



Chapter 16

Congenital Absence of Pigmentation in Skin and Hair with Diminished Vision

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A 6-year-old boy, born out of a consanguineous marriage presented with white skin and hair, photophobia and diminished vision. The onset was congenital. There was complete lack of pigment in the skin, hair, eyebrows and eyelashes (Fig. 16.1). The family history was absent. Ophthalmologic examination revealed bluish translucent iris, nystagmus, reduced visual acuity (1/10) and foveal hypoplasia. He had normal physical and mental development. His routine laboratory parameters (including peripheral blood smear) were within normal limits. No other congenital or systemic abnormalities was found. Based on the clinical details and physical examination, what is the diagnosis?

1. Chediak-Higashi syndrome
2. Cross Syndrome
3. Oculocutaneous albinism
4. Hermansky-Pudlak syndrome

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FIGURE 16.1 Generalized loss of pigmentation of skin and hair.
(Courtesy: Dr. Piyush Kumar)

Diagnosis

- Oculocutaneous albinism

Discussion

Oculocutaneous albinism (OCA) is the most common inherited, heterogeneous disorder of generalized hypopigmentation involving skin, hair and eyes. It has five forms: OCA1A, OCA1B (yellow albinism), OCA2 (brown albinism), OCA3 (rufous/red type) and OCA4 (least common) [1]. The global estimated frequency of OCA is 1:20000. The major two forms, OCA1 (tyrosine-negative) and OCA2 (tyrosine-positive) constitute 90% of the cases seen worldwide and OCA2 is the most prevalent form [2]. OCA3 and OCA4 are rare.

In OCA1A, genetic mutations in TYR gene completely abolish tyrosinase activity, while mutations rendering some enzyme activity result in OCA1B allowing some accumulation of melanin pigment over time. The gene implicated in OCA2 is P, important for normal processing and transport of melanosomal proteins such as TYR and TYRP1. Mutations in Tyrp1 gene in OCA3 result in delayed maturation and an early degradation of Tyr. Mutations in the membrane-associated transporter protein gene (MATP) cause OCA4 [1].

OCA1A is the most severe type showing complete absence of melanin production throughout life. The skin, hair, eyelashes and eyebrows are all white, and skin does not tan. Iris are light blue to pink and completely translucent along with intense photophobia and visual acuity 1/10 or less. The prominent ocular anomalies include congenital nystagmus, reduced pigmentation of the retinal pigment epithelium, foveal hypoplasia, misrouting of the optic nerve fibres at optic chiasma resulting in strabismus and reduced stereoscopic vision [2]. In OCA1B, OCA2 and OCA4, the hair and skin may develop some pigment with time, irises are green/

brown and visual acuity improves. OCA3 patients have red hair and reddish brown skin with no detectable visual anomalies are not always detectable [1]. A few other unusual ocular changes are Duane retraction syndrome, corneal mesodermal dysgenesis, and congenital glaucoma. Risk of development of non-melanoma skin cancer is also high in OCA [3].

Chediak–Higashi syndrome (CHS) is a rare, autosomal recessive multi-system disorder caused by mutation in *LYST* gene. It is characterized by hypopigmentation of the skin, eyes and hair, prolonged bleeding time, easy bruisability, recurrent infection, abnormal NK cell function and peripheral neuropathy [4]. Most of the patients develop an accelerated phase of the disease characterized by fever, jaundice, hepatosplenomegaly, lymphadenopathy, pancytopenia, coagulopathy and neurological abnormalities, unlike in OCA. The presence of massive peroxidase-positive lysosomal inclusion in the leukocytes, fibroblasts and melanocytes is diagnostic [4].

Hermansky-Pudlak syndrome is a rare autosomal recessive disorder characterized by reduced pigmentation of skin, hair, iris and retina, platelet storage-pool deficiency and lysosomal accumulation of ceroid lipofuscin in various tissues including reticuloendothelial system. It mostly results from the mutation in *HPS 1* and *3* genes associated with the formation of lysosome-related organelles. Although oculocutaneous presentation simulate the picture of OCA but the systemic findings such as bleeding diathesis, interstitial lung fibrosis, granulomatous colitis, cardiomyopathy and renal dysfunction help to differentiate it from OCA [5].

Cross syndrome or Cross-McKusick-Breen Syndrome is an inherited (autosomal recessive) oculocerebral syndrome, characterized by hypopigmentation of the skin and hair, and oculocerebral abnormalities. The common features shared with OCA include autosomal recessive trait, unusually light skin color, silvery-gray hair, hypopigmented iris and nystagmus [6]. There are certain other characteristic findings which are frequently present in this syndrome. These are delayed developmental milestones (psychomotor

retardation), corneal opacities, microphthalmia, iris atrophy, cataract, optic nerve atrophy, gingival fibromatosis, high arched palate, oligophrenia, dolichocephaly, athetosis, spastic paraplegia and Dandy-Walker type cystic malformation of posterior fossa [6].

Genetic counseling and prenatal diagnosis is an integral part of management of OCA. The gene mutational analysis is done by denaturing high performance liquid chromatography and single stranded conformational polymorphism followed by DNA sequencing.

Treatment is given according to the types and severity of OCA. Bifocal glasses help to correct low visual acuity and dark/photochromic lenses are used to prevent photophobia. Surgery of the ocular muscles may be done to cure nystagmus. For strabismus, it may be necessary to patch one eye in children to force the non-preferred eye to be used. Most people with severe forms of OCA do not tan and easily get sunburned, therefore sunscreens are recommended with at least a sun protection factor of 15.

Key Points

- OCA is the most common inherited disorder of generalized hypopigmentation due to genetic defects in melanin biosynthesis.
- It has five forms: OCA1A, OCA1B, OCA2, OCA3 and OCA4.
- OCA2 is the most common type and affects 1:4000 of the population in some parts of Africa.
- OCA1A is most severe type with complete lack of pigmentation in skin, hair and eyes. There is no pigment synthesis with age.
- Other types are milder and develop pigmentation over time.
- Hematologic tests, ophthalmic and systemic examination are mandatory to rule out other syndromic entities presenting with partial OCA.

References

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