A pericentric inversion duplication of the subcentromeric region of chromosome 12q

The proband, a 1 year old girl, was referred because of dysmorphic features and developmental delay. There was no family history of congenital abnormalities and the mother had received no drugs during her pregnancy.

The mother was 25 and the father 26 years old at the time of the birth. The pregnancy was normal and the birth uncomplicated. She learnt to sit at 3 months and to crawl at 5 months. She now walks unaided, yet she does not talk or make any sounds. She appears to understand what is said to her. The only abnormalities are a large protruding tongue and epicanthic folds.

Cultured peripheral lymphocytes were used for chromosomal analysis with GTG and R banding. All 15 cells examined showed an elongation of the short arm of one of the chromosomes 12. This was evaluated in the G banded slides as an inverted duplication in the short arm of the immediate subcentromeric region of the long arm: dup(12p)(q11→q12) (figure). The chromosomes of both parents were normal.

A P Albert, Jennifer Holdsworth, and Carol Massyn
Department of Cytogenetics, Eastern Province Blood Transfusion Service, Port Elizabeth 6000, South Africa.

Correspondence and requests for reprints to Dr A P Albert, Department of Cytogenetics, Eastern Province Blood Transfusion Service, Buckingham Road, Port Elizabeth 6000, South Africa.

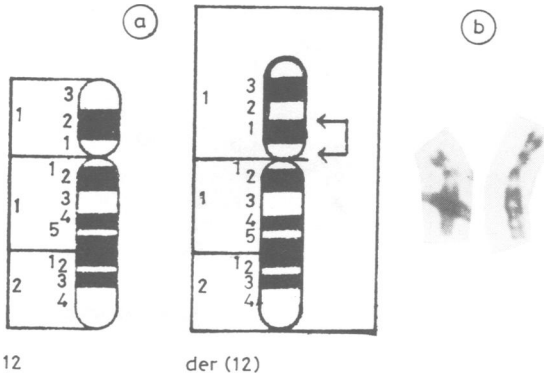

FIGURE *(a) Diagram of normal and abnormal chromosomes 12. (b) G banded partial karyotype showing the inversion duplication.*

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Partial trisomy 1q25→qter

A male infant, birth weight 2·78 kg, gestation 38 weeks, with chromosomally normal parents, had a karyotype 46,XY,−17,+der(17),t(1;17)(q25;p13) (figure). Clinical findings included moderate enlargement of the cranium with a prominent forehead naevus, long philtrum, thin upper lip, very small palpebral fissures, irregular gums, large asymmetrical ears, undescended testes, hypoplastic scrotum, bifid right thumb, syndactyly of the second and third toes of the left foot, and rockerbottom feet. The infant showed cardiorespiratory distress and died at 10 hours. Necropsy revealed a ventricular septal defect but the brain was well developed and the optic nerves and tracts, olfactory nerves, corpus callosum, and septum pellucidum all appeared normal.

E Janet Tawn*, M B R Roberts†, R G Ghazala‡, and Elizabeth M T Pyta*
**Cytogenetics Laboratory, Medical Department, British Nuclear Fuels plc, Seascale, Cumbria CA20 1PG; and Departments of Paediatrics† and Pathology‡, West Cumberland Hospital, Hensingham, Whitehaven, Cumbria CA28 8JG.*

Correspondence and requests for reprints to Mrs E J Tawn, Cytogenetics Laboratory, Medical Department, British Nuclear Fuels plc, Seascale, Cumbria CA20 1PG.

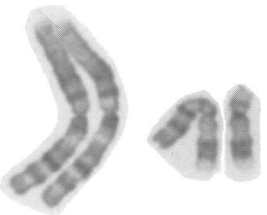

FIGURE *Partial karyotype of chromosomes 1 and 17.*

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Secondary amenorrhoea and 47,XX,i(Xq) karyotype

A 25 year old female underwent normal pubertal development with menarche at 10 years of age. Her menses were regular until 21 years of age when they became scanty and irregular. She received cyclic hormonal therapy with withdrawal bleeding, but for 18 months before being seen

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at 25 years of age she had received no hormonal therapy and had experienced no menstrual bleeding. At 6 years of age she had 'Bright's disease' which resolved after several months' stay in hospital. Her general health thereafter was excellent apart from intermittent, mild peripheral oedema.

Her physical examination showed a height of 155 cm, a weight of 62 kg, a blood pressure of 130/70, moderate obesity, and a grade 2/4 systolic ejection murmur. She had normal sexual development. The pelvic examination was normal apart from failure to palpate either ovary.

Laboratory studies included FSH of 183 IU/l (normal 2·5 to 27), LH of 256 IU/l (normal 3 to 250), T3 uptake of 30%, and T4 of 88 μg/dl. Analysis of peripheral lymphocytes by standard Q, G, and C banding showed a 47,XX,i(Xq) karyotype in all cells. Fibroblasts cultured from a forearm skin biopsy also showed only 47,XX,i(Xq). Late labelling studies with BrdU in lymphocytes and fibroblasts showed two late replicating X chromosomes in all cells analysed, one of which was the i(Xq) chromosome.

Two abnormal events must have given rise to the 47,XX,i(Xq) karyotype: non-disjunction resulting in the aneuploidy (47 chromosomes) and the formation of the isochromosome X. There is no simple explanation to relate the two abnormalities to a single event, or to explain one abnormality as predisposing to the other. Assuming that the 47,XX,i(Xq) karyotype in our patient was related to the premature ovarian failure, this would be difficult to reconcile with the report of King and Schimke.[1] Other explanations can be offered for this apparent discrepancy.

First, the 47,XX,i(Xq) state is not associated with abnormal gonadal function and our patient's gonadal failure is secondary to a cause unrelated to her karyotype. Secondly, the 47,XX,i(Xq) in our patient is the cause of her gonadal failure and the normal phenotype in the patient of King and Schimke occurred as the result of an undetected mosaicism for a normal cell line. Thirdly, the patient of King and Schimke represents the normal phenotypic expression of the 47,XX,i(Xq) karyotype and our patient's gonadal failure was the result of an undetected mosaicism. Either 45,X or 46,X,i(Xq) might be expected to have occurred and either would be an adequate explanation for the premature ovarian failure.

Reconciliation of the difference between these two cases will require additional reports of patients with the 47,XX,i(Xq) karyotype. It will be important that an extensive search for mosaicism is conducted in such cases.

THADDEUS E KELLY*, JOHN W WILKS†, AND HERMAN E WYANDT*
*Division of Medical Genetics, University of Virginia School of Medicine, Charlottesville, Virginia; and †Jefferson Surgical Clinic, Roanoke, Virginia, USA.

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Correspondence and requests for reprints to Dr Thaddeus E Kelly, Box 386, University Hospital, Charlottesville, Virginia 22908, USA.

Necropsy findings in a child with FG syndrome

In 1983, Burn and Martin[1] reported from this unit two male cousins with mental retardation, congenital hypotonia, intractable constipation, failure to thrive, and dysmorphic facies as possible examples of the X linked FG syndrome. Few pathological studies have been reported and we felt that it would be interesting to report the necropsy findings in the proband of Burn and Martin.

The brain. The brain weighed 800 g (normal for age 1100 g) and was brachycephalic. The convolutional pattern was simple with broader and fewer gyri than normal. A very large 'cystic' cavum septi pellucidi was present which communicated with the lateral and third ventricles through large fenestrations (figure). The corpus callosum was present throughout, but thin. Histologically, only acute anoxic changes and one isolated neuronal heterotopia in the cerebellar white matter were observed; no other evidence of migration defect was observed.

The septum pellucidum, which develops as a result of caudal growth of the corpus callosum, often shows a midline cleft-like space, called the cavum septi pellucidi, especially in fetuses and young children. Friede[2] has suggested that a large cavum septi pellucidi may be a 'forme fruste' of agenesis of the corpus callosum and may be associated with a thin corpus callosum. This finding is therefore of interest, since case 2 reported by Opitz and

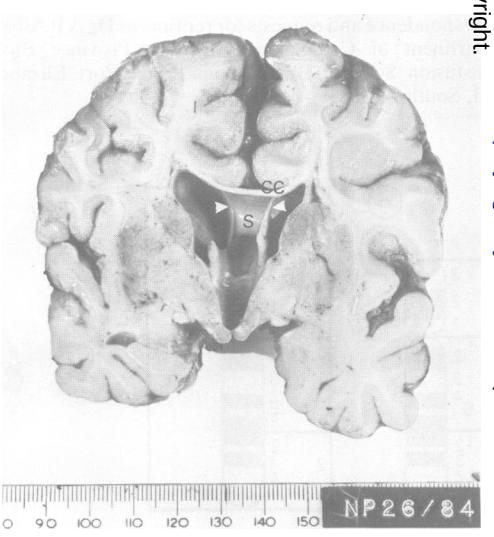

FIGURE *Coronal section of the brain at mammillary body level. A cystic cavum septi pellucidi (S) communicates with the lateral ventricles via large fenestrations (arrowheads). The corpus callosum (CC) is very thin and the gyral pattern slightly simplified.*

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