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Partial Monosomy For Chromosome 22 In A Girl With Mental Retardation

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ABSTRACT

This report describes a 5-year 6-month-old Chinese girl with partial monosomy for the long arm of chromosome 22. The karyotype was 46,XX / 46,XX,del (22) (q13.2). She presented with global developmental delay. Clinical features include seizures, failure-to-thrive, prominent ears, long philtrum and abnormal skin pigmentation on the face and limbs.

Keywords: mental retardation, partial monosomy 22

INTRODUCTION

Mental retardation in association with physical abnormalities is highly suggestive of chromosomal aberrations. With the availability of increasingly sophisticated techniques in the field of cytogenetics, more patients with so-called idiopathic mental retardation and minor dysmorphic facial features may in reality have an abnormal chromosome karyotype previously undetected. Therefore, mental retardation attributed to chromosomal abnormality will be better defined with increasing awareness and reporting.

CASE REPORT

The proband was a 5-year 6-month-old Chinese girl of non-consanguineous parents; mother aged 36 years and father aged 43 years. She has a 12-year-old sister who is phenotypically normal. She was delivered vaginally at 37 weeks gestation with a birthweight of 3225 g [between 50th to 90th centile], length 51 cm [90th centile] and head circumference 31.5 cm [<10th centile]. There was maternal pyrexia and moderate meconium-staining at delivery. APGAR scores were 9 at 1 and 5 minutes. She was well at birth except for microcephaly and mild bilateral clicky hips which subsequently resolved in infancy. At the age of 13 months, she developed febrile convulsions. At 2 years 6 months she was referred to the Development Assessment Clinic at Singapore General Hospital for global developmental delay. She walked unsupported at 20 months and had no speech. At 4 years 4 months she had 2 episodes of atonic fits associated with fever and the EEG done showed continuous generalised slow waves and multiple foci of sharp waves in both hemispheres consistent with secondary generalised epilepsy with multiple seizure types and mental retardation.

Psychological assessment at age 2 years 11 months confirmed global developmental delay with a functional age of approximately 15 months (Bayley's Scale of Infant development). Subsequent assessment at age 4 years 1 month showed her functioning profile to be about 17 months and speech and language skills at about 12 months.

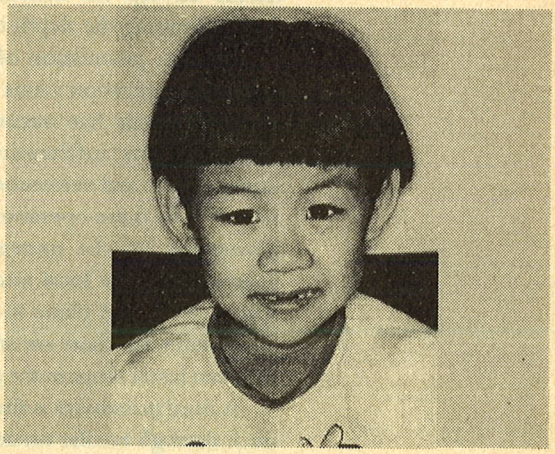

Fig 1 - Photograph of patient showing prominent ears and a long philtrum.

At 5 years 6 months, she weighed 15 kg (10th centile), height measured 97 cm (<3rd centile) and head circumference 49.5 cm (25th centile). She still had no expressive speech inspite of normal hearing. Abnormal clinical features included prominent ears, long philtrum and non-specific abnormal hyperpigmentation on her left cheek and lower limbs. The external genitalia were normal. She was treated with anti-convulsants and placed in a special pre-school education centre. Full blood count, thyroid function tests and serum amino acids levels were normal.

Cytogenetic studies

Chromosomal analysis was carried out on CTG banded metaphase obtained from cultures of PHA stimulated lymphocytes according to standard procedure. High resolution chromosomes were obtained by Methotrexate cell synchronisation. Analysis of CTG banded metaphases showed 46 chromosomes of female karyotype with an apparent deletion of one chromosome 22 at q13.2 in some cells.

For this reason fluorescent-in-situ hybridisation was performed using D22575 DiGeorge chromosome region probe because the control probe D22539 was located at q13.2. In all cells, a positive

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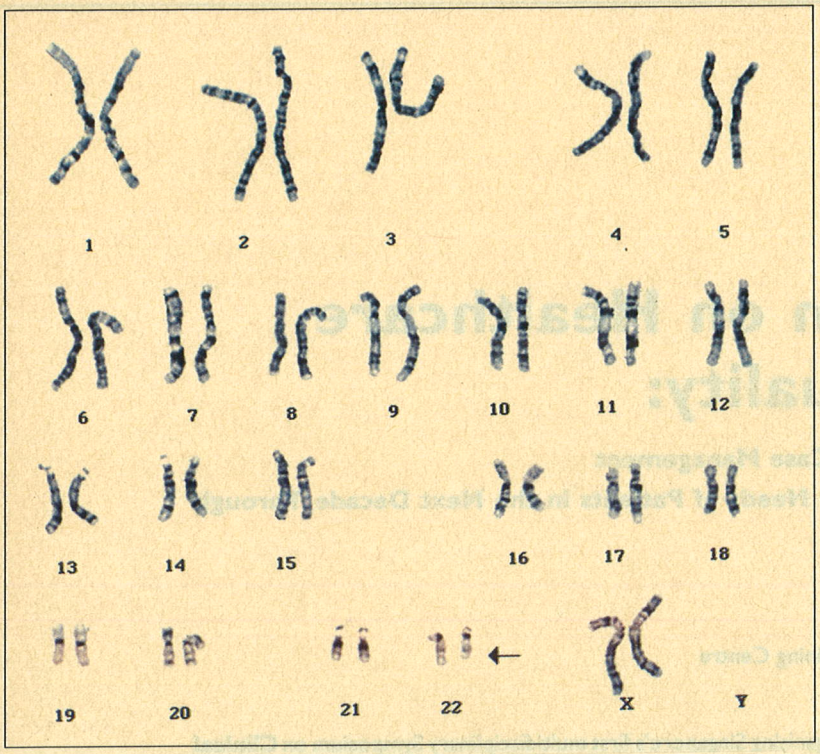

Fig 2 - Karyotype of patient showing deletion of chromosome 22

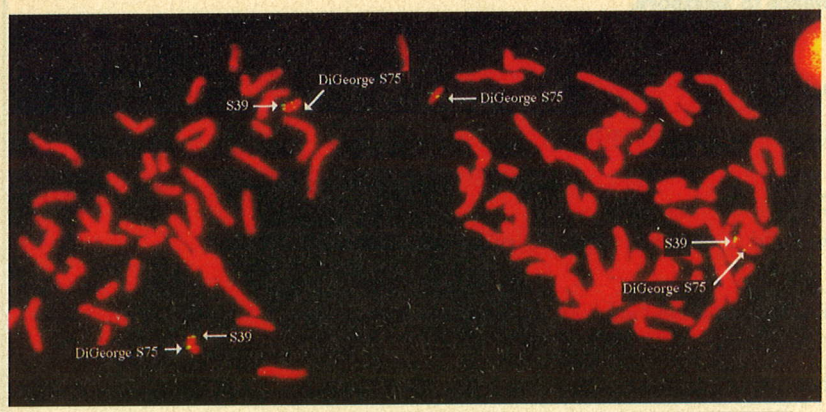

Fig 3 - FISH with Di George S75 probe showed a positive signal on both chromosomes 22.
FISH with S39 probe shows:
a) Left - a positive signal on both chromosomes 22.
b) Right - a positive signal on only one chromosome 22.

signal was observed on both chromosomes 22 at the DiGeorge region. On the other hand, in 14 of the 15 cells analysed, a positive signal was present on only one chromosome 22 at the S39 locus. This confirmed that there was a deletion of this chromosome region in the majority of cells.

DISCUSSION

Constitutional deletions of chromosome 22 most commonly involve loss of the short arm and proximal long arm due to *de novo* rearrangement or to unbalanced segregation of parental translocations. 'Pure' partial monosomy of 22q→ was first reported by Watt et al (1985) in a 14-year-old boy with a deletion of 22q12 → qter due to meiotic recombination of a maternal pericentric inversion[2]. Subsequently, in 1988, Herman et al described a three-month-old-baby with Goldenhar complex due to a terminal deletion of 22q[3]. In 1990, Romain et al reported an 18-month-old-girl with interstitial deletions involving 22q with global developmental delay and many features similar to the boy previously described by Watt et al such as full cheeks and eyebrows, epicanthic folds, long philtrum, wide, flat nasal bridge and long trunk[4]. More recently in 1992, Phelan et al reported a three-year-old with developmental delay, hypotonia, dolicocephaly, ptosis, epicanthal folds and posteriorly angulated auricles associated with cytogenetic, biochemical and molecular evidences of a 22q13 deletion[5]. Narahara et al (1992) described terminal 22q deletion associated with a partial deficiency of arylsulphatase A (ARSA) in a 7-month-old girl with psychomotor retardation, axial hypotonia and minor malformations[6]. They suggested that as the ARSA and Myoglobin (MB) loci have been mapped to 22q13.31 → qter (HGM10) and 22q11.2 → q13 (HGM10) respectively, the marked hypotonia may be due to a hemizygous deficiency of the MB or some other locus crucial to cerebellar embryogenesis.

There are few reports of terminal deletions of the long arm of chromosome 22. Although it is known that deletions of proximal 22q are associated with DiGeorge syndrome, the deletion of distal 22q has no distinctive phenotypes other than mental retardation.

The patient we have described is the first case of partial monosomy for chromosome 22 reported in the local population. Chromosomal analysis was done because chromosomal abnormality was suspected in the presence of severe global developmental delay, epilepsy and mild facial dysmorphism. Therefore, it must be emphasised that mental retardation with no apparent aetiology deserves a careful investigation with chromosomal study, especially when dysmorphic features are present.

REFERENCES

1. Yunis JJ. High resolution of human chromosomes - The attainment of 2000 bands. Science 1976; 191:1268-70.
2. Watt JL, Olson IA, Johnston AW, Ross HS, Couzin DA, Stephen GS. A familial pericentric inversion of chromosome 22 with a recombinant subject illustrating a "pure" partial monosomy syndrome. J Med Genetics 1985; 22:283-7.
3. Herman GE, Greenberg F, Ledbetter DH. Multiple congenital anomaly/mental retardation syndrome with Goldenhar complex due to a terminal del (22q). Am J Med Genetics 1988; 29:909-15.
4. Romain DR, Goldsmith J, Cairney H, Columbano - Green LM, Smythe RH, Parfitt RG. Partial monosomy for chromosome 22 in a patient with del (22) (pter → q13.1: q13.33 → qter). J Med Genetics 1990; 27:588-9.
5. Phelan MC, Thomas GR, Saul RA, Rogers RC, Taylor HA, Wenger DA, et al. Cytogenetic, biochemical and molecular analyses of a 22q 13 deletion. Am J Med Genetics 1992; 43:872-6.
6. Narahara K, Takahashi Y, Murakami M, Tsuji K, Yokohama Y, Murakami R, et al. Terminal 22q deletion associated with a partial deficiency of arylsulphatase A. Am J Med Genetics 1992; 29:432-3.