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The color of skin: gray diseases of the skin, nails, and mucosa

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Abstract Gray diseases are a group of skin disorders characterized mainly by gray discoloration with or without involving the mucous membranes and nails. These diseases may be hereditary or acquired. Some of the better-known hereditary entities are dermal melanocytosis, incontinentia pigmenti, hypomelanosis of Ito, hemochromatosis, ochronosis, and silvery hair syndrome. Acquired diseases with gray coloring include late-stage organ failure, lichen planus pigmentosus, erythema dyschromicum perstans, and drug reactions. The discoloration is due to either increased epidermal and or dermal melanin or dermal deposition of a chromogen or a combination of both. Investigations are directed to determining the underlying medical condition and a skin biopsy is usually unnecessary. Likewise, treatment is directed mainly toward the underlying medical disease. Although bleaching (lightening) agents may diminish the discoloration, better results may be obtained from using a Q-switched laser and intense pulsed light, either alone or in combination with topical agents.

Introduction

The unique skill of dermatologists, and "the raison d'être for the specialty of dermatology is the possibility of making a diagnosis with the naked eye." With this consideration, skin color represents the most important sign for establishing the diagnosis or the differential diagnoses. The milky white of vitiligo, violaceous of lichen, salmon pink of psoriasis, and yellow of xanthomas are examples of lesion skin colors that, in their absence, the diagnosis of the relevant disease(s) cannot be made with certainty. Similarly, gray skin is a characteristic color of several diseases that will be highlighted; however, artifacts of a light gray-brown following skin lines on the neck and shoulders may be attributed to a lack of vigorous washing to remove the build-up of stratum corneum (Figure 1), and allowing a dirty-gray color to be seen.[1,2]

Definition and general considerations

Gray diseases are characterized by gray skin and or hair, nails, and mucous membranes as the main characteristic and diagnostic feature. Gray skin may have unique and specific grays, namely battleship gray, gunmetal, iron gray, lead, pearl gray, silver, slate, smoke gray, steel gray, and taupe.[1] The gray color may be due to increased melanin, whether epidermal or

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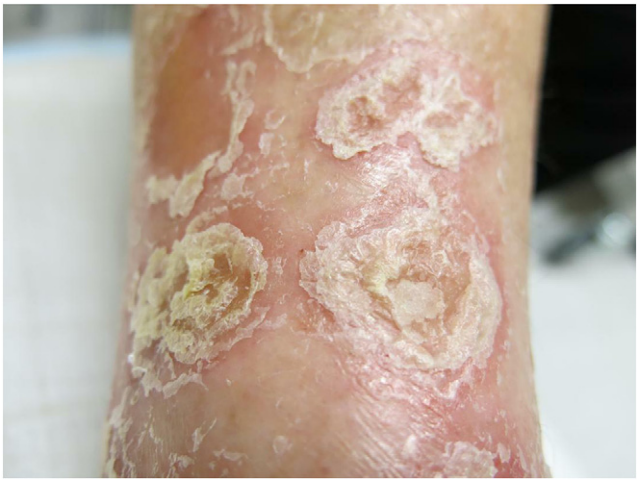

Fig. 1 An elderly patient with dermatitis neglectica (Terra firme dermatosis – Duncan's dirty dermatosis) showing accumulation of skin debris including stratum corneum (courtesy of Professor U. Wollina, Dresden, Germany).

dermal, or due to dermal deposition of a chromogen or a combination of both. The distinctive skin gray discoloration is generally due to the Tyndall effect of light scattered from dermal melanin. In general, lesions with increased epidermal melanin are accentuated and those with increased dermal melanin become less obvious, blending with uninvolved skin but distinguished through a Wood's lamp examination.[3,4] Gray diseases can be congenital or acquired. A skin biopsy is seldom required, and other investigations are usually directed to related medical illnesses.

Treatment of the gray discoloration of skin is usually not required, and in general, it is primarily directed to the extracutaneous manifestations. Genetic counseling is strongly indicated for inherited condition, whereas concealers may be useful for cover-up. There are several medical and surgical treatment options that can be tried, ranging from traditional depigmenting agents (eg, hydroquinone, corticosteroids, kojic acid) to active compounds isolated from plants and yeasts (eg, arbutin, aloesin, gentisic acid, flavonoids, hesperidin, licorice, niacinamide, yeast derivatives, polyphenols) that may inhibit melanogenesis without melanocytotoxicity. They are currently incorporated in several cosmetic lightening preparations.[5]

Topical application of tacrolimus or pimecrolimus or topical corticosteroids significantly diminish the erythema and vesicles (eg, in incontinentia pigmenti).[5,6] Various lasers, including the Q-switched ruby, Q-switched alexandrite, and Q-switched Nd:YAG lasers, may be helpful. The introduction of 755-nm picosecond and Q-switched Nd:YAG nanosecond lasers has proven useful.[7,8] Intense pulsed light may also provide lightening.[9] The choice of the treatment option depends on the availability of the machine and the experience of the treating dermatologist.

Etiology

Congenital/hereditary

- Dermal melanocytosis (Mongolian spot, nevus of Ota, nevus of Ito).
- Incontinentia pigmenti (Bloch-Sulzberger syndrome)
- Hypomelanosis of Ito
- Hemochromatosis (hereditary and secondary)
- Ochronosis (endogenous also called alkaptonuria-exogenous)
- Silvery hair syndrome

Acquired

- Disease-related
  - Late-stage organ failure (cardiovascular, renal, malignancy including paraneoplastic syndrome)
  - Lichen planus pigmentosus
  - Erythema dyschromicum perstans (ashy dermatitis)
  - Miscellaneous (Riehl melanosis, dermal melanocyte hamartoma, acquired nevus of Ota-like macules or Hori's nevus, patch blue nevus).
- Drug-related
  - Heavy metals (iron, silver, gold)
  - Antibiotics (chloramphenicol "Gray baby syndrome," tetracyclines)
  - Cardiopulmonary drugs (amoidarone, pirfenidone)
  - Miscellaneous (antimalarials, antipsychotics)

Congenital/hereditary

Dermal melanocytosis

Dermal melanocytosis is characterized by blue to blue-gray skin discoloration and includes several congenital and acquired entities. Mongolian spot, nevus of Ota, and nevus of Ito represent the most frequently encountered gray congenital dermatoses. Dermal melanocytosis is characterized histopathologically by a sparse number of dendritic, melanin-producing melanocytes that are scattered among the collagen bundles of the reticular dermis.

Mongolian spot (congenital dermal melanocytosis)

Mongolian spot (*syn.* congenital dermal melanocytosis) is very common and is characterized by blue to blue-gray patches present at birth, often in the lumbosacral region. It is more common in people of color, particularly Asians, and is due to entrapment of melanocytes in the dermis during their migration from the neural crest into the epidermis. The patch usually resolves during the first year of life.[10]

Although a Mongolian spot usually consists of a single or very few macules with round, oval, or angulated margins, multiple and widespread lesions involving the trunk, extremities, and face may occur. Its size varies from a few to more than 20 cm, and the color varies from light blue to dark blue to blue-gray. Extralumbosacral (aberrant) variants tend to be more persistent, and thus are easily confused with adult-onset dermal melanocytoses, nevus of Ota, Nevus of Ito, and patch blue nevus. Extensive and often persistent congenital dermal melanocytosis may be associated with inborn errors of metabolism, such as Hurler syndrome, Niemann-Pick disease, mannosidosis and Wolf-Hirschhorn syndrome.[11,12]

Nevus of Ota

Nevus of Ota (*syn.* nevus fuscoceruleus ophthalmomaxillaris, oculodermal melanocytosis, congenital melanosis bulbi, oculomucodermal melanocytosis) appears as blue to blue-gray to blue-brown unilateral, or occasionally bilateral, facial patch more common among Asians and Africans. It is characterized by a confluence of pinhead-sized to several millimeters in diameter round or oval individual macules, although the whole lesion appears as an irregularly demarcated and often mottled patch with variable size commonly along the distribution of the ophthalmic and maxillary branches of the trigeminal nerve. Involvement of the ipsilateral sclera is a characteristic feature that is seen in most patients (Figure 2). Other less frequently involved sites include conjunctiva, cornea, retina, tympanum, and oral and nasal mucosae.[13]

Nevus of Ota is persistent and may expand over time. The intensity of the gray may increase during menstruation, at puberty or menopause. The occurrence of uveal and cutaneous melanomas within the nevus has been rarely reported particularly in Caucasians.[14]

Nevus of Ito

Nevus of Ito (*syn.* nevus fuscoceruleus acromiodeltoideus) has a similar clinical appearance to nevus of Ota but differs by its location, as it appears on the supraclavicular, scapular, and deltoid regions. It may occur alone or in association with an ipsilateral or bilateral nevus of Ota. The color of the lesions and the histopathologic features are the same as nevus of Ota and, likewise, development of melanoma is very rare.[13,14]

Incontinentia pigmenti

Incontinentia pigmenti (*syn.* Bloch-Sulzberger syndrome) is an X-linked, dominantly inherited neurocutaneous syndrome with cutaneous, neurologic, ophthalmologic, and dental abnormalities.[15] Boys with the abnormal gene on their single X chromosome are hemizygous for this condition and may be so severely affected, unless mosaic, that they die *in utero.* The disease is caused by a mutation of the *IKBKG/NEMO* gene on Xq28, which results in loss of function of nuclear factor-κB, a critical protein that modulates cellular proliferation, apoptosis, and response to proinflammatory factors.[16] The skin manifestations have four stages, beginning with a phase of erythema and bullae in infancy, progressing to linear, verrucous lesions, followed by development of widely disseminated areas of hyperpigmentation (Figures 3A, B). In the fourth stage, seen in adults, faint, hypochromic, or atrophic lesions in a linear pattern are most apparent on the lower extremities and persist indefinitely. Hair, nail, and dental anomalies often first manifest during infancy and are permanent. Neurologic and ophthalmologic sequelae often appear during early infancy.[15]

The gray is a characteristic color for the stage of hyperpigmentation, which is ushered by the development of streaks and whorls of brown or slate-gray pigmentation along Blaschko lines mostly on the trunk (Figure 3B). The brown or slate gray lesions generally develop within the first few months of life and resolve slowly by adolescence. The histologic findings are suggestive of incontinentia pigmenti but not specific, and the observed slate gray is due to melanin incontinence and

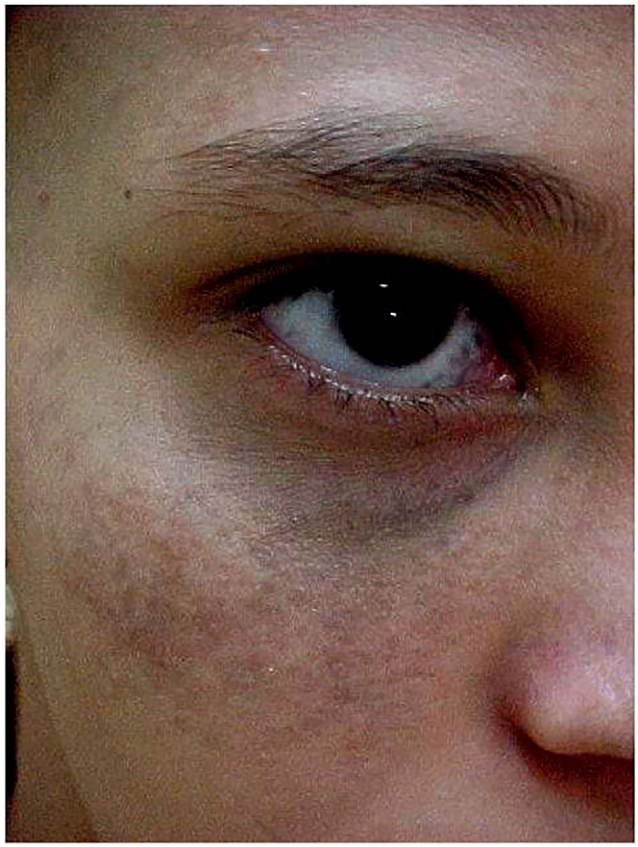

Fig. 2 Nevus of Ota showing the gray patches along the distribution of the ophthalmic and maxillary branches of the trigeminal nerve and including the ipsilateral sclera.

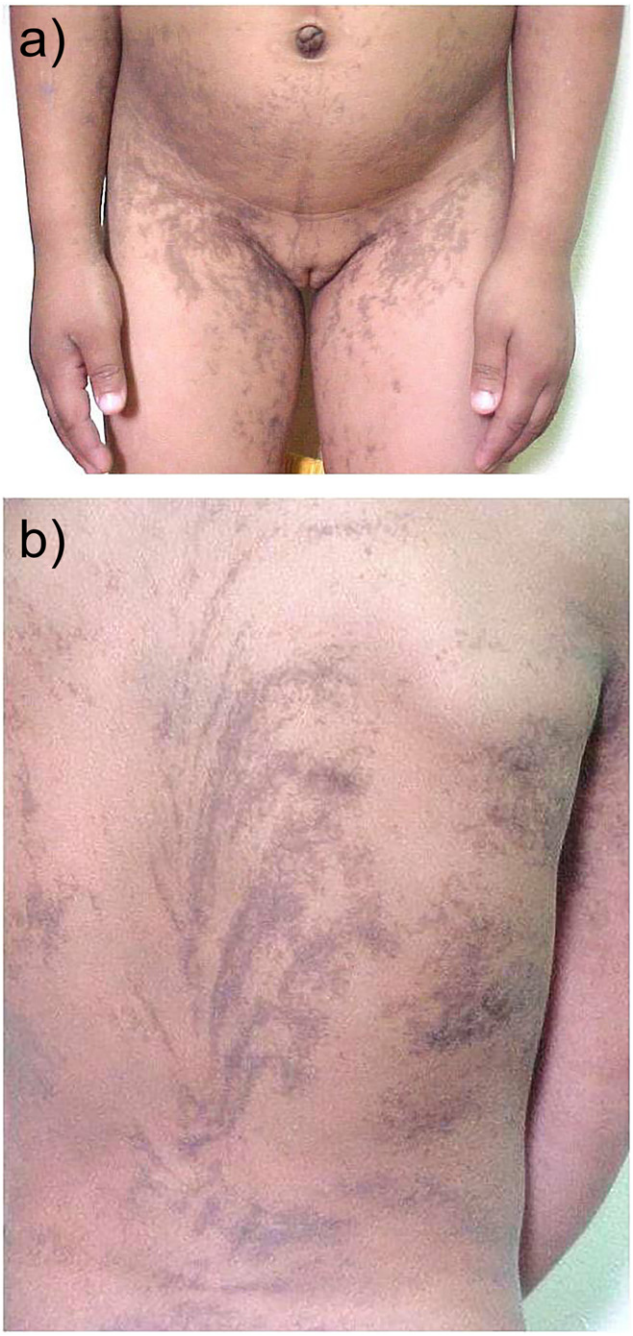

Fig. 3 A, A girl showing the characteristic gray lesions of incontinentia pigmenti on the groins and to lesser extent the lower abdomen. B, The same child showing linear streaks and whorled gray lesions along Blaschko lines on the back.

deposition in melanophages within a thickened papillary dermis.[15,17]

Differential diagnoses include linear and whorled nevoid hypermelanosis, hypomelanosis of Ito, dermatopathia pigmentosa reticularis, and Naegeli-Franceschetti-Jadassohn syndrome.

Persistent brown discoloration with no pigment incontinence and absent melanophages characterizes linear and whorled nevoid hypermelanosis. Pigmentation maculosa eruptiva idiopathica is a rare disease mainly affecting children and is characterized by asymptomatic, brown-gray nonconfluent macules involving the neck and trunk. Histopathologic examination shows basal cell layer hyperpigmentation, abundant melanophages, and mild perivascular lymphohistiocytic infiltrate in the papillary dermis. The condition is self-limiting, and lesions disappear spontaneously within several months.[18]

Naegeli-Franceschetti-Jadassohn syndrome is a rare, autosomal-dominant ectodermal dysplasia due to heterozygous mutations in the keratin 14 gene characterized by reticulate hyperpigmentation, hypohidrosis, dental anomalies, and palmoplantar keratoderma with nail dystrophy. Brown or gray-brown reticulate hyperpigmentation develops on the abdomen and periocular and perioral regions by the age of 2 years and fades at puberty.[19]

Hypomelanosis of Ito

Hypomelanosis of Ito (*syn.* Blaschkoid dyspigmentation, pigmentary mosaicism, segmental pigmentation disorder, incontinentia pigmenti achromians) is characterized by mosaic distribution of hypopigmented macules and bands of speckled or mottled, grayish-brown to blue-black patches involving the skin, conjunctiva, sclera, tympanic membrane, and oral and nasal mucosa. Genetic mosaicism is the most likely explanation for its inheritance. The skin lesions are present from birth, are asymptomatic, and can be associated with neurologic, skeletal, hair, and dental defects. The extracutaneous abnormalities are highly variable, most often affecting the central nervous system, eyes, and musculoskeletal system.[20]

Hemochromatosis

Hereditary (primary) hemochromatosis is a common autosomal-recessive disorder, whereas secondary hemochromatosis is seen in patients with erythropoetic disorders that require periodic blood transfusion, such as thalassemia, sickle cell anemia, and X-linked sideroblastic anemia. The disease includes cirrhosis, diabetes mellitus (bronze diabetes), hyperpigmentation of the skin, and cardiac failure. A color range of metallic gray or slate gray to brownish-bronze is an early sign of the disease that is most pronounced on sun-exposed areas, such as the face. Discoloration of genitalia, flexural folds, scars, nipple areolae, and oral mucosa are less commonly seen. The observed gray color is the result of increased melanin in basal cell layer rather than the iron and often accentuates during exacerbations and slowly regresses with therapy. Iron stain (eg, Perls Prussian blue stain) shows iron deposition around the blood vessels, within the basement membrane zone of sweat glands and the connective tissue cells surrounding them and the eccrine glands. The transferrin saturation test may detect the condition in an early stage.[21,22]

Treatment with phlebotomy does not immediately resolve the hyperpigmentation.

Mutations of the hemochromatosis gene (*HFE*) may be associated with porphyria cutanea tarda. *HFE C282Y* homozygotes (+/+) do not respond to chloroquine, and a decrease in serum iron concentration can only be achieved by phlebotomy.[23] Other cutaneous manifestations include ichthyosis, atrophy, koilonychia, and hair loss.[22]

Ochronosis

Endogenous ochronosis (*syn.* Alkaptonuria) is a very rare, autosomal-recessive disorder due to deficiency of homogentisate 1,2-dioxygenase. It is manifested by tissue deposition of homogentisic acid resulting in pigmentation of cartilage (eg, the helices), sclerae, and skin (eg, the axillae) in addition to darkening of urine on standing, arthritis, and valvular heart disease.[24]

The dermatologic features of alkaptonuria are rarely seen before 10 to 15 years of age and typically become apparent during adulthood, often in the fourth decade of life. Axillary skin may be one of the initial sites to develop hyperpigmentation, which can range in color from blue to yellow to brown. The classic blue-gray pigmentation associated with this disorder is often first noted on the helices of the ear and sclera. Later, it may affect the entire face, as well as the palmar and plantar surfaces, the buccal mucosa, and nail bed. Features that present early in life include brownish discoloration of diapers (due to the dark urine) and cerumen that is brown to black in color.[25]

Exogenous ochronosis is due to exposure to exogenous agents, such as antimalarials and noxious substances, including phenol, trinitrophenol, benzene, hydroquinone, mercury, resorcinol, and picric acid. In contrast to alkaptonuria, there is no arthropathy. Hydroquinone in bleaching creams is widely used by dark skin patients and is the major cause of exogenous ochronosis.[26,27]

Dermatoscopy is useful in determining exogenous ochronosis, as it shows densely pigmented structures obliterating some follicular openings and multiple thin, short, arciform structures.[28] The discoloration of the skin in ochronosis is a result of the formation and deposition of ochronotic (yellowish-brown), banana-shaped pigment granules in the dermis, macrophages, basement membrane, and in the apocrine glands.[26]

Silvery hair syndrome

Silvery hair syndrome (also considered as partial albinism) is a rare, autosomal-recessive condition characterized by silvery gray hair, eyebrows, and eyelashes and may be associated with immunologic and neurologic abnormalities. Two main types have been recognized as follows: (1) Chediak-Higashi syndrome, which is characterized by regularly arranged small clumps of melanin in the hair and large melanosomes in both melanocytes and keratinocytes in skin (Figure 4); and (2) Griscelli syndrome, which is similar to Chediak-Higashi syndrome but with prominent neurologic features and absence of the characteristic giant intracytoplasmic inclusion bodies in granulated cells.[29,30]

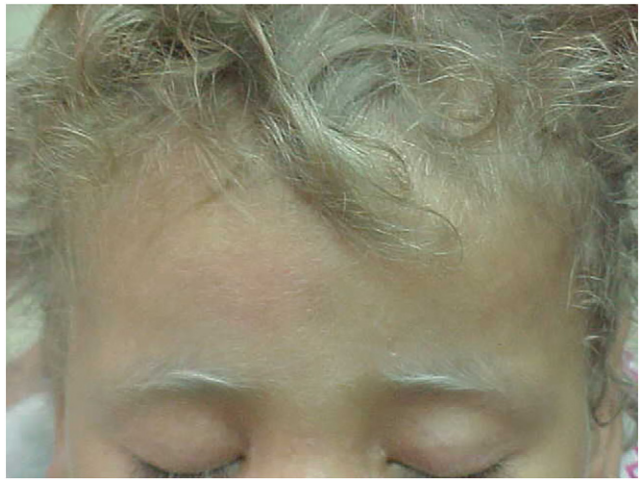

Fig. 4 A child with silvery hair syndrome showing the characteristic silver hair of the scalp, eyebrows and eye lashes without any neurologic manifestations (ie, Chediak-Higashi syndrome).

Light microscopy of hair shaft and skin is used to differentiate Chediak-Higashi syndrome from Griscelli syndrome. In contrast, Griscelli syndrome is characterized by small and large clumps of melanin in irregular pattern in hair medulla and hyperpigmented oval melanocytes with poorly pigmented keratinocytes in skin. The distribution of melanin granules in the skin correlates with that observed in the hair shaft, allowing Chediak-Higashi syndrome to be differentiated from Griscelli syndrome, at any age.[30]

Acquired

Several acquired conditions are characterized by the presence of gray skin, which may be localized to certain anatomic areas or generalized involving the entire integument with or without involvement of the nails and mucous membranes. Most of these conditions are observed in pigmented skin.[31]

Disease-related

Late-stage organ failure (cardiopulmonary, renal, paraneoplastic syndrome)

Late stages of diseases or organ failure, particularly of heart, lungs, and kidneys, is associated with slow blood flow

and inadequate tissue perfusion that ultimately produce a gray pallor. These diseases include late-stage chronic kidney disease (late-stage renal failure), terminal cancer as seen in the paraneoplastic syndrome, and congestive heart failure. The gray discoloration of the skin is generalized and is an important sign of increased deoxygenated blood and tissue ischemia. These cases are usually encountered in the emergency room, and further management of these patients is directed to the underlying condition.[32]

Lichen planus pigmentosus

Lichen planus pigmentosus is regarded as a pigmented variant of lichen planus, and it is primarily seen in heavily pigmented skin. It affects primarily the sun-exposed areas, such as the forehead and temples, and presents by slate gray, gray-brown, blue-brown color patches with ill-defined border and mild pruritus. Diffuse, reticular, and blotchy patterns have been observed on the face and neck.[33] Lichen planus pigmentosus has been associated with lichen planus elsewhere, frontal fibrosing alopecia, and hepatitis C virus infection.[34,35] Dermatoscopy may help for diagnosis (Figure 5).[35]

Erythema dyschromicum perstans

Erythema dyschromicum perstans (*syn.* ashy dermatosis) is a rare chronic-acquired skin disease characterized by gray hyperpigmented patches with erythematous borders. Its etiology is unknown and there is no specific treatment for the condition. It may be related to lichen planus pigmentosus with similar histology, although it typically involves the trunk and is characterized by circular hyperpigmented patches surrounded by erythema. In contrast to lichen planus, there is no affliction of the palms and soles and the mucous membranes. Exogenous ochronosis caused by hydroquinone can create a similar clinical appearance but with less inflammation than Lichen planus pigmentosus in addition to the pathognomonic banana-shaped deposition in the dermis.[34,36]

A recent consensus pointed to the marked overlap and confusing clinical features of lichen planus pigmentosus, erythema dyschromicum perstans, and ashy dermatosis. The group recommended their inclusion as a spectrum of acquired macular pigmentation of uncertain etiology. Treatment options of macular pigmentation of uncertain etiology include oral vitamin A, isotretinoin, tacrolimus ointment, Q-switched lasers in combination with chemical peeling with tretinoin, and/or azelaic acid.[34]

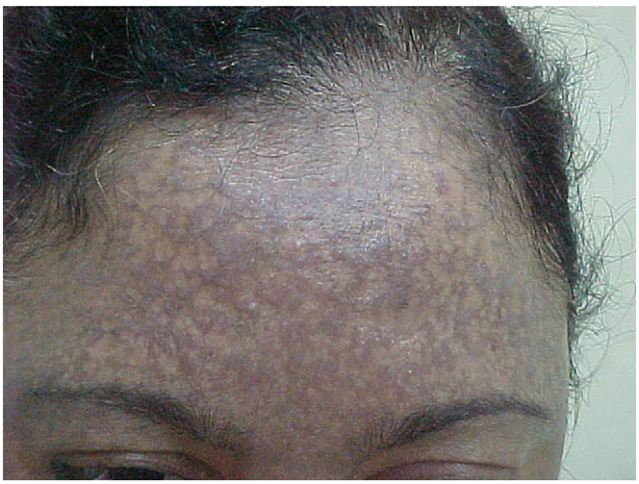

Fig. 5 A case of lichen planus pigmentosus showing gray-brown ill-defined patches in a diffuse reticular pattern on the sun exposed areas.

Miscellaneous

Riehl melanosis (*syn.* pigmented contact dermatitis) appears as gray-brown to blue-brown pigmentation most pronounced on the lateral aspects of the face, neck, and upper areas of the chest, often in a reticulate pattern. Occasionally, it occurs on other parts of the body, especially if the contact allergen is in textiles.[37] Recently, it has been recommended to consider Riehl melanosis of unknown etiology, whereas pigmented contact dermatitis when allergic or nonallergic contact or photo-contact dermatitis is established to different cosmetic, textile, occupational, or airborne allergens,[34] Ultraviolet light may play a role, because the lesions are found often in a photo-distributed manner, and some allergens are known to be photosensitizers. Patch tests are positive in many cases.[34,37] Poikiloderma of civatte may resemble Riehl melanosis; however, it is characterized by reddish-brown, reticulate pigmentation with atrophy and telangiectasia and is commonly seen among fair skinned individuals. Treatment is challenging; Q-switched Nd:YAG laser and intense pulsed light therapy was successfully used.[38,39]

Dermal melanocyte hamartoma appears as a single, very extensive area of gray-blue pigmentation that may be present from the time of birth. The skin involvement may be almost generalized, or there may be several coalescing blue macules that gradually extend within a circumscribed area from childhood. Acquired nevus of Ota-like macules (*syn.* Hori's nevus) is usually seen in adult Asian women and is manifested as bilateral blue-gray to gray-brown macules along the zygomatic area and, less often, on the forehead, upper-outer eyelids, and nose. In contrast to nevus of Ota, the eye and oronasal mucosa are not involved, and it is most commonly misdiagnosed as melasma. A patch blue nevus, which overlaps with the rare disorder adult-onset dermal melanocytosis, presents as a diffusely gray-blue area

that may have superimposed darker macules. The age of onset and sites of involvement vary, with some lesions having a linear distribution.[12,40,41]

Drug-related

Blue-gray hyperpigmentation is a possible side effect of several drugs and chemicals. It is mostly due to enhanced melanogenesis either by the medication or by cutaneous inflammation caused by the drug. Increased melanin pigment within dermal melanophages or dermal deposition of the drug or its metabolite is the characteristic histologic finding.[42,43]

Heavy metals, such as iron, silver, and gold, result in hemochromatosis, argyria, and chrysiasis respectively.

Argyria is a rare condition caused by ingestion of silver compounds. Silver salt deposits occur in the skin, nails, and mucous membranes, leading to permanent blue or blue-gray uniform pigmentation, especially on the face and other sun-exposed areas.[44] It commonly occurs in the setting of occupational exposure, or silver-containing medications, such as systemic absorption from topical silver sulfadiazine on extensive burns, and colloidal silver ingestion in alternative medicine.[44,45] The distinctive color is due to silver-induced increase in melanin and deposition of silver that histopathologically appears as tiny brownish granules in connective tissue surrounding sebaceous glands, in perineural tissue, and in arteriolar walls.[44,46] Medical treatment is ineffective.[45] Chrysiasis is due to dermal deposition of gold, which is rarely used as an alternative treatment of rheumatoid arthritis and pemphigus. It is a rare condition manifested as bluish to slate gray discoloration of the skin that predominantly occurs in sun-exposed areas and unlike argyria, nails, and mucous membranes are not affected. Ultraviolet light has been incriminated in induction of gold uptake and melanogenesis stimulation.[47,48] Histologic features of chrysiasis include dermal and perivascular gold deposition within the macrophages and endothelial cells as well as extracellular granules, creating an orange-red birefringence on fluorescent microscopy.[48,49]

Antibiotics, such as chloramphenicol and tetracyclines, can also result in gray discoloration of skin. Chloramphenicol causes gray baby syndrome, which is a serious and often fatal condition that affects premature neonates receiving systemic chloramphenicol. Renal and hepatic dysfunctions result in toxic elevation of the drug usually observed within 2 to 9 days and is manifested by development of abdominal distention, vomiting, hypothermia, cyanosis, and cardiovascular instability. Vasomotor collapse manifested as mottling of skin and eventual ashen-gray skin discoloration; hence, the name occurs.[50] Tetracyclines, particularly minocycline, are known to induce a dose-dependent dyschromia that most frequently affects areas of previous inflammation, as well as the shins, ankles, and arms.[51] Three distinct types are described with minocycline, including[1] type 1, which is a blue-black pigmentation at the site of scarring or prior inflammation due to deposition of minocycline,[2] type 2, which is a blue-gray pigmentation affecting normal skin, mainly the legs, and[3] type 3, also called dirty skin syndrome, that appears as muddy pigmentation due to increased melanin in sun exposed areas.[52,53]

Cardiopulmonary drugs may also induce gray skin. Amiodarone is a coronary vasodilator used in the treatment of ventricular arrhythmias that are refractory to other medications. Several systemic and dermatologic adverse effects are attributed to amiodarone, such as pulmonary fibrosis, thyroid affection, fulminant hepatitis, photosensitivity, and cutaneous hyperpigmentation, which affects 2% to 5% of patients. The pigmentation is characterized clinically by progressive blue-gray discoloration of predominantly sun-exposed areas. The pigmentary changes occur after several months and at doses greater than 400 mg/d. Cessation of therapy may not diminish the condition.[54] Pirfenidone, a novel antifibrotic drug, is effective in the treatment of idiopathic pulmonary fibrosis, which is a fatal lung disease characterized by chronic and progressive lung fibrosis.[55] Blue-gray pigmentation of sun-exposed areas, in addition to photosensitivity, are among its common cutaneous adverse effects. Adequate photoprotection and reduction of the dose of pirfenidone are effective treatments.[55,56]

Miscellanous drugs, such as antimalarials and antipsychotics, are known to induce gray pigmentation. In up to 25% of patients receiving antimalarials for more than 4 months, a blue-gray or purple color occurs. Although the gray is commonly seen in the pretibial area, other sites include the nail bed, face, and hard palate. The color is reversible, and it is due to increased epidermal pigmentation and dermal hemosiderin deposition (Figure 6).[57]

Antipsychotic medications produce adverse cutaneous effects in approximately 5% of patients. The use of henothiazines, imipramine, or desipramine frequently results in a progressive slate or blue-gray pigmentation in sun exposed areas of the skin. Histopathologically, the gray pigmentation is due to drug-melanin complexes along the basement membrane and their deposition within the dermal macrophages.[58] A newer antiepileptic ezogabine (retigabine) causes blue-gray mucocutaneous discoloration that affects the face, lips, hard palate, conjunctivae, and nails.[59]

Conclusions

Clearly, the gray discoloration of the skin can be observed in several hereditary and acquired diseases and that it is not the gray that is important but the underlying disease that can be fatal. With the introduction of new drugs and the growing desire for alternative medicine, more chemicals will be incriminated. Awareness of the diseases that may

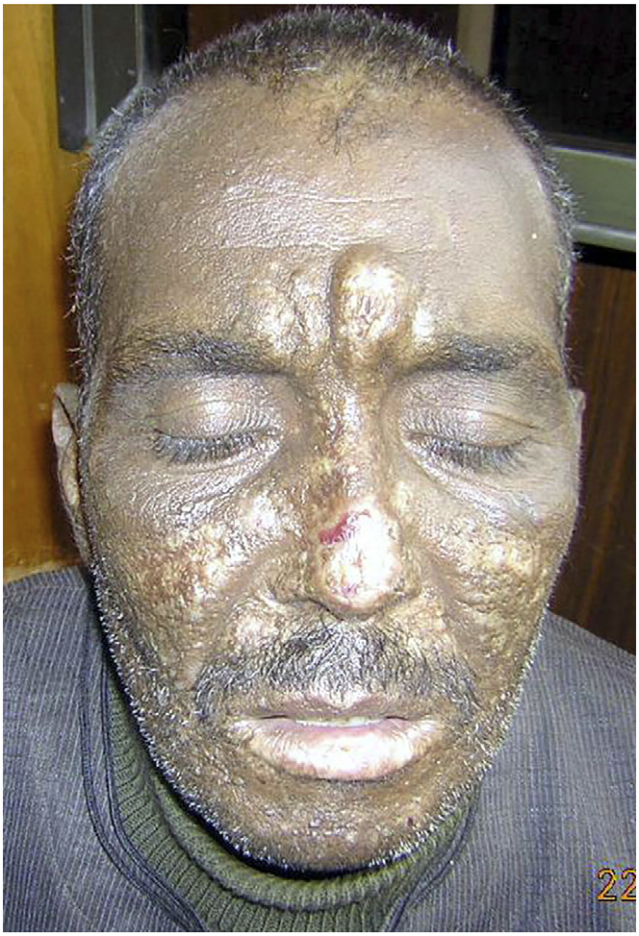

Fig. 6 A patient showing gray discoloration of the face appearing few months while on an antimalarial for treatment of discoid lupus erythematosus and marked photosensitivity. Swelling on the forehead is an unrelated lipoma.

manifest with gray discoloration helps in rapid establishment of the diagnosis, limiting the differential diagnoses and early treatment that can save lives.

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