first such case was reported in a 10 year old girl by Warburton and Shah in 1976.¹³ Her karyotype was 46,XX,t(9;11)(q34;q13). She responded well to busulphan and was alive 29 months after diagnosis. The patient reported by Verhest and Lustman¹⁴ had a complex karyotype with t(3;9;Y)(q35;q34;q12). A third case of Ph^{-ve} CML with a break at 9q34 was listed in Sandberg's review.¹⁵

c-abl has been shown by in situ hybridisation to be translocated from chromosome 9q34 to chromosome 22 in Ph⁺ CML, although it appears that the break site on chromosome 9 is variable.⁷ Amplification of c-abl occurs in the Ph⁺ k562 cell line and also in Ph⁺ CML.⁷ In addition, Canaani *et al*¹⁶ have demonstrated the presence of an 8 kb RNA transcript in five out of six patients with Ph⁺ CML. These data have led to the suggestion that c-abl may be of importance in the pathogenesis of CML. However, the rare cases of CML with variant translocations apparently not involving chromosome 9 and those cases who develop the Ph chromosome during the course of the disease would not lend support to this hypothesis.⁵ No translocation of c-abl was found in two cases of atypical CML with a normal karyotype.⁶ We are currently studying the cells of this patient using blot hybridisation with the human c-abl probe. The patient described in this report illustrates the differences in the clinical, haematological, and probably molecular behaviour of patients with Ph negative CML from those who possess the Ph chromosomal abnormality.

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Partial 2p deletion in a girl with a complex chromosome rearrangement involving chromosomes 2, 6, 11, and 21

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SUMMARY We describe the clinical and cytogenetic findings of a 9½ month old girl with a complex chromosome rearrangement

resulting in a probable deletion of band 2p14. She does not resemble other reported cases of del(2p).

Deletions of the short arm of chromosome 2 are exceedingly rare, having been reported in only five

patients. Two had terminal deletions of bands 2p23→pter^{1 2} and a third had deleted material distal to band 2p24.¹ The remaining two patients had interstitial deletions of bands 2p11→2p21³ and 2p13→2p15.⁴ We report a patient with a complex chromosome rearrangement involving chromosomes 2, 6, 11, and 21 resulting in a probable deletion of band 2p14.

Case report

The proband (fig 1) was a 9½ month old white girl of

FIG 1 The proband.

mixed European and American Indian ethnic background, born to a non-consanguineous 21 year old woman and 24 year old man. The mother's reproductive history included four pregnancies that resulted in one therapeutic abortion, a normal girl, a spontaneous abortion of a molar pregnancy at two months, and the proband. The pregnancy was complicated by nausea during the first trimester, but was otherwise uneventful. The mother reported no exposure to teratogenic agents. The family history was unremarkable except for an 18 year old maternal uncle with severe scoliosis.

The proband was delivered vaginally without complication at 37 weeks. She weighed 2.9 kg and measured 48 cm (both on the 50th centile). No abnormalities were noted at birth, but at the age of 2 months she was admitted to hospital with symptoms of spinal meningitis (vomiting, diarrhoea, high fever, congestion, and an unusual high pitched cry), although no infection was found. At that time, she was moderately hypotonic with minimal head and truncal control.

The proband was placed in an infant stimulation programme and seen monthly for assessment of her physical and mental growth parameters. A physical therapy programme established the left side of her body to be weaker than the right. Despite these

FIG 2 GTG banded karyotype of the proband.

FIG 3 (Top) GTG banded chromosomes involved in the complex chromosome rearrangement. For each of the four pairs, the normal chromosome is on the left and the derived chromosome on the right. (Bottom) Diagrammatic representation of the chromosomes presented above identifying breakpoints on the normal chromosomes and sources of chromosome segments in the derived chromosomes.

programmes, she made little progress in her developmental milestones and her physical growth rate slowed down appreciably.

She was referred for a genetics consultation at the age of 9½ months. Physical examination revealed a relatively normal appearing child with a weak, high pitched cry and lung congestion. Her length was 71.5 cm (30th centile), weight was 6.8 kg (−3 SD), and head circumference was 41 cm (−3 SD). She was brachycephalic, sutures were closed, and the anterior fontanelle was not palpable. Her palate was rugated and her palpebral fissures had a slight upward slant, but otherwise her facial features were normal. She had a pectus excavatum and considerable scoliosis in the upper thoracic area. Her fingernails were short, flat, and ridged and her dermatoglyphs had a few unusual features (bilateral *r'* axial triradii and radial loops on the second digits), but were not grossly abnormal.

LABORATORY STUDIES

The proband's chemical profile, complete blood count, urine analysis, metabolic screen, TORCH

titres, and CT scan were all normal. Her visual and auditory evoked potentials were also within normal limits. A skull and long bone radiograph series revealed a very small anterior fontanelle and normal bone age.

CYTOGENETIC STUDIES

Chromosome preparations from peripheral blood lymphocyte cultures obtained on two separate occasions were analysed with G, Q, or C banding (fig 2). A total of 60 metaphase cells was examined; the modal chromosome number was 46. Analysis of the banding patterns revealed a complex chromosome rearrangement involving chromosomes 2, 6, 11, and 21 in all cells. Seven breakpoints were identified in the four derivative chromosomes: 2p13-3, 2p15, 2p25-1, 6p12-3, 6q12, 11q14-1, and 21q21-1 (fig 3). The proband's karyotype is interpreted as 46,XX,t(2;6;11;21)(2qter→2p13-3::2p15→2p25-1::11q14-1→11qter;2pter→2p25-1::6p12-3→6q12::21q21-1→21qter;11pter→11q14-1::6p12-3→6pter;21pter→21q21-1::6q12→6qter). Only band 2p14 is unaccounted for.

TABLE Summary of clinical findings in patients with deletions of 2p.

	<i>Emanuel et al</i> ¹		<i>Duca et al</i> ²	<i>Fryns et al</i> ³	<i>Present case</i>
	<i>Case 1</i>	<i>Case 2</i>			
Deleted segment	2p24→pter	2p23→pter	2p13→p15	2p11→p21	2p14
MR or developmental delay	+	+	+	+	+
Failure to thrive	+	+	+	+	+
Normal birth weight and length	+	+	—	+	+
Short stature	+	+	+	—	—
Low weight	+	+	+	—	+
Hypotonia	+	—	—	+	+
Microcephaly	+	+	—	—	+
Delayed closure of fontanelles	+	+	+	—	—
Prominent occiput	—	+	—	—	—
Frontal bossing	—	—	+	+	—
Parietal bossing	—	—	+	—	—
Narrow forehead	—	—	+	+	—
High forehead	+	—	—	—	—
Sparse hair	+	—	—	—	—
Facial hirsutism	—	—	+	+	—
Facial asymmetry	—	—	+	—	—
Rectangular facies	+	—	—	—	—
Arched eyebrows	—	+	—	—	—
Ptosis	—	+	—	—	—
Small palpebral fissures	+	—	—	—	—
Downward slanting palpebral fissures	—	+	—	—	—
Upward slanting palpebral fissures	—	—	—	—	+
Microcornea	+	—	—	—	—
Nystagmus	+	—	—	—	—
Strabismus	—	+	+	+	—
Enophthalmos	—	—	+	—	—
Iridial pigmentation abnormalities	—	—	—	+	—
Posteriorly rotated ears	—	—	+	—	—
Low set ears	+	+	+	—	—
Abnormal ear shape	—	+	+	—	—
Small nose	+	—	—	—	—
Short philtrum	—	—	+	—	—
Large mouth	—	—	—	+	—
Cupid's bow mouth	+	—	—	—	—
High arched palate	—	+	—	—	—
Micrognathia	+	—	—	—	—
Short neck	—	—	+	+	—
Winged scapulae	—	—	+	—	—
Widely spaced nipples	—	—	+	—	—
Pectus excavatum	—	—	+	—	+
Kyphosis	—	—	+	+	—
Scoliosis	—	—	+	—	+
11 pairs of ribs	—	+	—	—	—
Narrow abdomen	+	—	—	—	—
Inguinal hernia	+	—	—	—	—
Cryptorchidism	NA	—	NA	+	NA
				(Left side)	
Joint contractures	—	+	—	—	—
Genu valgum	—	—	+	—	—
Single flexion crease on fifth fingers	+	+	—	—	—
Fifth finger clinodactyly	+	—	—	—	—
Prominent heels	—	+	—	—	—
Long broad halluces	—	—	+	+	—
Valgus deformity of halluces	—	—	+	+	—
Overlapping toes	—	—	+	+	—

+=trait present.

—=trait absent.

Blank=not reported to be present or absent.

NA=not applicable.

Lymphocyte studies revealed the mother's chromosomes to be normal. The father was unavailable for study.

Discussion

The clinical features of patients with deletions of 2p are summarised in the table. The patient of Ferguson-Smith *et al*² is not included in the tabulation because he was also partially trisomic for the distal four bands of 5q and so was not a pure case of partial 2p monosomy. The patient reported by Zachai *et al*⁵ is identical to case 2 of Emanuel *et al*.¹

Given the paucity of reported cases, only the most tentative statements can be made regarding the clinical picture associated with deletions of 2p. The two cases presented by Emanuel *et al*¹ have nearly identical deleted segments and share the following stigmata: mental retardation with microcephaly (−4 to −6 SD), failure to thrive, normal weight and length at birth with postnatal onset of growth deficiency (−4 to −5 SD), delayed closure of the anterior and posterior fontanelles (both patent at 17 months), low set ears, and single flexion crease on the fifth fingers.

Although the two reported cases of interstitial deletions have deleted bands in common (table), the missing segment in the patient of Fryns *et al*³ was over three times the length of the deleted segment in the patient of Duca *et al*,⁴ making a phenotypic comparison speculative at best. The patients of Fryns *et al* and Duca *et al* did, however, show some phenotypic similarities, particularly in the areas of the cranium (frontal bossing with narrow forehead), spine (kyphosis), and toes (long broad big toes with valgus deformity and overlapping toes). Our patient appears to have a single deleted band (2p14) although we cannot rule out the possibility that this

band has been incorporated into another breakpoint site. The smallness of the deleted segment may explain her minimal dysmorphogenetic features; however, there is a lack of clinical similarity between our patient and the other two cases of interstitial 2p deletions. For example, our patient had premature closure of her fontanelles, whereas three other patients, including one with a deleted segment incorporating band 2p14,⁴ had delayed closure of their fontanelles. It is possible that our patient's physical and mental stigmata are the consequence of a disruption in one or more gene's nucleotide sequence resulting from this child's numerous chromosome breaks. Given the uncertainty of our patient's karyotype and the limited number of 2p deletion cases, it is evident that more cases of 2p deletions are required before a clear cut 2p deletion syndrome, or syndromes, emerges.

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Sacrococcygeal teratoma and normal alphafetoprotein concentration in amniotic fluid

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SUMMARY It is usually assumed that in the case of sacrococcygeal teratoma the concentration of alphafetoprotein in the amniotic fluid is increased. In the case reported here the AFP

concentration in the amniotic fluid was found to be normal in spite of a large teratoma not covered with skin. Possible reasons for this are discussed and the histological characteristics of the tumour are reported. It is emphasised that this teratoma could not have been recognised