TABLE Summary of clinical findings in three cases of trisomy 9q.

	Turleau et al ¹	Faed et al ²	Present case
Trisomic segment	q11→q33	q12→q32	q12→q32
Pregnancy (wk)	40	36	37
Birth weight (g)	2300	1730	2300
Length (cm)	50		44
Head circumference (cm)	32.5		29
Sex	M	M	F
Asphyxia or neonatal problems	+	+	—
Microdolichocephaly	+	+	+
Slender face	+	(+)	+
Hypotelorism	+	— (Wide set)	+
Horizontal palpebral fissures	+	+	+
Epicanthic folds	+	+	+
Strabismus	+	+	—
Nose	Beaked	Beaked	Beaked
Mouth	Small	Small	Small
Lips			Thin upper lip overlaps lower lip
Micrognathia	+	+	+
Abnormality of the thumbs	+		+
Hip joint		Flexion contracture	Unilateral dislocation
Feet	Long toes with abnormal implantation		Normal
Internal malformation	Ventricular septal defect		
Thriving	Poor	Poor	Poor
Mental retardation	+	+	+
Natural history	Alive at 5 years	Alive at 4 years	Alive at 2 years

Discussion

As far as we are aware, there have been only two reported cases of trisomy 9q in which most of the long arm is involved (table). The clinical features common to all three cases are: low birth weight, failure to thrive, mental retardation, narrow face, epicanthic folds, beaked nose, small mouth, micrognathia, and good life expectancy during infancy. These similarities should make it possible to recognise this abnormality on the basis of clinical findings. It is remarkable that the presence of such a large extra segment has a relatively mild effect on the patient.

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Familial centric fission of chromosome 4

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SUMMARY A centric fission of chromosome 4 is described in the proband and his mother, both phenotypically normal. In addition, partial monosomy for the long arm or the short arm or

both of chromosome 4 may have been present in two of the proband's sibs who died in infancy and childhood, respectively.

Centric fission of a chromosome consists of a break in the centromeric region, which results in the

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separation of the centromere into two portions, and consequent formation of two stable telocentric chromosomes. Such an event, well known in animals, was first described in humans by Sinha *et al.*¹ Other cases of centric fission in man have been reported by Hansen,² Fryns *et al.*,³ and more recently by Janke.⁴

The only case of centric fission of chromosome 4 reported so far was described by Dallapiccola *et al.*⁵ in the mother of two patients with trisomy 4p.

Case report

A couple requested genetic counselling because of familial infertility. A pedigree analysis, which was uninformative for the wife, indicated, however, con-

sanguinity in the husband's family, his parents being first cousins (fig 1). In addition, the sibship of the husband's mother (IIIA) included three spontaneous abortions and two deaths in early childhood, and the husband's sibship (IVB) also included two spontaneous abortions and two deaths (IV.11 and IV.15).

Chromosome analysis showed a normal karyotype for the wife and a 47,XY,cen fiss 4 complement for the husband. As a result, the proband's parents were also examined. The father (III.7) had a normal karyotype, while the mother (III.8) was found to have a centric fission of chromosome 4.

The clinical data regarding the dead children, IV.11 and IV.15, were based on the mother's report and on examination of photographs (table 1).

FIG 1 Family pedigree.

TABLE 1 Clinical data of patients IV.11 and IV.15.

Clinical data	IV.11	IV.15
Birth weight	Normal	Normal
Growth	Normal	Normal
Psychomotor retardation	Severe	Severe
Delay in walking	—	Later than 2 years
Delay in language development	—	Later than 2 years
Convulsions	Frequent	Frequent
Microcephaly	Not identified	Present
Glabella	Normal	Prominent
Palpebral fissures	Mongoloid slant	Not identified
Strabismus	Absent	Present
Nose	Wide and flat bridge	Beaked
Ear abnormality	Pointed	Large, low set
Micrognathia	Doubtful	Present
Hypoplasia of mandible	Moderate	Present
Cardiac defects	Not identified	Present
Age at death	6 months	12 years

FIG 2 Chromosomal pattern of the proband (GTG banding).

TABLE 2 Clinical data identified in partial aberrations of chromosome 4.

Clinical data	4p—	4q—	4p+	4q+
Birth weight	Low +++	Normal	Low +	Low +++
Growth delay	+++	+++	+++	+++
Psychomotor retardation	+++	+++	+++	+++
Delay in language development	++	++	+++	++
Hypotonia	+++	++	+++	+++
Convulsions	+++	++	+++	+
Age of survival	17 years	4 years	Youth	—
CNS malformations	Frequent	Rare	Rare	Rare
Brachycephaly or oxycephaly	++	—	—	—
Microcephaly	+++	+++	++	+++
Haemangiomas	++	—	—	—
Absence of scalp	++	Normal	Low hairline	Normal
Hypertelorism	+++	+++	+++	++
Coloboma	++	+++	++	—
Strabismus	++	—	+++	+
Palpebral fissures	Antimongoloid	Horizontal mongoloid	Horizontal	Horizontal or slightly slanted
Glabella	Prominent	Prominent	Prominent	Prominent
Nose	Beaked	Wide and flat bridge	Low set, dysmorphic	Low set, dysmorphic
Micrognathia	+++	++	—	++
Cleft lip and/or palate	+++	—	—	—
Hypoplasia of mandible	+	—	—	—
Cardiac defects	++	++	+	+
Accessory ribs	+	++	—	—
Vertebral malformations	+	—	+++	—
Hypoplasia of pelvis	+	—	++	—
Renal anomalies	+	++	+	+++
Abdominal anomalies	+	+	+	+
Hip dislocation	+	++	—	+
Flexion creases of 4th finger	+++	—	+	++
Dermatoglyphs	Reduced	Normal	Increased	Normal
Camptodactyly	+	—	+++	—
Flat or displaced feet	++	++	++	+
Clinodactyly	++	++	++	+
Hypoplasia of external genitalia	+++	—	+++	—
Cryptorchidism	+++	—	+++	+++

+++ severe, ++ moderate, + mild, — absent.

FIG 3 Partial karyotypes of the proband showing centric fission of chromosome 4 (GTG banding).

Discussion

This appears to be the first published case report of transmitted centric fission of chromosome 4 so far. It is interesting to observe the particular stability of human telocentric chromosomes, which involve a high risk of transmission of non-balanced gametes.

In sibships A and B there are early spontaneous abortions which could be attributed to the unbalanced form of the aberration. Another point worthy of attention is the possible clinical interpretation of the two children of sibship B, who died at 6 months and 12 years, respectively. Their phenotype was deduced from the clinical history and the photographs.

Table 2 lists the symptoms described in cases of partial aberrations of chromosome 4 and allows a comparison with those present in the two dead children as a possible aid to a specific diagnosis.

Of the various clinical manifestations described in table 1, subject IV.11 presented with a normal birth weight, flat and wide nasal bridge, mongoloid slant, absence of strabismus, and died at 6 months. These symptoms are also found in cases

of partial 4q— suggesting that partial monosomy of the long arm of chromosome 4 was present in this child.

Subject IV.15 presented with a beaked nose, pronounced micrognathia, strabismus, and marked hypoplasia of the mandible. Death occurred at 12 years. This appears to be consistent with malformations found in partial monosomy of the short arm of chromosome 4. In particular, the age of death is similar to the only case reported⁶ of survival through the first year of life in a subject with partial 4p monosomy.

We would like to thank Mr Mario Sanchioni for his help with the photographs.

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Mosaic Down's syndrome with de novo 45,XX,-21,-22,+t(21q;22q)/46,XX,-21,+t(21q;21q) rearrangement

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SUMMARY The occurrence of mosaic Down's syndrome with two independent Robertsonian translocation cell lines is very rare. Such a patient is reported here, in whom an unbalanced Robertsonian translocation between two chromo-

somes 21 was detected in the majority of cells. The patient also revealed a minor cell line with a second Robertsonian translocation involving a chromosome 21 and a 22. The chromosome translocations detected in this patient were de novo in origin.

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