associated with significant neonatal mortality. The majority of reported cases are secondary to parental chromosome rearrangements.³ The phenotype in duplication 16q is difficult to ascertain fully because of the variable concomitant chromosome deletions, although common features include pre- and postnatal growth retardation, failure to thrive, low set, malformed ears, long philtrum, micrognathia, cryptorchidism, and joint contractures.

Three cases have been reported previously with deletion 9p and concomitant duplication 16q secondary to a parental translocation.^{1,4,5} One case⁵ is paternally derived with identical breakpoints to our patient. Two other cases have larger deletions of 9p and smaller duplications of 16q.^{1,4} The table outlines and compares the clinical features in our patient, the three previously reported patients, and the 9p phenotype.

Our patient clearly has many features of the deletion 9p syndrome and resembles the three cases previously described with an unbalanced translocation involving chromosomes 9 and 16. She has done well

with craniofacial surgery and is currently functioning at the 14 to 15 month level.

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De novo terminal deletion 7p22.1-pter in a child without craniosynostosis

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SUMMARY A patient with a de novo terminal deletion of the short arm of chromosome 7 (p22.1-pter) is described. Facial dysmorphism, a congenital heart defect, and genital hypoplasia were evident. There were no signs of craniosynostosis. Our observation confirms that deletion of 7p22 is not necessarily associated with craniosynostosis.

More than 20 patients with malformation syndromes resulting from partial deletions of the short arm of chromosome 7 have been reported. Most of the deletions are cytogenetically different. The majority of patients show variable clinical features most of which are common to congenital anomaly syndromes resulting from other types of aneuploidy.^{1,2} Craniosynostosis, however, has so far appeared to be consistently associated with deletion of a segment of band 7p21¹⁻³ and the exact location of the

chromosomal segment critically important for this type of craniosynostosis has been the subject of discussion.¹⁻³

We report on a patient with marked facial dysmorphism, tetralogy of Fallot, and genital hypoplasia but without craniosynostosis, whose karyotype showed a de novo terminal deletion of the short arm of chromosome 7 (7p22.1-pter). To our knowledge, this is only the second patient reported with a pure terminal 7p22 deletion.

Case report

A six year old boy was referred because of severe psychomotor retardation and a congenital heart defect. Weight was 96 kg, length 90.0 cm, and head circumference 44.5 cm (all <3rd centile). He was the second child of healthy, unrelated parents. He was delivered at 38 weeks' gestation with a birth weight of 2300 g, a length of 45 cm, and a head circumference of 32.5 cm. On clinical examination, facial dysmorphism was apparent with an antimongoloid eye slant, epicanthic folds, broad and flat nasal bridge, thin upper lip, triangular shaped

FIG 1 Facial appearance of the proband.

localise the breakpoint at 7p22.1 (fig 2b). The karyotypes of both parents were normal.

Discussion

Nine interstitial and 12 terminal deletions of 7p have been reported. Most cases have been reviewed by Motegi *et al*¹ and Schömig-Springler *et al*.² Fig 3 shows an ideogram of the short arm of chromosome 7 with a comparative representation of the reported deletions,^{1,2} together with an interstitial deletion reported by Garcia-Esquivel *et al*³ and the present patient. Clearly, there is considerable cytogenetic heterogeneity regarding size and localisation of the deleted segment. Seven patients had a terminal deletion of band 7p22 (fig 3 a-e). Five terminal deletions were monosomic for band 7p21 (fig 3 f-j). Three interstitial deletions had partial loss of 7p21 and partial or complete loss of 7p15 (fig 3 k-n). The remaining interstitial deletions

mouth, and low set and poorly lobulated ears. The hair was curly, silvery blond, and bristly (fig 1) and the anterior and posterior hairlines were low. A midfrontal haemangioma was noted. The palatal arch was asymmetrical but there was no midline defect. There was pectus carinatum. Both thumbs were hypoplastic and proximally implanted. Overlap of the second toe over the third was noted bilaterally. The penis was small and there was unilateral cryptorchidism. The clinical cardiological diagnosis of tetralogy of Fallot was confirmed by catheterisation, which showed an extreme degree of pulmonic stenosis and a large ventricular septal defect. Drumstick-like fingertips were noted. Ophthalmoscopy of the retina yielded normal results. Radiographical examination excluded craniosynostosis and any type of skeletal dysplasia.

CYTOGENETIC STUDIES

Peripheral blood lymphocytes were cultured according to standard synchronisation techniques. Forty R banded and 30 G banded cells were analysed. The R banded cells with good banding quality showed a small terminal deletion of the short arm of chromosome 7. G banding showed that the 7p21 band was intact and careful analysis indicated that the 7p22.2 band was deleted (fig 2a). We can therefore

FIG 2 (a) G banded (left) and R banded (right) chromosomes 7. (b) Ideogram of chromosome 7 showing the breakpoint of the deleted chromosome (arrow head).

FIG 3 Ideogram showing the deleted segments of the short arm of chromosome 7 found in published reports. +: with craniosynostosis, - without craniosynostosis, * a chromosome abnormality is present in addition to the deletion 7p. a: Winsor *et al* * (1978) (2 cases); b: Marcallo *et al* * (1977); c: Zackai and Breg * (1973) (2 cases)¹⁰; d: Fryns *et al* * (1985)⁵; e: Baccichetti *et al* (1982)⁴; f: Nakagome *et al* (1976)⁹; g: Wilson *et al* (1973)⁶; h: Schömg-Spangler *et al* (1986)²; i: Friedrich *et al* (1975)⁷; j: Dhadi and Smith * (1976); k: McPherson *et al* (1976)⁸; l: Motegi *et al* (1985)¹; m: Garcia-Esquivel *et al* (1986)³; n: Miller *et al* (1979)¹¹; o: Crawford *et al* (1979); p: Müller *et al* (1981); q: Bianchi *et al* (1981) (2 cases); r: Moedjono *et al* (1978); s: present case. Complete references of patients a, b, j, o, p, q, and r can be found in Motegi *et al*¹ or Schömg-Spangler *et al*.²

were monosomic for different bands proximal to 7p21 (fig 3 o-r). Interestingly, breakpoints are most frequently located at subbands 7p22.1 (fig 3 a-e, k, s) and 7p21.1 (fig 3 g-i, k, m, o-q). In view of this cytogenetic heterogeneity, it is not surprising that no consistent 7p- syndrome has emerged from the reported cases. Comparison of the clinical findings showed that there are some characteristic features which, however, do not seem to be correlated with loss of specific segments of 7p and are common findings in patients with any type of aneuploidy: cranial dysmorphism, cleft palate, saddle nose, small, dysplastic, low set ears, and foot malformations.^{1,2} Premature craniosynostosis, on the other hand, is an uncommon finding in patients with chromosome anomalies but was reported in nine patients with 7p deletions (fig 3). Craniosynostosis appears to be associated consistently with deletions of parts of band 7p21.^{1,3} Our patient showed some of the common findings reported in patients with monosomy 7p: a broad and flat nasal bridge, low set and poorly formed ears, antimongoloid slant of the palpebral fissures, overlapping of the toes, and genital hypoplasia. Cytogenetic analysis in our patient showed a small terminal deletion involving band 7p22. Only one other patient has been reported with a similar deletion without additional aneuploidy for another chromosome segment.⁴ We have compared the clinical findings in these two patients with

the main clinical characteristics in patients monosomic for band 7p21 or 7p22.⁶⁻⁹ (table). Even in the subgroup of patients with 7p deletions with clearly overlapping regions for the deleted segment there is considerable clinical heterogeneity. Our patient broadens this clinical spectrum; a normal forehead, overlap of the second toe over the third bilaterally, and tetralogy of Fallot are features which are not present in the six other patients.

An interesting conclusion can be drawn with regard to the craniosynostosis. Much interest has focused on the assignment of the critical segment for craniosynostosis. Baccichetti *et al*⁴ suggested that deletion of part of band p21 could be associated with craniosynostosis. Motegi *et al*¹ restricted the critical segment to the midportion of 7p21 (7p21.2 or the proximal part of 7p21.3). Garcia-Esquivel *et al*³ proposed the 7p21.1 subband. On the other hand, Schömg-Spangler *et al*² concluded that loss of a segment distal to the p21 band would be crucial, based on reports of patients with craniosynostosis but without involvement of band p21.^{5,10,11} Zackai and Breg¹⁰ described two cases with ring chromosome 7 in which possibly more than the terminal p22 band was involved. The patient with craniosynostosis reported by Fryns *et al*⁵ was also trisomic for 2q32-qter owing to an unbalanced t(2;7) and was explained by Garcia-Esquivel *et al*³ as a position effect. In the last case it is not clear to what extent

TABLE Clinical findings in patients with 7p2 deletion.

	Wilson et al ⁶	Friedrich et al ⁷	McPherson et al ⁸	Nakagome et al ⁹	Baccichetti et al ⁴	Schöning-Spangler et al ²	Present case
Deleted segment	15.3(?)–pter	15–22.3	21–22	21.3–22.3	22.1–22.3	21–pter	22.2–pter
Sex	F	F	M	F	M	F	M
Birth weight (g)	2665	2500	2900	1900	3200	2650	2300
Gestational age (wk)	38	40	37	40	38	40	38
Psychomotor retardation	+	+	+	+	+	+	+
Abnormality of skull	Acrocephaly	Trigonocephaly	Turricephaly, flat occiput			Trigonocephaly	
Craniosynostosis	+	+	+	–	–	+	–
Prominent forehead	+	+	+	+	+	+	–
Palpebral fissures	Downward slanting	Upward slanting	Short	Downward slanting	Short	–	Downward slanting
Epicanthic folds	–	–	+	+	+	–	+
Depressed nasal bridge	+	–	+	–	–	–	+
High arched palate	–	–	–	–	–	+	+
Cleft palate	–	–	–	–	–	–	–
Low set, dysplastic ears	+	+	+	+	+	–	+
Fingers	Long, slender	Overlapping 2, 5 over 3, 4	–	–	–	Drumstick thumbs with far ulnar-proximal insertion	Hypoplastic, proximally implanted thumbs
Feet	–	Rocker bottom feet	Talipes equinovarus	Pes varus	Club feet	–	–
Toes	Long, slender	–	–	–	–	–	Overlapping 2 over 3
Cardiovascular anomalies	–	Aortic stenosis	–	–	–	Persistent ductus arteriosus	Tetralogy of Fallot
Genital anomalies	–	Hypoplasia	–	–	Hypospadias Gr I	Hypoplasia	Hypoplasia

band p21 was involved in the deletion. Therefore, deletion of 7p21.1–p21.2 would be compatible with the association with premature craniosynostosis.

Our case and the patient of Baccichetti *et al*⁴ are the only two reported pure terminal deletions of 7p22. Neither patient had signs of craniosynostosis and they therefore provide additional evidence that partial or complete deletion of band 7p22 is not necessarily associated with craniosynostosis.

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A non-centromeric C band variant on chromosome 11q23.2

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SUMMARY An extra G band was found inserted into chromosome 11q23.2 in a boy who had severe developmental delay and anal stenosis. Cytogenetic characterisation of this extra band showed that it was composed of Q band brilliant, C band heterochromatin. It was also present in clinically normal subjects in two other generations and was therefore presumed to be unrelated to the clinical abnormalities in the proband. Although rare, this cytogenetic anomaly may be useful as a genetic marker for 11q23.2.

Chromosome polymorphism has been well described in the human genome and includes differences in amount, location, and type of pericentromeric constitutive heterochromatin.¹ These variations are attributed primarily to gain or loss of repetitive DNA sequences that have synonymously been referred to as satellite DNA.² Changes in the

amount of this material are believed to be caused by unequal recombination or over-replication or both.³ Occasionally, pericentromeric inversions of this genetically inert material are observed, most commonly on chromosome 9.⁴ There also appear to be different types of constitutive heterochromatin on different chromosomes as these can be distinguished cytochemically. For example, chromosome 9 contains a large block of heterochromatin that can be distinguished using the Giemsa 11 technique and has been used to determine the mechanisms responsible for rearrangement.⁴ Other regions of the genome can also be distinguished with a montage of other cytochemicals.

To date, very few chromosome variants have been described that involve translocation to parts of the genome other than those in which they are commonly found. Watt *et al*⁵ described a normal subject who had an insertion of the nucleolus organising region (NOR), normally found on the acrocentric chromosomes, along with some adjacent heterochromatin into chromosome 12p. The NOR, while differing from satellite DNA in that it is highly active transcriptionally, may also show a tremendous degree of variation in copy number without any