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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chromosome 7.¹⁻⁶ Although the affected patients have had several abnormalities in common, their facial features and general appearance are not sufficiently distinctive to constitute an easily recognisable clinical syndrome. It is of interest, however, that several of these patients have been described as having an abnormal cry, which may facilitate recognition of this particular chromosomal deletion.

Case report

This family requested referral for genetic counselling because of a 9-year-old daughter with mental retardation. An older sib was considering marriage and was concerned about the risks to his future offspring. The proband was born on 1.8.72 to a G5, P4, A0 mother after a 42-week pregnancy which was uneventful except for treatment with thyroid hormone for symptoms of hypothyroidism. Delivery occurred precipitously. The mother recalls that spontaneous breathing did not occur for 2 to 3 minutes and that the infant required some resuscitation, although Apgar scores were listed as 10 at 1 and 5 minutes. Birth weight was 3570 g, head circumference 35 cm, and chest circumference 35 cm. In the newborn nursery record, it was noted that she was "unable to cry well, does go through motions of crying, but a very feeble cry results".

Laryngoscopy was done at 3 days of life because the cry, also described at that time as 'cat-like', was associated with episodes of cyanosis. The vocal cords were noted to be flaccid and either oedematous or thickened. Also described was a bowing deformity with escape of air through the midportion of the vibrating edge of the vocal cords. The infant was sent home and was noted to feed poorly and have difficulty in sucking. The cat-like cry persisted for at least her first year of life, during which there were several admissions to a local hospital for choking spells and possible aspiration. At 1 year of age she was evaluated at the Rhode Island Hospital. A pneumoencephalogram showed dilation of the ventricles suggesting cerebral atrophy. Laryngoscopy was done but no unusual findings were noted. Chromosome analysis done in 1973 on peripheral blood and skin fibroblasts without banding showed no abnormality. Because of occasional febrile seizures, she was given anticonvulsant medication until she was aged 6. Psychomotor development has been slow. She did not walk until the age of 5, no speech has developed, and she is only partially toilet trained. There is no family history of similarly affected subjects and both parents and the five older sibs are all normal.

Physical examination revealed a severely retarded,

FIG 1 The proband at 9 years of age.

mildly dysmorphic, but friendly and co-operative child (fig 1). The height was 114 cm (50th centile for a 5½-year-old), weight was 25.8 kg (10th centile), and head circumference was 50.75 cm (low normal). The body was rather stocky with a relatively large thorax. The cranial vault was somewhat unusual in shape, with a bony protuberance over the area of the anterior fontanelle and mild underdevelopment of the frontal areas. The pinnae were normally

FIG 2 Interstitial deletion of chromosome 7: *del(7) (pter→q22::q32→qter)*.

TABLE Clinical features of patients with interstitial deletion of the distal 7q segment.

Reference	Deleted segment	Sex	Birth weight/ gestational age	Head	Ears	Mouth	CNS	Cry	Other	Course
2	21-31	F	1740 g 36 wk	Microcephaly	Low-set, pointed	Large lips	L brain hypoplastic, arrhinencephaly	Not mentioned	Hyperplasia of islets of Langerhans	Died 2nd mth
1	21-32	F	2320 g 40 wk	Low normal	Low-set, dysplastic	Large with turned-down corners	Hypertonia, seizures	Feeble until 3 mth		Early feeding difficulty, developmental delay
4 (case 1)	21-32	F	1500 g Term	3rd centile at birth; 25th centile at 6 yr	Large, prominent antihelix	Large	Poor suck, hypotonia with hypertonia of lower limbs	Not noted		Severe MR, no speech, recurrent respiratory and urinary infections
3	22-32	F	2300 g Term		Malformed, low-set		Seizures, congenital glaucoma	Not noted	Small palpebral fissures with upward slant, contractures of fingers	Poor suck, gavage feeding, died of CHF at 39 d (AS and VSD)
5	22-31	F	3200 g 40 wk	Normal at birth and 17 mth	Thin outer ear cartilage	Normal	Broad-based gait, clumsy movements	Aphonic, unusual	Short distal phalanges of 3rd-5th fingers, clitoral hypertrophy	Swallowing difficulty, moderate MR
6	31-34	F	2368 g 9 mth	Less than 5th centile at 10 wk	Low-set, prominent antitragus	Turned-down thin upper lip	Moderate hypertonia	Weak, cat- like	Reflux, digitalised R thumb, extra vaginal mucous membrane	
Present case	22-32	F	4000 g 42 wk	Low normal at 9 yr	Protuberant R preauricular sinus	Large	Hypertonia lower extremities, broad- based-gait	Weak, cat- like, aphonic		Early feeding difficulty, severe MR

shaped, but slightly protuberant, and there was a left preauricular sinus. The mouth appeared large. The hands had mild bilateral 5th finger clinodactyly. There was moderate hypertonia of the lower extremities and a slow broad-based gait. Her cry was quite unusual, with initial aphonia and difficulty with initiation of sound, followed by a fairly normal cry of slightly diminished volume but normal pitch.

Another chromosome analysis with banding was requested. An abnormality was found consisting of an interstitial deletion of the long arm of chromosome 7 (fig 2). The deleted portion appeared to be the segment lying between band 7q22 and 7q32. Both parental karyotypes were normal.

Discussion

In attempting to obtain a specific diagnosis for this patient, we requested that the karyotype preparation be specifically examined for a possible small deletion of the midportion of the 5p15 band, which is considered to be the phenotypically relevant segment in the cri-du-chat syndrome.⁷ The discovery of the 7q deletion prompted us to review previously published cases in an attempt to determine whether or not this is a clinically recognisable syndrome.

The table records pertinent data on seven patients, including the present case, with interstitial deletions involving this portion of the long arm of chromosome 7. Ear malformations were mentioned in all patients, but were of differing morphology. All were thought to have mental retardation. Other neurological abnormalities, such as epilepsy and hypo- or hypertonia, were frequent. Early swallowing and feeding difficulties were present in five of the seven, and a large mouth was noted in four. Unfortunately, there are no normal values available at present for mouth size during childhood, so that the impression of a relatively large mouth is a subjective one. It is, however, an unusual finding in chromosomal syndromes.

It is noteworthy, however, that a feeble, weak, or cat-like cry was specifically mentioned in four of the seven patients. Initial aphonia on attempts to cry was present in our case and one other⁵ which suggests either a structural anomaly of the larynx or poor co-ordination of the laryngeal musculature, or both. The chromosomal breakpoints in these four cases were not identical, but the involvement of q31 was common to all, suggesting that the unusual cry might be correlated with the q31 segment. The

aetiology of the abnormal cry in the cri-du-chat syndrome has remained controversial,⁷ but in some cases the cry has improved with age as has occurred in our patient and one other.¹ All the patients so far reported with interstitial 7q deletions have been females which raises the possibility of lethality in males, a question which can be resolved when further cases are discovered. In addition, increased resolution of chromosomal fine structure in the future will hopefully allow better karyotype-phenotype correlation than is possible at present.

In summary, although it is not possible to describe an easily recognisable phenotype to correspond with this chromosomal deletion, infants who are affected frequently have a cat-like cry. We suggest that as part of evaluations of infants with feeding difficulties, failure to thrive, mild dysmorphism, delayed development, and unusual cry, particular attention be paid to the 7q segment of the karyotype.

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