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Synchrony of oculocutaneous albinism, the Prader-Willi syndrome, and a normal karyotype

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SUMMARY A Chinese girl with oculocutaneous albinism has the Prader-Willi syndrome and a normal karyotype. This association emphasises the importance of further molecular study of the 15(q12) region of the genome in the search for the locus of an albinism gene.

Using current cytogenetic techniques, about 50% of subjects with the Prader-Willi syndrome are shown to have a normal karyotype, while the remainder display an interstitial deletion of 15(q12).¹ There are no distinguishing phenotypic features between these two groups.²

Hypopigmentation has been recognised as a component of Prader-Willi syndrome^{3,4} and a black infant with albinism, the Prader-Willi phenotype, and a deletion involving band 15(q11.2) has recently been documented.⁵

In this report we present the clinical features of a girl with oculocutaneous albinism and the Prader-Willi syndrome who has a normal karyotype. This observation prompts further speculation regarding the potential presence of a gene for albinism at the locus 15(q12).

Case report

The proband, a girl born in 1981 (figure), was the first child of young, non-consanguineous, Chinese parents living on the Indian Ocean island of Mauritius. Both parents and two younger sibs were in good health and there was no history of genetic disease in the extended family. The pregnancy was uncomplicated and delivery occurred normally at term. During the neonatal period the child was hypotonic and required tube feeding for the first 10

weeks of life. By six months of age oculocutaneous albinism was diagnosed clinically. At this time her psychomotor development was delayed by three months.

At the age of three years, she walked and understood simple commands although she was unable to speak. Her behaviour was characterised by temper tantrums, she had a voracious appetite, and her weight was on the 97th centile.

In 1987 at the age of six years, physical examination showed the following features. Her height was 115 cm (50th centile) and she weighed 24 kg (90th centile). Her skin, hair, and irides lacked pigment and she had nystagmus, photophobia, a right convergent squint, severe myopia, and pale retinæ. She had truncal obesity with tapering of the limbs and small hands and feet. Her IQ was estimated to be in the 30 to 50 range, vocabulary was limited to a few single words, and gross motor function was delayed. Hearing was normal, there was no evidence of any neuromuscular deficit or systemic disease, and there were no additional dysmorphic features. Her genitalia were normal for a prepubertal female.

Cytogenetic studies were performed on peripheral blood lymphocytes. Analysis of G banded chromosomes, containing up to 850 bands per haploid set, showed a normal karyotype without evidence of a deletion in the long arm of chromosome 15. No facilities were available for measurement of hair bulb tyrosinase activity.

FIGURE The proband aged six years. In addition to the truncal obesity and small extremities which characterise the Prader-Willi syndrome, she has hypopigmentation of the skin, hair, and irides which typify albinism.

Discussion

The girl discussed in this article had the Prader-Willi syndrome, classical albinism, and a normal karyotype. The Prader-Willi syndrome was diagnosed on the basis of hypotonia during infancy, hyperphagia with obesity after the neonatal period, mental retardation, and the small hands and feet. Her normal cytogenetic status is in keeping with the fact that a karyotype without a deletion 15(q12) is observed in almost half of the subjects with the Prader-Willi syndrome.¹

A decrease in pigmentation has been described as a component of the multisystem involvement in the Prader-Willi syndrome^{1 3 4} and a positive correlation between the presence of a 15(q12) deletion and hypopigmentation has been mentioned in some reports.^{1 3} Further evidence for a causal link between the Prader-Willi syndrome and albinism derives from the fact that a significant proportion of

persons with the syndrome have optic misrouting and a defect in retinal and optic tract pigmentation.⁵ These abnormalities are indistinguishable from the changes recorded in albinism.

A possible association between the Prader-Willi syndrome and oculocutaneous albinism has previously been suggested by the documentation of families where one member has the Prader-Willi syndrome and other relatives have albinism.^{3 6} A recent report described these two conditions occurring together in a black child with a deletion of chromosome 15.⁷ In the child whom we studied, the occurrence of oculocutaneous albinism and the Prader-Willi syndrome in the presence of a normal karyotype warrants further consideration.

A chromosomal deletion of 15(q12), either visible on karyotyping or at a submicroscopic level, may result in the Prader-Willi phenotype. A gene in this region of the genome could have a controlling influence on tyrosinase activity; hypopigmentation might be the consequence of the heterozygous state of this gene in the Prader-Willi syndrome, as the result of an overt or covert chromosomal deletion. If, in addition, the 'gene for albinism' is inherited on the homologous chromosome, then a combination of the Prader-Willi syndrome and oculocutaneous albinism would be the phenotypic outcome.

The use of molecular markers at 15(q12) could prove of value in the detection of submicroscopic deletions in persons with the Prader-Willi syndrome and a normal karyotype. In this context, the synchronous occurrence of this syndrome and oculocutaneous albinism suggests that the 15q11-q13 region might be a candidate locus for an albinism gene.

Financial assistance for this study was provided by the Guy Elliot Scholarship, the South African Medical Research Council, the Mauerberger Foundation, the Harry Crossley Fund, and the University of Cape Town Staff Research Fund. We thank the Mauritian Ministry of Health for permission to undertake this project and the staff of APEIM for their invaluable assistance.

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A new recessive syndrome of unusual facies, digital abnormalities, and ichthyosis

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SUMMARY Two sibs with a similar pattern of unusual facial features, limb malformations, and postnatal onset of ichthyosis are reported. The parents are first cousins and neither shows any stigmata of the disorder. The presence of ichthyosis suggests that there may be a metabolic component to this syndrome. In view of the consanguinity and pattern of the malformations, autosomal recessive inheritance seems likely.

In communities where consanguinity is common there is an increased incidence of autosomal recessive disorders, some of which are provisionally 'private' syndromes. We describe a family where a male infant was born with multiple symmetrical malformations, those in the limbs affecting the middle rays more than the outer rays. Chromosome analysis was normal and autosomal recessive inheritance was suggested to the parents, who were consanguineous. They went on to have two normal children, followed by a daughter with a similar pattern of malformations. Both affected children failed to thrive and died in infancy. The features of this syndrome are reported here for the first time.

Case reports

CASE 1

This male infant was the second child born to healthy Pakistani parents who are first cousins. The mother was 24 years old and the father 46 years. Their first child was a healthy female and the father has four healthy children from a previous marriage. The patient was born in 1984 by normal vaginal delivery at term after an uneventful pregnancy. Birth weight was 2550 g (3rd to 10th centile), length 50 cm (50th centile), and OFC 31.9 cm (10th to 25th centile). He was noted to have unusual facial features at birth with bilateral inner epicanthic folds,

short forehead, and fullness of the lateral part of the eyelid. He had a small mouth with a thin upper lip and a midline groove in the lower lip. He tended to suck his lips inwards (fig 1). He had a short neck with redundant skin posteriorly and a prominent ear

FIG 1 Case 1 aged two weeks. Note the thin upper lip, the midline groove in the lower lip, and fullness of the lateral part of the eyelid.

Received for publication 3 September 1988.

Revised version accepted for publication 11 November 1988.