

Y material in a small percentage of cells is insufficient to explain the clinical defect. (C) It is possible that position effect may have produced the abnormal phenotype by inducing hemizygoty for a distal portion of 6q. In *Drosophila* (Baker, 1968) position effect variegation is caused by breakage in both heterochromatic and euchromatic segments followed by an exchange which places the euchromatic segment adjacent to the broken heterochromatin. A similar effect has not been shown in man, though our case may fit the cytological criteria. (D) The cytogenetic findings indicate that both small acrocentrics are der Y's; however, an alternative source for the extra chromosome cannot be completely disregarded. (E) Neither pregnancy nor delivery was uneventful, and the translocation and mosaicism may be benign karyotypic abnormalities coincidental or secondary to prenatal trauma. Because of these confounding factors, a diagnosis of chromosomal disease remains unclear.

The origin of the karyotype can be traced initially to the translocation which must have occurred before first cleavage, since no normal cell line has been found in the patient. Non-disjunction giving rise to the 47 line must have occurred after the exchange, since the additional chromosome appears identical to the translocation product. Two explanations can be offered regarding the proximity of the cytological events. If both exchange and non-disjunction occurred in gametogenesis, a zygote with 47 chromosomes would have resulted. Subsequent loss of one der Y would have had to occur to produce the 46 chromosome line. Alternatively, exchange before first cleavage, mitotic non disjunction of the der Y, and selective loss of the resulting X line might have occurred. Non-disjunction might have been the result of structural damage caused by the antecedent translocation, perhaps through a bridge-breakage-fusion event followed by stabilisation of the Y chromosomes. There is no cytological evidence for present instability of the der Y in our patient. Both der Y's appear to have the same structure and length, and in no cells was a dicentric observed.

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A dicentric no. 15 chromosome with two satellite regions

SUMMARY A case of an inherited chromosome no. 15 with two centromeres and two satellite regions is described and its origin postulated. The chromosome appears to have no clinical significance.

Stable dicentric chromosomes have been reported for X and Y isochromosomes (Cohen *et al.*, 1973; de la Chapelle and Stenstrand, 1974; Howell *et al.*, 1976) and for some Robertsonian translocations (Niebuhr, 1972a; Daniel and Lam-po-tang, 1976). Less common are those formed by translocations between acrocentrics and other autosomes (Niebuhr, 1972b; Warburton *et al.*, 1973).

A case of a no. 15 chromosome with two centromeric regions and two regions of satellite material is presented which was first encountered during routine analysis of an amniotic fluid.

Case report

Two samples of amniotic fluid from a 35-year-old woman at 22 weeks' gestation were sent to the authors from outside this region. The indication for amniocentesis was advanced maternal age. Preliminary ultrasound examination had revealed a twin pregnancy and an attempt was made to obtain fluid from each sac.

The patient had two previous children, both clinically normal.

Karyotypes of the cultured amniotic fluid cells showed a chromosomal aberration of doubtful significance in both samples. The referring physician was asked for blood from the parents for chromosome analysis. Before parental karyotypes could be studied, the parents decided that termination would be indicated if there was any doubt about the normality of the fetuses. In view of the extreme anxiety provoked by this situation, their request was agreed to by the referring physician and the gynaecologist. Diamniotic, monochorionic twins, both male, were aborted. Necropsy showed no clinical abnormalities.

Cytogenetic studies

The amniotic fluid was cultured on 6×22 mm coverslips in 5 cm petri dishes (7 to each of 2 dishes). The first harvest of 4 coverslips made after 11 days was G-banded with trypsin. Analysis revealed an abnormal no. 15 chromosome which appeared to have extra material containing a centromere added on to the short arms (Fig. 1a). No other abnormalities were detected. Further coverslips were harvested two days later, some stained with Giemsa and some C-banded with barium hydroxide and $2 \times$ S.S.C. C-banding disclosed two regions of centromeric heterochromatin, one being at a constriction and one which appeared as two separate dots (Fig. 1b). Studies of satellite association patterns showed the presence of two sets of satellite material, one between the two centromeric regions and one terminal (Fig. 1c and d).

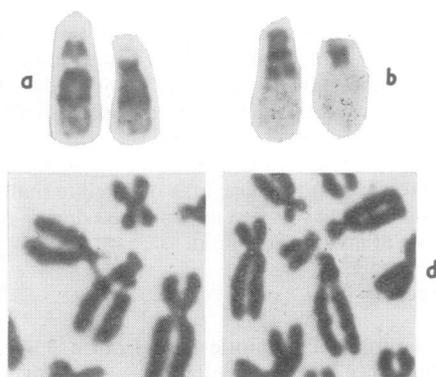


Fig. 1 (a) G-banded no. 15 chromosomes. (b) C-banding of the abnormal no. 15 chromosome and another D group chromosome. (c) Giemsa staining showing association with the intercalary satellites. (d) Giemsa staining showing association with the terminal satellites.

The mother was subsequently found to have the same abnormal chromosome. All her other chromosomes appeared normal. Culture of amniotic fluid and skin taken at termination from both fetuses showed that both had the abnormal chromosome.

Discussion

Since the abnormal chromosome was first encountered in an amniotic fluid, its clinical significance could not immediately be ascertained. G-banding, C-banding, and satellite association studies indicated that the material added on to the end of the short arms of the no. 15 chromosome contained the short arms and centromere of an acrocentric chromosome. However, it was not known if any long arm material was also present. As the abnormal chromosome was later found in the clinically normal mother, the additional material is probably just centromere and short arm material.

The abnormal chromosome appears to be stable. The lower centromere divides prematurely as indicated by the presence of two distinct spots with C-banding (Fig. 1b) and by the monocentric appearance of the chromosome with conventional Giemsa staining (Fig. 1c and d). It is, therefore, inactive at metaphase. This early division of one centromere has been reported for other dicentric and explains their stability through cell division (Niebuhr, 1972b; Warburton *et al.*, 1973; de la Chapelle and Stenstrand, 1974; Daniel and Lam-potang, 1976; Howell *et al.*, 1976).

Giemsa staining shows a pale region underneath the centromeric constriction. This was confirmed by association studies to be satellite material (Fig. 1c). Associations were also seen between the region above the active centromere and other acrocentric chromosomes (Fig. 1d). Warburton *et al.* (1973) have also reported a case of a dicentric chromosome with intercalary satellite material which underwent associations. The inclusion of satellite material within a chromosome as opposed to being terminal does not seem to prevent its activity as a nucleolar organizer.

The origin of the abnormal chromosome could not be determined. It could have arisen as a result of a direct duplication of the centromere and short arms of the no. 15 chromosome. The karyotype of the amniotic fluid would then be written 46,XY, dir dup (15) (pter → cen → q11::p13 → q11::q11 → qter). Alternatively, a translocation in meiosis between a no. 15 chromosome and another acrocentric chromosome could have occurred. The other product would be acentric and the cell line containing it lost. The karyotype would then be 46,XY,-15+dic,t(?):15

(q11;p13). The study of polymorphisms in previous generations of the family might have helped resolve the origin of the abnormal chromosome but this was not possible.

In patients found to have a twin pregnancy, amniocentesis is likely to be attempted at a later gestation than usual. In these circumstances it appears advisable to carry out preliminary parental karyotyping and thus avoid the situation described.

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Leprechaunism with mosaicism 46,XX/47,XX extra ring chromosome

SUMMARY A case of leprechaunism with a chromosomal abnormality is reported. The patient was a female infant, born to healthy, consanguineous young parents. Her course was one of extreme marasmus, with death at 3

months of age. She presented the classical features of the syndrome and chromosome mosaicism 46,XX/47,XX,+r(?). It was not possible to identify the origin of the extra ring chromosome. It is difficult to establish the role of such a cytogenetic finding in the aetiology of the syndrome.

This report concerns a female infant with the clinical features of leprechaunism, whose chromosome complement was mosaic. One cell line was normal while the other included 47 chromosomes, the additional chromosome being a small ring. This is the first instance in which an infant with leprechaunism has been found to have such abnormal karyotype.

Case report

The patient was born at term to healthy parents who are second cousins. The father was 30 years old when the infant was born, the mother 26. The mother had had five previous pregnancies. Four had been normal offspring while one had ended in a spontaneous abortion. The pregnancy which produced the proband was uncomplicated. The infant's birthweight was 3750 g and the length was 51 cm. The infant was cyanotic. The facies was grotesque, with hypertelorism and oblique palpebral fissures. The nasal bridge was broad and flat, and the nostrils large. The lower lip was thick and everted. The palate was widely cleft. Other abnormalities included occipital prominence; low set, oblique ears with obvious malformations of the lobules (Figs. 1 and 2); and extension of the scalp hair over the forehead. In addition, fine lanugototype hair was noted in the preauricular areas, and on the arms and back. The nipples appeared to be normal but were low and widely placed. The external genitalia were prominent. The infant was hypertonic and maintained an opisthotonic posture lying on her side. The hips were held in a position of adduction. Both feet revealed an equinovarus malformation with the third toes overlying the fourth. The fists were held tightly clenched. A simian crease was present on each palm. The skin was inelastic, forming prominent folds, and subcutaneous tissue was severely deficient.

Laboratory determinations, including urinary amino acid analysis, yielded normal results. X-ray films revealed a narrow pelvis (Fig. 3), and advanced skeletal maturation. The bone age was 6 to 9 months when the infant was 2 months old, on the basis of the evaluation of carpal and tarsal ossification centres.

The infant's course was one of progressive marasmus and she died at the age of 3 months.