Short communications

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15/15 translocation in Prader-Willi syndrome

SUMMARY Two further cases (one previously published as D/D translocation) of 15/15 translocation in Prader-Willi syndrome are reported, which brings the total cases of this specific chromosomal anomaly in connection with this specific syndrome up to three or possibly four. It is suggested that Prader-Willi syndrome might be caused by loss of short arm material of chromosome 15.

Chromosome 15 seems to be involved in the pathogenesis of Prader-Willi syndrome. Hawkey and Smithies (1976) have found a 15/15 translocation in a male with Prader-Willi syndrome. Yoshida *et al.* (1972) found the same translocation in a newborn female who may have had Prader-Willi syndrome since she was reported to be a poor feeder and to have sluggish body movement. Translocations between homologous chromosomes of the D group are rare and especially so the 15/15 type. The only other reported case of 15/15 translocation is that by Lucas (1969) in a normal female who had repeated abortions. The diagnosis in this case was made by autoradiography and not by banding techniques. We have seen 2 further cases of Prader-Willi syndrome in males with a 15/15 translocation (Fig. 1). The male:female ratio reported in the literature is 3:1.

G-banded D chromosomes

Fig. 1 Chromosomes 13, 14, and 15/15 translocated chromosomes.

Our first case was described as a D/D translocation by Bühler *et al.* in 1963. As pointed out by Hawkey and Smithies (1976), though not diagnosed as such in 1963, this patient had most of the cardinal symptoms of Prader-Willi syndrome and the diagnosis was later confirmed by obtaining further anamnestic data

about his early development, such as neonatal hypotonia, poor feeding, and complete absence of crying up to the age of 6 months.

The second case of 15/15 translocation was found in Pavia in an 8-year-old boy who had all the cardinal features of Prader-Willi syndrome, such as neonatal hypotonia, diminished spontaneous movement, weak cry, hypogonadism and cryptorchidism, mental retardation, obesity, and short stature. He also had strabismus, almond-shaped eyes, fish-shaped mouth, and kyphoscoliosis which are present only in a proportion of cases. His mother recalled weak fetal movements during pregnancy.

In this case the chromosome composed of the two homologous 15 chromosomes had only one centromere as shown by the C-banding technique. In the Swiss case reported by Bühler *et al.* (1963) in metaphases with extended chromosomes there were clearly two C-bands separated by a constriction or by a short less staining segment (Fig. 2). In metaphases with condensed chromosomes, however, the 15/15 translocation chromosome looked monocentric. Both patients' parents' chromosomes were normal as were the chromosomes of two sisters of the Swiss case.

C-banded D chromosomes

Fig. 2 Chromosomes 13, 14, and 15/15 translocated chromosome.

The finding of three or possibly four cases of 15/15 translocation associated with Prader-Willi syndrome leaves little doubt that chromosome 15 is involved in the pathogenesis of this syndrome. If the 15/15 chromosome is monocentric one has to assume that there has been a total loss of the short arm and a segment of the long arm of one 15 and also of a segment of the short arm of the other 15. If it is dicentric at least short arm material of both chromosomes 15 must have been deleted. We suggest that all cases of Prader-Willi syndrome should be carefully evaluated for involvement of chromosomes 15 minor abnormalities, such as loss of short arm.

We are sure, however, that several cases will continue to show a normal karyotype. The next effort, therefore, should be in the direction of isolating, by careful comparison of the phenotypes, the eventual existence of a new syndrome similar to the Prader-Willi syndrome whose pathogenesis is the result of the genetical imbalance resulting from a 15/15 translocation.

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References

- Bühler, E. M., Rossier, R., Bodis, I., Vulliet, V., Bühler, U. K., and Stalder, G. (1963). Chromosomal translocation in a mentally deficient child with cryptorchidism. *Acta Paediatrica*, **52**, 177-182.
- Hawkey, C. J., and Smithies, A. (1976). The Prader-Willi syndrome with a 15/15 translocation. *Journal of Medical Genetics*, **13**, 152-157.
- Lucas, M. (1969). Translocation between both members of chromosome pair number 15 causing recurrent abortions. *Annals of Human Genetics*, **32**, 347-352.
- Yoshida, M. C., Nomoto, N., and Sasaki, M. (1972). Quinacrine fluorescence patterns in somatic chromosomes of a t(15q 15q) carrier. *Humangenetik*, **15**, 66-70.

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Echinocytes in families with Duchenne muscular dystrophy

SUMMARY The results of the present investigation have failed to confirm the suggestion that there is a significant increase in the proportion of echinocytes in preparation of fresh erythrocytes in patients with Duchenne muscular dystrophy and heterozygous carriers of this disorder.

It has been reported that the frequency of deformed or more easily deformable erythrocytes is greater in males with X-linked Duchenne muscular dystrophy and heterozygous females than in controls (Matheson and Howland, 1974; Miller *et al.*, 1976; Percy and Miller, 1975). However, a previous study showed that

there was considerable overlap between the results in controls and carriers and between controls and affected boys (Lumb and Emery, 1975). The present more extensive study was undertaken in order to investigate this problem more fully.

Subjects and methods

Blood samples were obtained from 10 families where Duchenne dystrophy had occurred, living within a 70 kilometre radius of Edinburgh. The control sample included healthy laboratory and university personnel. Heparinized blood, 20 μ l, drawn not more than 4 hours previously, was added to each of 6 Luckham plastic tubes containing 180 μ l 0.9% NaCl solution previously adjusted to 284 mosm/kg. The contents of the tubes were mixed gently and left for 2 minutes. They were then centrifuged for 3 minutes, the supernatant removed, and a further 180 μ l saline added. After 2 minutes the supernatant was again removed after centrifugation and the cells were fixed by adding 180 μ l of fresh 3% glutaraldehyde in 0.01 M sodium cacodylate adjusted to pH 7.4 and 316 mosm/kg. After 1 hour the tubes were gently agitated to facilitate mixing and the cells remained in fixative for 2 hours. After two washes in saline, 100 erythrocytes from each tube were counted and classified by examining random fields of view. Each cell was classified as either echinocyte (Class I, II, or III) or non-echinocyte (Bessis, 1972). For two families examination under phase contrast was also performed, but since the proportion of echinocytes using this method did not differ significantly from the proportions obtained from the same tubes using standard light microscopy, examination by phase contrast was discontinued.

Serum creatine kinase (CK) determinations were estimated by the Rosalki method using the kit supplied by Calbiochem (Rosalki, 1967).

Results and discussion

The proportions of echinocytes observed together with means and 95th centiles are depicted in the Fig. grouped under the categories of controls, possible carriers, definite carriers, and boys affected with Duchenne muscular dystrophy. There was no significant difference between any of the mean values in these various groups. These results clearly indicate that a simple echinocyte count on a 'fresh' blood sample is of no value in carrier detection which confirms Lumb and Emery's (1975) previous findings. Further, there was no significant correlation between the proportion of echinocytes and the serum level of creatine kinase.

Matheson and Howland's (1975) sample was small