Myelodysplastic syndromes: a scoring system with prognostic significance. *Br J Haematol* 1985;59:425-33.

- ⁹ Mukerjee D, Bowen J, Anderson DE. Simian papovirus 40 transformation of cells from cancer patient with XY-XXY mosaic Klinefelter's syndrome. *Cancer Res* 1970;30:1769-72.

Correspondence and requests for reprints to Dr D G Oscier, Department of Haematology, Royal Victoria Hospital, Shelley Road, Bournemouth BH1 4JG.

Partial trisomy 6p and partial trisomy 22 resulting from 3:1 meiotic disjunction of maternal (6p;22q) translocation

P R SCARBROUGH*, A J CARROLL*, S C FINLEY*†, AND K HAMERICK*

*Laboratory of Medical Genetics and †Department of Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama, USA.

SUMMARY A male infant, partially trisomic for a small segment of chromosomes 6 and 22 resulting from a maternal translocation, is described. Comparison of the phenotypic features of the proband with those noted in partial 6p and partial 22 trisomies revealed some common features found in both chromosome anomalies but especially reinforced those features thought to be characteristic of 6p trisomy syndrome.

Case report

A 13 day old white male (fig 1) was the 2780 g product of a 38 to 39 week gestation for a 22 year old gravida 2 (FO, PO, Abl, LO) mother. Admission to

hospital and hormone injections were required to maintain the pregnancy complicated by first trimester bleeding. Maternal drug or alcohol abuse, radiation or chemical exposure, and smoking were denied. Family history was remarkable for several maternal relatives with multiple miscarriages and several unexplained early infant deaths.

Caesarean section was performed because of maternal toxemia. Polyhydramnios was noted at delivery. The neonatal course was complicated by hyperbilirubinaemia and hypoglycaemia.

Physical examination showed a vigorous infant with microcephaly, facial asymmetry, overriding sagittal suture, small anterior fontanelle, right sided microphthalmia, blepharophimosis, blepharoptosis, downward slanting palpebral fissures, mild hypertelorism, slightly flattened nasal bridge, flammeus naevus over the nasal bridge and nape of the neck, bilateral preauricular pits, holosystolic murmur, partial soft tissue syndactyly of the second to fourth

FIG 1 The proband at 15 months.

Received for publication 3 January 1985.

Revised version accepted for publication 13 February 1985.

toes, penile chordee, and cryptorchidism. Re-evaluation at 18 months revealed significant developmental delay.

CYTOGENETIC STUDIES

Cultured peripheral leucocytes from the proband contained 47 chromosomes with an extra atypical acrocentric chromosome approximately one-quarter to one-third the size of a G group chromosome (fig 2a). Clarification of its derivation was made possible by analysis of parental chromosomes. The father's karyotype was normal. GTG banding of maternal chromosomes revealed a reciprocal translocation

between the short arm of a chromosome 6 and the long arm of a chromosome 22: 46,XX,t(6;22)(p25;q11·2) (fig 2b and c). The proband's karyotype, interpreted as 47,XY,+der(22),(22pter→22q11·2::6p25→6pter)mat, indicated trisomy for 6pter→6p25 and 22pter→22q11·2. Six of ten maternal relatives studied were balanced translocation carriers.

Discussion

Partial trisomy 6p is considered to be a clinically recognisable syndrome. Comparison of the clinical

FIG 2 (a) Partial karyotype of the proband. Normal chromosomes 6 and 22 and atypical supernumerary chromosome 22. (b) Partial karyotype of carrier: rcp t(6;22)(p25;q11·2). (c) Diagrammatic illustration of the translocation. Breakpoints are indicated by arrows.

TABLE Phenotypic features of partial trisomy 6p.

Reference	1				2	3	4	5	6	7	8	Present case
	IV.33	IV.34	IV.6	IV.21								
Trisomic segment					pter→p21	pter→p23	pter→p21	pter→p21	pter→p22	pter→p21	pter→p22	pter→p25
Growth retardation	+	+	+	+		+	+	+	+	+	+	+
Developmental delay	+	+	+	+	+	+	+	+	+	+	+	+
High forehead	+	+	+	+	+		+		+	+	+	+
Thin, sparse hair	+	+						+				+
Abnormal sutures	+	+	+	+			+	-	+	+	+	+
Close set eyes	+	+	+	+			±				+	-
Microphthalmia			+						+	+	+	+
Blepharoptosis	+	+	+	+	+	+	+	+	+	+	+	+
Blepharophimosis	+	+	+			+	+	+	+	+	+	+
Strabismus or nystagmus			+	+	+		+		+	+	+	+
Bulbous nose	±	+			+	+	+			+		+
Microstomia	+	+	+				-				+	-
Thin lips	+	+	+			-			+	+	+	+
Small, pointed chin	+	+						+	+		+	-
Low set/malformed ears	+	+	+	+	+		+	+	+	+	+	+
Heart murmur and/or defect	+	+	+	+			+	-	+	+	+	+
Small kidneys	+	+	+	+			+					
Proteinuria	+	+	+				+	+		-	+	

findings (table) of previously reported cases¹⁻⁸ and our case supports and amplifies the phenotype suggested by Breuning *et al.*⁴ Frequently noted anomalies include term gestation; low birth weight; delayed psychomotor and somatic development; high, prominent forehead; thin, sparse hair; large anterior fontanelle; abnormal sutures (split or overlapping); flat occiput; bulbous nose; microstomia; thin lips; small pointed chin; skin haemangiomas; low set, malformed ears; heart murmur or defect; proteinuria and small kidneys. Ocular abnormalities, including close set eyes, microphthalmia, blepharoptosis, blepharophimosis, strabismus, and nystagmus, appear to be prominent features of trisomy 6p.

The duplication of genetic material has been fairly constant in published cases with breakpoints between 6p21 and p23. However, the proband was trisomic for a smaller segment of 6p (6pter→p25) when compared to these cases (6pter→p21-23), indicating that many of the phenotypic features of partial trisomy 6p can be demonstrated with trisomy of only an extremely small amount of 6p.

In cases resulting from malsegregation of a parental translocation, there is an overlap of phenotypes. However, comparison of the clinical findings in the resulting chromosomally abnormal offspring should allow further delineation and segregation of the clinical presentation associated with specific chromosome segments. Such correlation of phenotypes with monosomy or trisomy of particular chromosome regions would seem most important in understanding the full range of expression of the

respective cytogenetic anomalies especially in counselling for prenatal diagnosis.

The expert technical assistance of John Woods and secretarial assistance of Shirley Gann are gratefully acknowledged. The cooperation and patience of the very special parents of this patient and their relatives who were studied is also appreciated. This study was supported in part by Project 905, MCH, DHHS.

References

- Therkelsen AJ, Klinge T, Henningsen K, Mikkelsen M, Schmidt G. A family with a presumptive C/F translocation in five generations. *Ann Genet (Paris)* 1971;14:13-21.
- Chiyo H, Kuroki Y, Matsui I, Yanagida K, Nakagome Y. A 6p trisomy detected in a family with a 'giant satellite'. *Humangenetik* 1975;30:63-7.
- Turleau C, Chavin-Colin F, de Grouchy J. La trisomie 6p partielle. *Ann Genet (Paris)* 1978;21:88-91.
- Breuning MH, Bijlsma JB, de France HF. Partial trisomy 6p due to a familial translocation t(6;20)(p21;p13). *Hum Genet* 1977;38:7-13.
- Coté GB, Papadakou-Lagoyanni S, Sbyrakos S. Partial trisomy 6p with karyotype 46,XY,der(22),t(6;22)(p22;q13)mat. *J Med Genet* 1978;5:479-81.
- Pearson G, Mann JD, Bensen J, Bull RW. Inversion duplication of chromosome 6 with trisomic codominant expression of HLA antigens. *Am J Hum Genet* 1979;31:29-34.
- Rosi G, Venti G, Migliorini Bruscelli G, Dotti E, Bocchini V, Armellini R. Trisomy 6p22→6pter due to a familial t(6;13)(p22;q34 or 33) translocation. *Hum Genet* 1979;51:67-72.
- Bernheim A, Berger R, Vaugier G, Thieffry JC, Matet Y. Partial 6p trisomy. *Hum Genet* 1979;48:13-6.

Correspondence and requests for reprints to Dr P R Scarbrough, Laboratory of Medical Genetics, University Station, University of Alabama at Birmingham, Birmingham, Alabama 35294, USA.