Oculocutaneous albinism in an isolated Tonga community in Zimbabwe

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Abstract

Oculocutaneous albinism (OCA) is a recessively inherited genetic condition prevalent throughout sub-Saharan Africa. We now describe a cluster of tyrosinase positive OCA (OCA2) cases belonging to the Tonga ethnic group living in the Zambezi valley of northern Zimbabwe. The prevalence in this region was 1 in 1000, which is four times higher than that for the country as a whole. The gene frequency for OCA2 in this population was calculated as 0.0316, with a carrier rate of 1 in 16. Molecular analysis showed that all five affected subjects from two independent families examined were found to be homozygous for an interstitial 2.7 kb deletion mutation commonly found in OCA2 subjects in Africa. An obligate carrier from another family was heterozygous for this deletion allele. Affected subjects in this isolated community suffered health, social, and economic problems.

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Oculocutaneous albinism (OCA) is a recessively inherited genetic condition where there is hypopigmentation of the skin, hair, and eyes. One form, tyrosinase positive OCA (OCA2), is by far the most common type in southern Africa.¹ In indigenous African ethnic groups OCA2 subjects have sandy coloured hair, pale, chalky white skin, often burned by the sun, and light brown eyes showing nystagmus, photophobia, lack of binocular vision, and poor visual acuity. Their appearance contrasts sharply with that of their darkly pigmented peers.

OCA2 has a relatively high prevalence throughout sub-Saharan Africa. In southern Africa, the prevalence of the condition ranges from 1 in 1279 among the Swazi in Swaziland² to 1 in 4182 in Zimbabwe³ where the Shona are the predominant group. OCA2 cases were not evenly distributed throughout Zimbabwe, with a higher prevalence in the capital⁴ and along the eastern border of the country where the Ndaou and Manyika subgroups of the Shona ethnic group live.³

The gene for OCA2, on chromosome 15,⁵ encodes an integral melanosomal membrane protein with transmembrane domains.^{6,7} The function of this protein has not been elucidated to date but the existence of multiple transmembrane regions suggests that it may function as a porter in a membrane. A 2.7 kb deletion muta-

tion which removes exon 7 of the gene has been found among OCA2 subjects in various parts of Africa including Zaire,⁸ Tanzania,⁹ Cameroon,¹⁰ and South Africa.¹ This report describes a high prevalence of OCA2 in an isolated Tonga community in the west of Zimbabwe where this common 2.7 kb deletion allele was found in all OCA2 subjects tested, as well as in one obligate carrier.

Methods

During a postal survey of schools throughout Zimbabwe reported elsewhere,^{3,4} a cluster of cases of OCA2 was identified in an isolated lakeside valley in western Zimbabwe. These OCA2 subjects belonged to the Tonga, a minority ethnic group in the country. At the time of the visit there was no doctor serving the community. The local clinic was run by a nursing sister.

SUBJECTS

OCA2 cases were identified on a visit to the community. Five adults and one schoolgirl (and her mother) were interviewed with the help of an interpreter from the local school. Subjects T1 to T3 were sibs, two male and one female, from a family of 12, three of whom were OCA2. T4 was a female and T5 a male member of an independent family of seven sibs, three of whom were affected. The age range for subjects T1 to T5 was 18 to 32 years, although a few were uncertain of their exact age. All affected subjects showed the same phenotype with sandy coloured hair and light brown eyes. Their skin was chalky white without naevi and all showed nystagmus and photophobia.

MOLECULAR ANALYSIS

Blood samples from all five OCA2 subjects (T1 to T5) and an obligate carrier, the mother of a young girl with OCA2 attending the local school, were taken and dried on filter paper. PCR analysis using a test designed to detect the 2.7 kb interstitial deletion of the P gene was performed as described previously¹¹ on these six subjects and two controls, a homozygote for the deletion allele (CE) and a normally pigmented white subject (LH). For PCR amplification from purified DNA, reactions included 0.5 µmol/l of each primer (MHB 71, MHB72, and MHB107), 30 ng genomic DNA, 1.2 units of AmpliTaq (Perkin Elmer Cetus) in a total volume of 60 µl. For PCR amplification using filter paper, 20 µl of Gene Releaser (Bioventures, Inc) was added to 1 mm² of filter

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paper, mixed by vortexing, and allowed to stand for 10 minutes. The samples were then treated per GeneReleaser protocol as described before.¹¹ Following this procedure 0.5 µmol/l of each primer (MHB107, MHB71, and MHB72) and 1.2 units of *AmpliTaq* were added to the 20 µl of Gene Releaser/filter paper tube to a total final volume of 60 µl. The following conditions were used for PCR: denaturation at 94°C for one minute, annealing at 60°C for one minute, synthesis at 72°C for one minute, repeated 35 times. PCR products were separated on a 2% agarose gel (1% GTG/1% NuSieve, FMC) and visualised by ethidium bromide staining. For enhanced accuracy and sensitivity in determining the allele status, most sets of PCR products were subsequently transferred to Hybond N⁺ (Amersham) filter paper and subjected to hybridisation with a 2.4 kb *SstI-SphI* genomic fragment ("Probe II"²⁸) that corresponds to portions of the specific PCR products. After washing at high stringency (0.5 × SSC at 65°C) the specific products were visualised by autoradiography.

Results

PREVALENCE

The total community in the area numbers some 11 000, bounded by mountains and the lake. A total of 11 OCA2 cases were identified, giving a prevalence of about 1 in 1000 in this community. The affected subjects belonged to five different families. Members of three of these were available for interview. One 10 year old girl was the youngest member of the family, with eight unaffected older sibs, born to normally pigmented carrier parents. In another family, including subjects T4 and T5, there were three affected sibs in the family, with the affected female married to a normally pigmented male from the community and having two unaffected children. In the other there were three members with OCA2 (T1 to T3) in a large family of 12 children. None of these people was married. Both of these families reported that there had been cases of albinism in previous generations on either the mother's or father's side, or both. Using the Hardy-Weinberg equation the gene frequency for OCA2 in this population was calculated as 0.0316 and the carrier rate 1 in 16.

THE MUTATION OF THE P GENE

All five subjects investigated were found to be homozygous for the deletion allele. The results from two Tonga OCA2 subjects (T1 and T2) are shown in fig 1. The carrier mother of the schoolgirl was heterozygous for the allele. A blood sample was not taken from the girl as she was considered too young. As her father had died it was not possible to determine the nature of the other mutation allele.

HEALTH AND SOCIAL ISSUES

Although a mobile eye clinic visited the area from time to time none of the six affected subjects interviewed wore spectacles. Only one male had sunglasses and a hat to protect his eyes from the severe glare of the Zambezi valley and his skin from the intense sun. None of the

Figure 1 PCR analysis of two controls and two Africans with OCA2 from the Tonga ethnic group in Zimbabwe. In this assay the common deletion allele produces a 420 bp fragment and a non-deletion allele produces a 240 bp fragment. Lanes 1 and 2 are PCR products from controls: CE, a homozygote for the deletion allele, and LH, a normally pigmented subject without the deletion allele. Lanes 3 and 4 are from T1 and T2, sibs belonging to the Tonga group, who are both homozygous for the deletion allele.

others wore protective clothing, being dressed in shorts or dresses. All had sunburn and sun induced skin lesions. The young girl of school going age was attending the local primary school and clearly received support from her teachers, although she had no aids of any kind to help improve her poor vision. The adults interviewed were all living at home and being supported by their extended families. The teachers at the local school reported that albinism was still considered a curse in this area and evidence of "marital misdemeanour".

Discussion

Members of the Tonga ethnic group, belonging to the Bantu speaking Negroid people, live in the Zambezi valley where they survive on fishing in the nearby lake and tilling crops. The area is geographically isolated as it is bounded by mountains and the lake. The prevalence of OCA2 reported here, 1 in 1000, is about four times higher than that for the country as a whole, 1 in 4182.³ The carrier rate among the Tonga in this valley was 1 in 16, compared with the rate of 1 in 33 for all Zimbabweans, the majority of whom belong to the Shona group. The affected families recalled being told of cases of albinism in previous generations and it is probable that OCA2 has been present at a relatively high frequency in this small community for generations. Although the Tonga marriage patterns prohibit marriages between close relatives, all members of the group are likely to have recent common ancestors. The observation that the same deletion mutation is found at all mutant OCA2 loci examined suggests that the mutation exists at a high frequency in a relatively inbred community with limited choice of marriage partners. Molecular analysis of OCA2 cases from South Africa,¹ Tanzania,⁹ Cameroon,¹⁰ and Zimbabwe¹⁰ indicates that this deletion allele is common throughout central and southern Africa, although other mutant alleles have also been reported.

The Zambezi valley is extremely hot for much of the year and those with albinism living in this environment are at high risk of developing skin cancers, especially if they fail to wear protective clothing. The sensitive skin and photophobia of those interviewed prohibited their participation in the agricultural and fish-

ing activities of a community where there are few other job opportunities. Although treatment for skin lesions was not available and the families were unable to afford barrier creams, they may have been able to obtain assistance from the mobile eye clinics. In fact, such a clinic had visited the area on the day before the visit made by one of us, but it had not occurred to those with OCA2 to attend. The provision of simple magnifiers would enhance the quality of life of those with OCA2, especially in the case of the girl attending school. Information pamphlets were left with the subjects, the local school, and at the clinic. The belief that albinism is a curse is a further burden the OCA2 families had to bear. The notion that the mother had been unfaithful was an explanation to account for the appearance of a baby differing so markedly in appearance from either parent. The presence of women with OCA2 having normally pigmented babies appeared not to counter this myth. Although albinism was considered a curse, those with OCA2 were living with and being supported by members of their extended families.

There was clearly a need for affected subjects to be alerted to the health facilities that were available and to have information about albinism to enable them to manage and to understand their condition better.

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