What You Should Know About Albinism and the Eye

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Albinism is a general name given to a family of diseases in which the production of melanin (a dark pigment) is disordered. There are many pigmented tissues in the body including the skin, hair, and parts of the eye. Genetic mutations that involve melanin pathways can produce different degrees of hypopigmentation or absence of pigmentation in the skin and the eye. Figure 1 shows the pigmentary pattern of a normal eye. Figure 2 shows that of a patient with albinism. It is evident that the fundus has less pigment, and the choroidal vessels, which lay beneath the retina and retinal pigment epithelium, are more visible.

Figure 1 Normal Fundus Pigmentation

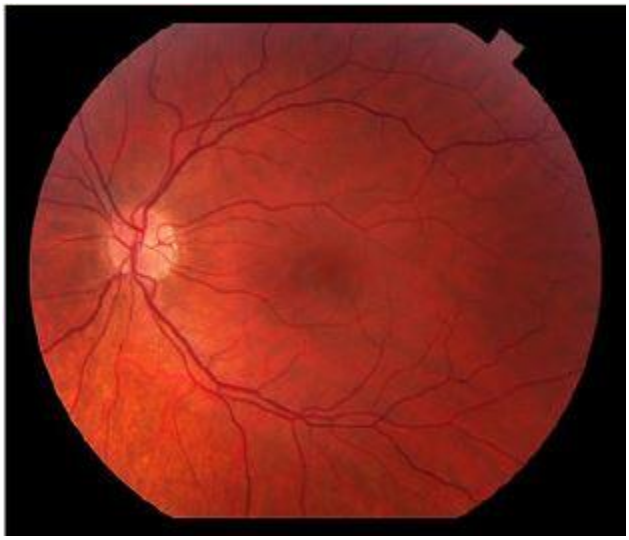
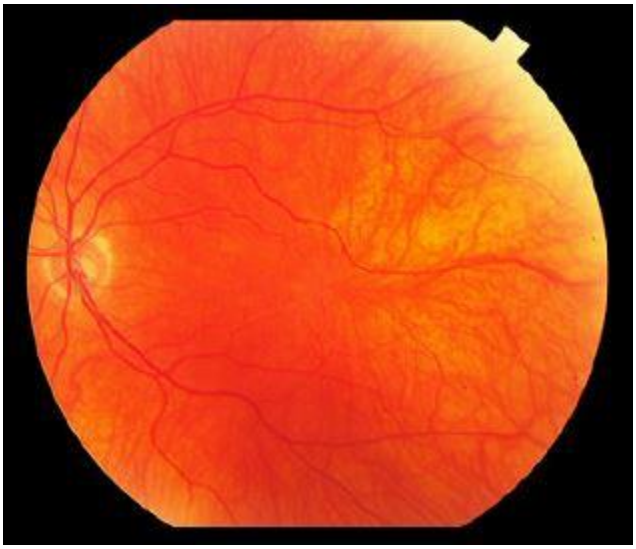
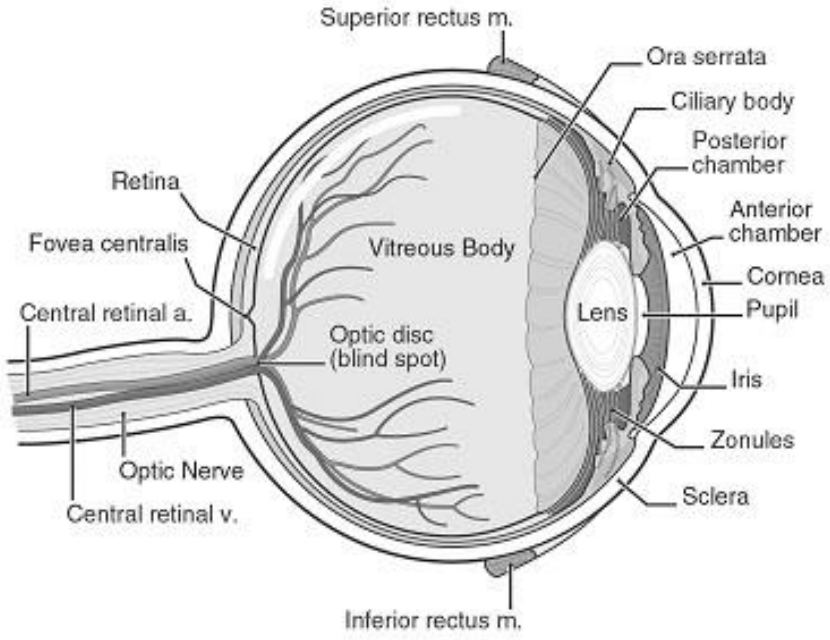


Figure 2 Fundus Pigmentary Pattern in Albinism



The eye can show many abnormalities in albinism. Figure 3 shows the anatomy of the eye. The tissues involved in the albinism include the iris, the ciliary body, the uvea, and the retina.

Figure 3



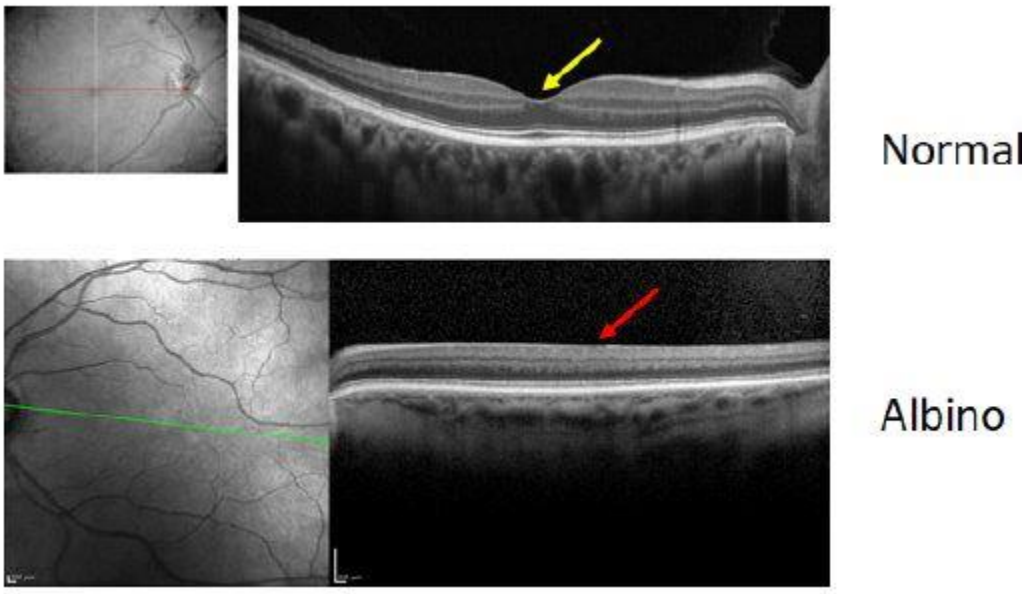
Melanin is important in the embryogenesis of the visual pathways. Pigmented cells of the retinal pigment epithelium, pigmented epithelium of the ciliary body and pigmented epithelium of the iris are derived from the neuroectoderm of the embryo. Melanogenesis in pigment epithelial cells begins by the fifth week of fetal life and is completed soon after birth. Melanogenesis of uveal cells continues after birth, which is why different patients with albinism can have differing degrees of skin and hair pigmentation.

Levels of melanin in embryogenesis correlate with many ocular abnormalities including foveal anatomy, decussation of axons of retinal

ganglion cells, strabismus, refractive error, and nystagmus. Patients with albinism frequently have foveal hypoplasia (figure 4) and can have reduced perifoveal vascular density. Besides eye problems, patients with albinism also have anomalous auditory fiber projections. Reduction in skin pigmentation leads to a higher rate of skin cancer.

There are two ancillary tests that are useful in diagnosing ocular albinism. The optical coherence tomograph (OCT) can show foveal hypoplasia. Visual evoked potentials (VEP) can be done one eye at a time and the responses compared. Generally patients have symmetric responses. Patients with albinism frequently have asymmetric monocular visual evoked potentials.

Figure 4 Foveal Hypoplasia in Albinism



Legend: The normal OCT has a foveal depression (yellow arrow). The Albino macula has no foveal depression (red arrow).

Types of Albinism

There are many forms of albinism.These include the following:

Oculocutaneous Albinism

There are many sub-forms of oculocutaneous albinism, but to simplify, there are two main groupings based on the amount of activity of the enzyme tyrosinase. Tyrosinase mediates the conversion of tyrosine into melanin through a complex biochemical pathway. 55 mutations of the tyrosinase gene on chromosome 11 have already been found and more being found all the time. Thus oculocutaneous albinism is not one disease but rather many diseases all grouped under a single rubric.

The first subtype of oculocutaneous albinism is tyrosinase positive oculocutaneous albinism. These patients have some activity of the enzyme tyrosinase on a hair bulb assay. The patients may have some cutaneous pigmentation but they clearly hypopigmented.

The other major subtype is tyrosinase negative oculocutaneous albinism. These patients have no activity of the enzyme tyrosinase on a hair bulb assay. They have no skin or hair pigment nor any ocular pigment.

Both types have photophobia, iris transillumination, increased visibility of choroidal vessels, a high prevalence of refractive errors,

strabismus, nystagmus, foveal hypoplasia, and misrouting of ganglion cell axons.They have a normal to a supernormal electroretinogram and a normal electrooculogram (special electrical tests done in the ophthalmologist's office).

Black patients with oculocutaneous albinism may lack iris transillumination and may have some fundus pigmentation, but they uniformly have foveal hypoplasia. On average, their visual acuity may be slightly better than in white patients.

Female heterozygotes have a mosaic fundus with patchy hypo-and hyperpigmentation.

Ocular Albinism

Ocular albinism involves decreased pigmentation in the eye and lessened but present pigmentation and skin and hair. It is inherited in 2 forms. One is X-linked and the other is autosomal recessive. In both types patients have strabismus, nystagmus, foveal hypoplasia, and reduced visual acuity. They are distinguished most simply by the appearance of the melanosomes in skin cells viewed through a microscope. Normal

melanosomes are less than 1.5 µm in diameter. Macromelanosomes, which are the hallmark of ocular albinism of the x-linked type (Nettleship-Falls type), are larger, ranging from 3-3.5 µm in diameter. The autosomal recessive Foresee-Erickson type (Aland Island Eye Disease) features no macromelanosomes but only normal melanosomes. Patients with Aland Island Eye Disease may have color vision abnormalities not seen in x-linked ocular albinism.

The prevalence of x-linked ocular albinism 1: 50,000. The gene mutation occurs at P22.3 of the x chromosome most commonly arising from a mutation of the GPR143 gene, which results in a mutated G-protein coupled receptor present in endosomes, lusosomes, and melanosomes. Carrier femals can be detected by three signs: a.) reduced zone of foveal hypoautofluorescence on fundus autofluorescence imaging, b.) radiating streaks of increased auofluorescence, and c.) persistence of the retinal ganglion cell layer in the fovea with reduced depth foveal depression on OCT. The prevalence of autosomal recessive ocular albinism is much less.

Certain Forms of Albinism of Special Note:

Chediak-Higashi Syndrome

This is an autosomal recessive form of albinism featuring ocular hypopigmentation, cutaneous pigment dilution, hair with a metallic frosted gray coloration. hepatosplenomegaly, and recurrent, recalcitrant infections.They have an increased incidence of lymphoma. Death in these patients usually occurs in the first 10 years of life.

The mutated gene is located on chromosome 1q42.1. The Chediak-Higashi syndrome gene product is unknown. Patients have a decrease in natural killer cell activity. They show giant intracytoplasmic inclusion bodies in their neutrophils, lymphocytes, platelets, and melanosomes. The only treatment is a bone marrow transplant.

Hermansky-Pudlak Syndrome

Hermansky-Pudlak syndrome is an autosomal recessive condition which there is an accumulation of ceroid. These patients have a platelet defect, develop an interstitial form of pulmonary fibrosis, inflammatory bowel disease, cardiomyopathy, and renal failure. It is particularly common in Puerto Rico with a carrier frequency of 1: 21.

The gene that is mutated is found on chromosome 10q23.1-23.3. On blood smear, these patients have an absence of dense bodies in the platelets which leads to bleeding problems.

Wardenburg Syndrome

Wardenburg syndrome is characterized by melanocytes that failed to populate certain areas of the body during the embryogenesis. Affected patients have broad nasal roots, telecanthus (widely spaced eyes), hyperplasia of the medial eyebrows, a broad high nasal bridge, white forelock, segmental iris hyperchromia, strabismus, fundus hypopigmentation, and congenital neurosensory deafness. The responsible gene mutation involves the PAX3 gene that is localized to chromosome 2q35.2-37.3.

Albinoidism

In albinoidism, patients have normal visual acuity, but manifest transillumination of the iris and hypopigmentation of the fundus. They do not have strabismus or nystagmus.

Final Comments

All patients who are extremely fair should be checked for iris transillumination. If other signs of albinism are present, it is important to rule out systemic associations such as Chediak-Higashi disease and Hermansky-Pudlak syndrome. A hair bulb test for the presence of tyrosinase activity may be useful. A skin biopsy to check for macromelanosomes may be informative if ocular albinism of the x-linked inheritance type is suspected. Rarely, genetic sequencing may be performed. This test may not be easy to get, and may not be covered by insurance. If these are not present, low vision consultation may benefit patients in performing their daily tasks.

References

1. Carden SM, et al. Albinism: modern molecular diagnosis. Br J Ophthalmol 1998: 82:189-195.

2. Bouzas EA et al. Evoked potential analysis of visual pathways in human albinism. Ophthalmol 1994; 101: 309-314.

3. Mietz H, et al. Foveal hypoplasia in complete oculocutaneous albinism. A histopathologic study. Retina 1992; 12: 254-260.

4. Khan KN, et al. Detailed retinal imaging in carriers of ocular albinism. Retina 2018; 38:620-628.

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