Disorders of Pigmentation in Infants and Children

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Disturbances of melanin pigmentation in children comprise a heterogeneous group of diseases with different etiologies. These include genetic, metabolic, endocrine, nutritional, chemical, physical, and inflammatory disorders (see Table 1).

Disorders of Hypopigmentation

Vitiligo

Vitiligo is an autoimmune disorder characterized by ivory-white patches secondary to melanocyte destruction. The disease is inherited as autosomal dominant with variable penetrance and is estimated to affect 1–2% of the population.1 Thirty percent of patients have either a positive family history of vitiligo or a history of halo nevi or premature hair graying.2,3 Vitiligo usually affects young adults, with 50% of cases occurring before the age of 20 and 25% before the age of 8 years.4 The disease is uncommon in infancy.

In most cases, symmetrical lesions develop on sun-exposed areas like the dorsa of hands, the face, and neck.5 Other favored sites include body folds like the axilla and groin and body orifices such as the mouth, nose, umbilicus, genitalia, and anus. Vitiligo lesions can also arise over bony prominences like the elbows and knees. Lesions are usually variable in size and shape and consist of well-defined depigmented macules and patches. Loss of pigment may not be apparent in fair-skinned individuals but may be disfiguring in blacks. Vitiligo can appear at sites of trauma or sunburn (Koebner's phenomenon).

A variant of vitiligo is the segmental type, which consists of asymmetrically distributed, depigmented macules confined to one nerve segment (Fig 1). This form is more common in children and is highly associated with autoimmune disorders and premature graying.6

Associations

There is a 10–20% incidence of vitiligo in endocrine autoimmune disorders like Hashimoto’s thyroiditis, diabetes mellitus, polyendocrine deficiencies, and parathyroid abnormalities.7 In addition, patients with lymphoma, leukemia, myasthenia gravis, scleroderma, and alopecia areata have a higher incidence of vitiligo. It is estimated that 20% of patients with malignant melanoma have vitiligo, and its presence is a poor prognostic factor.2,8 Vitiligo patients are prone to multiple ocular abnormalities, including discrete depigmentation in the choroid and retinal pigment epithelium, chorioretinitis, uveitis, and iritis.

The Vogt-Koyanagi-Harada syndrome is a rare disorder characterized by bilateral uveitis, alopecia, vitiligo, deafness, and possible meningeal irritation.9 The Alezzandrini syndrome consists of bilateral deafness with unilateral degenerative retinitis, unilateral vitiligo and poliosis.10

The differential diagnosis of vitiligo includes postinflammatory hypopigmentation, pityriasis alba, tinea versicolor, albinism, and the ash leaf macule of tuberous sclerosis.

Course and Treatment

The course of vitiligo is one of remission and exacerbation. Complete spontaneous repigmentation is unusual. Partial and temporary repigmentation has been reported in children for lesions of <2 years’ duration and in summer. The repigmentation process is slow, and usually the face and trunk respond better than the dorsa of hands and feet.11

Localized patches of vitiligo can be treated with topical steroids (class III); a good response occurs in 30–50% of patients.12–14 Narrow-band UVB (311 nm) therapy is an effective and valuable option for the treatment of extensive vitiligo in children.15 Topical psoralen followed by sun or UVA exposure should be reserved for compliant patients because of the risk of phototoxicity and sunburn.16 Oral psoralen with UVA is recommended for children > 10 years.17 Significant repigmentation is seen in up to 30% of cases. Preliminary studies using topical calcipotriol in combination with either sun exposure or oral psoralen and UVA have shown some beneficial results.18,19 In unresponsive, localized, stable
vitiligo patches, autologous skin graft or topical 5-fluorouracil with epidermal abrasion can be attempted.\(^{20,21}\)

If vitiliginous patches affect > 50% of the body, then depigmentation with 20% monobenzyl ether of hydroquinone or a Q-switched ruby laser may be an option.\(^{11,22}\)

**Albinism**

Albinism is an uncommon disorder characterized by congenital lack of pigment in the skin, hair, and eyes. There are two major forms of the disease, the oculocutaneous and the ocular. In oculocutaneous albinism, melanin synthesis is affected in the melanocytes of the skin, hair, and eyes, while in the ocular form, it is limited to the eyes.

Oculocutaneous albinism consists of several variants; most are inherited as autosomal recessive.\(^{17}\) In whites, the skin is milky white, and the hair is white to yellow or sometimes light brown (Fig 2). Affected individuals have pink pupils and grey-blue irises and suffer from photophobia. In blacks, the skin is usually white or lightly tanned with freckles on sun-exposed areas. The eyes are blue or hazel and the hair is blond. The number of melanocytes and melanosomes is normal; however, there is no melanin production because of mutations in the tyrosinase gene that result in inactive, less active, or temperature-sensitive tyrosinase.\(^{23}\)

The Hermansky-Pudlack variant of oculocutaneous albinism is characterized by a bleeding tendency secondary to a platelet storage defect. Waxlike, ceroid depositions are found in the lungs, reticuloendothelial system, oral and intestinal mucosa, and urine.\(^{24}\)

The Chediak-Higashi syndrome of oculocutaneous albinism is characterized by giant lysosomal granules in leukocytes, platelets, and other cells.\(^{25}\) Major manifestations include recurrent infections, bleeding tendency, and neurological abnormalities. Fifty percent of patients die before the age of 10 secondary to hemorrhage or infection.\(^{26}\)

In ocular albinism the abnormal pigmentation is limited to the eyes. Male patients often present with iris...
translucency, photophobia, and nystagmus. Female patients usually are less affected.

Piebaldism

Piebaldism is an autosomal dominant disorder characterized by congenital patches of depigmentation that lack melanocytes. These include a white forelock, a depigmented triangular patch over the forehead and scalp, and variable symmetrical patches over the body. Hyperpigmented thumbprint macules may be seen within the patches of leukoderma (Fig 3). Associated abnormalities include heterochromic irises, motor incoordination, mental retardation, and defective cell-mediated immunity. Piebaldism results from mutations of the kit proto-oncogene (chromosome 4), which encodes a cell surface receptor for the stem cell growth factor.

Hypomelanosis of Ito

This is a neurocutaneous disorder that is usually sporadic, although there have been some reports of autosomal dominant inheritance. The disorder is characterized by bilateral, asymmetrical, hypopigmented macules in a whorled or streaked pattern, parallel to one another and often following Blaschko’s lines. The trunk and extremities are usually involved. Lesions may be present at birth or appear early in childhood; affected areas increase in number and extent initially, then stabilize, and tend to fade with time. Melanocytes may be decreased, are usually poorly dendritic and have few small melanosomes. The disease is often associated with neurological, musculoskeletal, and ocular abnormalities. These include seizures, mental retardation, developmental delay, macrocephaly, scoliosis, limb defects, hypotonia, strabismus, nystagmus, and hypertelorism, among others. In addition, alopecia, nail ridging, and dental anomalies have also been reported. Abnormal chromosomal patterns have been found in many cases of hypomelanosis of Ito, and the disorder seems to be the result of genetic mosaicism.

Nevus Depigmentosus

This uncommon congenital, nonhereditary, hypomelanicotic lesion appears mostly over the trunk as a unilateral hypopigmented macular patch with irregular, serrated borders (Fig 4). The patch is off-white and remains stable in its size and distribution throughout

Figure 2. Oculocutaneous albinism in a child (Courtesy of Dr. Shukrallah Zaynoun).

Figure 3. Melanotic macules within patches of leukoderma in piebaldism (Courtesy of Dr. Shukrallah Zaynoun).

Figure 4. Nevus depigmentosus over the arm that appeared at 5 months of age (Courtesy of Dr. Shukrallah Zaynoun).
life. It has very rarely been associated with seizures and limb hypertrophy. On histopathology, there is a normal complement of melanocytes but a reduction in the number of melanosomes in melanocytes and keratinocytes as well as membrane-bound melanosomal aggregates. Nevus depigmentosus has to be differentiated from segmental vitiligo, hypomelanosis of Ito, and the ash leaf spot of tuberous sclerosis.

Pityriasis Alba

Pityriasis alba is a very common finding in prepubertal children with a personal or family history of atopy. Lesions most commonly appear on the face, neck, and arms. They consist of ill-defined, hypopigmented macules, a few centimeter in size with a powdery white scale (Fig 5). Extensive pityriasis alba involving the trunk and extremities is an unusual form observed mainly in adolescents and young adults.

Tinea Versicolor

Tinea versicolor, uncommonly reported in children, is a chronic, asymptomatic skin infection caused by the yeast Malassezia furfur. The condition is common in warm, humid climates and is characterized by hypopigmented, scaly macules located mainly over the upper trunk in adults, whereas in children there is a preferential facial localization (Fig 6).

Mycosis Fungoides

Hypopigmented mycosis fungoides is an uncommon presentation of the disease. It has an earlier age of onset and is more prevalent in individuals with dark skin color. Hypopigmented macules and patches that may be scaly, most commonly located over the trunk, characterize it clinically (Fig 7). The diagnosis is often delayed because it may be mistaken for vitiligo, tinea versicolor, generalized pityriasis alba, and postinflam-
mostly on the face, shoulders, and upper back. They darken in summer and fade in winter. Freckles could be inherited as an autosomal dominant trait in individuals with red-blond hair and blue eyes. They are present in several disorders, including xeroderma pigmentosum, progeria, and neurofibromatosis. The melanocyte number is normal.

Lentigines

Lentigines are small, dark brown to black, oval to circular macules usually 1–2 cm in diameter. They appear in childhood and increase in number up to adulthood. Lesions can appear on any skin surface, including mucous membranes. Lentigines are unaffected by sun exposure, and their color is darker and more uniform than freckles. They have an increased number of melanocytes. Multiple syndromes manifest lentigines as part of their cutaneous manifestations, and these include Peutz-Jeghers, Leopard, and Lamb syndromes.

Peutz-Jeghers Syndrome is an autosomal dominant disorder characterized by hyperpigmented macules and multiple gastrointestinal polyps. Multiple brown, blue, or black macules can appear on the lips, buccal mucosa, perinasal, periorbital, perianal, and labial regions as well as on the dorsa of fingers and toes and on the palms and soles (Fig 8). The majority of the gastrointestinal polyps are found in the small intestine; they have a low malignant potential. This syndrome usually occurs in the second decade of life and is uncommon in children. Presenting symptoms in the pediatric age group include abdominal pain, melena, intussusception, and hematemesis. Patients with Peutz-Jeghers Syndrome are also at risk of developing carcinomas in the uterus, ovary, breast, and other organs.

The Peutz-Jeghers Syndrome gene (LKB1) encoding a serine/threonine kinase STK11 was mapped to chromosome 19p13.3. LKB1 is a tumor suppressor gene; germline mutations of this gene have been detected in many Peutz-Jeghers Syndrome families.

Treatment consists of relieving obstructions and of multiple individual polypectomies with regular endoscopic and cytological examinations.

Café au Lait Macules (CALMs)

CALMs are oval to round, light brown macules measuring 0.5–20 cm in diameter. They appear at birth or shortly thereafter. They are present in 10–20% of normal people; however, they can be a sign of neurofibromatosis as 90% of neurofibromatosis patients have multiple CALMs. According to Growe and Schull, the presence of six or more CALMs, each 1.5 cm in diameter, or 0.5 cm in prepubertal children, is a presumptive sign of the presence of neurofibromatosis. Other syndromes that have a definite association with CALMs are McCune-Albright syndrome, Watson syndrome, and ring chromosome syndromes. CALMs have also been reported in tuberous sclerosis, epidermal nevus syndrome, ataxia telangiectasia, Bloom's syndrome, LEOPARD syndrome, Silver-Russell syndrome, and Turner syndrome. In CALMs, there is an increased number of melanosomes with a variable number of melanocytes.

References


Pharmacy Labels—From the collection of Lawrence Charles Parish, MD, Philadelphia, PA.