

Egyptian Dermatology Online Journal

Volume 2 Number 2

A review of Oculocutaneous Albinism and its syndromes.

Dr. (Mrs.) O. A. OLASODE FWACP

Dr. O. A. OLATEJU. FMCO

Dr. J. K OLABANJI. FMCS

Dr. B. J. OLASODE. FWACP

Correspondence to:

Dr Babatunde J Olasode
Department of Histopathology
University of Calabar Teaching Hospital
Calabar, Cross Rivers State.
Nigeria.

<mailto:bjshalom428@yahoo.com>

Egyptian Dermatology Online Journal 2 (2):6, December 2006

Accepted for publication in : July, 2006.

A review of Oculocutaneous Albinism and its syndromes.

Oculocutaneous albinism (OCA) represents a group of inherited abnormalities of melanin synthesis. There is congenital reduction or total absence of melanin pigment in OCA. Melanin pigment is produced in a specific cell type called the melanocyte located in the lower layers of the skin, in hair bulbs, in the eye especially the iris and the pigment epithelium of the eye [1]. The melanocyte is present in all individuals and is only rarely absent in some. Melanin is produced by the hydroxylation of the amino acid L-tyrosine to dihydroxyphenylalanine (DOPA), which is then oxidized to DOPA quinone by the copper containing enzyme tyrosinase. The product is a black brown pigment, which in the presence of sulfhydryl compound produces a red yellow pheomelanin. The pigment polymer is then deposited on a protein matrix within the melanosome, which is then transferred to keratinocytes in the skin via the dendrites of the melanocyte. OCA results when the pathway is disrupted[2].

Melanin Synthetic pathway

The first step of the synthetic pathway for both eumelanins and pheomelanins is mediated by tyrosinase

Tyrosine → DOPA → dopaquinone

Dopaquinone can combine with cysteine by two pathways to benzothiazines and pheomelanins

Dopaquinone + cysteine → 5-S-cysteinyl-dopa → benzothiazine intermediate → pheomelanin

Dopaquinone + cysteine → 2-S-cysteinyl-dopa → benzothiazine intermediate → pheomelanin

Alternatively, dopaquinone can be converted to leucodopachrome and follow two more pathways to the eumelanins

Dopaquinone → leucodopachrome → dopachrome → 5,6-dihydroxyindole-2-carboxylic acid → quinone → eumelanin

Dopaquinone → leucodopachrome → dopachrome → 5,6-dihydroxyindole → quinone → eumelanin[2].

Sir Archibald Garrod first included albinism as inborn error of metabolism [2],[3] but it is now believed to be a heterogeneous genetic disorder caused by mutations in several different genes. Population studies have revealed a genetic heterogeneity with evidence pointing to several loci [3]. There has been a report of OCA in both parents while the offspring had normal pigmentation. This is an example in which the parents are homozygous for a mutation at distinct but different loci from their pigmented child who is heterozygous at both loci [4]. In this example the hair bulb incubation test suggested a biochemical basis for this type of albinism as the hair bulb from the parents were unable to produce melanin pigment when incubated in a solution containing tyrosine or DOPA, this is the type of albinism referred to as Tyrosinase negative OCA.

Classification of Oculocutaneous Albinism.

The classification of OCA has changed a great deal over the years, with much of the work coming from the international Albinism Center and the help of all of the wonderful individuals and families who have helped with these studies. For many years, the term "albinism" referred only to people who had white hair, white skin, and blue eyes. Individuals who had OCA and pigmented hair and eyes were identified, particularly in the African[5] and African-American population, and terms such as 'incomplete albinism', 'partial albinism' or 'imperfect albinism' were used for them, but these terms are inappropriate and are no longer used. In the 1960's, Dr. Carl Witkop[6],[7] developed the hair bulb incubation test to separate pigmented and non-pigmented types of OCA and started to use the terms "ty-neg" or "negative-negative" and "ty-pos" or "positive-positive" OCA. Freshly plucked hair bulbs from a person with OCA were placed in a solution of tyrosine or DOPA in a

test tube and watched to see if pigment formed in the pigment cells in the hair bulb. If no pigment formed, the test was negative and the diagnosis was ty-neg OCA. If pigment formed in the hair bulb, the test was positive and the diagnosis was ty-pos OCA. Although this simple test showed that there were different types of OCA, subsequent studies have shown that the hair bulb incubation test is not very sensitive and has many false negative and false positive responses. As result, the hair bulb incubation test is no longer used in the evaluation of an individual with OCA.

A sensitive hair bulb tyrosinase enzyme activity assay was developed in an attempt to improve the specifically of the hair bulb test. Unfortunately, biochemical studies of hair bulb tyrosinase activity also proved to be unreliable and did not have the specificity necessary for accurate diagnosis. The hair bulb tyrosinase assay test is no longer used in the evaluation of an individual with OCA.

In the 1980's the classification of OCA was expanded using very careful skin, hair and eye examinations [6]. The reason for this was the knowledge that there were more than 50 gene loci that controlled pigmentation in the mouse, and it was suggested that careful analysis of skin, hair, and eye pigmentation of individuals with OCA could help identify the human equivalent of each genes. A number of types of OCA were identified, including platinum OCA, minimal pigment OCA, yellow OCA, temperature-sensitive OCA, autosomal recessive ocular albinism and brown OCA, and it was hoped that each would be caused by a different gene. In the 1990's, we have been able to identify the genes involved in most types of OCA, and have found that the classifications based on hair, skin and eye color is not accurate and that it was better to classify OCA types based on the specific gene involved.

We have now identified five genes that are associated with the development of OCA and one gene that is involved in OA.[7].

Basic Inheritance And Genetics.

Gene	Type of Albinism
Tyrosine's gene	OCA1 (OCA1A and OCA1B)
P gene	OCA2
TRP1 gene	OCA3

HPS gene	Hermansky-Pudlak syndrome
CHS gene	Chediak Higashi syndrome
OA1 gene	X-linked ocular albinism

Table 1. Genes Associated with Albinism

The pigmentation (phenotype) range for OCA at each gene locus is broad. Most of the various types or subtypes of OCA that were defined over the past 20 years can now be associated with a specific genetic locus.

OCA1. Tyrosinase Related Oculocutaneous Albinism.

One of the two most common types of albinism is tyrosinase related OCA, produced by loss of function of the tyrosinase enzyme in the melanocyte. This results from inherited mutations of the tyrosinase gene.

Classical OCA, with a total absence of melanin in the skin, hair and eyes over the lifetime of the affected individual is the most obvious types of OCA1, but there is a wide range of pigmentation associated with tyrosinase gene mutations. The range in phenotypes extends from total absence to near normal cutaneous pigmentation, but the ocular features are always present and help identify an individual as having albinism.

Many different mutations of the tyrosinase gene have been identified in individuals and families with OCA I. Most mutations lead to the production of tyrosinase enzyme that does not work. As a result, the first two critical conversations in the melanin pathway (tyrosine--> DOPA--> DOPA quinone) are not made and no melanin pigment forms, the pathway is "blocked" at the start. Mutations that produce an inactive enzyme or no enzyme at all are called "null" mutations.

Some tyrosinase gene mutations are not null mutations but are called "leaky" mutations. These mutations lead to the production of a tyrosinase enzyme that has a little activity but nowhere near the normal amount of activity (often in the range of 1-10% of normal activity). Leaky mutations and the resultant tyrosinase enzyme allow some melanin to form. The formation of melanin can be very small (the minimal pigment type of OCA) or can range to nearly normal (the type of OCA that was mistakenly called autosomal recessive ocular albinism).

An important distinguishing characteristic of OCA1 is the presence of marked hypopigmentation at birth.

Most individuals affected with a type of OCA1 have white hair, milky white skin, and blue eyes at birth. The irises can be very light blue and translucent such that the whole iris appears pink or red in ambient or bright light. During the first and second decade of life, the irides usually become a darker blue and may remain translucent or become lightly pigmented with reduced translucency. The skin remains white or appears to have more color with time. Sun exposure produces erythema and a burn if the skin has little pigment and is unprotected but may tan well if cutaneous pigment has developed. Pigmented lesions (nevi,

freckles, lentigines) develop in the skin of individuals who have developed pigmented hair and skin[6]

OCA1A.

Individuals with OCA1A or the classic negative-negative OCA are unable to make melanin in their skin, hair or eyes, because they have no active tyrosinase enzyme. They are born with hair and skin and blue eyes, and there is no change as they mature into teenagers and adults. They never develop melanin in these tissues. The phenotype is the same in all ethnic group around the world and at all ages. With time, the hair may develop a dense rather than a translucent white or a slight yellow tint but this is usually from the denaturing of the hair protein with the use of different shampoos. The irides are translucent and appear pink early in life and often turn a gray- blue color with time. No pigmented lesions develop in the skin, although amelanotic nevi can be present.

Visual acuity for OCA1A is usually in the legally blind range, 20/200 to 20/400[8], although near vision may be better if the print is held close to the eyes. Vision usually does not improve with age. Photophobia and nystagmus cause more problems with OCA1A than with other types. Vision often does not correct well with glasses, but low vision aids help.

OCA1B.

OCA1B is produced by mutations of the tyrosinase gene that result in enzyme with residual or "leaky" activity. The variation in the pigmentation in individuals with OCA1B is wide from very little cutaneous pigment to nearly normal skin and hair pigment. Mutations coding for enzyme with differing amounts of residual activity are the primary cause of this variation, and a moderate amount of residual activity can lead to near normal cutaneous pigmentation and the mistaken diagnosis of ocular albinism. Ethnic and family pigment patterns influence the pigmentation of an individual with OCA1B, and hair color can be light red or brown in some families where this is the predominant pigment pattern.[9]

The original OCA1B phenotype was called yellow albinism because of the yellow blond or golden color of the melanin that develops in the hair of affected individuals. It is now known that the hair color is the result of pheomelanin synthesis and the formulation of this type of melanin is related to the reduced tyrosinase function. Only small amounts of DOPA quinone form and these combine quickly with sulfur-containing compounds present in the cell and produce the pheomelanin. Other types of OCA1B have been described as minimal pigment OCA, platinum OCA, temperature-sensitive OCA, and autosomal recessive ocular albinism.[7],[8]

All variations of OCA1B are characterized by having very little or

no pigment present at birth followed by the development of varying amounts of melanin in the hair and the skin in the first or second decade. In some cases, the melanin develops within the first year. The hair color changes to light yellow, light blond or golden blond first, and may eventually turn dark blond or brown in the adolescent and the adult. One interesting feature of OCA1B is the development of dark eyelashes. Eyelash hair pigment is often darker than that of the scalp hair. The irides can develop hazel, light tan or brown pigment, sometimes limited to the inner third of the iris, and iris pigment can be present on globe Tran illumination. Some degree of iris translucency, as demonstrated by slit-lamp examination, is usually present. Visual acuity is in the range of 20/90 to 20/400, and may improve with age.[6],[8] Many individuals with OCA1B will tan with sun exposure while it is common to burn without tanning after sun exposure. Pigmented nevi can develop with time, although most developing nevi are amelanotic. Very few freckles develop.

Another type of OCA1B is temperature-sensitive OCA. Affected individuals are thought to have OCA1A during the first years of life, with white hair and skin, and blue eyes. With further development, some of the body hair develops pigment. The hair under the arms remains white and the scalp hair remains white but may develop a slight yellow tint. In contrast to this is the arm and leg hair that develop light to dark pigment. The eyes stay blue and the skin remains white and does not tan. This type of OCA1B is caused by a mutation of the tyrosinase gene that produces an enzyme that does not work at regular body temperature (scalp and under the arms) but does work in cooler parts of the body (arms and legs). As a result, melanin synthesis occurs in the cooler but not the warmer areas of the body such as the arms and legs.

Autosomal recessive ocular albinism.

Some years ago a series of families were described which children of normally pigmented parents had the ocular feature of albinism but not appear to have significant cutaneous hypopigmentation. This was called autosomal recessive ocular albinism (AROA) because males and females were affected in these families. Studies now show that calling this AROA is not correct and most of the individuals and families like this have OCA1B or OCA2 with nearly normal or normal cutaneous pigmentation. One family has been described in which the individual with OCA1B was not diagnosed with albinism until mid-life, although she had always been aware of her reduced visual acuity. [4]

OCA2 P-Gene Related Oculocutaneous Albinism.

The common features of OCA2 include the presence of hair pigment at birth and iris pigment at birth or early in life. Localized (nevi, freckles, and lentigines) skin pigment can develop, often in sun-exposed regions of the skin, but tanning is unusual. It was one thought that the ethnic and constitutional pigment background of an affected individual

had a more profound effect on the OCA2 phenotype than on the OCA1 phenotype, but this no longer appears to be the case. Both OCA1B and OCA2 have a broad range of pigmentation that, in part, reflects the genetic background of the affected individual. There may be some accumulation of pigment in the hair with age but this is much less pronounced as that found in OCA1B and many individuals with OCA2 have the same color throughout life. OCA2 is the most common type of OCA in the world, primary because of the high frequency in equatorial Africa.[5]

In Caucasian individuals with OCA2, the amount of pigment present at birth varies from minimal to moderate. The hair can be very lightly pigmented at birth, having a light yellow or blond color or more pigmented with a definite blond, golden blond or even red color. The normal delayed maturation of the pigment system in northern European individuals (i.e., very blond or towheaded as a child with later development of dark blond or brown hair) and lack of long hair can make it difficult to distinguish OCA1 from OCA2 in the first few months of life. The skin is white and does not tan on sun exposure. Iris color is blue-gray or lighted pigmented and the degree of iris translucency correlates with the amount of pigment present. With time, pigmented nevi and lentigines may develop and pigmented freckles are seen in exposed areas with repeated sun exposure. The hair in Caucasian individuals may slowly turn darker through the first two or more decades of life. There is a distinctive OCA2 phenotype in African-American and in African individuals.[7] The hair is yellow at birth and remains yellow through life, although the color may turn darker. Interestingly, the hair can turn lighter in older individuals, and this probably represents the normal graying with age. The skin is white at birth with little change over time, and no tan develops. Localized pigmented lesions such as pigmented nevi, lentigines and freckles can develop in some individuals. The irides are blue/gray or lightly pigmented. There appears to be a wide OCA2 pigment phenotypic range in African-Americans, in that some individuals with OCA2 (defined as having pigmented hair at birth and the ocular features of albinism) have brown, ginger, auburn or red hair. Some of this variation may reflect genetic admixture in this population, and some may result from different mutations of the P gene and their different effect on the function of the P protein. Some individuals who were previously thought to have autosomal recessive ocular albinism have now been shown to have OCA2.

Brown OCA

Brown OCA is a type of albinism that is recognized in the African and the African-American populations, but not in other populations. In African and African-American individuals with Brown OCA, the hair and skin color are light brown, and the irides are gray to tan at birth. With time there is little change in skin color, but the hair may turn darker and the irides may accumulate more tan pigment. Affected

individuals are recognized as having albinism because they have all of the ocular features of albinism. The iris has punctuated and radial translucency, and moderate retinal pigment is present. The skin may darken with sun exposure[6] Visual acuity ranges from 20/60 to 20/150. The phenotype in Caucasian individuals is unknown at present.[8]

Brown OCA is part of the spectrum of OCA2, resulting from alteration of the P gene. These gene alterations are associated with the development of yellow or red pheomelanin and a lack of development of brown or black eumelanin. As with OCA1B, Brown OCA may arise from a mutation that reduces ("leaky" mutation) the function of the P gene product while the more common OCA2 results from completely knocking out ("null" mutation) the function of the P protein[8]

Prader-Willi and Angelman Syndrome.[4]

There is an association with OCA2 and the hypopigmentation found with Prader-Willi syndrome and Angelman Syndrome. Prader-Willi syndrome is a development syndrome with neonatal hypotonia, hyperphagia and obesity, hypogonadism, small hands and feet, and mental retardation associated with characteristic behavior. Many individuals with Prader-Willi syndrome are hypopigmented but most do not have the typical ocular features of albinism, but a number of individuals with Prader-Willi syndrome and OCA have been identified. For those without obvious OCA, hair and skin are lighter than unaffected family members, and childhood nystagmus and strabismus are common and often transient [6]. The irides are pigmented with some translucency on globe transillumination, and retinal pigment is reduced in amount. The fovea may not appear entirely normal but is present. Some individuals with Prader-Willi syndrome have OCA2 with cutaneous hypopigmentation associated with all of the typical ocular features of albinism. Angelman syndrome is a complex developmental disorder that includes developmental delay and severe mental retardation, microcephaly, neonatal hypotonia, ataxic movements, and inappropriate laughter [4]. In Angelman syndrome, the hypopigmentation is characterized by light skin and hair. There may be a history of nystagmus or strabismus, and iris translucency and reduced retinal pigment may be present. No analysis of the optic tract organization is available. It is expected that individuals with Angelman syndrome having OCA2 will be described, because of the location of the P gene in the Prader-Willi Angelman syndrome region at chromosome[7].

OCA3 TRP1-Related OCA [4],[6]

The first evidence that variations in human pigmentation could be related to mutations of the TRP1 gene came from the description of an African-American newborn twin boy who had light skin light brown hair, and blue/gray irides while his fraternal twin brother had normal pigmentation. Subsequent studies have shown that a type of OCA

known as 'rufous' or 'red OCA' in the South African population results from mutations of the gene for TRP1.

Rufous or red OCA has only been partially documented. Individuals with OCA who have red hair and reddish-brown pigmented skin have been reported in Africa and in New Guinea, but clinical descriptions are incomplete, and similar individuals in the U.S. population have not been identified and reported. The cases are described in the literature as 'red', 'refocus', or 'xanthous' albinism. Individuals with red hair who have either OCA1 or OCA2 are also recognized, but the reddish-brown skin pigment is usually not present, and they should not be confused with rufous OCA. The pigment phenotype in South African individuals includes red or reddish brown skin, ginger or reddish hair, and hazel or brown irides. The ocular features are not fully consistent with the diagnosis of OCA, however, as many do not have iris translucency, nystagmus, strabismus, or foveal hypoplasia. Furthermore, no misrouting of the optic nerves has been demonstrated by a visual evoked potential, suggesting either that this is not a true of albinism, or that the hypopigmentation is not sufficient to consistently alter optic nerve development. At this time, the phenotype for TRP1-related OCA in the Caucasian and the Asian populations is unknown[7].

Hermansky-Pudlak Syndrome[9],[10]

The Hermansky-Pudlak Syndrome includes OCA, an abnormality of platelets that usually leads to mild bleeding, and the accumulation of a material called ceroid in tissues throughout the body. Hermansky and Pudlak first described this condition in two Czechoslovakian individuals in 1959 and it has subsequently been recognized throughout the world with the majority of affected individuals in the Puerto Rican population. HPS is not common, except in the latter population, and does not constitute a major type of OCA; however, the frequency in Puerto Rico is approximately 1:1,800. HPS is not found on other Caribbean islands.

HPS is a pigmented type of OCA and skin and eye pigment develop in many affected individuals, but the amount of pigment that forms is quite variable. Some affected individuals have marked hypopigmentation of their skin and hair similar to that of OCA1A, others have white skin and yellow or blond hair similar to OCA1B or OCA2, and others have only moderate hypopigmentation suggesting that they may have OA rather than OCA. The variation can be seen within families as well as within families. Individuals with HPS in the Puerto Rican population have hair color that varies from white to yellow to brown. Skin color is creamy white and definitely lighter than individuals without HPS in this population. Freckles are often present in the sun exposed regions (face, neck, arms and hands), often enlarging and overlapping into large areas that look like normal dark skin pigment, but tanning does not occur. Pigmented nevi are common. Iris color varies from blue to brown, and all of the ocular features of albinism are

present. Visual acuity ranges from 20/60 to 20/400[6]. Affected individuals have been identified in other populations infrequently, and the phenotype shows the same degree of variation in pigmentation as is found in Puerto Rico. Hair color varies from white to brown and this correlates with the ethnic group. The skin is white and does not tan. Eye color varies from blue to pigmented. The most important medical problems in HPS are usually related to the lung and the gastrointestinal tract changes. Interstitial lung fibrosis (or scarring of the lungs) develops in many individuals with HPS, although the actual prevalence is unknown. The fibrosis results in an inability of the lungs to expand and contract, reducing their ability to take in oxygen and exhale carbon dioxide. This is called restrictive lung disease. Fewer individuals with HPS develop colitis of inflammation of the intestinal tract. This is called granulomatous colitis, and the medical problems include abdominal pain and bloody diarrhea in a child or an adult. The presence of ceroid material in the lungs and the intestines suggest that this material may be involved in the development of these complications, but this has not been proven[10].

The bleeding problem in HPS is related to a deficiency of granules in the platelets (i.e. storage pool-deficient platelets) that store material needed for normal platelet function. Platelets are cells in the blood that are responsible for forming the initial clot after a blood vessel is cut or opened. Platelets work by first attaching to exposed material in the blood vessel wall, and then sticking together and contracting into small plug to close the hole. Platelets stick together because they secrete chemicals from storage compartments that are inside each platelet. In HPS, these storage compartments do not form (storage granules do not form) and the platelets are unable to secrete this necessary chemical. The platelets first stick to the cut blood vessel wall but do not aggregate and contact and do not form a firm plug at the hole. This produces mild bleeding episodes in many affected individuals, including easy bruisability, epistaxis, hemoptysis, bleeding of the gums with brushing or dental extraction and postpartum bleeding. Occasional severe bleeding is observed which in part may be related to normal variation in Von Willebrand factor.

Chediak-Higashi Syndrome (CHS)[6],[7]

The Chediak-Higashi Syndrome is a rare syndrome that includes an increased susceptibility to bacterial infections, hypopigmentation, and the presence of giant granules in white blood cells. The skin, hair, and eye pigment is reduced or diluted in CHS but the affected individuals often do not have obvious albinism and the hypopigmentation may rarely be noted when compared to other family members. Hair color is light brown to blond and the hair has a metallic silver-gray sheen. The skin is creamy white to slate gray. Iris pigment is present and nystagmus and photophobia may be present or absent.

OAI X-Linked Ocular Albinism[4]

Ocular albinism involves the eyes only. X-linked ocular albinism occurs primarily in males. Skin color is usually normal or slightly lighter than the skin of other family members. Eye color may be in the normal range, but examination of the back of the eye (retina) through the pupil shows that there is no pigment in the retina. Females who carry the gene for X-linked ocular albinism may show a mixture of pigmented and non-pigmented areas in their retinas.

Visual acuity in X-linked albinism is in the range 20/50 to 20/400.

It is often possible to identify females who carry the gene by examining their eyes. "X-linked" means that the gene for ocular albinism is passed from mothers who carry the gene to sons who have ocular albinism.

Autosomal Recessive Ocular Albinism (ARO) [4],[6],[7]

In the 1970's, a type of albinism associated with relatively normal skin and hair pigment was described in families that contained affected females and males. This appeared to be a type of ocular albinism that was caused by a gene on an autosomal chromosome (non-sex chromosome) rather than on the X chromosome; hence, the name of autosomal recessive ocular albinism. We now know that this was incorrect and these families are actually part of the spectrum found in OCA1 and OCA2. At this time, there is no evidence for a true ARO type of albinism, and this term should not be used.

Conclusion

Albinism is varied and has numerous syndromes which should be recognized. We have tried to review the common syndromes and describe them.

References

1. Carden S.M., Boissy R.E. Schoettker P.J., Good W.V. Albinism: Modern molecular diagnosis. Br. J. Ophthalmol. 82: 189-195; 1998.
2. Wildsoet CF, Oswald PJ, Clark S. Albinism its implications for refractive development. Investigative Ophthalmology and visual science 41 (1): 1-7, 2000.
3. Kasmann Kellner B, Hille K, Pfau B. Ruprecht KW. Eye and general illnesses in the public school for the blind and usually handicapped students in Saarland Development in the last 20 years. Ophthalmology. 95 (1):51-54. 1998.

4. O'Donnell E.F. Jr; WR Green. The Eye in Albinism. 38 in Duane's Clinical Ophthalmology Vol.4. W. Tasman and E.A. Jarger (Eds.), N.Y. 1982, Lippincott Williams & Wilkins (LWW).
5. Donaldson DD (1974): Transillumination of the iris. Trans Am Ophthalmol Soc 72: 89 -106.
6. Krill A.E., Lee GB: The electroretinogram in albino and carrier of the ocular albino tract. Arch Ophthalmol. 69: 32, 1963.
7. Shawkat FS, Kriss A. Thompson D, Russell-Eggitt I, Taylor D, Harris C. Vertical or asymmetric Nystagmus need not imply neurological disease. Br. J. Ophthalmol 2000 Feb. 84 (2): 175-80.
8. Shaw Fs, Kriss A, Russell Eggih I, Taylor D. Harris C. Diagnosing children presenting with asymmetric pendular nystagmus. Dev Med. Child Neuro. 43(9) 622-7, 2001.
9. Choi YC, Kim Sk, Lee SH, Lee MS, Choi PS, Chung UK. Eye movement changes in albinism - a case report with electronystagmographic findings. Yonsei Medical Journal 34 (2): 195-200, 1993.
10. Holmes JM, Cronin CM. Duane Syndrome associated with Oculocutaneous albinism. Journal of Pediatric Ophthalmology and Strabismus 28(1) 32-4, 1991.