Robertsonian translocations which are generally inherited,⁷ balanced homologous Robertsonian translocations are considered to originate de novo immediately after fertilisation or in early embryogenesis.^{18,19} However, in two cases transmission of a balanced homologous t(22q22q) from a mother to a phenotypically normal daughter has been established.^{17,19} This anomalous inheritance could be explained either by fertilisation of an ovum carrying the translocation by a sperm nullisomic for chromosome 22 or by early post-zygotic loss of a chromosome 22 from a trisomic zygote.^{17,19}

These latter reports therefore complicate the issue of genetic counselling in couples where one partner has a homologous Robertsonian translocation. Previously it was assumed that phenotypically normal offspring were not possible and sterilisation has been advocated.³ However, carriers might now be counselled that, although the chance of having a normal child is probably very small, it remains an unquantifiable possibility and that, if couples elect for a pregnancy, fetal karyotyping could be undertaken should the gestation reach 16 weeks.

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References

- Caspersson T, Hultén M, Lindsten J, Therkelsen ÅJ, Zech L. Identification of different Robertsonian translocations in man by quinacrine mustard fluorescence analysis. *Hereditas* 1971;**67**:213–20.
- Lucas M, Wallace I, Hirschhorn K. Recurrent abortions and chromosome abnormalities. *J Obstet Gynaecol Br Commonw* 1972;**79**:1119–27.
- Parslow MI, Gardner RJM, Veale AMO. Giemsa banding in the t(13q13q) carrier mother of a translocation trisomy 13 abortus. *Humangenetik* 1973;**18**:183–4.
- Lewis BV, Ridler MAC. Recurrent abortion associated with a balanced 22:22 translocation, or isochromosome 22q in a monozygous twin. *Hum Genet* 1977;**37**:81–5.
- Žizka J, Baliček P, Finková A. Translocation D/D involving two homologous chromosomes of the pair 15. *Hum Genet* 1977;**36**:123–5.
- Hultén M, Lindsten J. The behaviour of structural aberrations at male meiosis. In: Jacobs PA, Price WH, Law P, eds. *Human population cytogenetics*. Edinburgh: Edinburgh University Press, 1970:23–61.
- Hamerton JL, Canning N, Ray M, Smith S. A cytogenetic survey of 14,069 newborn infants. 1. Incidence of chromosome abnormalities. *Clin Genet* 1975;**8**:223–43.
- Guanti G. A new case of rearrangement of chromosome 15 associated with Prader-Willi syndrome. *Clin Genet* 1980;**17**:423–7.
- Ledbetter DH, Riccardi VM, Airhart SD, Strobel RJ, Keenan BS, Crawford JD. Deletions of chromosome 15 as a cause of the Prader-Willi syndrome. *N Engl J Med* 1981;**304**:325–9.
- Ferguson-Smith M, Ellis PM. Personal communication, 1970. Cited in Cohen MM. The chromosomal constitution of 165 human translocations involving D group chromosomes identified by autoradiography. *Ann Genet (Paris)* 1971;**14**:87–96.
- Furbetta M, Falorni A, Antignani P, Cao A. Sibship (21q21q) translocation Down's syndrome with maternal transmission. *J Med Genet* 1973;**10**:371–5.
- Murken JD, Bauchinger M, Palitzsch D, Pfeifer H, Suschke J, Haendle H. Trisomie D₂ bei einem 2½ jährigen Mädchen (47,XX,14+). *Humangenetik* 1970;**10**:254–68.
- Coldwell S, Fitzgerald B, Semmens JM, Ede R, Bateman C. A case of trisomy of chromosome 15. *J Med Genet* 1981;**18**:146–8.
- Shokeir MHK. Complete trisomy 22. *Clin Genet* 1978;**14**:139–46.
- Kajii T, Ferrier A, Niikawa N, Takahara H, Ohama K, Avirachan S. Anatomic and chromosomal anomalies in 639 spontaneous abortions. *Hum Genet* 1980;**55**:87–98.
- Boué J, Daketsé MJ, Deluchat C, Ravisé N, Yvert F, Boué A. Identification par les bandes Q et G des anomalies chromosomiques dans les avortements spontanés. *Ann Genet (Paris)* 1976;**19**:233–9.
- Kirkels VGHJ, Hustinx TWJ, Scheres JMJC. Habitual abortion and translocation (22q:22q): unexpected transmission from a mother to her phenotypically normal daughter. *Clin Genet* 1980;**18**:456–61.
- Gardner RJM, Parslow MI, Veale AMO. The formation of the abnormal chromosome in balanced homologous Robertsonian translocation carriers. *Humangenetik* 1974;**21**:279–82.
- Palmer CG, Schwartz S, Hodes ME. Transmission of a balanced homologous t(22q:22q) translocation from mother to normal daughter. *Clin Genet* 1980;**17**:418–22.

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Pregnancy in a patient with 47,XX,i(Xq) karyotype

SUMMARY A phenotypically normal woman with a 47,XX,i(Xq) karyotype is reported. She has had two successful pregnancies monitored by prenatal diagnosis with the delivery of normal offspring. The presence of a structurally abnormal third X chromosome has not demonstrably affected this patient or her reproduction.

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The importance of the human X and Y chromosomes in sexual differentiation is readily apparent. Patients with anomalies of the X chromosome most frequently have clinical features of Turner's syndrome. Much less clearly defined are patients who possess additional X chromosome material. For example, triple X females are not easily distinguishable from 46,XX females.^{1,2} Only a few cases have been reported of patients who have a 47,XXX karyotype with the third X chromosome being structurally abnormal.³ This report describes a patient with a 47,XX,i(Xq)(qter→cen→qter) karyotype.

Case report

The patient presented at the age of 14 because of short stature. At that time she was 137 cm in height and a diagnosis of hypothyroidism was made. Thyroid replacement therapy was started and over the subsequent 2 years she grew 15.2 cm in height. An incidental buccal smear was done and this identified a very large Barr body in 43% of the cells. A normal sized Barr body was not seen. Complete karyotypic analysis with G banding demonstrated a 47,XX,i(Xq)(qter→cen→qter) chromosome complement. A single centromere was identified with C banding. Mosaicism was not identified in either peripheral lymphocytes (200 cells) or skin fibroblasts (150 cells). Chromosome analyses of the patient's parents and sibs were normal. Spontaneous pubertal development began at 15½ years of age with menarche following 3 months later. Her adult height is 157.5 cm.

At the time of birth the patient weighed 2920 g and was 47 cm in length. Her growth since birth was approximately at the level of the 10th to 15th centile and then increased after starting the thyroid replacement therapy. The patient's physical examination at the age of 14 was within normal limits with the exception of the short stature. Eighteen months after the initiation of the thyroid replacement therapy pubertal changes started, with normal breast development, pubic hair growth, and onset of spontaneous menses. Her menses have continued normally into adult life.

She has had two spontaneous pregnancies, both ending with the birth of normal infants. Her first born child was a normal male, 46,XY, Apgar 9, 3289 g in weight. The second pregnancy resulted in a female infant, 46,XX, Apgar 10, weighing 3487 g. Both pregnancies were monitored with prenatal diagnosis by amniocentesis and chromosome analysis.

Discussion

Patients with a variety of structural abnormalities of

the X chromosome, including deletions and isochromosomes, have been reported to have features of Turner's syndrome.⁴ In contrast, patients with an additional X chromosome, such as the 47,XXX female, have frequently been reported to be normal. In fact, so far it has not been possible to establish a specific clinical syndrome associated with the 47,XXX karyotype.^{1,2}

Many triple X patients are phenotypically normal and have only been identified during large scale population screening.^{1,2} Some exhibit mental retardation although the majority of 47,XXX females do not. Other patients have been reported with reproductive failure, such as pregnancy wastage or menstrual irregularities or both.⁵ However, no specific clinical syndrome has been identified for these XXX persons or for patients with a structurally abnormal third X chromosome.³

The presence of a normal phenotype plus the identification of an abnormally large Barr body in the buccal smear of our patient would suggest that in the majority of her cells the abnormal X chromosome is inactivated. BrdU studies to show X chromosome inactivation were not performed. This patient has no evidence of mental retardation; in fact she has successfully completed a college degree.

Although we feel that patients with a sex chromosome abnormality are obviously at higher risk of transmitting an abnormal X chromosome to their offspring,⁶ it does appear that in some cases a successful pregnancy may occur. To ensure a successful outcome of pregnancy, however, prenatal diagnosis is advisable for these patients. A third structurally abnormal X chromosome does not appear to markedly interfere with reproduction or with other cellular function in some patients,⁷ including the case described here. The inactivation of the structurally abnormal X chromosome presumably minimises the disturbance of cellular function and may explain the normal phenotype and reproductive outcome of this patient. However, the presence of an unrecognised 46,XX cell line could account for the normal phenotype and reproductive history of our patient.

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References

- ¹ Barr ML, Sergovich FR, Carr DH, Shaver EL. The triplo-X female: an appraisal based on a study of 12 cases and a review of the literature. *Can Med Assoc J* 1969; **101**:247-58.
- ² Tennes K, Puck M, Bryant K, Frankenburg W, Robinson

- A. A developmental study of girls with trisomy X. *Am J Hum Genet* 1975;27:71-80.
- ³ Borgaonkar DS. *Chromosomal variation in man. A catalog of chromosomal variants and anomalies*. 2nd ed. New York: Liss, 1977.
- ⁴ Simpson JL. *Disorder of sexual differentiation. Etiology and clinical delineation*. New York: Academic Press, 1976.
- ⁵ King CR, Magenis E, Bennett S. Pregnancy and the Turner syndrome. *Obstet Gynecol* 1978;52:617-24.
- ⁶ Dewhurst J. Fertility in 47,XXX and 45,X patients. *J Med Genet* 1978;15:132-5.
- ⁷ Mattei MG, Mattei JF, Vidal I, Giraud F. Structural anomalies of the X chromosome and inactivation center. *Hum Genet* 1981;56:401-8.

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A homozygote for pericentric inversion of chromosome 4

SUMMARY A child with developmental and language delay was found to be homozygous for a pericentric inversion of chromosome 4 (inv(4)(p15·2q12)). Her normal mother and aunt are inversion heterozygotes. It is suggested that the phenotypic abnormalities may have resulted from damage at chromosomal breakpoints or from a position effect which is expressed only in homozygous form.

The incidence of pericentric inversions in the general population is quite low (0·01% in surveys of unselected newborns),¹ although higher frequencies of 1·0% to 2·8% have been reported in selected populations.²⁻⁴

Inversions are often ascertained as a result of their occurrence in abnormal subjects but may be coincidental findings. Although inversion heterozygosity has been associated with infertility⁵ or reduced fertility, and high neonatal mortality,⁶ as well as increased risk of offspring with chromosome aberrations or mental retardation,⁷⁻⁹ it is the general impression that pericentric inversions are usually harmless in a single dose. The effect of homozygosity of pericentric inversions on the phenotype has not been firmly established since only a few cases have been reported.^{2 10-13}

We present a developmentally and mentally retarded child who is homozygous for a pericentric inversion of chromosome 4. Her mother and maternal aunt, who are phenotypically normal, are heterozygotes. We suggest that the abnormalities

seen in this child are the result of damage at the chromosomal breakpoints or of a position effect which is expressed only in homozygous form.

Case report

A black female was first seen at 4 years 8 months of age because of developmental and severe language delay. She was the only child of a 20-year-old mother and a 21-year-old father. Consanguinity in this relationship was denied. The pregnancy was complicated by prolonged nausea and vomiting and the delivery was by caesarean section. Her birth weight was 1930 g.

Physical examination on admission to this hospital showed a small child with a prominent forehead, mild dolichocephaly, pointed chin, and a broad nasal bridge. The eyes were deep set and the ears were large with accentuated lobes. Both height and weight (97·8 cm and 14·3 kg) corresponded to the 3rd centile although the head circumference (48·6 cm) was in the normal range. The extremities were slender with long hands and feet. Muscle mass was poorly developed. Her movements were jerky and her gait was flat footed.

The patient's early development was delayed. She stood at 12 months and walked at 3 years of age. She was shown to be functioning with gross motor skills at the 2½ year level and with fine motor skills at the 18 to 24 month level. She achieved a cognitive developmental index of 71 and a motor developmental index of 74 on the Bailey Mental Scale and Bailey Motor Scale, respectively. Her receptive and expressive language skills were both at the 1 year level on the Receptive-Expressive Emergent Language Scale. She had a moderate bilateral sensorineural hearing loss, more severe on the right side.

The results of routine laboratory studies, including full blood count, urine analysis, blood and urine amino-acids, T4 and TSH, x-rays and hand pattern profile analysis were normal. An electroencephalogram was normal and a CT brain scan showed no abnormalities. Dermatoglyphic analysis showed normal palmar creases, an *atd* angle of 98°, a total finger ridge count of 115, and seven ulnar loops, two arches, and one whorl on the fingertips.

Chromosome analysis of peripheral blood lymphocytes and skin fibroblasts showed a homozygous pericentric inversion of chromosome 4, using GTG and RBA banding. Her karyotype was 46,XX,inv(4)(pter→p15·2::q12→p15·2::q12→qter), inv(4)(pter→p15·2::q12→p15·2::q12→qter). The inversion appeared to be the same in both chromosomes and was present in all cells examined (figs 1a, 2).

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