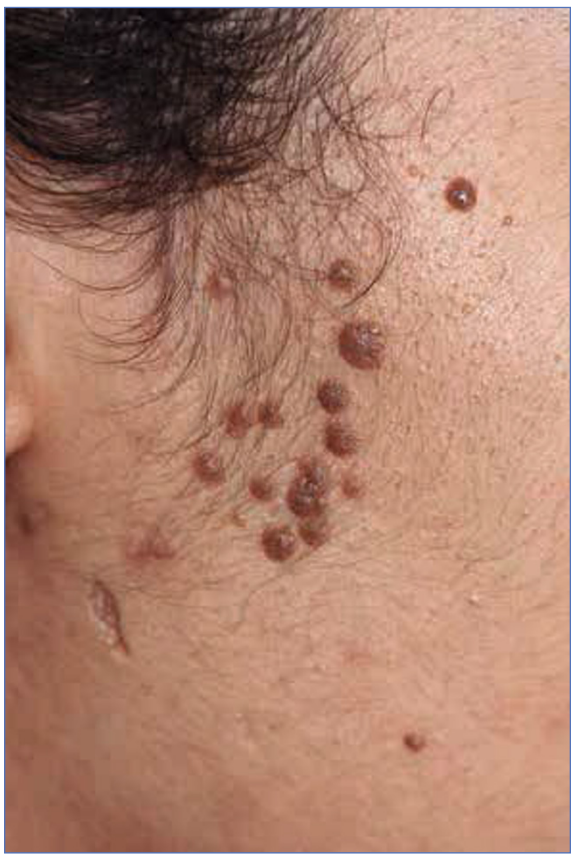
DERMATOSIS PAPULOSA NIGRA



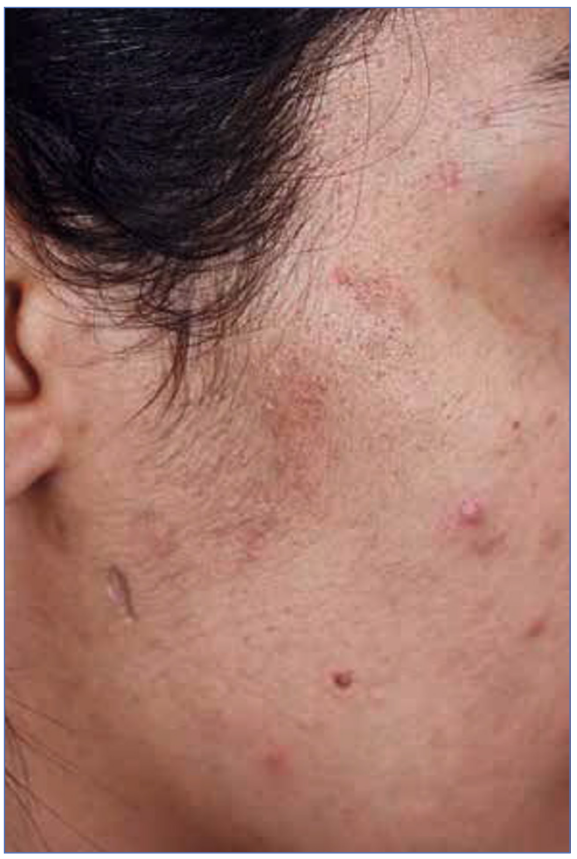
Dermatosis papulosa nigra. Black papules mostly located on the malar area.



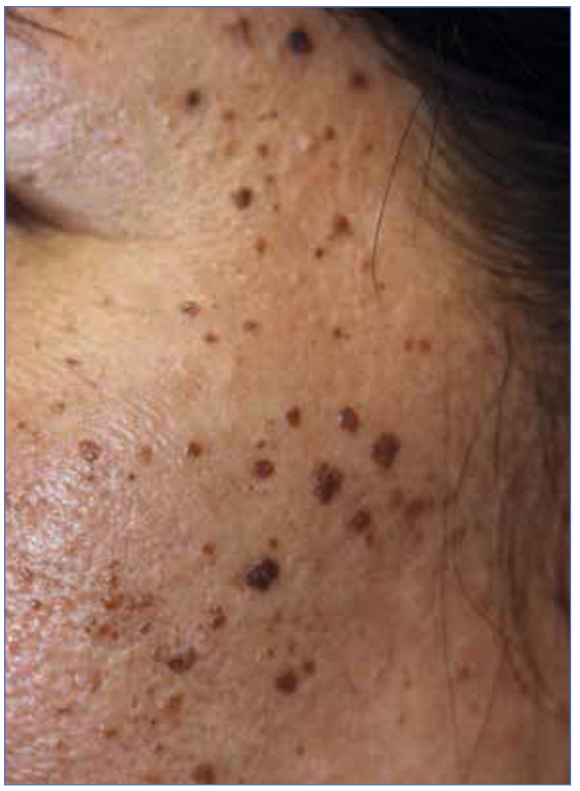
More widespread presentation of dermatosis papulosa nigra with involvement of the cheeks spreading to the forehead and the neck.



Papules of dermatosis papulosa nigra on the malar area.



Two months after dermabrasion of the lesions using erbium laser.



More widespread presentation of dermatosis papulosa nigra with involvement of the cheeks spreading to the forehead and the neck.

EPIDEMIOLOGY

Observed mostly in the Negroid population (up to 35% in African-American people) but has been described in Asian, Latin American and Mediterranean populations.
Female to male ratio: 2.
Genetic background (half of affected people with at least one family member affected).

PATHOPHYSIOLOGY

Unknown, but the occasional positive family history may suggest a genetic propensity.

CLINICAL DERMATOLOGICAL PRESENTATION

Light brown to black, well defined asymptomatic papules from 1 to 5 mm in diameter.
Onset at puberty with a progressive increase in size and number.
Localization: peri-ocular, cheeks, neck, less frequently on the upper trunk.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Appearance of acanthotic seborrheic keratoses with irregular acanthosis, hyperkeratosis, keratin-filled invaginations of the epidermis (horn cysts), and marked hyperpigmentation of the basal layer. Melanophages can be present in the upper dermis.

DIFFERENTIAL DIAGNOSIS

- Seborrheic keratoses.
- Syringoma.
- Nevi.

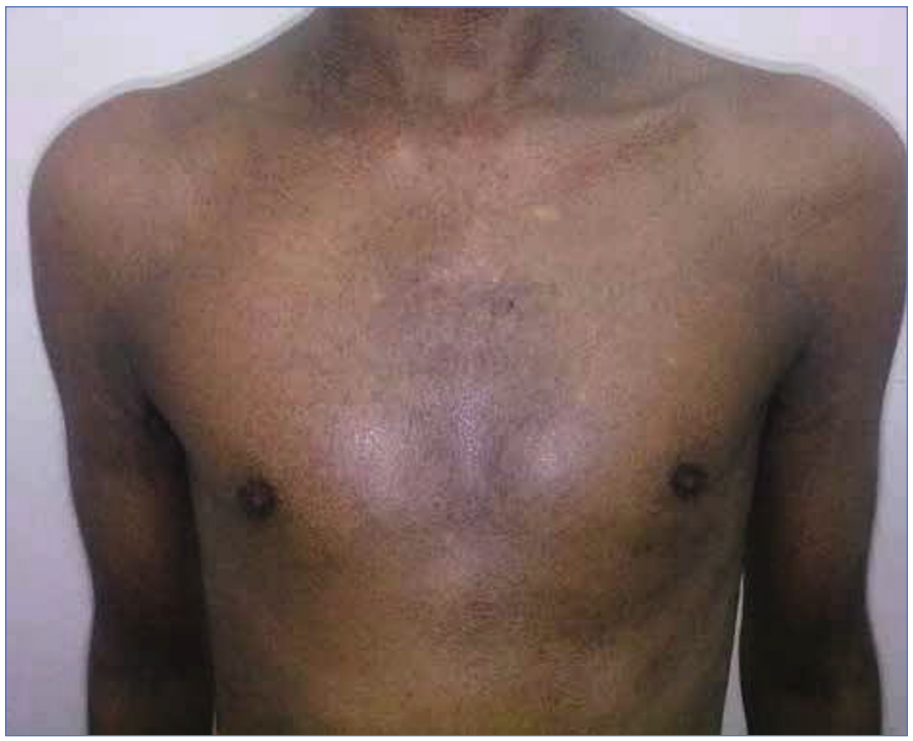
TREATMENT

The lesions are benign. Shave excision, electrodessication, cryotherapy, lasers (CO_2, erbium, pulsed dye, and NdYAG 1064 nm) have been proposed. Dyschromic or scarring sequelae can be observed after treatment so caution has to be taken.

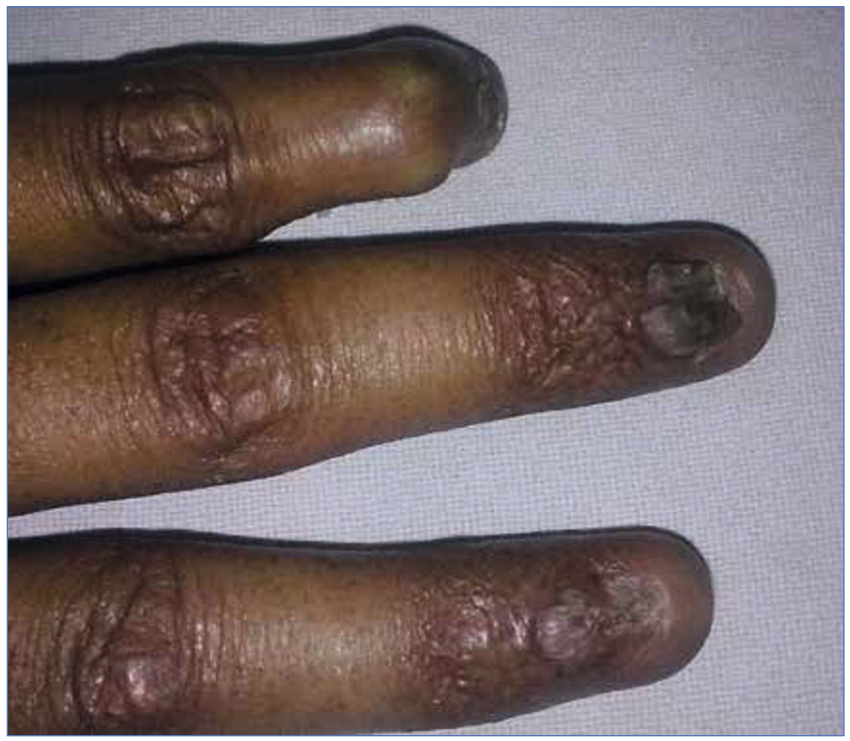
KEY REFERENCES

- Grimes PE, Arora S, Minus HR, Kenney JA Jr. Dermatosis papulosa nigra. Cutis. 1983;32:385-6.
- Garcia MS, Azari R, Eisen DB. Treatment of dermatosis papulosa nigra in 10 patients: a comparison trial of electrodesiccation, pulsed dye laser, and curettage. Dermatol Surg. 2010;36:1968-72.

DYSKERATOSIS CONGENITA



Reticulated hyperpigmentation of the trunk in a patient with dyskeratosis congenita (coll. Shivam Sinha).



Severe nail dystrophy in a patient with dyskeratosis congenita (coll. Shivam Sinha).

EPIDEMIOLOGY
Dyskeratosis congenita is a rare genodermatosis.

PATHOPHYSIOLOGY
Mutation in the genes encoding telomerase RNA component leading to defective telomere maintenance.

DKCA1
(Dyskeratosis congenita, autosomal dominant 1)

OMIM: #127550
GENETICS
Autosomal dominant inheritance with mutations in the TERC gene (10q24.2).

DKCA2
(Dyskeratosis congenita, autosomal dominant 2)

OMIM: #613989
GENETICS
Autosomal dominant inheritance with mutations in the TERT gene (5p15.33).

DKCA3
(Dyskeratosis congenita, autosomal dominant 3)

OMIM: #613990
GENETICS
Autosomal dominant inheritance with mutations in the TINF2 gene (14q12).

DKCB1
(Dyskeratosis congenita, autosomal recessive 1)

OMIM: #224230
GENETICS
Autosomal recessive inheritance with mutations in the NOLA3 gene (15q14).

DKCB2
(Dyskeratosis congenita, autosomal recessive 2)

OMIM: #224230
GENETICS
Autosomal recessive inheritance with mutations in the NOLA2 gene (5q35.3).

DKCB3
(Dyskeratosis congenita, autosomal recessive 3)

OMIM: #613988
GENETICS
Autosomal recessive inheritance with mutations in the TCAB1 gene (17p13.1).

DKCB4
(Dyskeratosis congenita, autosomal recessive 4)

OMIM: #613989
GENETICS
Autosomal recessive inheritance with mutations in the TERT gene (5p15.33).

DKCB5
(Dyskeratosis congenita, autosomal recessive 5)

OMIM: #613989
GENETICS
Autosomal recessive inheritance with mutations in the RTEL1 gene (20q13.33).

DKCX (Dyskeratosis congenita, X-linked)

OMIM: #305000
GENETICS
X-linked inheritance with mutations in the DKC1 gene (Xq28).

CLINICAL DERMATOLOGICAL PRESENTATION
Reticulated hyperpigmentation.
Hypopigmented nevus anemicus-like macules can be observed on the reticulated hyperpigmentation.
Localization: neck, upper chest, and proximal parts of the limbs, then generalized.
Premature graying of the hair.
Poikiloderma with telangiectasia and atrophy.
Leukoplakia of mucous membrane, nail dystrophy, loss of dermatoglyphics.
The classic triad with reticulated hyperpigmentation, leukoplakia and dystrophy of nails appears in childhood (between 4 and 10 years).

EXTRACUTANEOUS SIGNS
Bone marrow failure, predisposition to malignancy, osteoporosis, aseptic necrosis of the hip, mild to moderate mental retardation, and pulmonary and hepatic fibrosis.

HISTOPATHOLOGY
Melanophages and amyloid deposits in the upper dermis.
Focal epidermal atrophy, mononuclear cell infiltrate and increased vascularization in the legions of poikiloderma.

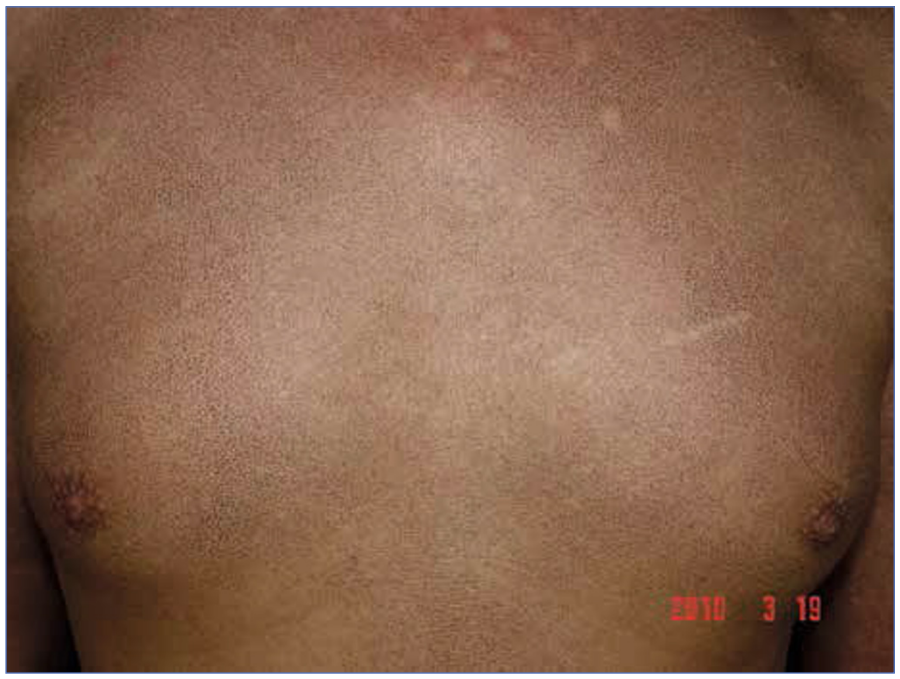
DIFFERENTIAL DIAGNOSIS
- Rothmund-Thomson syndrome.
- Chronic graft-versus-host disease.

TREATMENT
Genetic counseling. The disease worsens with time and prognosis is poor, with life expectancy below 50 years of age.
Oral or topical retinoids can be useful for leukoplakia.
Hematopoietic stem cell transplantation is the only curative option for bone marrow failure.

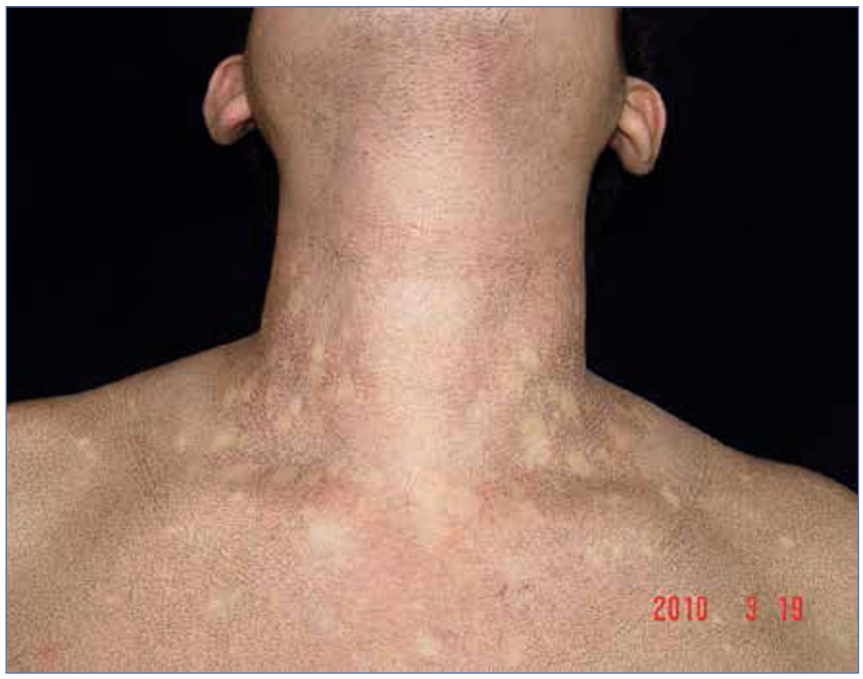
KEY REFERENCES

- Yi-Pei Lee, Sheau-Chiou Chao and Julia Yu-Yun Lee. Naevus anaemicus-like hypopigmented macules in dyskeratosis congenita. Australasian Journal of Dermatology. 2011;52:142-5.
- Mason PJ, Bessler M. The genetics of dyskeratosis congenita. Cancer Genet. 2011;204:635-45.
- Calado RT, Young NS. Telomere diseases. N Engl J Med. 2009;361:2353-65.

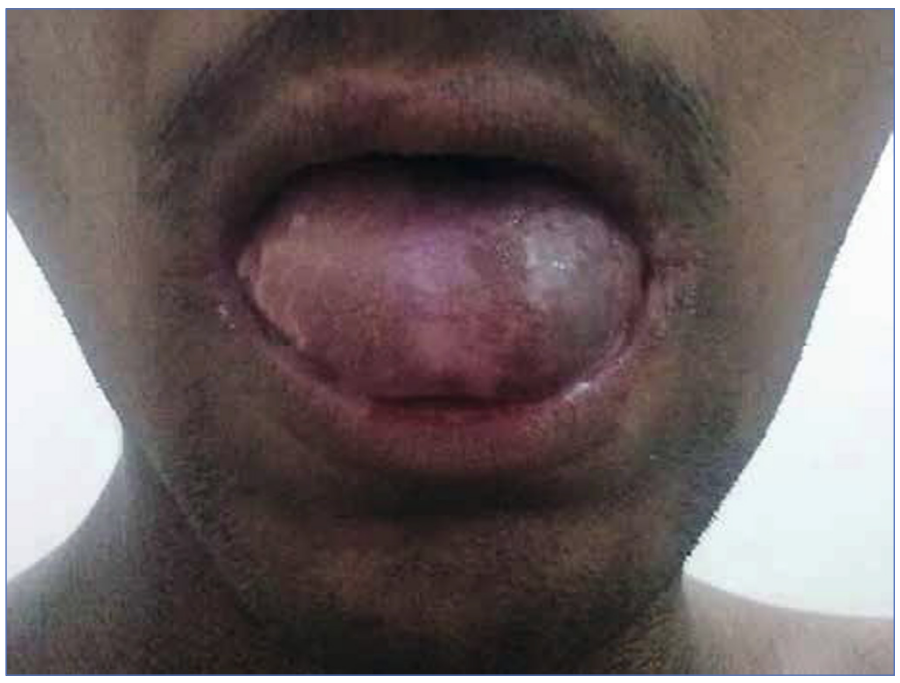
DYSKERATOSIS CONGENITA



Reticulated hyperpigmentation and nevus anemicus-like hypopigmented macules in a patient with dyskeratosis congenita (coll. J. Yu-Yun Lee).

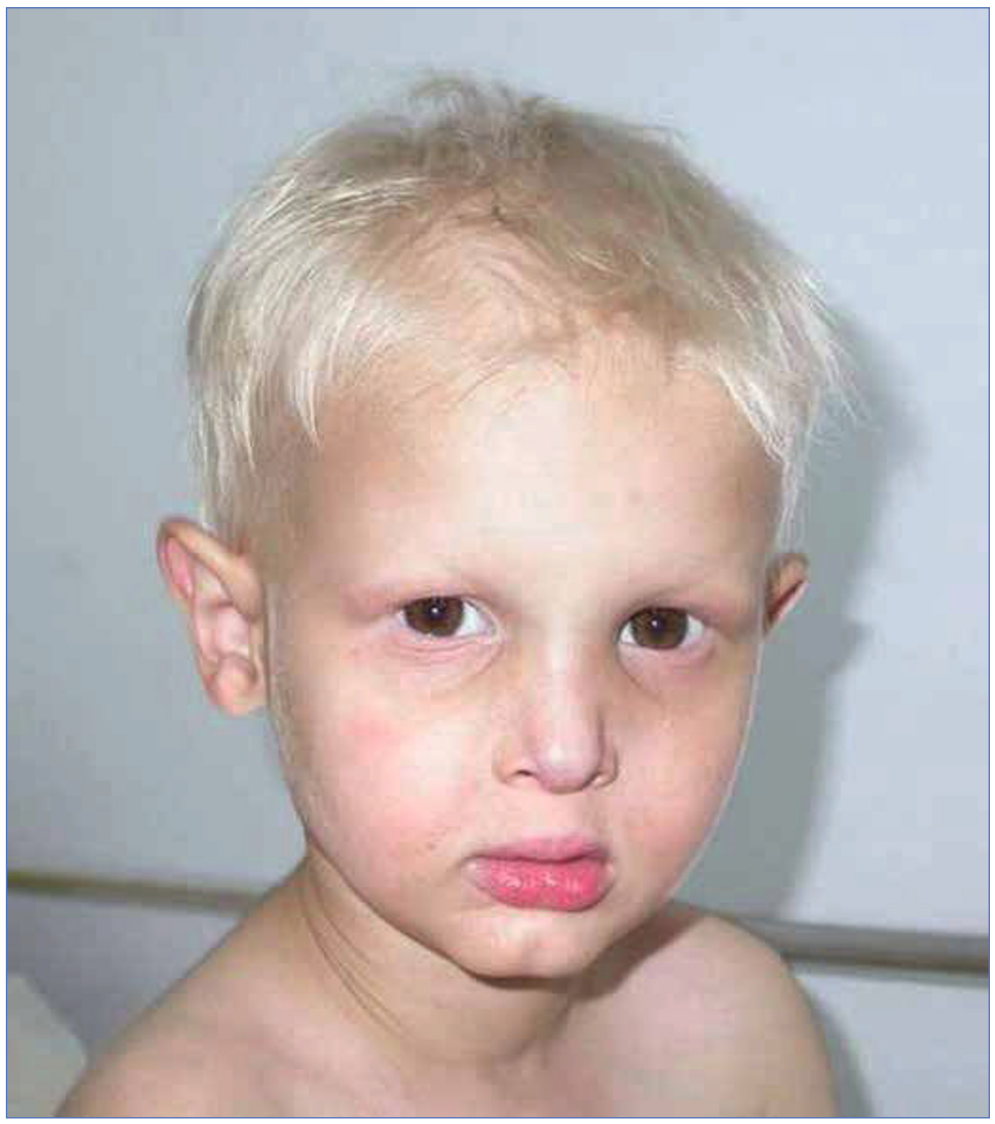


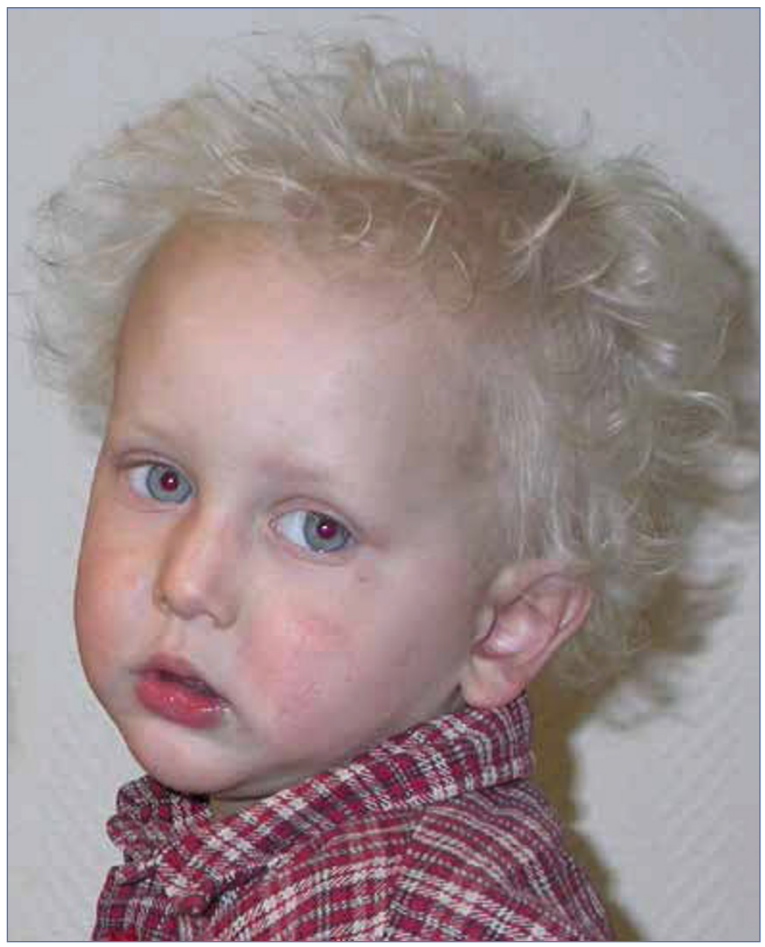
Reticulated hyperpigmentation and nevus anemicus-like hypopigmented macules in a patient with dyskeratosis congenita (coll. J. Yu-Yun Lee).



Leukoplakia in a patient with dyskeratosis congenita (coll. Shivam Sinha).

ECTODERMAL DYSPLASIA





Ectodermal dysplasia 1 hypohidrotic, X-linked. Note the hypopigmented skin and hair, which is sparce.

Ectodermal dysplasia 1 hypohidrotic, X-linked with pale skin and hair. Note the typical face with thick, everted lips; the frontal bossing, the wrinkled and slightly hyperpigmented periorbital skin; and large, low-set ears.

OMIM: #305100

EPIDEMIOLOGY

Ectodermal dysplasia is a large and heterogeneous group of genodermatoses.
The prevalence is estimated to be 7 cases per 10,000 births.

GENETICS

The ectodermal dysplasia 1 hypohidrotic, X-linked, is the most common variant. It has an X-linked inheritance with mutations in the EDA (ectodysplasin-A) gene (Xq13.1).
The ectodermal dysplasias comprise a large and heterogeneous group of inherited disorders with more than 190 distinct disorders described to date, including also autosomal recessive and autosomal dominant forms.

MOUSE MODEL

Tabby mouse.

PATHOPHYSIOLOGY

Mutations in genes leading to an abnormal development in two or more ectodermal structures (hair, nails, teeth, and sweat glands) without other systemic findings.
Only some ectodermal dysplasias are associated with hyperpigmentation.

CLINICAL DERMATOLOGICAL PRESENTATION

Classic triad:
- Inability to sweat (anhidrosis or hypohidrosis).
- Sparse hair (hypotrichosis).
- Abnormal or missing teeth (anodontia or hypodontia).

Patchy, mottled or reticulated hyperpigmentation can be observed in several ectodermal dysplasias. Hyperpigmentation around the eyes and lips are highly suggestive of hypohidrodic ectodermal dysplasia syndrome.
Diffuse hypopigmented skin and hair can be noted.
Dryness of skin and eyes is classical. Chronic eczematous dermatitis can be observed.

EXTRACUTANEOUS SIGNS

Dysmorphic features.
Growth failure.
Hyperthermia with fever and seizures.

HISTOPATHOLOGY

Reduction in the number of sweat glands, hair follicles, and sebaceous glands.

DIFFERENTIAL DIAGNOSIS

- Pachyonychia congenita.
- Aplasia cutis congenita.
- Focal dermal hypoplasia syndrome.

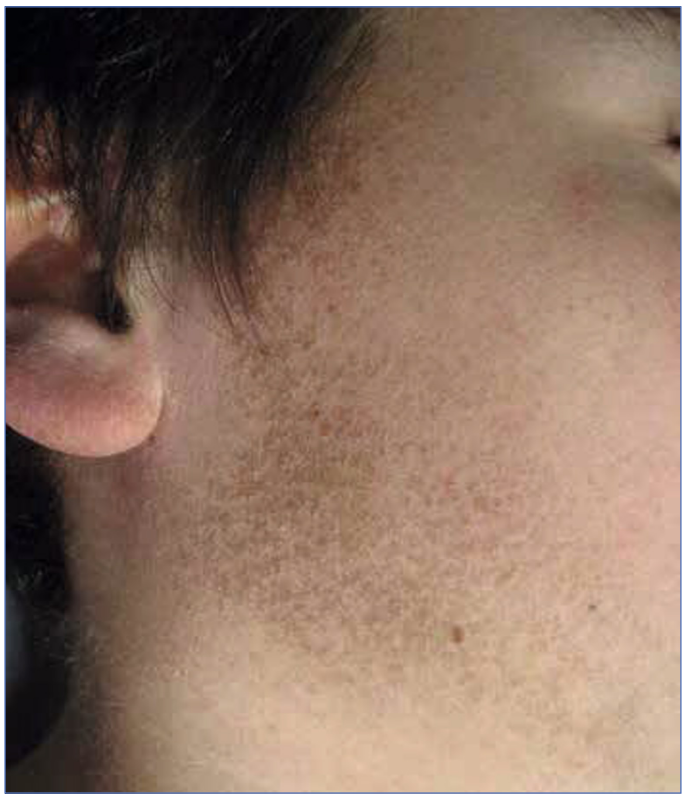
TREATMENT

Genetic and educational counseling.
Topical emollients, artificial tears.

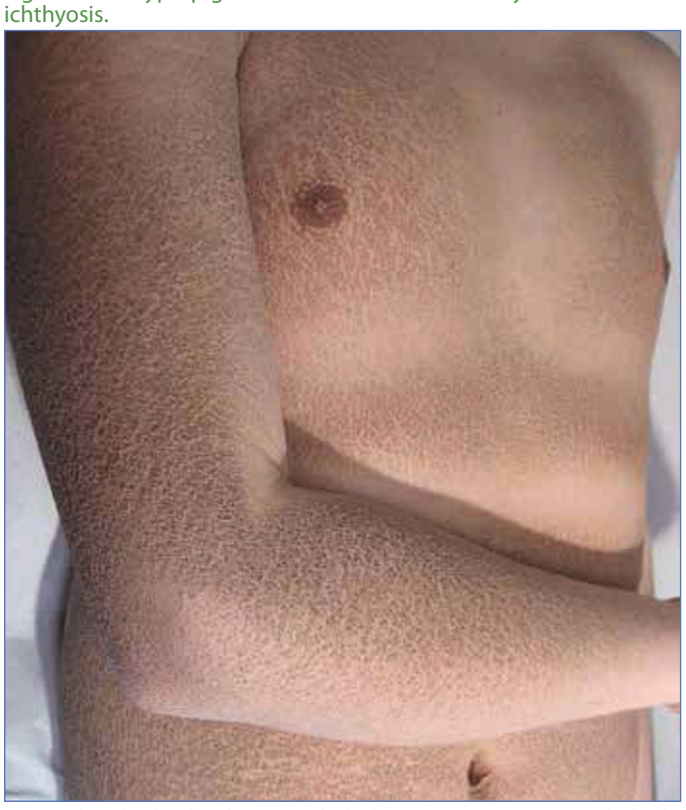
KEY REFERENCES

- Knaudt B, Volz T, Krug M, Burgdorf W, Röcken M, Berneburg M. Skin symptoms in four ectodermal dysplasia syndromes including two case reports of Rapp-Hodgkin-Syndrome. Eur J Dermatol. 2012;22:605-13.
- McGrath JA, Mellerio JE. Ectodermal dysplasia-skin fragility syndrome. Dermatol Clin. 2010;28:125-9.
- Mikkola ML. Molecular aspects of hypohidrotic ectodermal dysplasia. Am J Med Genet A. 2009;149A:2031-6.

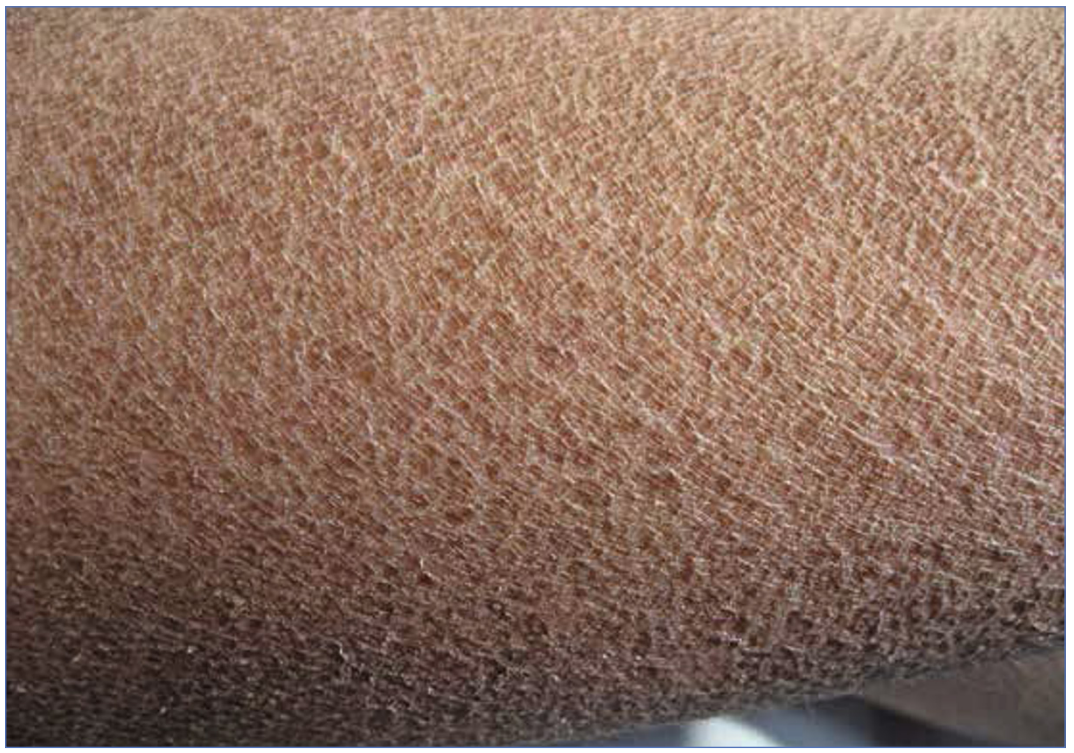
ICHTYOSIS



Light brown hyperpigmentation of the face in a boy with X-linked ichthyosis.



Dry and scaly skin leading to a dark skin appearance in an X-linked ichthyosis. Note that the folds are spared.



Brown discoloration due to the hyperkeratosis in an X-linked ichthyosis.

Acquired ichthyosis in a patient suffering from malnutrition and AIDS.

OMIM: #146700; #308100; #242300; #601277; #604777; #146750; #606545; #146800

EPIDEMIOLOGY

Acquired forms are rare and have to been seen as a marker of a systemic disorder (cancers [lymphomas], AIDS, malnutrition, chronic renal failure, leprosy, sarcoidosis, lupus, dermato-myositis, etc).
Some drugs such as clofazimine, can induce an ichthyosis.
Ichthyosis vulgaris is the most common form of hereditary ichthyosis (95% of the cases). The other types of hereditary ichthyosis such as X-linked ichthyosis and lamellar ichthyosis have a more severe presentation.

PATHOPHYSIOLOGY

The discoloration is linked to an increased thickness of the epidermis with an abnormal stratum corneum.

CLINICAL DERMATOLOGICAL PRESENTATION

The skin is rough and dry with dark appearance.
Scaling is most prominent on the extensor surfaces of the extremities and usually spares the folds.

EXTRACUTANEOUS SIGNS

None in most of cases.
Some hereditary ichthyosis can be part of a multi-organ genetic disorder.

HISTOPATHOLOGY

All ichthyosis is characterized by a hyperkeratosis.

DIFFERENTIAL DIAGNOSIS

- Atopic or contact dermatitis.

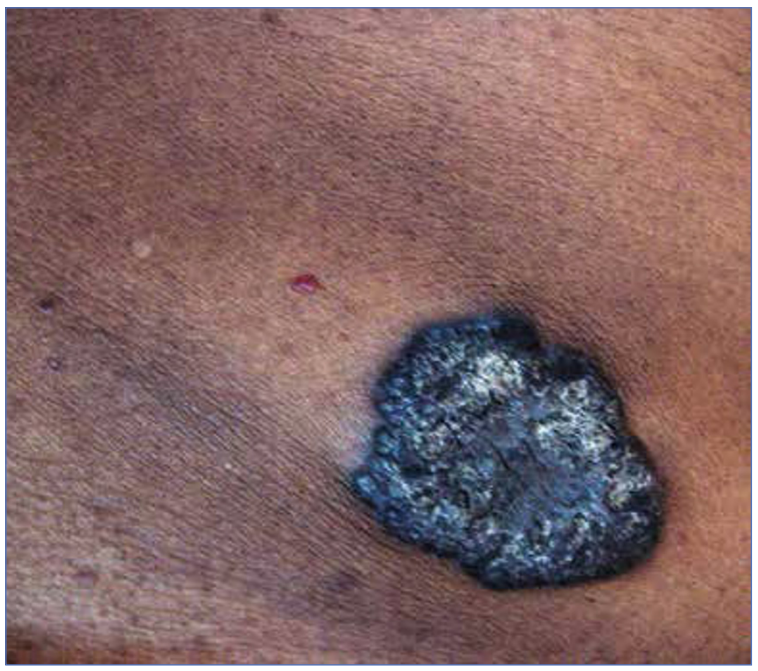
TREATMENT

Topical keratolytics, emollients.
Topical tretinoin.
Acitretin.
Treatment of the underlying disorder or discontinuation of the responsible drug if acquired ichthyosis.

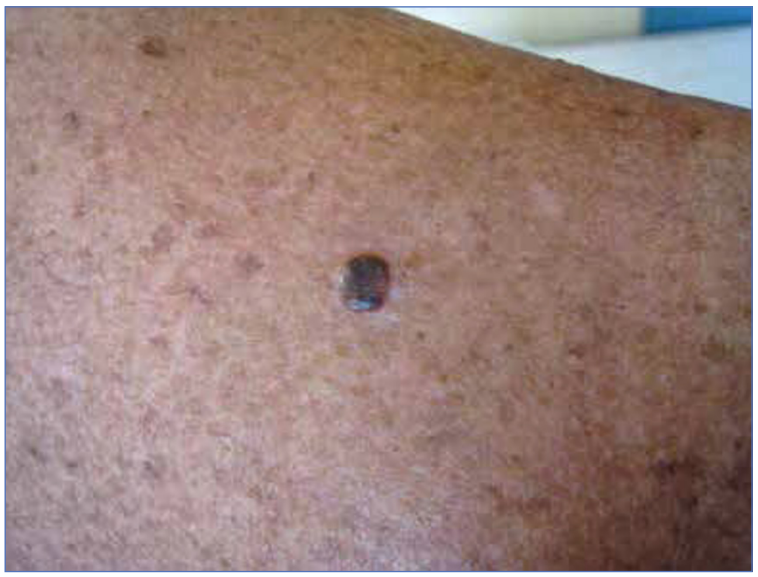
KEY REFERENCE

- Patel N, Spencer LA, English JC 3rd, Zirwas MJ. Acquired ichthyosis. J Am Acad Dermatol. 2006;55:647-56.

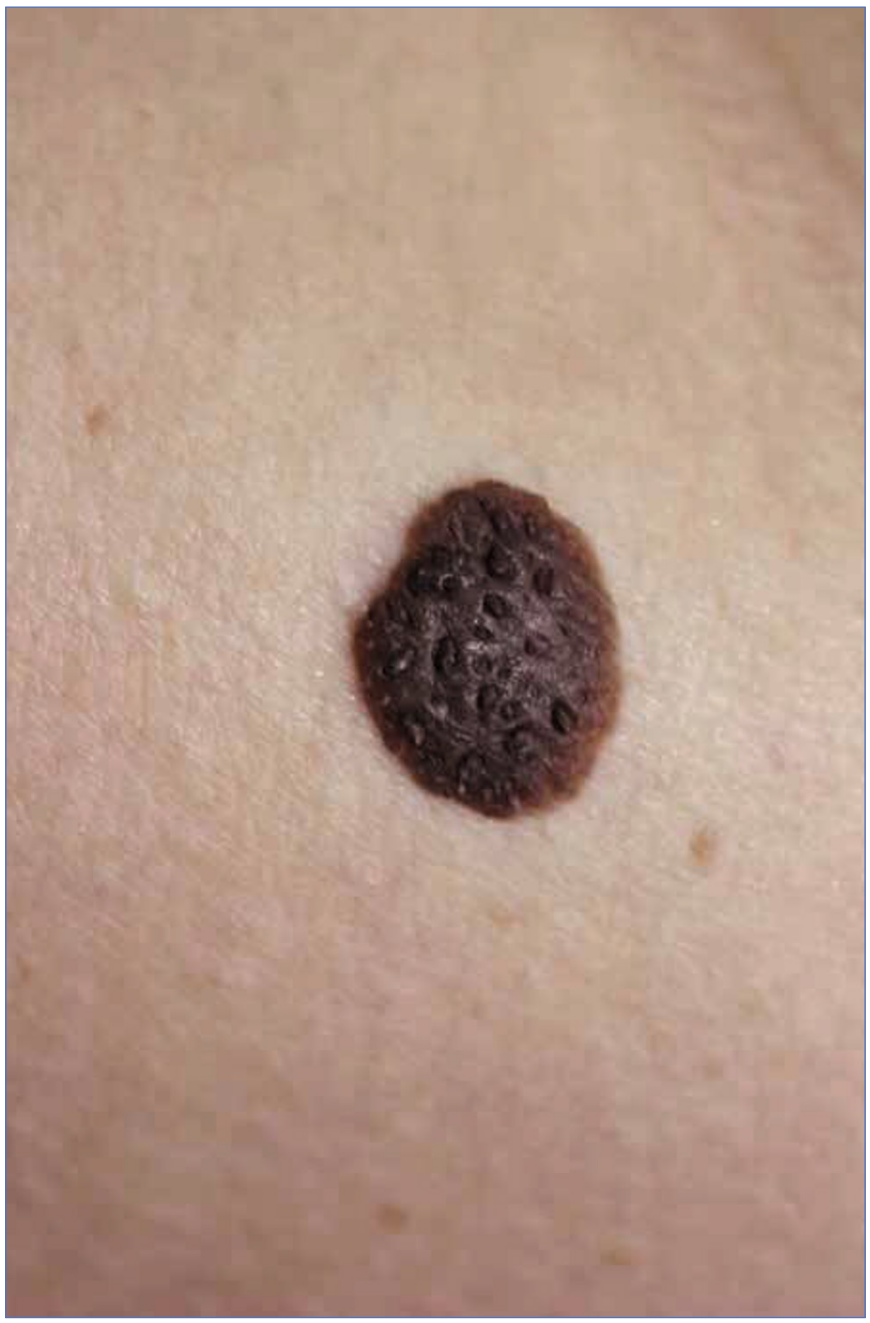
MELANOACANTHOMA



Voluminous melanoacanthoma of the abdomen presenting as a solitary black and verrucous lesion (coll. Arun C. Inamadar).



Some lesions can be suggestive of melanoma. Dermoscopy and histological analysis are sometimes required.



Melanoacanthoma of the trunk.

EPIDEMIOLOGY

Cutaneous and mucosal melanoacanthomas are described.
The cutaneous form occurs from the forth to eighth decades of life. Males and females are equally affected and it is more frequent in White populations.
The mucosal form is observed primarily in young to middle-aged Black females.

PATHOPHYSIOLOGY

Benign proliferation of keratinocytes with dendritic melanocytes. The hyperpigmentation could be due to a blockade of melanin transfer from melanocytes to the keratinocytes, leading to an increased amount of melanin within melanocytes. Originally reported as a distinct entity, melanoacanthomas are now considered by most authors as a highly pigmented variant of seborrheic keratosis.

CLINICAL DERMATOLOGICAL PRESENTATION

Cutaneous melanoacanthoma: solitary brown to black lesion from few millimeters to several centimeters in diameter.
The surface is rough and can become verrucous.
Localization: mainly on trunk, scalp, face (often on lip or eyelid), penis and extremities.
Mucosal melanoacanthoma: dark-brown, black or blue-black solitary lesion from few millimeters to several centimeters in diameter.
The surface is usually flat. Verrucous lesions are rare.
Localization: lips, oral mucosa and oropharynx.
NB. In both types, multiples lesions have been reported, but are rare.

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Proliferation of keratinocytes with dendritic melanocytes without cytologic atypia. The epithelial hyperplasia is minimal in mucosal forms.
Acanthosis, hyperkeratosis, parakeratosis, papillomatosis, and small horn pearls can be observed.

DIFFERENTIAL DIAGNOSIS

- Melanoma.
- Nevus.
- Fixed drug eruption.
- Amalgam tattoos.

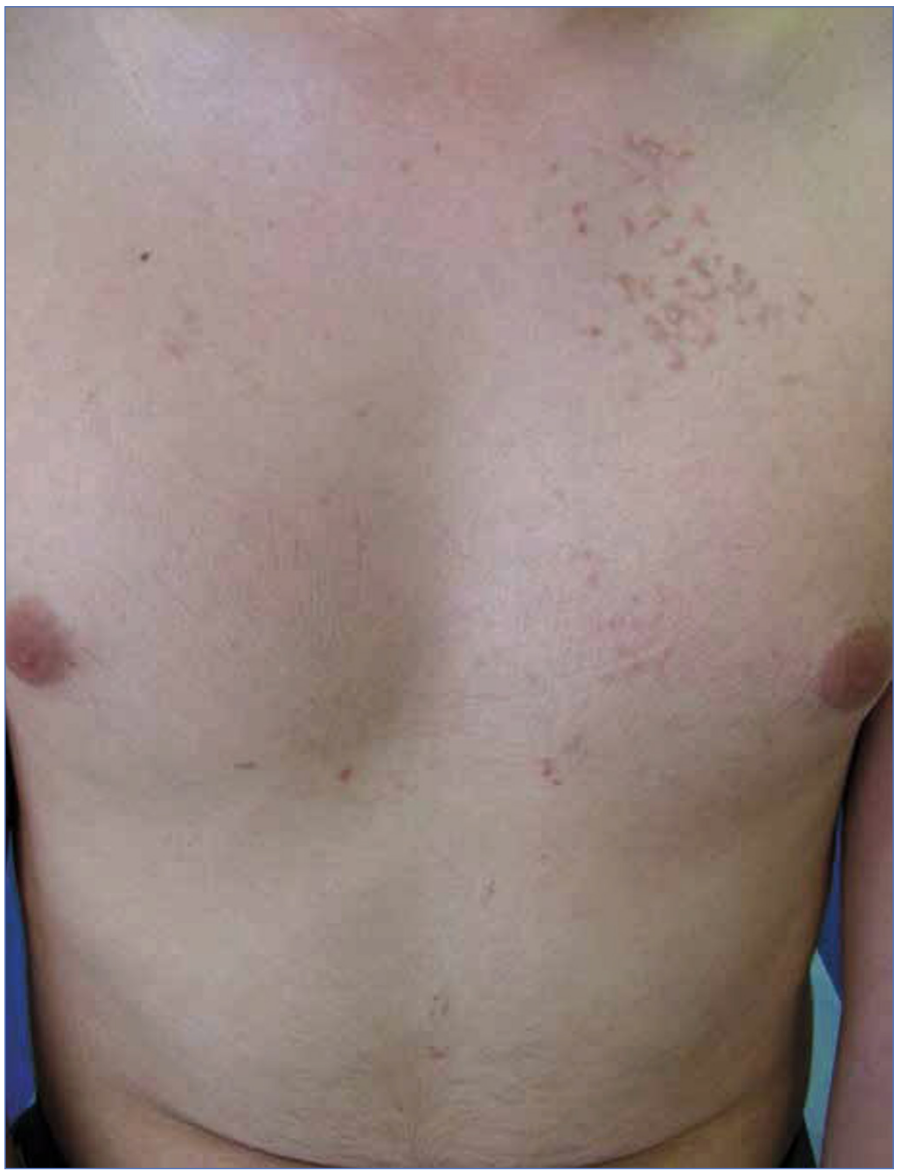
TREATMENT

Surgery, shaving, cryotherapy or ablative laser can be proposed if the patient wants the lesion to be removed. If needed a skin biopsy can be performed to rule out melanoma

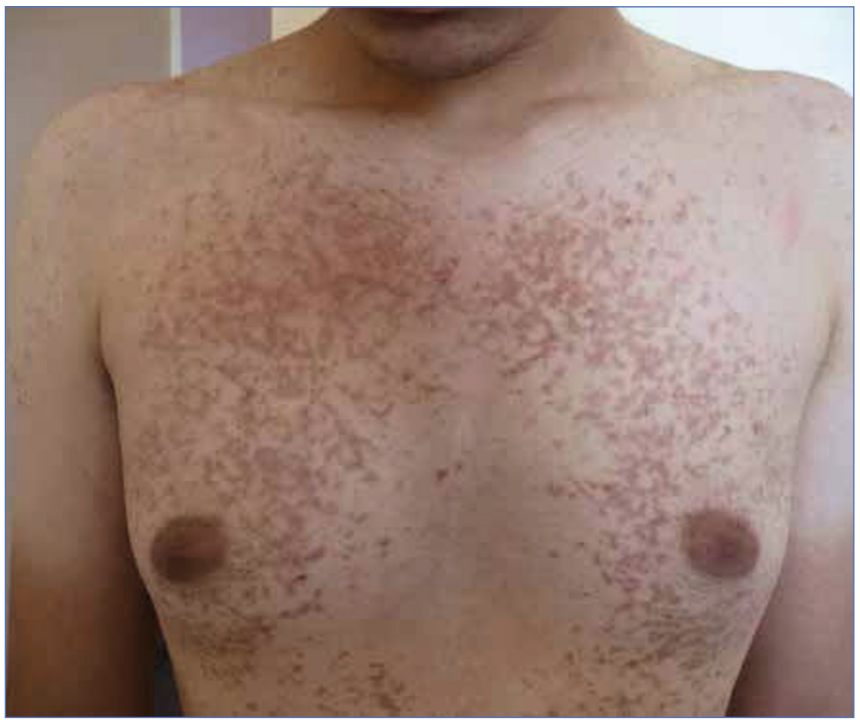
KEY REFERENCES

- Yarom N, Hirshberg A, Buchner A. Solitary and multifocal oral melanoacanthoma. Int J Dermatol. 2007;46:1232-6.
- Lambert WC, Lambert MW, Mesa ML, et al. Melanoacanthoma and related disorders. Simulants of acral-lentiginous (P-P-S-M) melanoma. Int J Dermatol. 1987;26:508-10.

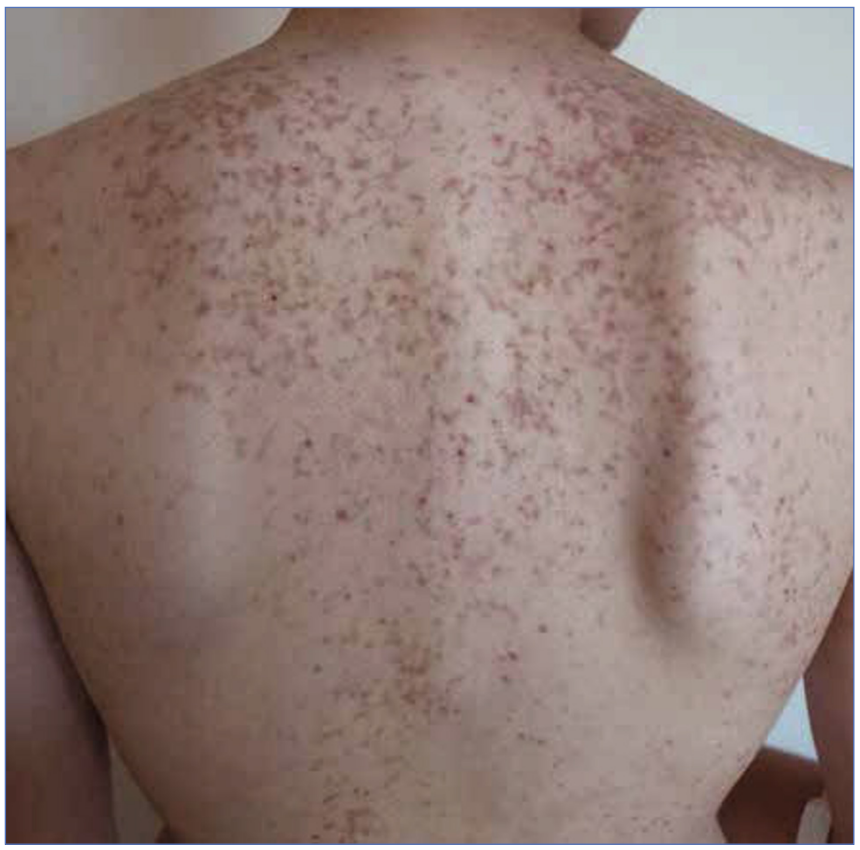
PRURIGO PIGMENTOSA



Mild and mostly unilateral form of prurigo pigmentosa in a young man.



Erythematous pruritic papules coalescing to form a reticulate pattern getting progressively hyper-pigmentated.



Back of the same patient.

EPIDEMIOLOGY

Rare inflammatory dermatosis. Most cases have been described in Japan.
Mostly young adults with female predominance (sex ratio from 2:1 to 7:1 depending on series).

PATHOPHYSIOLOGY

Prurigo pigmentosa is characterized by an inflammatory phase with pruritic erythematous papules and a resolution phase with reticulated pigmentation. The etiology is unknown.
Association with diabetes mellitus, ketosis, pregnancy, and fasting or dieting has been reported.

CLINICAL DERMATOLOGICAL PRESENTATION

Sudden onset of erythematous pruritic papules that coalesce to form a reticulate pattern.
Resolution of the primary lesions occurs within days, leaving a mottled or reticulate hyperpigmentation.
Localization: mainly on the trunk. The abdomen, lumbosacral regions, antecubital fossae, limbs, and forehead can also be affected. The mucous membranes are spared.
Duration from 1 month to 8 years (mean 1 year).

EXTRACUTANEOUS SIGNS

None.

HISTOPATHOLOGY

Early lesions: neutrophil infiltration, spongiosis, ballooning degeneration and necrotic keratinocytes.
Then the infiltrate gets a patchy lichenoid pattern, with a predominance of eosinophils and lymphocytes.
Late lesions: parakeratosis, epidermal hyperplasia, melanophages with sparse lymphocytes in the upper dermis.

DIFFERENTIAL DIAGNOSIS

- Confluent and reticulated papillomatosis of Gougerot and Carteaud.
- Macular amyloid.

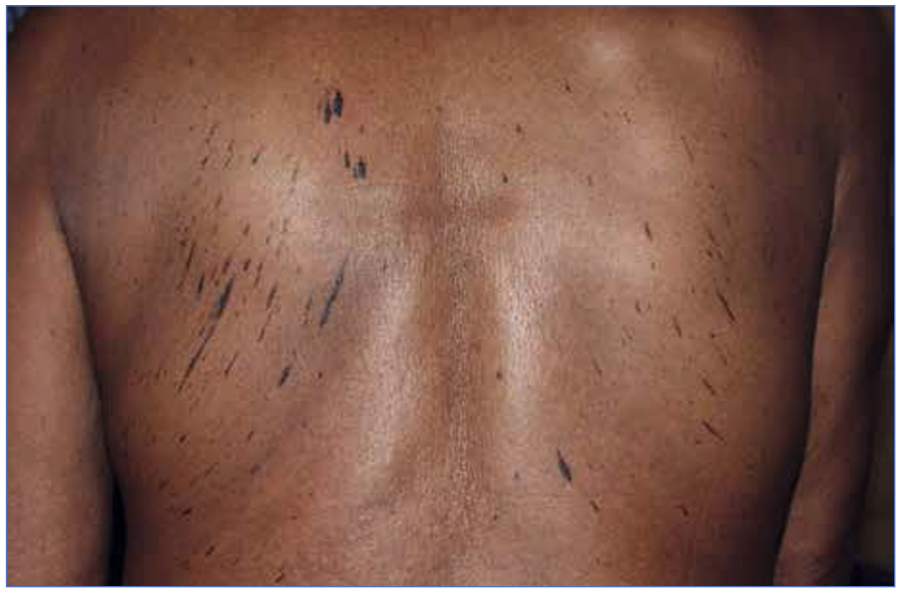
TREATMENT

Minocycline is considered as a standard treatment.
Doxycycline, dapsone, macrolides can be proposed.

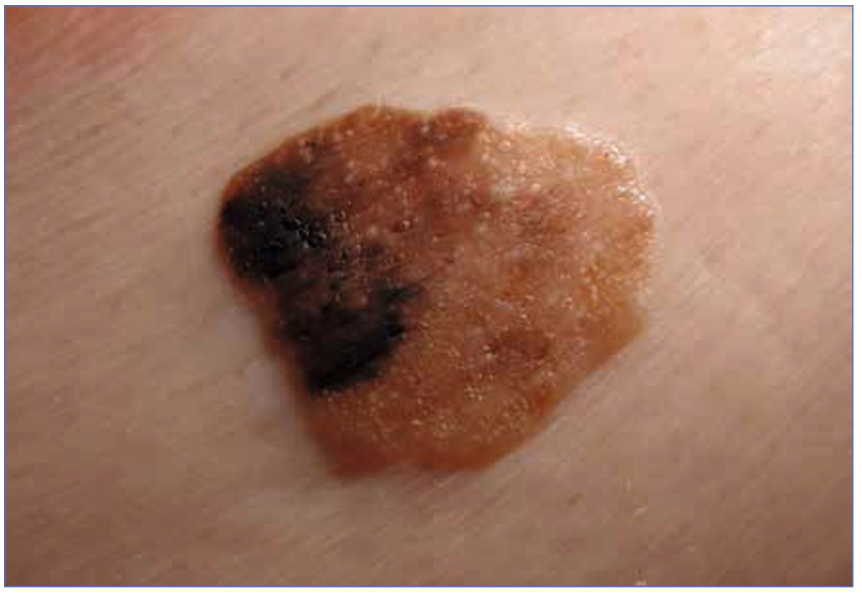
KEY REFERENCES

- Oh YJ, Lee MH. Prurigo pigmentosa: a clinicopathologic study of 16 cases. J Eur Acad Dermatol Venereol. 2012;26:1149-53.
- Boer A, Misago N, Wolter M et al. Prurigo pigmentosa: a distinctive inflammatory disease of the skin. Am J Dermatopathol. 2003;25:117-29.

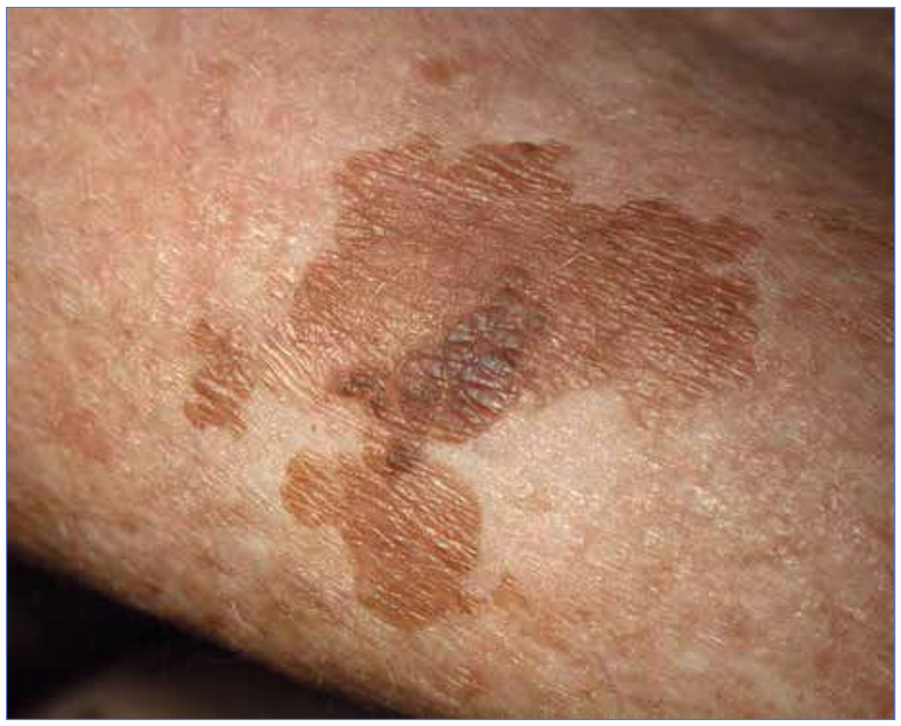
SEBORRHEIC KERATOSIS



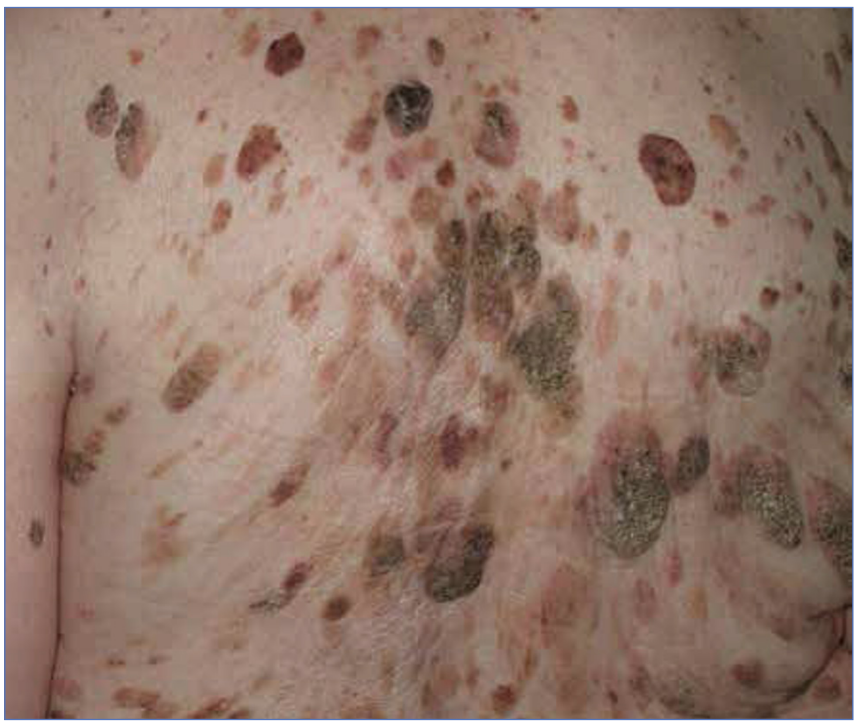
Hyperpigmented seborrheic keratoses of the back with a christmas tree disposition.



Seborrheic keratoses. Note the keratin plugs.



Velvety pigmented lesions with well-defined borders.



Multiple seborrheic keratoses from light brown macules to large verrucous lesions in an elderly woman.

EPIDEMIOLOGY

Very common benign tumor with an increased frequency with age. The prevalence was shown from almost 80% at 40 years to 98% in people over 60 years of age. However, a prevalence of 23% has been found in people aged 15 to 30 years.
A familial trait to develop multiple seborrheic keratoses is found in about half of the patients (autosomal dominant transmission).

PATHOPHYSIOLOGY

The pathophysiology of seborrheic keratoses is not fully understood but the implication of epidermal growth factors is suspected. Sunlight exposure has been reported to have a causative role.
The discoloration is linked to an increased thickness of the epidermis with an abnormal stratum corneum. In hyperpigmented seborrheic keratoses the melanocytes are stimulated by the cytokines produced by the surrounding keratinocytes, leading to an increased production of melanins and their transfer to the keratinocytes.

CLINICAL DERMATOLOGICAL PRESENTATION

Asymptomatic (sometimes pruriginous) macules with well-defined borders getting progressively velvety to verrucous with multiple plugged follicles.
Color: light brown to black.
Localization: mostly on the trunk but any site of the body can be affected. A Christmas tree disposition is frequently observed on the back.

EXTRACUTANEOUS SIGNS

None in most of cases.
Rapid onset of numerous seborrheic keratoses can be a paraneoplastic sign (Leser-Trelat syndrome). Malignant acanthosis nigricans is frequently associated. It should prompt the search for an underlying malignancy (mostly gastric and colon adenocarcinomas, but other solid and blood cancers have been reported).

HISTOPATHOLOGY

Papillomatous epithelial proliferation with horn cysts. Pronounced hyperkeratosis and papillomatosis can be observed in older verrucous lesions. Melanocytes can be found in aberrant places.

DIFFERENTIAL DIAGNOSIS

- Lentigo actinicus.
- Melanoma.
- Melanoacanthoma.
- Warts.
- Actinic keratoses.
- Squamous and basal cell carcinomas.

TREATMENT

Liquid nitrogen application, curettage, and ablative lasers are effective options.
Histological examination should be performed before any procedure if a melanoma or a skin carcinoma is suspected.

KEY REFERENCES

- Gill D, Dorevitch A, Marks R. The prevalence of seborrheic keratoses in people aged 15 to 30 years: is the term senile keratosis redundant? Arch Dermatol. 2000;136:759-62.
- Kwon OS, Hwang EJ, Bae JH, Park HE, Lee JC, Youn JI, Chung JH. Seborrheic keratosis in the Korean males: causative role of sunlight. Photodermatol Photoimmunol Photomed. 2003;19:73-80.

NON-MELANIC PIGMENTARY DISORDERS

Sweat discoloration

CHROMHIDROSIS

EPIDEMIOLOGY
The incidence of chromhidrosis is rare, without sexual predilection. It begins after puberty, when the apocrine glands are activated.

PATHOPHYSIOLOGY
Chromhidrosis refers to the excretion by the apocrine glands of sweat containing lipofuscin pigments. Depending on the various oxidative states of the lipofuscin pigments, the secretion turns yellow, green, blue to brown or black.
Eccrine chromhidrosis has been described with ingestion of drugs and dyes.

CLINICAL DERMATOLOGICAL PRESENTATION
Odorless colored staining of the skin restricted to areas with apocrine glands and more pronounced in the follicular orifices and pores.
The coloration of the skin can be yellow, green, blue to brown or black and can be easily removed by swabbing with cotton and water.
Underwear and clothes can be colored by the secretions.
Localization: because of the restricted distribution of the apocrine glands, the chromhidrosis is localized to the face, axillae and the breat areolae.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Apocrine glands are normal in size and morphology, but an increased number of lipofuscin granules is noted in the cytoplasm of secretory cells.

DIFFERENTIAL DIAGNOSIS
- Pseudochromhidrosis.

TREATMENT
Topical capsaicin and botilinum toxin type A have been reported to improve the condition.

KEY REFERENCES

- Marks JG Jr. Treatment of apocrine chromhidrosis with topical capsaicin. J Am Acad Dermatol. 1989;21:418-20.
- Matarasso SL. Treatment of facial chromhidrosis with botulinum toxin type A. J Am Acad Dermatol. 2005;52:89-91.

PSEUDOCHROMHIDROSIS

SYNONYMS
Extrinsic chromhidrosis.

EPIDEMIOLOGY
Pseudochromhidrosis is not uncommon. In most cases deposits of extrinsic dyes of clothes is the casual factor.

PATHOPHYSIOLOGY
The eccrine sweat is colored on the surface of the skin as a result of the deposit of extrinsic dyes or paints, or by the transformation by chromogenic bacteria.
Only few fungi and bacteria are known to induce pseudochromhidrosis. Corynebacteria are responsible for red pseudochromhidrosis whereas *Malassezia furfur* and *Bacillus* spp are the agents involved in the blue pseudochromhidrosis.
Several drugs have been reported to promote this microbial proliferation and to induce pseudochromhidrosis.

CLINICAL DERMATOLOGICAL PRESENTATION
Acquired discoloration of the skin.
The color is blue or red if bacterial or fungal proliferation is involved. All ranges of color can be observed when dyes or paints are deposited to the skin.
Localization: every part of the body can be affected but the face and the folds are usually spared.
Discoloration disapperas with swabbing.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
Normal.

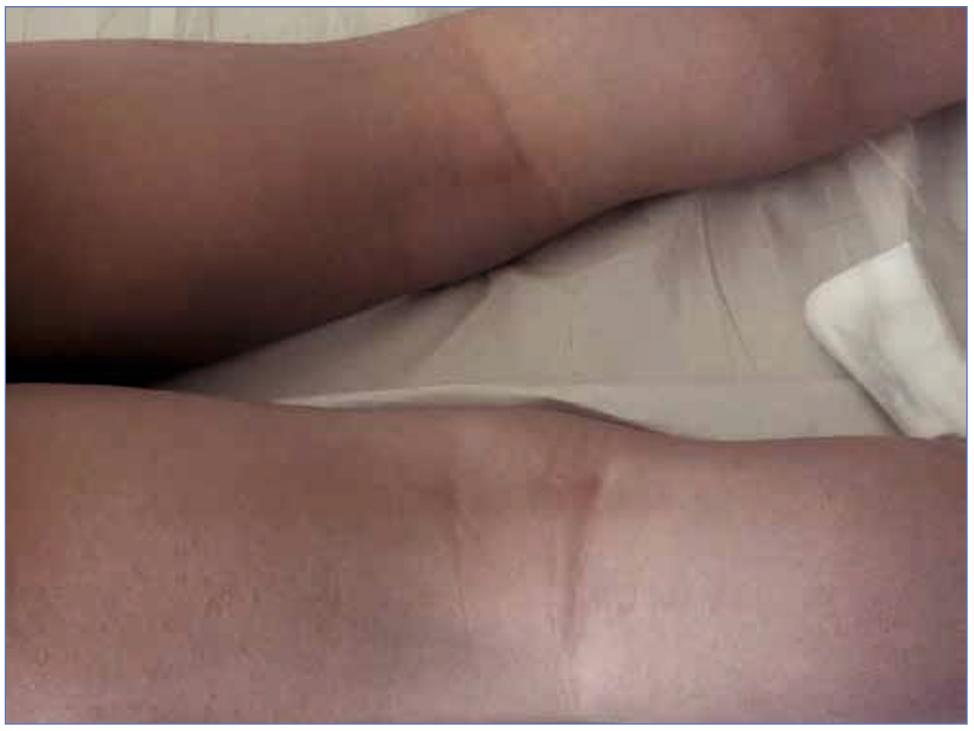
DIFFERENTIAL DIAGNOSIS
- Chromhidrosis.

TREATMENT
The discoloration is removed with washing.
Discontinuation of the drug if it is the cause.
First wash a new cloth before wearing it.

KEY REFERENCES

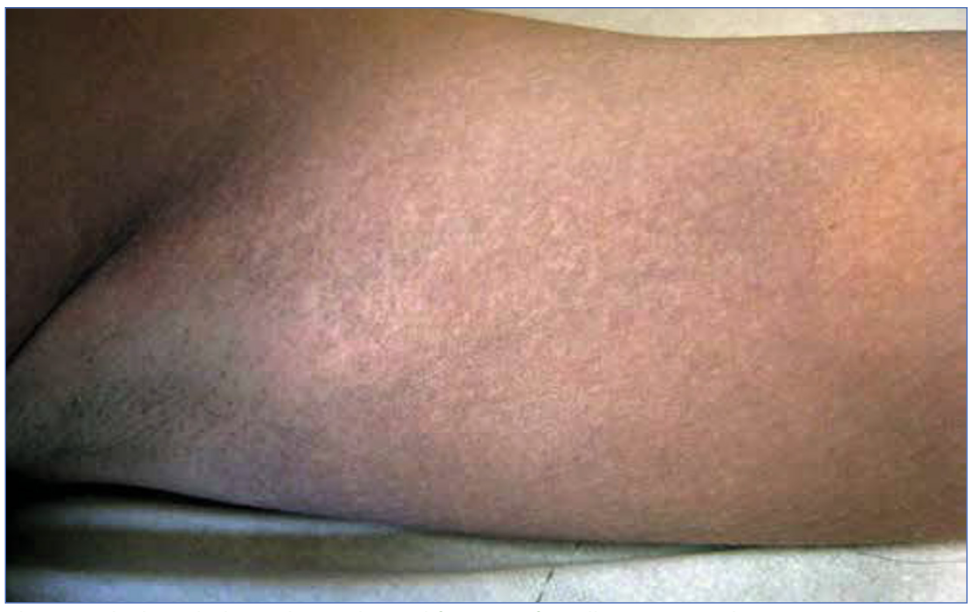
- Castela E, Thomas P, Bronsard V, Lacour JP, Ortonne JP, Passeron T. Blue pseudochromhidrosis secondary to topiramate treatment. Acta Derm Venereol. 2009;89:538-9.
- Hill S, Duffill M, Lamont D, Rademaker M, Yung A. Pseudochromhidrosis: blue discolouration of the head and neck. Australas J Dermatol. 2007;48:239-41.

PSEUDOCHROMHIDROSIS

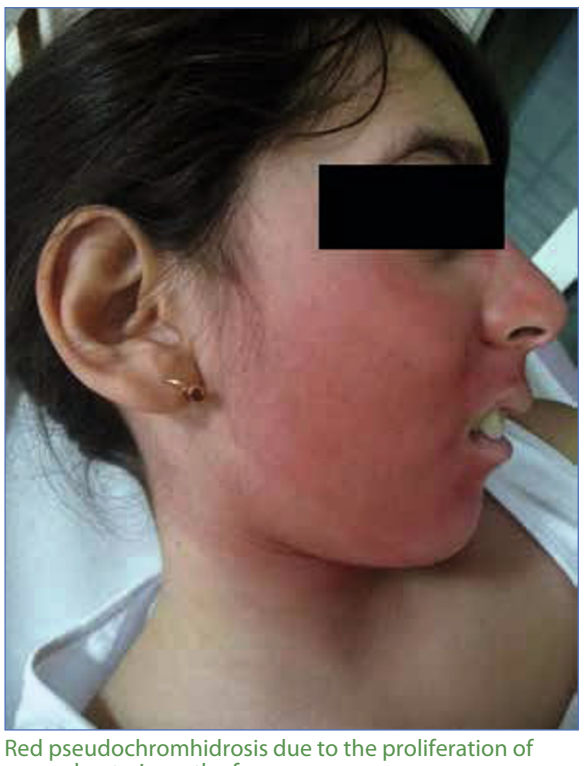


Pseudochromhidrosis of the leg in a young boy. Note that the blue discoloration is less pronounced in the folds and the faint blue coloration of the gauze compress after swabbing.

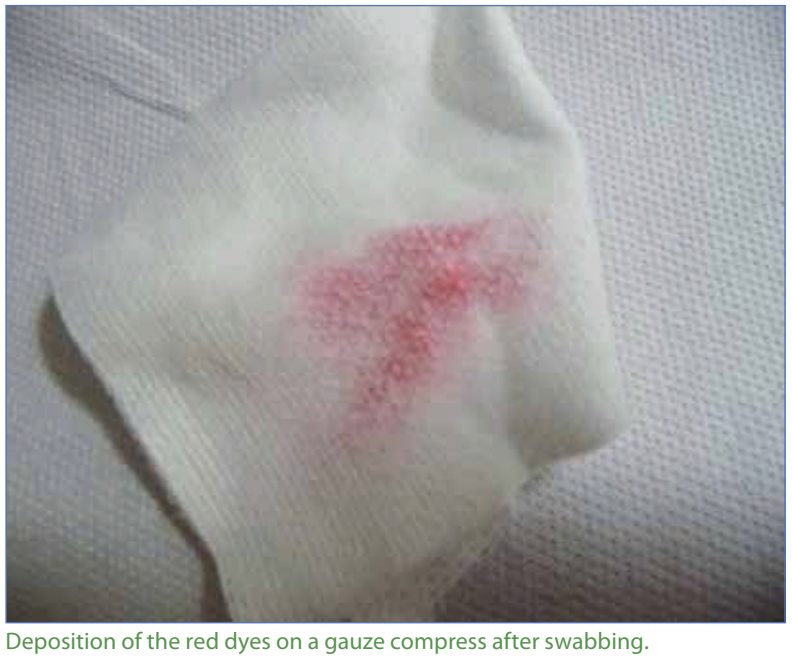
The same boy with the new pants responsible for the pseudochromhidrosis.



Blue pseudochromhidrosis due to the proliferation of *Bacillus* spp secondary to topiramate treatment.



Red pseudochromhidrosis due to the proliferation of corynebacteria on the face.

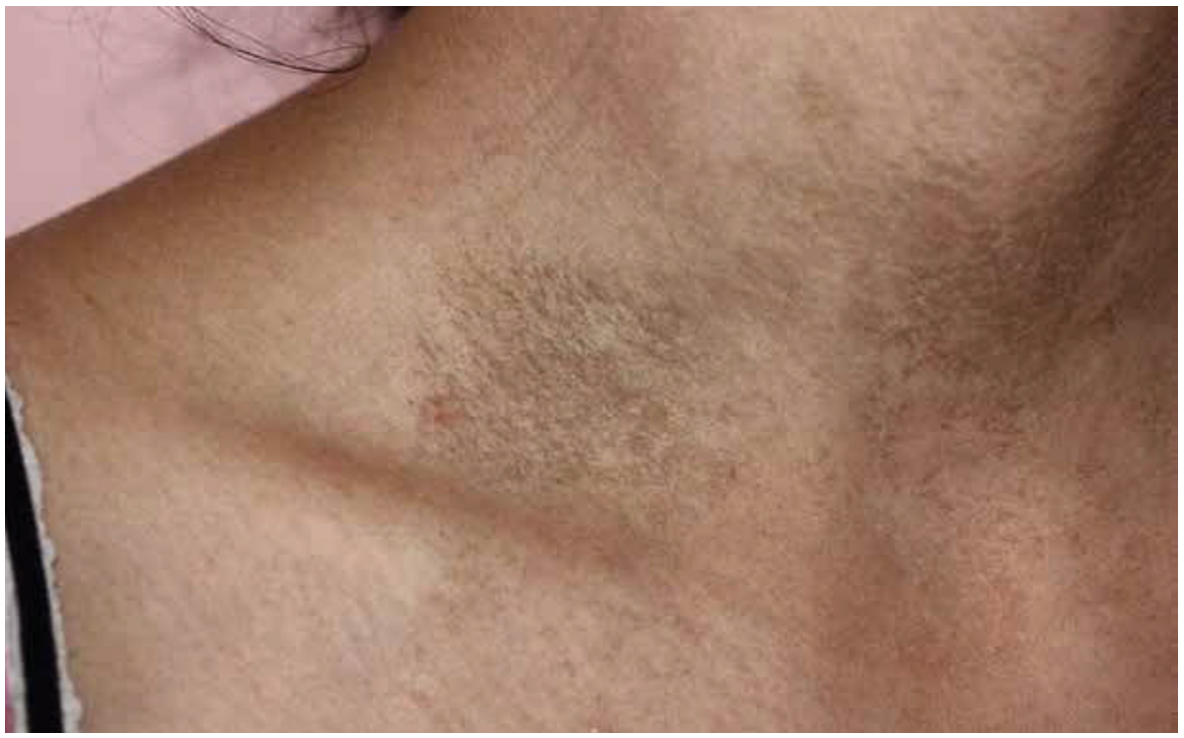


Deposition of the red dyes on a gauze compress after swabbing.

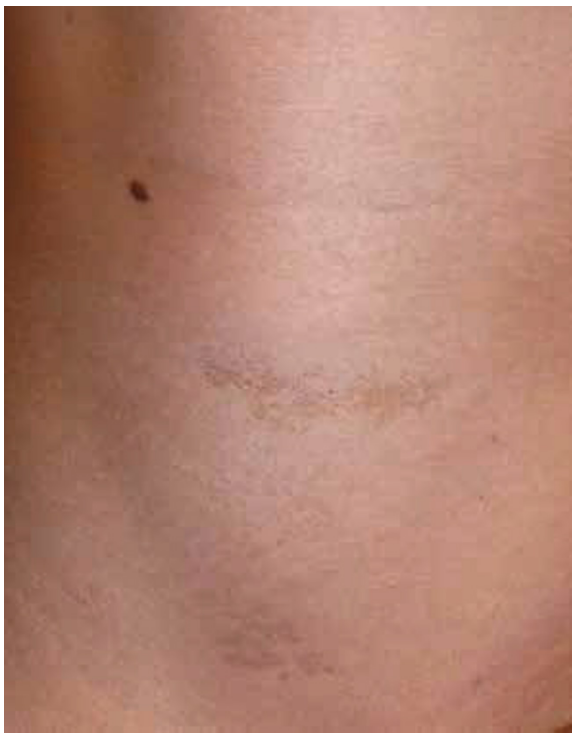
NON-MELANIC PIGMENTARY DISORDERS

Other

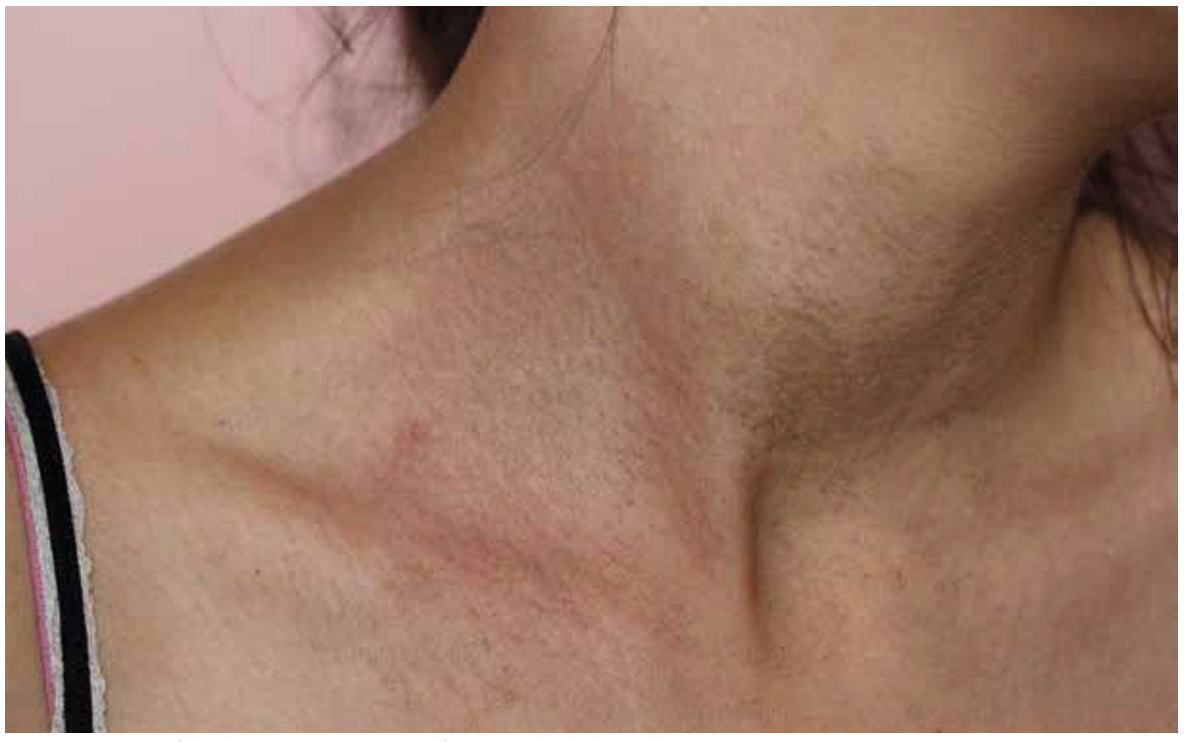
DIRT PIGMENTATION



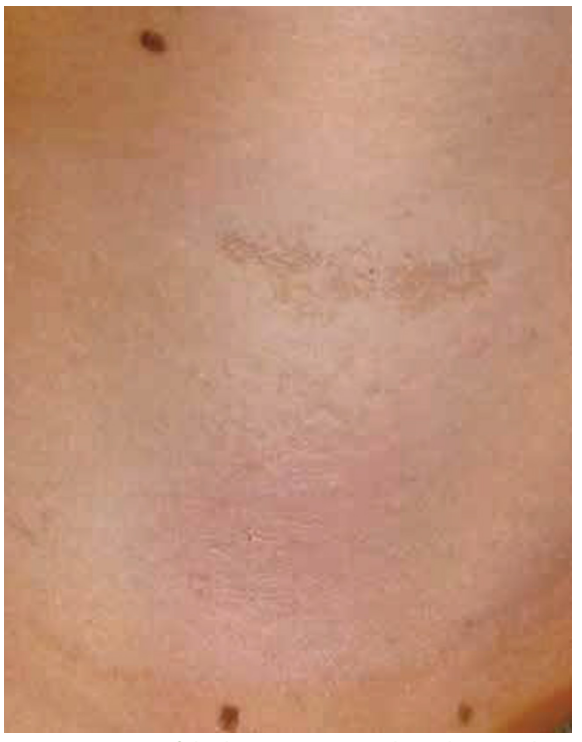
Terra firma-forme of the neck in a 13-year-old girl.



Pigmented and papillomatous pigmentation strictly located in the neck folds in an 8-year-old boy.



Disappearance of the hyperpigmentation after 70% alcohol swabbing.



Disappearance of the lower pigmented patch immediately after 70% alcohol swabbing.

SYNONYMS
Dermatosis neglecta, terra firma-forme dermatosis.

EPIDEMIOLOGY
Mostly observed in children when they started washing themselves but the condition is also observed in adults.

PATHOPHYSIOLOGY
Chronic avoidance of washing. The patches of the terra firma-forme dermatosis are resistant to a regular wash with soap and water but can be removed by alcohol swabbing with substantial shearing force.

CLINICAL DERMATOLOGICAL PRESENTATION
Acquired pigmented and sometimes keratotic patches.
Localization: mostly on the folds and the genital area.

EXTRACUTANEOUS SIGNS
None.

HISTOPATHOLOGY
None.

DIFFERENTIAL DIAGNOSIS
- Dirty neck of atopic dermatitis (atopic dermatitis with post inflammatory hyperpigmentation).
- Gougerot-Carteaud disease (confluent and reticulated papillomatosis).
- Acanthosis nigricans.
- X-linked icthyosis.

TREATMENT
Soap and water cleaning. 70% alcohol swabbing sometimes required.

KEY REFERENCES

- Tan C. Dirt-adherent dermatosis: not worth an additional name. Arch Dermatol. 2010;146:679-80.
- Ruiz-Maldonado R, Durán-McKinster C, Tamayo-Sánchez L, Orozco-Covarrubias ML. Dermatosis neglecta: dirt crusts simulating verrucous nevi. Arch Dermatol. 1999;135:728-9.
- Duncan WC, Tschen JA, Knox JM. Terra firma-forme dermatosis. Arch Dermatol. 1987;123:567-9.