the proximal or the distal portion of the short arm of chromosome 4 have been described but they have distinctly different and much more severe malformations than our patient.^{19 20} In all of the cases reported with intersitial or terminal deletions of the long arm of chromosome 4, the breakpoints have been distal to that observed in our patient and the phenotypic expressions have been, for the most part, much more severe.^{21 22}

We suggest that a pericentric inversion, which in heterozygous form has no adverse phenotypic expression, may have such an effect in homozygous form. The developmental and language delays seen in our patient may have resulted from damage of critical genetic material at the breakpoints or from a position effect caused by gene rearrangement resulting from the inversion which is expressed only in the homozygous form. However, the possibility that other recessive alleles may be involved cannot be ruled out.

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The phenotype of ring chromosome 3

SUMMARY A male child with mental retardation and poor growth was found to have a 46,XY,r3 (p26→q29) karyotype in 92% of his peripheral lymphocytes and 90% of his cultured fibroblasts. Comparison of this patient's dysmorphic features with previously reported cases of ring 3 or deletion 3p suggests a clinical syndrome derived mainly from deletion of 3p26→pter. The syndrome consists of mental retardation, pre-

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and postnatal growth retardation, microcephaly, hypertonia, digital anomalies, and a characteristic facies with ptosis, epicanthal folds, broad nasal root, down-turned corners of the mouth, and dysplastic ears.

Ring chromosome 3 has been previously reported in only two liveborn infants. We describe a third case and discuss clinical features which define a ring 3/deletion 3p chromosomal syndrome.

Case report

The proband (fig 1) was the first child of non-consanguineous, 21-year-old parents with negative family histories. The uncomplicated gestation lasted 38 weeks before a normal labour and vaginal delivery. The birth weight was 2.3 kg (< 3rd centile for 38 weeks) and the patient exhibited poor feeding, hypotonia, and irritability in the nursery. These problems and the patient's unusual facies prompted referral to Mott Children's Hospital for evaluation.

Physical examination at the age of 2 months showed a height of 52.5 cm, a weight of 3.3 kg, and a head circumference of 32.5 cm. The head was small in proportion to the height and weight, and all parameters were far below the 3rd centile for age. The facies was flattened with small palpebral fissures, bilateral ptosis, epicanthal folds, rounded and simplified ears, and a small mouth with down-turned corners. A high-arched palate, redundant skin behind the neck, hypoplastic nipples, extra creases in the antecubital fossa, a deep sacral dimple, primary hypospadias, and deep plantar creases between the first and second toes were also noted. There was no heart murmur and the testes were not descended. Hypotonia, lethargy, and decreased tendon reflexes were evident upon neurological

FIG 1 Front and lateral views of the proband.

FIG 2 Giemsa banded karyotype of the proband showing ring 3 (p26→q29).

examination. The patient's partial karyotype is shown in fig 2.

The subsequent clinical course has involved severe failure to thrive, gradual development of mild spasticity requiring physical therapy, and mental retardation. At the age of 3½ years, the patient's height was 81 cm, his weight 7.1 kg, and his head circumference 41 cm. His development was at the 6-month level.

CYTOGENETIC STUDIES

Using standard methods, analysis of Giemsa banded chromosomes showed ring 3 in 46 of 50 (92%) peripheral lymphocyte and 45 of 50 (90%) skin fibroblast metaphase spreads. The mother's karyotype was normal and the father refused study.

Discussion

Two previous cases^{1,2} of ring chromosome 3 were growth retarded males with dysmorphic features. Although breakpoints were not defined in these studies, the size of the ring and its lack of variability were similar to the partial karyotypes in fig 2. Our case and that of Picciano *et al*¹ exhibited mosaicism in both lymphocytes and fibroblasts, while the peripheral lymphocytes examined by Witkowski *et al*² all contained the ring 3 chromosome.

Anomalies of chromosome 3 have usually involved duplication rather than deletion. Several cases of 3p+³ and 3q+^{4,5} have been reported and recognisable syndromes have been defined. Fine-man *et al*⁶ reported a family with a previously documented pericentric inversion of chromosome 3⁷ which included a patient with partial monosomy 3p. The resemblance of this case and the monosomy 3p case of Gonzales *et al*⁸ to ring 3 patients suggests that 3p deletion is a major factor in generating the phenotype of ring chromosome 3.

TABLE Features of patients with ring chromosome 3 or deletion 3p.

	Present case	Picciano et al ¹	Witkowski et al ²	Fineman et al ⁶	Gonzales et al ⁸	Total
Sex	M	M	M	F	F	
Prenatal growth retardation	+	+	—	—	+	3/5
Postnatal growth retardation	+	?	+	+	+	4/4
Microcephaly	+	?	+	+	+	4/4
Ptosis	+	—	—	+	+	3/5
Epicanthal folds	+	?	+	+	+	4/4
Strabismus	—	?	+	—	+	2/4
Broad nasal root	+	?	+	+	+	4/5
Dysplastic ears	+	+	?	?	+	3/3
Micrognathia	+	+	+	—	—	3/5
Down-turned corners of the mouth	+	+	+	+	+	5/5
Hypospadias	+	+	—	—	—	2/3
Undescended testes	+	?	—	—	—	1/2
Deep sacral dimple	+	?	?	—	+	2/3
Anal anomaly	—	+	—	—	+	2/5
Renal anomaly	?	+	—	—	?	1/3
Digital anomaly	+	+	—	+	+	4/5
Hypertonicity	?	?	?	+	+	3/3
Mental retardation	Severe	Mild	Moderate	Severe	Severe	5/5
Karyotype	r3(p26→q29)	r3	r3	del 3(p25→pter)	del 3(p25→pter)	

+ anomaly present; — anomaly absent; ? anomaly not excluded.

Clinical features of patients with ring chromosome 3 or partial monosomy 3p are compared in the table. There is some resemblance in facies as shown by the microcephaly, ptosis, epicanthal folds, dysplastic ears, broad nasal root, and down-turned corners of the mouth in the patient's photographs. Three patients had intrauterine growth retardation while four had severe failure to thrive. None had evidence of heart disease, while various digital, genitourinary, and anal anomalies were noted. Mental impairment ranged from mild to severe and three patients developed hypertonicity. The concordant features and the similar facies seen in photographs offers a preliminary view of a ring 3/deletion 3p chromosomal syndrome. Further delineation of this phenotype will require additional cases of ring 3/deletion 3p and, if such an anomaly exists in liveborns, reports of distal monosomy 3q —.

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Cat-like cry and mental retardation owing to 7q interstitial deletion (7q22→7q32)

SUMMARY A patient with mental retardation and mild facial dysmorphism had a karyotype which was considered to be normal before the availability of chromosomal banding techniques. She had a history of a cat-like cry and severe feeding problems during infancy. At the age of 9, she was still found to have initial aphonia on trying to initiate sounds. Repeat chromosome analysis with G banding showed an interstitial deletion of the long arm of chromosome 7.

Several patients have been reported with interstitial deletions of the midportion of the long arm of

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