

# Case reports

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## De novo paracentric inversion in an X chromosome

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**SUMMARY** A 10½ year old female with skeletal abnormalities was referred for genetic consultation because of learning disabilities and a suggestion of 'Turner-like' stigmata. Cytogenetic analysis revealed a paracentric inversion of an X(q13·1q26·1) chromosome.

Before the advent of chromosome banding techniques paracentric inversions were virtually undetectable. Although high resolution banding is now being used regularly to detect small structural rearrangements, paracentric inversions apparently remain relatively rare. We have been able to find fewer than 25 published cases since the first report of Del Solar and Uchida in 1974<sup>1</sup> and none of them involved an X chromosome. In 1981 Ridler and Sutton<sup>2</sup> cited 15 unpublished cases of paracentric inversions, one of which was reportedly an Xq. One other Xq case, by Shabtai *et al.*,<sup>3</sup> was cited in the Abstracts of the European Society of Human Genetics Symposium on X-linked Diseases in 1982. We report here a paracentric inversion in an X(q13·1q26·1) of a prepubertal female with learning disabilities and skeletal anomalies.

### Case report

The patient (fig 1), a 10½ year old white female, was the product of the only pregnancy of a 24 year old woman and her 29 year old non-consanguineous husband. The pregnancy was complicated by cholestasis requiring cholecystectomy eight weeks after delivery. The gallbladder disease contributed to persistent nausea which was treated with either Bendectine or Compazine throughout the pregnancy. There also was a vaginal infection early in gestation which was treated topically. Failure of cervical dilation beyond three fingers following a 30 hour labour necessitated delivery by caesarean

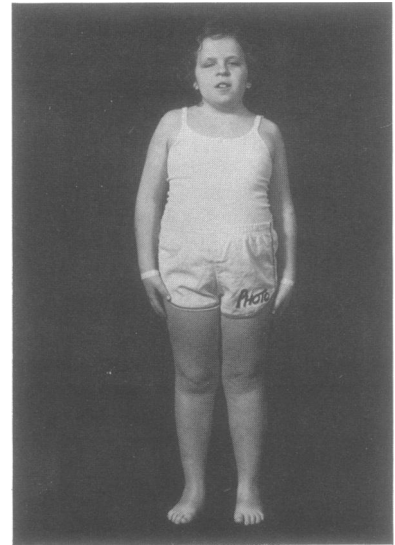


FIG 1 The proband aged 10.

section. Birth weight was 3·68 kg and length was 50·8 cm.

No abnormalities were noted at birth, and early developmental milestones were considered to be within normal limits. Learning difficulty, however, became apparent at school age, and the patient has always been in special schools for the neurologically impaired. She has minimal brain dysfunction with gross and fine motor incoordination as well as visual perceptive defects. At the age of 9 an abnormal gait was detected and she was referred for orthopaedic evaluation. The left femoral head was consistent with osteonecrosis and acetabular dysplasia, and mild thoracic scoliosis was noted. An arthrogram showed a voluminous joint capsule with mild lateral displacement of the left femur. Diagnostic studies, including T3, T4, and TSH, were within normal limits. A CT scan confirmed an enlarged thymus

considered to be due to benign hyperplasia. Because somewhat 'Turner-like' facies and habitus were noted, a genetics consultation was requested while the patient was in hospital for orthopaedic procedures.

On physical examination at the age of 10½ years, her height (140.2 cm) was at the 50th centile for age, but her weight (42.5 kg) was at the 50th centile for 12 years. Her head circumference was greatly increased (55.2 cm), representing the 50th centile for 18 years. The face was large with heavy jowls, the neck was very short, and the nuchal hairline quite low. The broad chest was symmetrical. The breasts were prepubertal, as were the external genitalia. There were no cardiac thrills or murmurs and the lungs were clear. Obesity was marked, but no abdominal organomegaly was present. Numerous dark brown pigmented macular moles were scattered over most of her body. Bilateral brachydactyly of the fifth fingers was noted. The feet were short and broad and the patient walked with a Trendelenberg gait to the left.

CYTOGENETIC STUDIES

Chromosome analysis, using high resolution banding techniques,<sup>4</sup> revealed a modal number of 46 with a paracentric inversion of one of the X chromosomes in all cells examined. Replication studies determined that the inverted X was active 50% of the time. The karyotype was 46,XX,inv(X)(q13·1q26·1) (figs 2a and b). A buccal smear showed 9% Barr bodies. Dermatoglyphic analysis was essentially unremarkable, except for an accessory interdigital triradius on the right hand and thenar patterns bilaterally. The total finger ridge count was not raised. High resolution banded chromosomes from both parents revealed normal 46,XX and 46,XY karyotypes.

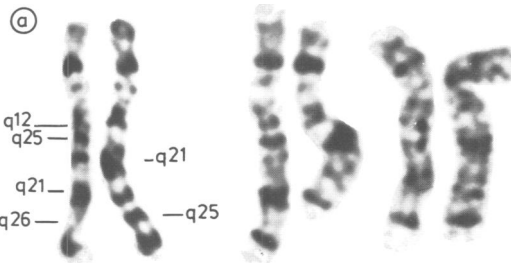


FIG 2a Representative pairs of X chromosomes with inverted X on the left.

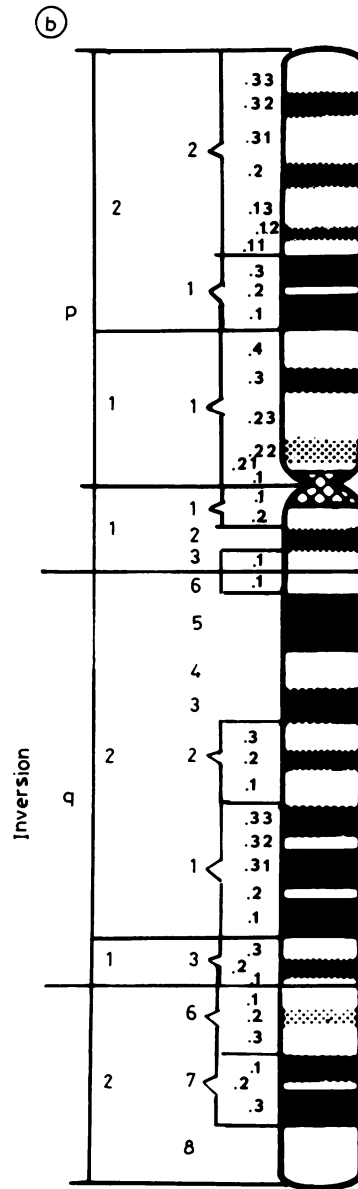


FIG 2b Diagram of the X chromosome with inversion.

Discussion

With so few cases of paracentric inversions having been reported, none of which involved an X chromosome, the phenotypic effect of such a rearrangement cannot be clearly defined. It is possible, however, that there is a relationship

between the structural abnormality of the X chromosome and the physical findings in this case. Although the banding studies indicated a rearrangement of chromosome material, no visible deletion could be detected. The 'critical region' hypothesis of Sarto *et al*<sup>5</sup> proposed that breaks from Xq21 to Xq25 result in gonadal dysgenesis. However, Summitt *et al*<sup>6</sup> extended this region proximally to include Xq13 and the upper breakpoint in our patient is at band Xq13.1. Since the patient was prepubescent and surgery was imminent, a complete endocrine evaluation was declined by the family. It will be important to follow her progress over the next few years, and if puberty does not ensue, efforts will be made to obtain the endocrine studies. Should she achieve spontaneous sexual maturation and menarche, we could not predict with certainty the phenotype of any offspring, but it would seem reasonable to assume that fertility might be reduced. Unequal crossovers within the loop of the inverted chromosome could result in unstable derivative chromosomes. In addition, liveborn children with multiple anomalies due to rearrangements of duplication or deletion might result, for which antenatal diagnosis could be performed.

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## Monosomy 13q32.3→qter: report of two cases

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**SUMMARY** Two unrelated patients with monosomy 13q32.3→qter are reported. Comparison with six similar cases previously published indicates that the craniofacial dysmorphism of the 13qter monosomy syndrome is related to band 13q34, the thumb hypoplasia to band 13q32, and an apparently different phenotype to band 13q33. Coagulation deficiency appears to be non-specific in monosomy 13qter.

The purpose of this report is to describe two cases of monosomy 13q32.3→qter and to review the karyotype-phenotype correlation.

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#### Case reports

##### CASE 1

The proband, a girl, was the product of the 12th pregnancy and normal delivery. She suffered from mild hypoxia during the neonatal period. Developmental milestones were delayed and at 5 months of age she was unable to control her head or to sit unsupported. At this age, physical examination (fig 1) revealed multiple abnormalities (table), including low set posterior hairline, large ears with overdeveloped lobules and prominent antitragus, inverted left nipple, slender fingers, sacral dimple, muscular hypotonia, and weak cry. No cardiac murmur was audible. A CT scan disclosed enlarged ventricles and basal cisternae. A skeletal x-ray showed abnormal ossification of the T3 vertebral