deletions in different patients are different in size and extent towards the centromere and telomere, thus leading to varying additional malformations. However, cardinal features are probably caused by a deletion of always the same segment, 8q23.2→q24.1. In a minority of patients with LGS, even in prometaphase preparations of excellent quality, no deletion in 8q can be found. These latter patients are less severely mentally retarded and they less frequently have additional malformations than those with visible deletions. Schinzel⁵ suggested that the minimal pathognomonic segment for the manifestation of the cardinal features of LGS is too small to be detected by present prometaphase banding. Our four cases had no cardinal features of LGS, that is, multiple cartilaginous exostoses, cone shaped epiphyses, and facial dysmorphism. Furthermore, the visual disturbances in our cases are not found in typical LGS.

On the other hand, anomalies of chromosome 11p have been reported in Beckwith-Wiedemann syndrome (BWS) and in WAGR. Duplication of 11p has been found in over a dozen patients with cardinal features of BWS and mental retardation. Schmutz⁶ reported a case of deletion of chromosome 11p13 with BWS and macroglossia, umbilical hernia, high birth weight, facial naevus flammeus, and mental retardation. The clinical features of WAGR are Wilms' tumour, aniridia, mental retardation, and gonadoblastoma. Our four cases showed no resemblance to BWS or WAGR except for mental retardation. From a review of previously reported patients with del(11)(p15.1p13) or del(11)(p15.1p12),

Gilgenkrantz *et al*⁷ confirmed many ophthalmic symptoms, such as glaucoma, cataracts, nystagmus, ptosis, and exotropia, in addition to aniridia. Furthermore, most of these patients had growth deficiency, mental retardation, abnormal genitalia, and nephroblastoma. From these findings, it is likely that a break in band 11p15.1 caused growth and mental retardation and amblyopia in our four cases.

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A new interstitial deletion of 4q (q21.1::q22.1)

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SUMMARY A unique case of de novo interstitial deletion of chromosome 4 is described involving loss of band q21. The male newborn had multiple abnormalities including frontal bossing, prominent occiput, low set ears, micrognathia, short sternum, short, broad hands and feet, agenesis of the corpus callosum, and cardiac defects. The phenotypic abnormalities are compared with other reported cases of deletion 4q involving adjacent regions.

Interstitial deletions of the long arm of chromosome 4 are said to be relatively rare; in fact, 16 cases have been published to date with most of these reports having different breakpoints. So far, attempts at deletion mapping in this portion of the human genome have only indicated a tentative assignment of the piebald trait¹ gene to band 4q12 and the locus of the group component (Gc) system² (vitamin D binding protein) to 4q11→q13.

Case report

The proband was born at term after an uneventful pregnancy to unrelated parents. The G1P0 mother

was 24 years and the father 28 years old. There was no known family history of miscarriages or abnormal children. Signs of fetal distress appeared late in labour and delivery was by forceps. Apgar scores were 2, 2, 3, and 4 at one, five, 10, and 45 minutes, respectively. Weight was 3540 g (50th centile), head circumference was 39.5 cm (>97th centile), and length was 53.3 cm (90th centile).

Dysmorphic features noted at birth included: bossing of the forehead, prominent occiput, hypertelorism, low set ears, broad nasal root, small

mouth, micrognathia, short sternum, short, broad hands and feet, and clinodactyly of both hands (fig 1). The feet showed deep plantar grooves between the big and second toes. Ultrasound examination indicated partial agenesis of the corpus callosum. There was echocardiographic evidence of pulmonary hypertension.

The baby was persistently cyanosed despite full ventilatory support. In the light of the multiple abnormalities treatment was withdrawn and the baby died at 13 hours.

FIG 1 Full face and lateral view of the patient at necropsy.

FIG 2 Partial banded karyotype showing the deleted chromosome 4. (i) GTG bands with the deleted 4 on the left. (ii) RBG bands with the deleted 4 on the right.

FIG 3 Diagram of 4q interstitial deletions.

Necropsy confirmed absence of the corpus callosum. The brain was otherwise normal. Examination of the heart showed normal anatomical connections. The right chambers were dilated. A widely patent atrial septal defect and a membranous ventricular septal defect were found. Pulmonary outflow tracts were normal but the pulmonary veins were extremely small. All other internal organs appeared normal.

CYTOGENETIC ANALYSIS

Chromosome analysis performed urgently on a bone marrow specimen showed no abnormality on solid staining. However, high resolution GTG banding performed on a whole blood culture using the harvest method of Ibraimov³ later showed a small interstitial deletion of the long arm of a chromosome 4. RBG banding was performed according to the method of Eichenbaum *et al.*⁴ The karyotype was interpreted as 46,XY,del(4)(pter→q21.1::q22.1→qter) (fig 2). Chromosome analysis of the parents was normal.

Discussion

Fig 3 shows schematically the published reports of deletions involving interstitial segments of the long arm of chromosome 4. Only two of these cases^{5,6} correspond to the deleted q21 region which we report. Phenotypic anomalies in both these cases, which coincide with features of our patient, included: shortness of limbs, short, broad hands and feet, very prominent occiput, frontal bossing, low set ears, and hypotonia. Both these cases had significant developmental delay. The patient of Mitchell *et al.*⁶ died at five months of sepsis from bilateral otitis media.

Another six reports of interstitial deletions of the long arm of chromosome 4 involve loss of part of the q21 segment only.^{1-7,10} These cases and our patient have the following features in common: short

fingers, prominent forehead, small, low set ears, and hypotonia. The prenatally diagnosed case of Campbell *et al.*¹⁰ also had cleft lip and palate, coarctation of the aorta, double vena cava, and digital flexion deformities, and was detected after raised maternal serum AFP at 15 weeks' gestation. Three of the four patients with deletion of the q12 segment of chromosome 4 also had the piebald trait.^{1,7,8} The most proximal deletion described² suggested the location of the Gc system in this region owing to abnormal segregation of this marker in a mentally retarded girl.

Deletions which are distal to the one we describe appear to have six different breakpoints involving various segments from q22 to q35.^{6,11-16} All the patients had developmental delay; otherwise the phenotype is varied with individual patients exhibiting the following features: infant death owing to intrauterine growth retardation, hypotonia, short limbs, and malrotation of the gut¹¹; cardiac abnormalities and death at four years¹⁵; craniosynostosis¹⁵; Rieger's syndrome¹²; coloboma, micrognathia, and growth retardation¹⁴; and multiple congenital abnormalities, VSD, and left ventricular hypertrophy.⁶ One report is of direct transmission of a deletion in an 'educationally subnormal' mother to her subnormal son.¹⁶

Conclusion

There is a heterogeneous, non-specific range of phenotypes attributable to partial deletion of 4q. This may simply reflect a common disruption of developmental homeostasis caused by chromosomal monosomy. It is clearly not possible to delineate new syndromes based on single cases, but it is of interest that all three patients so far described with a deletion of the 4q21 segment displayed shortness of limbs and digits.

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Cat eye syndrome associated with aganglionosis of the small and large intestine

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SUMMARY A newborn male infant is presented with the characteristic phenotype of the cat eye syndrome and a small supernumerary chromosome shorter than a 22. He also had complete absence of parasympathetic ganglion cells throughout the small and large intestine.

The cat eye syndrome is characterised by anal atresia, ocular coloboma, cardiac defects, preauricular tags or sinuses, abnormalities of the urinary tract, mental retardation, and a small supernumerary, bisatellited, isodicentric chromosome. Molecular hybridisation with chromosome 22 specific probes have shown that the isodicentric chromosome

FIG 1 Coloboma of the iris and preauricular pits.