Unseen Impairment: Pediatric Primary Care Management of Oculocutaneous Albinism 2

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ABSTRACT

Oculocutaneous albinism type 2 (OCA2), an autosomal recessive mutation of the *OCA2* gene on chromosome 15, results in ocular and dermatologic manifestations. In primary care, nurse practitioners must detect the condition, refer to specialists, provide psychosocial support, refer to community resources, and coordinate care for children with this disorder. This article discusses the pathophysiology, epidemiology, and differential diagnosis of OCA2 as well as a discussion of the clinical implications and nurse practitioner management of the condition. The unique psychosocial effects of having the OCA2 mutation are less frequently explored in the current literature and are highlighted in this article.

Keywords: genetics, oculocutaneous albinism, pediatric primary care, visual impairment

The diagnosis of albinism can be confusing for parents, and adjusting to life with the condition can be difficult for affected children. Speaking about the experience of raising her daughter with albinism, 1 mother said, "We thought she was a super alert baby, but around eight weeks we realized she actually wasn't tracking at all, her eyes were just moving back and forth. Suddenly everything changed. We didn't know what she needed and no one told us what to expect. It would have been nice to know sooner what resources were available to us." Oculocutaneous albinism type 2 (OCA2) is a complex subtype of albinism associated with a wide range of visual impairments without the traditional physical stigmata of disease. Children with the condition may face different obstacles than those typically discussed with relation to albinism. This article will discuss the pathophysiology, epidemiology, clinical presentation, and differential diagnosis. The unique developmental and psychosocial effects of having the OCA2 mutation are less frequently explored in the current literature and are highlighted in the article.

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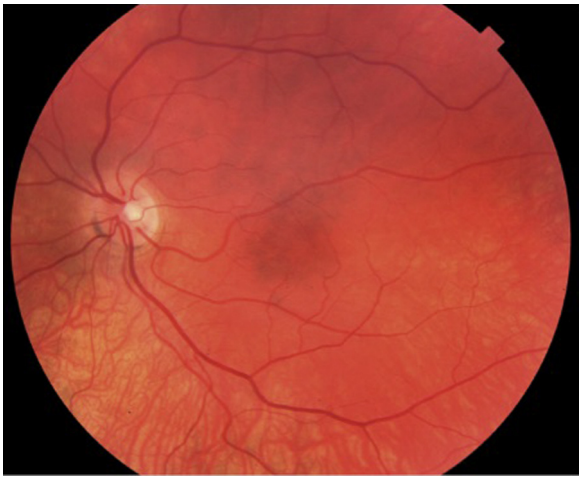
OVERVIEW

OCA2 is a form of albinism, a genetic disorder consisting of varying degrees of hypopigmentation and characteristic ocular features.[1] In general, clinical features of OCA2 are milder than oculocutaneous albinism type 1 (OCA1) because there is some degree of melanin production with age. The typical presentation of OCA2 is on a spectrum of severity.[2] Most OCA2 patients are detected by the 4th month of life because of nystagmus; strabismus manifests later.[3] Other ocular findings include light irides, blonde fundi, foveal hypoplasia with abnormal vasculature (Figure 1), and mild to severe deficit in visual acuity.[1]

Phenotypic presentation of OCA2 includes white to fair skin with or without scattered pigmentation and hair color ranging from blond to black. Pigmentation of those with OCA2 ranges from minimal to near normal when compared with others of the same family or ethnicity.[3] Brown OCA, recently identified as a variant of OCA2 found primarily in African and African American

Figure 1. Foveal hypoplasia and abnormal retinal vessels in a normally avascular area in the fundus of this patient with OCA2. Also note peripheral and midperipheral blondeness consistent with albinism.



populations, presents with light brown skin and hair. Brown OCA among other ethnic groups presents as slightly less pigmented than direct family members but in line with ethnicity.[4]

PATHOPHYSIOLOGY

OCA2 is an autosomal recessive disorder of the *OCA2* gene (originally called the *P* gene) on chromosome 15. The *OCA2* gene codes for a melanosomal membrane protein. The gene, on the long arm of chromosome 15, 15q11.2-11.3, controls both the entry of tyrosine and the pH balance of the melanosome.[1] Tyrosine is a precursor to melanin, and a mutation will result in a dysfunctional melanosome that cannot properly produce pigment.[5] Unlike in OCA1, OCA2 patients show positive tyrosinase activity, thus increasing pigmentation.

The variability in the phenotype is caused by whether the child's mutation is compound heterozygous or homozygous.[3] Nonpathogenic polymorphisms of the *OCA2* gene may be related to variation in iris color in all people.[1] In 2015, the Human Gene Mutation Database categorized 178 known mutations of the *OCA2* gene; the majority were missense mutations (91) followed by small deletions (20) and splicing (16).[6,7]

EPIDEMIOLOGY

The prevalence of OCA2 is 1:38,000 to 1:40,000 worldwide across most ethnicities.[3] Among Africans, the prevalence is 1:1,500 to 1:3,900 and among African Americans 1:10,000. Most albinism in these populations is attributable to OCA2 mutations.[3,8] Therefore, children of African ancestry are at highest risk. The mutation carrier prevalence is estimated to be 1:100 worldwide, 1:22 to 1:32 in the African population, and 1:50 or less in the African American population with no documented sex difference.[3]

DIFFERENTIAL DIAGNOSIS

The diagnosis of albinism can be made clinically, with confirmation and subtyping most commonly completed by microarray. In the future, whole exome sequencing may be more accessible.[3] The differential diagnosis of OCA2 should include 4 major categories: 1) other forms of albinism, 2) other genetic conditions, 3) neurologic, 4) ocular conditions that result in infantile nystagmus (Figure 2).

Subtypes of albinism associated with varied systemic abnormalities exist (Supplementary Table 1). Hermansky-Pudlak syndrome is a variant of OCA accompanied by neutropenia, platelet dysfunction, pulmonary fibrosis, and colitis and is more common in the Puerto Rican population.[9] Chediak-Higashi syndrome is an immunologic-associated OCA seen with recurrent bacterial infections, easy bruising, and peripheral neuropathy.[2] Griscelli syndrome types 1 through 3 present with varying degrees of pancytopenia, immunodeficiency, hemophagocytic syndrome, and/or central nervous system dysfunction along with the ocular manifestations of albinism.[10]

Aside from albinism, there are multiple genetic disorders resembling OCA2. Angleman syndrome and Prader-Willi syndrome are both the result of mutations on chromosome 15 on either side of the *OCA2* gene.[11,12] As a result, 1 in 100 patients with either syndrome also has OCA2.[1] Many patients with Angleman syndrome and Prader-Willi syndrome without ocular features of OCA2 will present with cutaneous manifestations.[3] Waanderburg syndrome type 2 presents as hypopigmentation and progressive hearing loss without ocular symptoms; it should be considered in the workup of a hypopigmented patient but will be quickly ruled out in a child with OCA2. FRMD7-related infantile nystagmus (congenital motor nystagmus) is an X-linked disorder resulting