

Iris coloboma, ptosis, hypertelorism, and mental retardation: a new syndrome

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SUMMARY Two sibs and an unrelated single patient have a combination of iris coloboma, ptosis, hypertelorism, broad nasal bridge, short stature, and mental retardation. The London Dysmorphology Database was used to determine whether this is a new syndrome.

The concept of a provisionally unique syndrome was formulated by Cohen¹ in 1982 to describe the occurrence in a single person of a syndrome that had not previously been reported. He suggested that it should remain 'private' until other reports appeared. He used the designation 'a pedigree syndrome' to refer to a unique condition in a family. The reason for differentiating between the two was to indicate that the pedigree syndrome was of known genesis whereas the provisionally private or unique syndrome could be either genetic or environmentally caused.

It is a commonplace occurrence for a so called 'new' or 'private' syndrome to be subsequently found in old, often obscure publications. If authors had better access to old published reports it is likely that many of the 'new' syndromes would be encountered. One of the functions of the London Dysmorphology Database is to allow the clinician rapid access to these reports so that clinically similar cases can be ascertained.² We report two sibs and a third single case with an unusual combination of dysmorphic features which could constitute a new autosomal recessive syndrome.

Case reports

CASE 1

Case 1 was first seen when she was seven years of age. She was born after a normal pregnancy to non-consanguineous Asian parents. Her birth weight was appropriate for gestational age and there were no perinatal problems. Her parents first became concerned when she was not sitting at six months and her development has been globally retarded ever since. Now at the age of seven years

she can walk but she has no understandable speech. On examination her height was below the 3rd centile whereas her head circumference was on the 25th centile, as was her weight. She has bilateral ptosis, hypertelorism, a broad nasal bridge, and prominent epicanthic folds (fig 1). In addition, she has bilateral

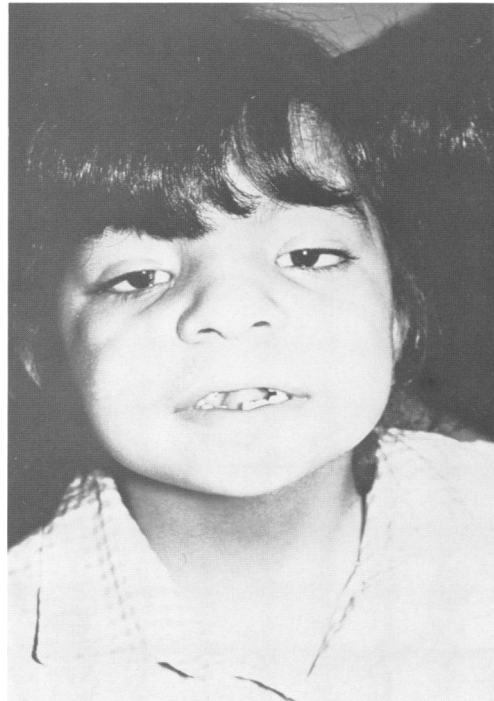


FIG 1 Case 1. Note the bilateral ptosis, hypertelorism, and epicanthus inversus giving an appearance of a broad nasal bridge.

iris colobomata. The rest of the examination was entirely normal.

CASE 2

Case 2, the younger brother of case 1, has a similar history. He is globally retarded. His height is below the 3rd centile, and he has bilateral iris colobomata, ptosis, and prominent epicanthic folds with inferior epicanthus which gives the impression of a broad nasal bridge (fig 2). All investigations including thyroid function and chromosomes were normal.

CASE 3

Case 3 was born by caesarean section and weighed 3.6 kg at birth. She has a normal older sister and her parents are unrelated Caucasians. At seven months of age the parents first became anxious by their daughter's developmental delay and by her unusual appearance. When seen at that stage she was found to have a skull circumference on the 10th centile and a height below the 3rd centile. Her face was characterised by a metopic ridge, broad nasal bridge, bilateral ptosis, and hypertelorism. She had a left sided iris coloboma (fig 3). She was generally hypotonic and globally delayed. She subsequently sat unaided at 14 months and was able to pull herself

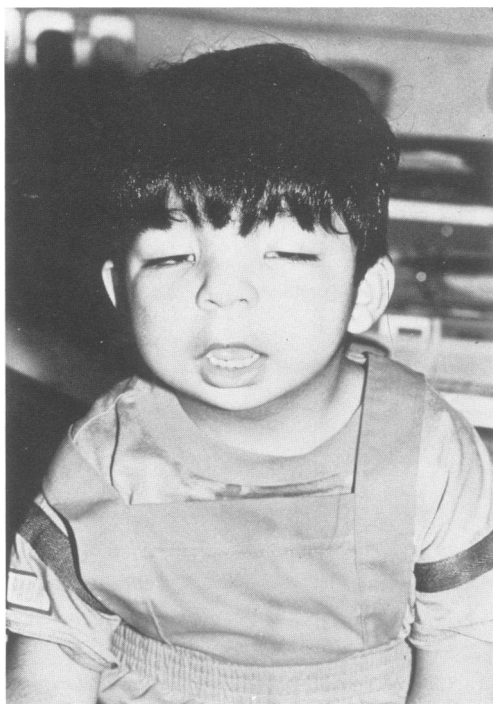


FIG 2 Sib of case 1. Note the similar facial features.

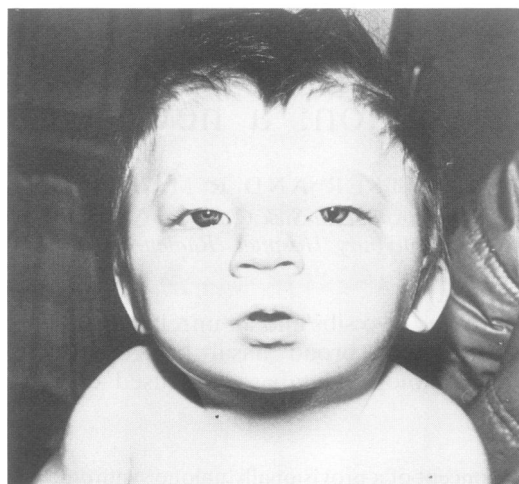


FIG 3 Single patient with left sided iris coloboma, hypertelorism, ptosis, and broad nasal bridge.

up on to furniture at 23 months; she had single words at 17 months. When seen at the age of four years the above features were noted and, in addition, she had a short neck and low posterior hairline. Her stature had remained short, below the 3rd centile, and her development was still greatly delayed. A chromosomal analysis with G banding was normal.

Discussion

The main clinical features in these three children were the presence of colobomata of the iris, ptosis, telecanthus, hypertelorism, mental handicap, and short stature. The nasal bridge appears wide, possibly because of the prominent inferior margin of the broad epicanthus. The cheeks are prominent and slope down to a pointed chin.

Using the London Dysmorphology Database, no conditions had a combination of iris coloboma, mental retardation, and ptosis. On using the combination of iris coloboma and mental retardation, a list of 17 conditions were suggested, but none of these fitted. We considered CHARGE association but two criteria (coloboma and retardation or growth or development or both) are insufficient for a diagnosis. Joubert syndrome⁴ was also considered as iris coloboma and mental retardation are two of the features, but these children did not show an unusual breathing pattern, nor did they have abnormal eye movements or a cerebellar ataxia. The short stature, hypertelorism, ptosis, short neck, and low

posterior hairline did lead us to consider Noonan syndrome⁵ in case 3 but, to date, colobomata of the iris have not been reported and the facial gestalt (figs 1, 2, and 3) is different.

We present these three children to draw to the attention of clinical geneticists a new autosomal recessive syndrome.

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