

# Article ▶ Pediatric Patient with Oculocutaneous Albinism: A Case Report

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## ABSTRACT

**Background:** Oculocutaneous albinism (OCA) is a rare genetic disorder that occurs due to a mutation in one of the genes that affects the melanin biosynthesis pathway. OCA is autosomal recessive and affects people of all ethnic backgrounds. Oculocutaneous albinism often presents with nystagmus and pale coloring of the skin and hair. The patient with OCA has normal development, intelligence, fertility, and lifespan.

**Case Report:** A two-month-old female presented with a new-onset intermittent nystagmus. A complete vision exam resulted in a diagnosis of oculocutaneous albinism with nystagmus secondary to foveal hypoplasia. The findings were discussed with the parents, and a follow-up was scheduled. At the five-month follow-up, the patient was progressing well and had a reduction in the amplitude of her nystagmus.

**Conclusion:** Oculocutaneous albinism is often discovered first with a visit to the eye care professional due to a recent onset of nystagmus. Foveal hypoplasia causes an onset of nystagmus between two and three months. Additional ocular manifestations include reduced visual acuity, strabismus, high refractive error, amblyopia, increased decussation of visual fibers, color vision defects, photophobia, transillumination, and hypopigmentation of the retinal pigmented epithelium. Assistance for the child with OCA consists of correcting the refractive error; amblyopia treatment when necessary; and concurrent physical, occupational, and low vision therapy. Communication and collaboration with other medical specialties is warranted throughout life.

**Keywords:** genetic disorder, low vision, nystagmus, oculocutaneous albinism, pediatric

## Case Report

### Initial Visit

A two-month-old female was taken to the emergency department when her parents noted an onset of what they described as intermittent shaky movements of the eyes. The doctor in the emergency department noted intermittent horizontal nystagmus of high frequency that was more prominent in lateral gaze. The patient was referred to the ophthalmology department for a complete eye exam.

The following week, the patient presented to our office for a complete eye exam. The patient's mother accompanied her to the exam. The mother reported the onset of the nystagmus within the past week and believed that it occurred more frequently when the patient was trying to focus on something in particular.

A complete medical history was taken. The child was full term with no complications during birth. She was taking Zantac (ranitidine) for reflux but was otherwise healthy with no known drug allergies. Family ocular history was unremarkable.

Upon examination, it was noted that the patient fixed and followed bright, lighted toys binocularly. She was grossly aligned with no strabismus noted during the Hirschberg test. The pupils were equal in size, round, and reactive to light. No afferent pupillary defect was noted. A large-amplitude, low-frequency, horizontal jerk nystagmus was observed. The patient's overall pigmentation, both skin and hair, was

very fair. The patient was then dilated with one drop of Cyclomydril OU.

Anterior segment evaluation showed light blue irides but was otherwise normal. A mild hyperopic refractive error of +1.75 sphere OU was found with cycloplegic retinoscopy. Posterior segment evaluation revealed foveal hypoplasia in both eyes and a pale fundus bilaterally that was transparent enough to allow visualization of the underlying choroidal vasculature. The remaining posterior ocular structures were unremarkable.

Due to the clinical findings of hypopigmentation and foveal hypoplasia, a diagnosis of ocular albinism with secondary nystagmus was given. The discussion of findings with the mother included the strong possibility of oculocutaneous albinism (OCA) and a high probability of decreased vision for the entirety of the patient's life. Best corrected verbal visual acuity (VA) was unable to be obtained due to age. A more specific VA measurement will be obtained when the child is old enough to complete verbal acuity tests. Tests for recognition VA include but are not limited to Lea Symbols, HOTV, and Allen symbols. A visually evoked potential (VEP) or forced preferential looking could have been performed to obtain resolution VA but was not deemed necessary at that point in time as they would not alter the course of treatment. Close monitoring of the patient and reevaluation of visual behavior was deemed to be necessary, and a six-month follow-up was scheduled.

A referral to a local center for children with visual impairment was provided. The center focuses on young children from birth through preschool. They work with children of varying visual deficiencies to help both the patient and the family learn adaptations in order to provide the best success possible as the child continues to grow. Services focus on the individual child and can include any of the following: orientation and mobility, low vision training, Braille instruction, occupational and physical therapy, and speech training. These services allow them to help prepare the visually impaired child for success in mainstream school environments and beyond.

### Five-month Follow-up Examination

The patient returned for follow-up at the age of 6.5 months. Both parents accompanied the patient for the examination. Neither had any concerns. They noted that her hair had fallen out and grown back in very pale, almost white, in color. The parents had begun the relationship with the local center for children with visual impairment and were very pleased with their interactions thus far. Medical history remained unchanged from the previous visit.

Gross examination showed pale hair and eyelashes, as well as very pale, hypopigmented blue irides. At this time, it was not possible to visualize iris transillumination with gross observation. Transillumination of the iris would be best visualized with the biomicroscope, which was not feasible at this age. Fixation was measured as central, non-steady, maintained at near OD, OS with a 10<sup>A</sup> base down prism. The patient was aligned by unilateral cover test at near with no strabismus noted. A horizontal jerk nystagmus was noted to have a small to moderate amplitude and low frequency. At this exam, one drop of cyclopentolate 1% was instilled in each eye. Cycloplegic refraction revealed -1.00+1.00x090 OD, -1.00+1.00x090 OS. Fundus examination was unchanged from the previous exam, showing an albinotic fundus with foveal hypoplasia OU.

At this follow-up examination, a definitive diagnosis of OCA with secondary nystagmus was made. The parents stated that the patient's pediatrician also agreed with the diagnosis. Because of the obvious clinical diagnosis, genetic testing for verification was not ordered at this time. Decreased visual function and visual impairment were reviewed with the parents. It was discussed that due to the patient's current age, a specific VA was not determined during this exam. Our office did not have a VEP, and as there were no indications that monocular amblyopia existed (secondary to strabismus or anisometropia), it was decided not to pursue forced preferential looking or to refer out for a VEP. The parents agreed with the treatment plan. Had they requested a measurement, the patient would have been scheduled to return for testing with the Teller Acuity Cards.

While glasses were not prescribed at this exam, the possibility of glasses in the future was discussed today due

**Table 1: Type of OCA, Genes Affected, and Genetic Loci**

Name	Abbreviation	Gene Affected	Locus
Oculocutaneous albinism type IA	OCA1A	Tyrosinase (TYR)	11q14.3
Oculocutaneous albinism type IB	OCA1B	Tyrosinase (TYR)	11q14.3
Oculocutaneous albinism type II	OCA2	OCA2 gene (OCA2)	15q12-q13
Oculocutaneous albinism type III	OCA3	Tyrosinase-related protein (TYRP1)	9p23
Oculocutaneous albinism type IV	OCA4	Membrane associated transport protein (SLC45A2)	5p13.2
Ocular albinism	OA	GPR143	Xp22.2

Information for table taken from Online Mendelian Inheritance in Man (OMIM)<sup>12</sup>

to the increasing shift in myopia. When glasses are needed they will include both the refraction and a note for medically necessary photochromic lenses. The photochromic lenses are indicated for the patient's protection from UV light as well as for comfort. Follow-up was scheduled for six months in order to continue to assess visual function and development as well as refractive error.

## Discussion

### Etiology and Genetics

Oculocutaneous albinism is an autosomal recessive disorder that presents with heterogeneous expressivity. Albinism can and does affect all ethnic backgrounds. Prevalence is dependent on subtype but has been reported to have an overall incidence of 1 in 16,000-20,000 live births. Carrier rates have been documented to be as high as 1 in 70.<sup>1-5</sup> Individuals with albinism have normal lifespan, development, intelligence, and fertility.

There are four main categories of OCA, each caused by mutations in a separate gene. The four types, OCA1, OCA2, OCA3, and OCA4, are due to mutations in tyrosinase, the OCA2 gene (formerly known as the P gene), tyrosinase-related protein (TYRP), and a membrane associated transport protein (MATP), respectively, all of which are found at different loci (Table 1).<sup>1,2,4,6-8</sup> There are many phenotype similarities amongst the different types of OCA, and the only definitive way correctly to diagnose the type is by genetic testing.

Ocular pigment has two different origins. The uveal melanocytes are derived from the neural crest, while the retinal pigment epithelium (RPE) melanocytes are derived from the neuroectoderm.<sup>1,8</sup> This explains why an individual can have different pigmentation throughout the ocular structures. In addition, the pigmentation of the iris and skin is determined not by the melanocytes but by the size and number of melanosomes.<sup>1</sup> Different proteins are involved in the melanin pathway, and disruption can happen in any of the steps.

The first type of OCA can be broken down into two subtypes, OCA1A and OCA1B. OCA1A is the most severe

form of oculocutaneous albinism. The patient with OCA1A completely lacks tyrosinase, a key step in the melanogenesis pathway. Because of this pathway breakdown, no pigment formation occurs. This will manifest as pale white skin that does not tan, white hair, and very light blue to pink irides. Due to the complete lack of pigment, patients with OCA1A tend to have the most reduced visual acuity of all albinism patients.<sup>1,2,6</sup>

OCA1B has an overall decrease in tyrosinase enzymatic activity that allows the accumulation of some pigment. Over the course of the first three years of life, the patient may develop some pigmentation of the hair, skin, and eyes. OCA1B also has a temperature-sensitive subtype that presents with hypopigmented hairs in the warmer-temperature areas of the axial and pubic regions and body hair with pigment in the colder-temperature extremities.<sup>1,6-8</sup>

OCA2 is caused by mutations in the OCA2 gene, which assists in the regulation of the amount of tyrosine. The phenotypes in type 2 OCA vary widely, with even black hair being reported in some cases. Because the phenotype presentation can appear as a very mild form of albinism, visual acuity prognosis is often more positive in patients with this genetic mutation.<sup>1,2</sup> This form of OCA is more prevalent in sub-Saharan African populations.<sup>6</sup>

A mutation in the tyrosinase-related protein gene is the cause for OCA3. The mutation of TYRP1 often presents with red hair and reddish-brown skin. It is far more common in patients of southern African descent than other ethnic backgrounds. Type 4 OCA is related to a mutation in the MATP gene SLC45A2. It is phenotypically very similar to OCA type 2, with a wide spectrum of clinical presentation.<sup>1,2,6,7</sup>

Ocular albinism (OA) is an X-linked recessive trait. It presents with the ocular manifestations but lacks the cutaneous manifestations found in other forms of albinism. In many cases, the female carrier presents with a “mud-splattered” fundus, patches of pigment next to patches of hypopigmentation in the retina.<sup>1,4,7</sup> This appearance is due to lyonization, the phenomenon that allows X-linked recessive genotypes to be partially expressed.

With almost 200 mutations in the TYR gene alone, it is highly unlikely that all genetic abnormalities related to albinism have been discovered.<sup>2</sup> Additional research and case studies are likely going to continue to provide us with additional mutations that contribute to albinism.

## Clinical Presentation

The clinical presentation for OCA varies widely depending on the specific genetic mutation. In addition, the heterogeneous nature of the genetic mutation allows a spectrum of phenotypic expression to occur. Typically, skin, hair, and ocular structures are either hypopigmented or lighter in pigment than in other people with the same ethnic background. In families of darker-pigmented individuals, diagnosis can often be made at birth due to the obvious lack of pigment in the child. In

children whose family background contains lighter-pigmented individuals, diagnoses can be delayed.

Skin color can fluctuate from no pigment to normal pigmentation. Furthermore, patients with one type of albinism (OCA1B) can develop some pigmentation over the first one to three years of life. Hair color, including eyelashes and eyebrows, varies from no pigment to brown.

Ocular presentation also has a wide spectrum, and lack of pigment will be evident during examination due to iris transillumination, foveal hypoplasia, and hypopigmentation of the RPE. Additional ocular features include nystagmus, high refractive error, reduced visual acuity, possible strabismus and amblyopia, photophobia, color vision defects, and an increase in decussation of optic fibers.<sup>1,6-9</sup>

Variability of pigment in the iris structures manifests as a range of colors from pink to dark brown. Iris transillumination is a rare finding in normal, healthy individuals, even in those with lighter pigmentation. Transillumination can range from small specs to so diffuse that the outline of the intraocular lens can be seen through the iris.

Foveal hypoplasia is a constant in all types of albinism and is often the visually limiting factor. Visual acuity in patients with albinism spans from 20/20 to less than 20/400.<sup>2,7-10</sup> The RPE is often hypoplastic and can be translucent, allowing the choroidal vascular structures to be seen with binocular indirect ophthalmoscopy. This is often viewed more readily in the mid-peripheral and peripheral retina.<sup>1</sup> The hypopigmentation of the iris and retinal structures contributes greatly to the photophobia that is reported by the majority of albinism patients.

Nystagmus is not present at birth but develops in the second to third month of life.<sup>7,8</sup> Typically, the fovea begins to develop during this time period, allowing the eyes to fixate on their target. With hypoplasia of the fovea, the eyes develop a searching motion. In lighter-pigmented families, the onset of nystagmus is often the first indication of the disease and warrants a visit to their eye care professional. The nystagmus seen with albinism falls under the category of infantile nystagmus syndrome (formally known as congenital nystagmus). Nystagmus generally begins with a large amplitude and low frequency. Over time, the nystagmus may improve, but it is important to note that any type of nystagmus is possible: horizontal, vertical, or rotary.<sup>1,4,8</sup>

In an individual without albinism, the nasal retinal fibers, which make up 55% of the total fibers, cross at the optic chiasm. An individual with albinism has a larger amount, up to 75-85% of the fibers, decussating to the contralateral side.<sup>1,8</sup> The increase in decussating fibers is not due to an increase in nasal fibers, but rather to a portion of the temporal retinal fibers also crossing at the chiasm. It was previously believed that only patients who had an increase of crossing fibers could truly be diagnosed with albinism, but recent literature has documented the genetic mutation for albinism in patients without the abnormal decussation.<sup>1</sup> The miswiring of the

optical system contributes to the increase in strabismus and reduced stereopsis in this patient population.<sup>2,8,9</sup>

High refractive errors are common in albinism patients. Literature indicates that the refractive errors have no predilection for one type and can be hyperopic, myopic, or astigmatic.<sup>3,9</sup> Due to the high incidence of strabismus and larger refractive errors, amblyopia can occur and needs to be considered if the measured corrected visual acuity is more than one line different between the two eyes. If the child is too young to respond to verbal VA tests, forced preferential looking or a VEP can be utilized to gain insight into their visual abilities. Both tests will result in resolution visual acuities. While resolution visual acuity cannot be compared directly to recognition VA, it can give the doctor insight as to differences in acuities between the two eyes, and amblyopia treatment can be initiated with more confidence.<sup>8</sup>

### Associated Syndromes

While OCA is generally found without any concurrent systemic conditions, it is also known to be associated with certain syndromes. Common syndromes in which albinism is a component are Hermansky-Pudlak syndrome and Chédiak-Higashi syndrome. Both syndromes have vesicular formation irregularities.<sup>1,4,6</sup>

Hermansky-Pudlak syndrome is more common in patients of Puerto Rican descent, with rates of 1 in 1800 reported.<sup>2,11</sup> Vesicles affected include platelets, which can result in bleeding problems. Furthermore, some individuals with Hermansky-Pudlak syndrome have ceroid lipofuscin deposits, which can cause additional health problems. These problems include granulomatous colitis, interstitial lung disease, renal failure, and/or cardiomyopathy.<sup>1,6-8,11</sup> Chédiak-Higashi syndrome patients have increased susceptibility to bacterial infections.<sup>6-8</sup> Due to the additional health complications that exist with Hermansky-Pudlak syndrome and Chédiak-Higashi syndrome, additional testing for the patient with OCA may be warranted. Particular care and timely referral should occur in patients with particular backgrounds or frequent bleeding, bruising, or infections.

Additional syndromes include Griscelli syndrome, Waardenburg syndrome type II, Elejalde syndrome, Angelman syndrome, and Prader-Willi syndrome. In Prader-Willi and Angelman syndromes, the albinism is often OCA2.<sup>1,2,8</sup>

### Ocular Treatment and Follow-Up

Clinical diagnosis of albinism usually requires a referral to an eye care specialist. In some cases, where the patient's family has darker pigmentation, diagnosis can be made at birth. Complete ocular examination is necessary at diagnosis and will be essential throughout the patient's life. Due to the increased incidence of high refractive error, strabismus, and amblyopia, examinations may need to be more frequent during the first few years of life, as frequent as every six months. Once the child

is older, if there is no concurrent strabismus and/or amblyopia, the visits can be spread out to once per year.

Since many patients have nystagmus, VA may be better binocularly or when taken through a fogging lens, which helps to minimize any latent nystagmus that may be present. Even still, it is prudent to obtain monocular VA in order to rule out amblyopia. If amblyopia occurs due to refractive error differences or strabismus, it is critical to ensure that proper treatment is given.

If necessary, glasses can help improve vision. Many practitioners believe that visual acuity will still be diminished and may not provide the option to the parents or the patient. It has been shown that adaptation to glasses, when necessary, is excellent and can improve overall acuity.<sup>3</sup> Photochromic lenses can be very helpful and should be strongly considered, especially in the pediatric patient who may not be able to verbalize their discomfort. In addition, these lenses will help to protect the ocular structures from ultraviolet light; a medically necessary indication can be included with their glasses prescription.

Special testing can help to determine the level of foveal hypoplasia and the percentage of optic fibers that decussate. Optical coherence tomography can be used to determine the true amount of hypoplasia in the macula. This test can be difficult due to the secondary nystagmus, but studies have shown its feasibility to help reveal structural changes to the retina. Typically, complete foveal hypoplasia will show as a tram-track appearance on the scan and a complete lack of foveal depression. If some foveal depression exists, better VA is expected.<sup>4,9</sup> Verification of optic fiber decussation to the contralateral side can be determined by monocular VEP. The VEP can be used to help diagnose albinism in a patient with minimal hypopigmentation but is not necessary for the diagnosis in all cases.<sup>1,3,4,8</sup>

Because of the overall reduced acuity, it is crucial to monitor the child's developmental milestones and to seek assistance from other specialties such as physical or occupational therapy. As the child begins school, special accommodations may need to be instituted. An individual educational plan (IEP) can be instituted to allow the use of low vision aids and special accommodations throughout the child's educational career. Often higher-contrast papers, magnifiers, and enlargement machines (closed circuit televisions, iPads, etc.) are the most beneficial. As the patient ages and enters the work force, additional accommodations such as added time to complete assignments or special equipment may be necessary.<sup>1,2,6,10</sup>

### Additional Considerations:

Patients with OCA have an increased risk of skin cancer due to their lack of pigment. Avoidance of direct sunlight, particularly during the critical times between 10:00 am and 3:00 pm when the UVA and UVB rays are at their strongest, is recommended. In addition, the patient should be diligent about using sunscreen and protective clothing. Referrals

to dermatology should be considered early in life. The dermatologist can discuss more details and risks with the patient and parents and will most likely schedule frequent exams to check for any abnormal skin changes.<sup>2,11</sup>

In some situations, patients may have psychological issues associated with being different than their peers. In those instances, psychological counseling is warranted. In some areas of the world, albinism patients are treated very poorly, and even killed, as historical superstitions still prevail.<sup>1,6</sup>

Genetic testing is often unnecessary for diagnosis since the clinical presentation is so well defined. In some instances, genetic testing may be of benefit to the patient or family members. If the parents of a child with albinism are considering additional children, their risk of having another child with OCA is one in four. Any unaffected children by the same parents have a 67% chance of being a carrier of the trait. If a patient with oculocutaneous albinism has children, their offspring with either be carriers or will express the trait themselves, depending on the genetics of the second parent. If the OCA patient's spouse is a carrier of the trait, the chance of their children having OCA increases. The patient and spouse may wish to undergo genetic testing before reproduction. Prenatal testing is possible if requested, but warrants a detailed conversation with a geneticist.<sup>2</sup>

## Conclusion

Albinism is a rare condition that affects individuals of all ethnic backgrounds. Since the onset of nystagmus is often the first sign, many of these patients are diagnosed during a visit to their eye care provider. It is critical for the eye care professional to be able to detect the clinical signs of albinism so that the family and patient do not undergo unnecessary medical testing. In addition, frequent eye exams are necessary during the first few years of the patient's life. The examinations must routinely verify any need for glasses as well as ensure that no amblyopia or strabismus has developed. If necessary, the practitioner must be prepared to treat these conditions accurately and efficiently.

Permanent vision impairment is a constant in all forms of OCA. Patients and their families may need counseling both to understand and to accept the reality of visual impairment, which has a wide prognosis depending on the expressivity of the albinism. As the child ages, an IEP and special accommodations are often necessary during the school years. These accommodations can be continued throughout the patient's life, even into the working years. Patients with OCA

have normal development, intelligence, and lifespan. With proper care, the life of a patient with albinism is not restricted beyond the visual limitations.

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