now described, or from insult occurring after organogenesis, such as infection or retinopathy of prematurity (ROP). Although born prematurely, our patient had no neonatal problems and he did not require oxygen therapy. ROP has been reported in similar circumstances but the ocular signs are different. The boy we describe is hypermetropic whereas in cicatricial ROP, myopia is the rule and extensive vitreous bands are not seen.

From the genetic viewpoint retinal folds are found in several entities. In isolation they may show autosomal dominant, autosomal recessive, or sex linked recessive inheritance.[2] In this latter form minor ocular abnormalities may be detected in carrier females.[3] They may also be a manifestation of autosomal dominant familial exudative vitreoretinopathy[4] but insert equatorially in this condition, whereas in the present case the vitreous strands extend further forwards to the ora serrata. Furthermore, no retinal changes have been detected in other family members.

Pleiotropic autosomal recessive syndromes which may feature retinal folds include the Seckel-like syndrome described by Bixler and Antley[5] and the combination of hydrocephalus with microphthalmos documented by Warburg.[6] Retinal folds have also been observed in one of four patients who had a sex linked recessive disorder characterised by microphthalmos, corneal clouding, cataracts, microcephaly, hypospadias, and cryptorchidism,[7] and in a blind retarded boy who was found to have an interstitial deletion of the long arm of chromosome 13.[8]

The combination of microcephaly, microphthalmos, and retinal folds has been described in a male offspring of first cousin parents,[9] to a variable degree in four persons from two sibships in a large inbred family,[10] and in the aforementioned brothers reported by Jarmas *et al.*[1] One of these brothers also had pedal oedema and both showed mildly anteverted nares, these features also being present in our own patient, in whom the pedal oedema resolved slowly over the first three months of life. In the family of Jarmas *et al*[1] the boys' mother showed microcephaly and microphthalmos. Taken in conjunction with the findings in our patient's mother and sister, this would suggest that there is an inherited form of microcephaly, microphthalmos, and retinal folds in which males show the full stigmata with females being more mildly affected. Inheritance could be sex linked dominant or sex influenced autosomal dominant.

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A de novo 3p;8p unbalanced translocation resulting in partial dup(3p) and partial del(8p)

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SUMMARY We present the first case of a de novo translocation resulting in dup(3p). Giemsa banding studies tentatively identified the source of the extra genetic material as 3p. Clinical findings were compatible with those previously reported in dup(3p) patients, further defining this cytogenetic anomaly as a distinct, clinically identifiable syndrome.

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Both partial dup(3p) and partial del(8p) have been reported. The phenotype of del(8p) is considered to be non-specific while that of dup(3p) is considered to be clinically recognisable. Previously reported cases of dup(3p) have mostly resulted from malsegregation of parental translocations, allowing identification of the specific chromosomal aberration not only by clinical findings but also by extrapolation from parental karyotypes.

Case report

The proband (fig 1), a newborn white female, was the 2850 g product of a 40 week gestation for a gravida 4 (G4 P0 Ab0 L4) 34 year old mother and 44 year old father. Pregnancy was complicated by class B maternal diabetes requiring up to 40 units of insulin each day for control, but was otherwise unremarkable. Labour and delivery were uncompli-

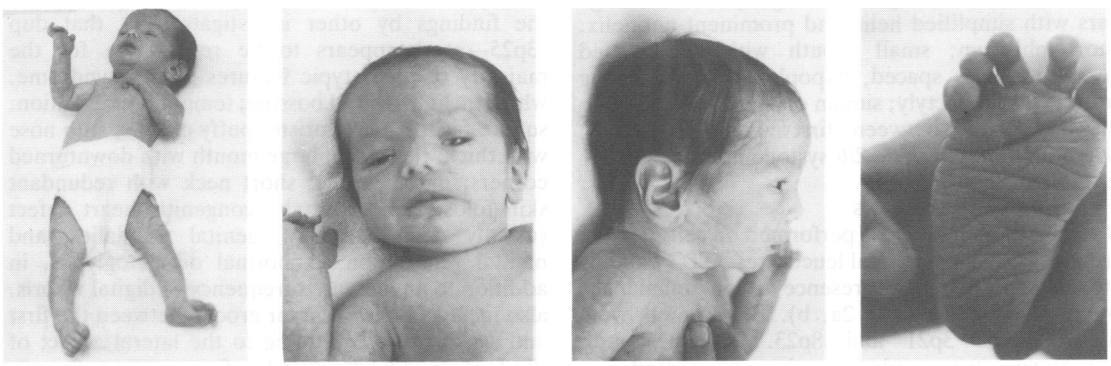

FIG 1 *The proband at four weeks of age.*

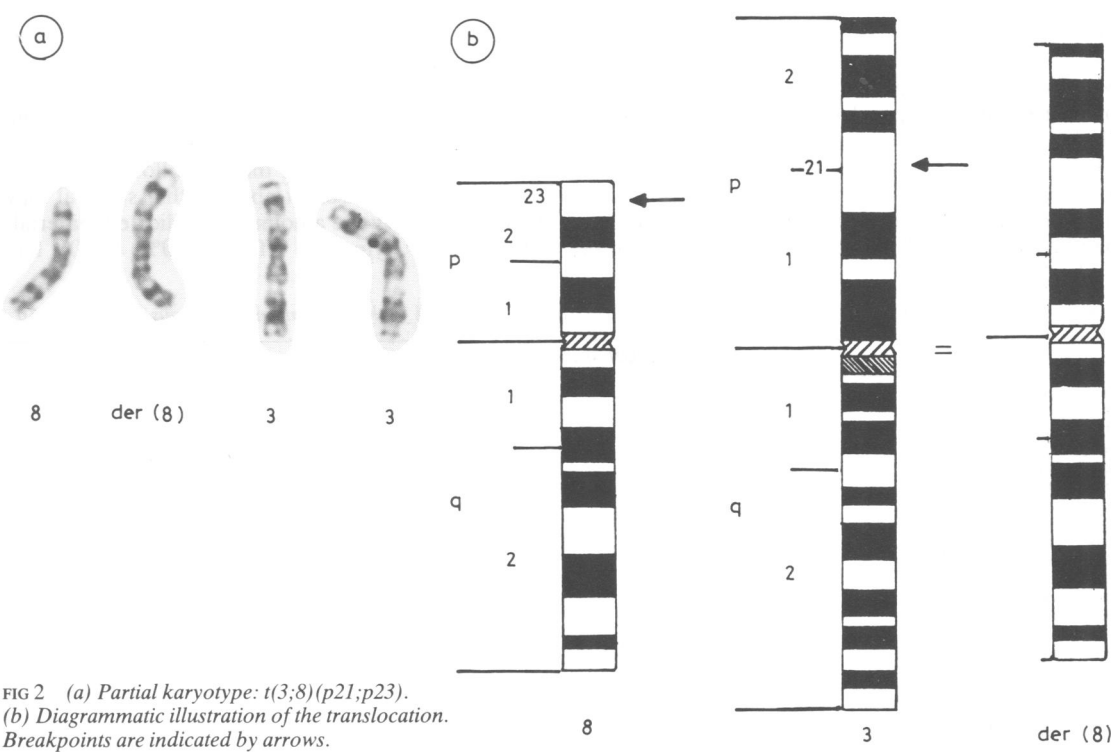

FIG 2 *(a) Partial karyotype: t(3;8)(p21;p23). (b) Diagrammatic illustration of the translocation. Breakpoints are indicated by arrows.*

cated and Apgar scores of 7 at one minute and 9 at five minutes were assigned. Both parents denied exposure to radiation or chemicals and the mother did not smoke or drink during pregnancy. Family histories were non-contributory.

Genetic consultation was requested at one day of age for evaluation of multiple dysmorphic features, including prominent forehead; slight temporal indentation; square facies; full cheeks; hypertelorism; short neck with redundant skin folds; low posterior hair line; mild micrognathia; slightly low set, large ears with simplified helix and prominent antihelix; short philtrum; small mouth with downturned corners; widely spaced, hypoplastic nipples, long trunk; camptodactyly; simian creases; gap and deep plantar furrow between first and second toes; hypotonia; and a grade 2/6 systolic mumur.

CYTOGENETIC STUDIES

Cytogenetic studies were performed on cells derived from culture of peripheral leucocytes. GTG banding studies identified the presence of an unbalanced 3p;8p translocation (fig 2a, b). Breakpoints were identified as 3p21 and 8p23. The proband's karyotype was subsequently designated as 46,XX,−8,+der(8),t(3;8)(p21;p23). Cytogenetic studies on both parents were normal.

Discussion

Martin and Steinberg[1] reviewed 17 definitely identified cases of dup(3p). Two other reports not included in this study were also reviewed by us.[2 3] These cases mostly resulted from malsegregation of a maternal translocation. Our case represents the first de novo translocation identified by Giemsa banding studies, with clinical features thought to be characteristic of the dup(3p) syndrome. Associated duplication or deletion of other chromosomes is varied and appears to be insignificant in modifying the dup(3p) phenotype. This is consistent with our case, in which none of the infant's dysmorphic features could be specifically attributed to del(8p).

The duplicated genetic material has included 3p2→pter, with breakpoints at 3p21, 3p23, or 3p25. In two cases, no sub-band was identified.[4 5] Comparison of the frequency of phenotypic features (table) noted in these subgroups of dup(3p) supports the findings by other investigators[1 6 7] that dup (3p25→pter) appears to be responsible for the majority of phenotypic features of this syndrome, which include frontal bossing; temporal indentation; square face; hypertelorism; puffy cheeks; stub nose with thick, fleshy tip; large mouth with downturned corners; micrognathia; short neck with redundant skin folds; camptodactyly; congenital heart defect (usually ASD or VSD); genital anomalies; and mental retardation. Abnormal dermatoglyphs, in addition to an increased frequency of digital whorls, also include a deep plantar groove between the first and second toes extending to the lateral aspect of the foot, specifically noted in five cases.

Though the overall phenotypic expression of dup(3p) does not seem to vary significantly with increase or decrease in the amount of duplicated genetic material, two exceptions were noted. Cleft lip and palate have been reported in cases of dup(3p21→pter) and dup(3p23→pter), but not in dup(3p25→pter). Therefore, the duplication of the 3p23→p25 region might be necessary for this specific anomaly. Also, even though follow up time is limited in some cases, it appears that survival may be influenced by the amount of duplicated material. Of patients dying in infancy, 70% (7/10) had

TABLE *Comparison of frequency of phenotypic features specifically noted with duplication of various regions of 3p.*

	Present case	*dup(3p21→pter)*	*dup(3p23→pter)*	*dup(3p25→pter)*
Brachycephaly	+	9/9	4/4	?
Frontal bossing	+	8/9	4/4	3/4
Microcephaly	+	5/9	3/6	1/4
Temporal indentation	+	8/9	3/3	2/2
Square face	+	7/9	6/6	3/4
Prominent cheeks	+	9/9	3/3	4/4
Hypertelorism	+	10/11	6/6	3/5
Epicanthic folds	+	8/10	2/3	0/2
Carp shaped mouth	+	8/9	6/6	2/2
Micrognathia	+	9/10	5/5	1/2
Cleft lip/palate	−	3/9	1/6	0/5
Short neck	+	11/11	5/6	1/2
Cardiac defects		9/10	3/6	4/5
Septal defects	+	4/9	3/3	4/4
Genital anomalies	−	6/9	3/4	3/4
Sex ratio (M:F)		7:5	4:2	5:0
Infant death	?	7/12	1/6	2/5
Holoprosencephaly	−	0/12	1/6	2/5
Mental retardation	?	3/3	5/5	2/2

dup(3p21→pter). Excluding the three patients with holoprosencephaly, the average age at time of reporting of patients with dup(3p23 or 25→pter) was 6·3 years. The reason for this is unclear since the occurrence of cleft lip and palate, type and severity of cardiac malformations, occurrence of seizures, frequency of gastrointestinal or renal malformations, etc, seems to be fairly uniform in distribution among patients with early death and those with longer survival times.

In summary, dup(3p) does appear to be a recognisable clinical entity. Most are secondary to malsegregation of parental chromosome rearrangements. However, in de novo chromosome rearrangements, the specificity of clinical anomalies and Giemsa banding studies should allow easy identification of affected subjects. Detailed initial reports and extended follow up reporting of these patients may allow further correlation between specific phenotypic features, suggested influence on survival, and duplication of specific chromosome segments.

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Presumptive mosaic origin of an XX/XY female with ambiguous genitalia

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SUMMARY A child with ambiguous genitalia had an XX/XY karyotype in all tissues examined. Analyses of 11 informative polymorphisms, both chromosomal and genetic (Rh and HLA), showed no difference between the two cell lines. It is unlikely that the child originated from fertilisation of the egg and the second polar body by two sperms; therefore, we hypothesise that the child originated from an XXY zygote after mitotic errors during cleavage. Recent findings of differences in the chromosome constitution between the extra-embryonic tissues and the fetus support this view.

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Persons with both 46,XX and 46,XY cell lines have been reported for many years. Race and Sanger[1] and Tippett[2] present an excellent summary of their characteristics including detailed information of individual cases.

There are two main types. One frequently presents with ambiguous genitalia and XX and XY cells are present in blood and other tissues. Analysis of genetic markers shows evidence of two separate and partly complementary contributions by the mother as well as two independent contributions from the father. It is presumed that two separate acts of fertilisation of two distinct haploid products from one oocyte have occurred. Therefore, they have been defined as dispermic or primary chimera.

The other type is invariably associated with twinning. Detection has usually been fortuitous