had a long and prominent upper lip and all displayed microretrognathia. Bilateral cleft lip and palate was present only in our proband, but a cleft palate was reported in two other cases.²⁻⁷ Additional features of the syndrome were low set and malformed ears, short neck, and narrow and dysmorphic chest. Congenital heart defects were found in five of the seven patients. Cryptorchidism and hypoplastic genitalia were observed in the two males. Although skeletal defects do not appear as a distinguishing feature, hip dislocations were present in two cases. Dermatoglyphs were examined in three subjects and considered unremarkable. Two patients died within 3 months of birth; the surviving ones investigated beyond the first year of life were severely mentally retarded.

In five patients the cytogenetic abnormality consisted of a clone with an extra chromosome 14 in 8 to 93% of blood lymphocytes. Turleau *et al*⁶ described a mosaic trisomy 14 resulting from a de novo formation of an isodicentric chromosome, and Jenkins *et al*⁷ found a mosaic isochromosome of the long arm of chromosome 14 in a 14q15q heterozygote. In general, the proportion of trisomic cells was lower in fibroblasts than lymphocytes.

No single enzymatic abnormality was demonstrated by extensive red blood cell studies performed in two cases. Even the nucleoside phosphorylase activity did not show the expected gene dosage effect in our patient. This result could well be due to the presence of a mosaic trisomy.

Special comment is needed on the observation in the present case of consistent nuclear abnormalities in the neutrophils. The high frequency of appendages of variable size and shape, together with the tendency of the individual lobes to be poorly separated, make these granulocytes very similar to those originally described in trisomy 13 syndrome.⁹ Available data have pointed to a relationship between these nuclear projections and the extra set

of satellites carried by the extra chromosome 13. In fact, an increased number of small clubs is not a feature in the neutrophils of patients with translocation trisomy 13. However, the same also holds true in subjects with extra G group chromosomes or with partial aneuploidy of D group chromosomes retaining the satellite regions. Huehns *et al*⁹ stated that nuclear abnormalities of the neutrophils are specific to trisomy D. Our patient with trisomy 14 mosaicism proves that this is not so. Rather, we think that it could also be a feature of the other, usually lethal, conditions associated with extra chromosomes 14 or 15.

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A rare heterochromatic variant of chromosome 4

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SUMMARY A variant chromosome 4 with a large G positive heterochromatic block is described and discussed in relation to chromo-

some 4 heteromorphisms observed with other banding techniques. The extra heterochromatin is C positive and fluoresces brilliantly with Q banding, but differs from Yqh with some methods of staining.

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Heteromorphisms of chromosome 4 with Q banding and C banding are relatively common.^{1,2} In contrast, variants detected with G banding appear to be rare.³ We discuss here such a variant detected during fetal antenatal diagnosis.

Cytogenetic studies

G banded metaphases from amniotic fluid cell cultures revealed a chromosome 4 with a large darkly staining segment proximal to the centromere in the short arm (figure a). The extra material was C positive (figure c), and in many cells the short arm appeared remarkably similar to the long arm of chromosome 16. However, the extra heterochromatin fluoresced brightly when Q stained, indicating that it was not derived from a whole arm translocation between a chromosome 4 and a 16. Parental karyotypes showed that the anomalous chromosome was also present in the father (figure b, c) while the rest of the chromosomes in his karyotype were unremarkable. The pregnancy was continued and a phenotypically normal infant was born at term. The karyotype may be described as: 46,XY,var(4)(p12:00,G40,Q45,CB40)pat with the extra band located between 4p11 and 4p12.

In G banded preparations, the extra heterochromatin in 4p was consistently darker than the Yqh

segment (figure a), and a difference between these two regions was also observed with a silver staining technique (Goyanes,⁴ 1st step) which shows a staining affinity roughly coinciding with the loci rich in satellite III DNA. This shows as black metallic staining of the secondary constriction of chromosome 9, the short arms of the acrocentrics, and some of the euchromatin of the Y chromosome. With this method most of the karyotype turns a golden-brown colour, including the heterochromatin of Yqh. The heterochromatic segment in our variant remained unstained and pale, as do the secondary constrictions of chromosomes 1 and 16. This region therefore differed from the heterochromatin in Yqh (figure d).

Discussion

There is, to our knowledge, only one report of a variant chromosome 4 detected with G banding³ which appears similar to the one described here. In neither case was the presence of the G positive segment associated with any detectable phenotypic effects.

It seems likely that these chromosomes are extreme variants in size of the heterochromatic band which is sometimes present in chromosome 4, located paracentromerically, either in the short or in

FIGURE Partial karyotypes of the antenatally screened fetus (a,d) and of the father (b,c) showing the variant chromosome 4 (arrowed). (a) G banding using trypsin after pretreatment with acetic saline, (b) G banding using trypsin after pretreatment with hydrogen peroxide, (c) C banding, (d) silver staining.⁴

the long arm. This extra heterochromatin is usually detected as a Q band heteromorphism because it fluoresces brightly and conspicuously, and very high frequencies of these heteromorphisms have been reported from some population studies (reviewed by Al-Nassar *et al*¹). From the lack of reported G heteromorphisms, on the other hand, it appears that on G banding variants with small amounts of this heterochromatin are unremarkable, especially since some variation is expected around the centromere region. Therefore, only chromosomes with exceptionally large segments of heterochromatin become particularly noticeable. The brightly Q fluorescing and G positive heterochromatin is also likely to be consistently C positive, as has been found by Pearson *et al*.⁵ The inconsistencies between Q and C variants reported by other investigators^{2 6 7} can probably be attributed to two factors: firstly, many Q variants have a small bright band which would not produce a noticeable increase in the size of the pericentromeric C band and, secondly, in some of the C variants the large C positive segment could be the result of an increased amount of the usual centromeric heterochromatin which does not fluoresce.

In conclusion it is considered that there is a heterochromatic region in chromosome 4 which is variable in size from cases where it is not detectable to large segments like the one seen in our variant. This heterochromatin is located paracentromerically, in addition to the heterochromatin which usually surrounds the centromere. It fluoresces brightly on Q staining, is C positive, and, where large enough to be detected with these methods,

G positive and selectively unstained with the silver stain method of Goyanes.⁴ It is therefore structurally distinct from the centromeric heterochromatin, the secondary constriction heterochromatin of chromosomes 1, 9, and 16, and also from the brightly Q fluorescing region of the Y chromosome.

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