

# Two pericentric inversions of human chromosome 11

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**SUMMARY** A pericentric inv(11) (p15q23) detectable by G-, Q-, and R-banding and occurring in 1 member of each of 3 generations of a family is described. In another family studied by several banding methods in search of chromosomal markers, a pericentric inv(11) (p11q11) was found. It was detectable only by C-banding, the darkly staining band being located on the short-arm side of the centromere. The reasons for defining this aberration as an inversion rather than a location variant are outlined. This inversion occurred in 9 members of 3 generations of a large family.

There was no clear-cut evidence of any clinical consequences of these inversions either in heterozygotes or their offspring.

With the chromosome banding methods now available it has been established that pericentric inversions are not infrequent in the human chromosome complement. The clinical significance of these heritable marker chromosomes is not yet clear, but the available evidence suggests that the inversion itself does not cause clinical abnormalities (de la Chapelle *et al.*, 1974). Recent findings reviewed by Moorhead (1976) indicate that the proportion of clinically abnormal offspring resulting from duplication-deficiency after crossing over within the inverted segment is small. Likewise, infertility in inversion carriers has not generally been noted. It may be, therefore, that some or most pericentric inversions cause little clinical harm.

The object of this paper is to describe two previously unrecorded pericentric inversions in chromosome 11 and their segregation.

## Methods

Chromosome preparations were obtained from lymphocyte cultures with standard methods. Conventional staining of the chromosomes; G-banding (Seabright, 1971); C-banding (Arrighi and Hsu, 1971); Q-banding (Caspersson *et al.*, 1970); and R-banding (Dutrillaux and Lejeune, 1971) techniques were used.

## Results

### INV(11) (P15Q23)

The abnormal chromosome No. 11 was almost metacentric. In G-banded cells (Fig. 1) the terminal

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lightly staining part of the short arm appeared longer than normal while the terminal part of the long arm was correspondingly shorter. Though band q24 is seldom visible in G-banded cells, a few cells showed it located towards the end of the short arm in the abnormal chromosome. These findings are compatible with a pericentric inversion comprising the greater part of both arms, with breakpoints at p15 and q23. Q- and R-banding were compatible with this interpretation while C-banding was uninformative.

The proposita was studied cytogenetically after having had a normal boy followed by 3 spontaneous first trimester abortions (Fig. 2). She had inherited the inv(11) chromosome from her father, and had also passed it to her son. All 3 inversion heterozygotes were healthy and had no apparent anomalies. After the investigation the proposita gave birth to a healthy boy, who had a normal karyotype on pre- and post-natal investigations. Unfortunately all other relatives refused to co-operate so the further segregation of inv(11) in this large family could not be determined.

### INV(11) (P11Q11)

This inversion was only detectable in C-banded cells. The position of the centromere was not measurably altered and G-, Q-, and R-banding showed nothing abnormal. In C-banded cells, the two No. 9 chromosomes could be identified on account of their large C-bands. In the individuals heterozygous for the inversion in No. 11, a third C-group chromosome could be consistently identified because its darkly staining C-band was on the short-arm side of the

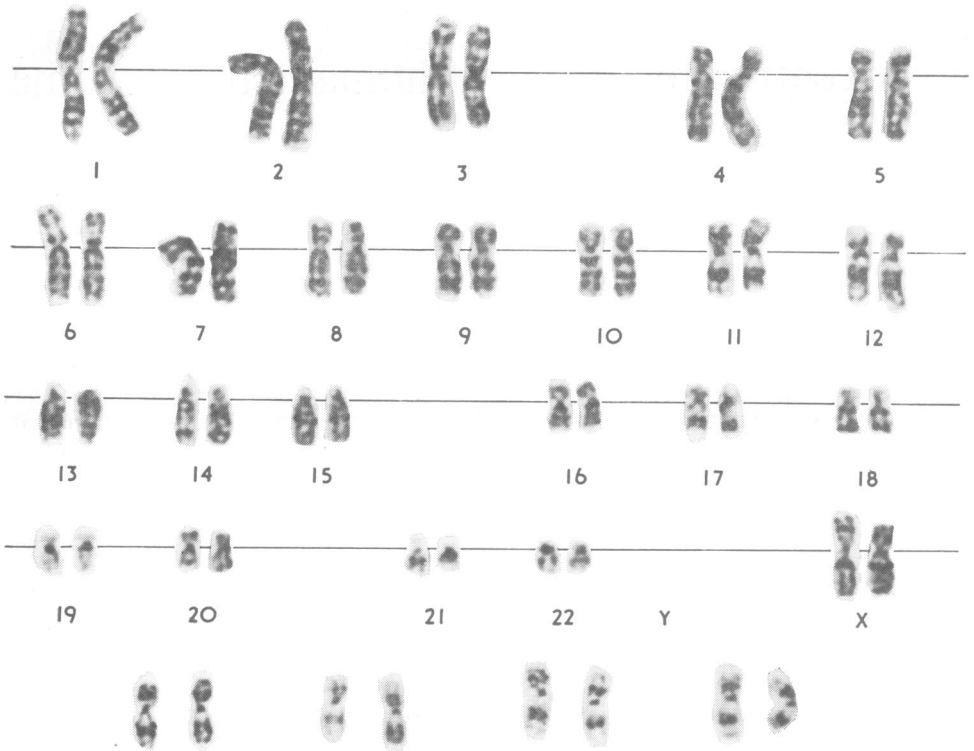


Fig. 1 G-banded karyotype of the proposita with *inv(11) (p15q23)*. The bottom line shows the No. 11 chromosomes from 4 other metaphases. The right-hand homologue carries the inversion.

centromere while in all the others it was at the centromere itself (Fig. 3). The abnormal chromosome was a No. 11 as shown by cells successively stained by Q- and C-banding (Fig. 4).

This inversion was found during an investigation of chromosomal markers in a family in which the autosomal dominant gene for myotonic dystrophy was segregating. The proposita (Fig. 5) did not have the *inv(11)* chromosome, but was heterozygous for the common inversion of chromosome 9, *inv(9)*

(p1q13), which segregated independently of the *inv(11)*. It should be noted that the mother of the proposita had the *inv(11)* without being related to the other carriers. Genealogical studies going back 5 and partly 6 generations failed to indicate a common ancestor from whom both she and her husband's brother might have inherited the marker. However, a connection might well still exist, since both families originated from the same isolated parish.

Four persons heterozygous for *inv(11)* but without myotonic dystrophy were all healthy, whereas the anomalies displayed by the five *inv(11)* heterozygotes with myotonic dystrophy, such as high arched palate, spina bifida, pes equinovarus, and mental retardation, could all be attributed to the disease (Pruzanski, 1966), and their dystrophic relatives with normal karyotypes also had similar anomalies. No spontaneous abortions or perinatal deaths were recorded in the family.

**Discussion**

*Inv(11) (p15q23)* is the most likely interpretation of the chromosomal abnormality seen in the first

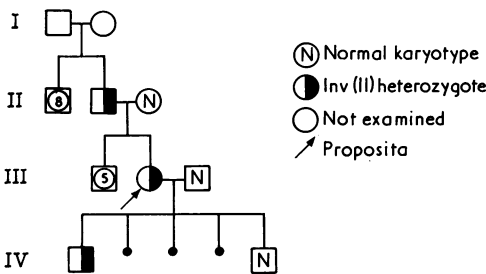


Fig. 2 Pedigree of the *inv(11) (p15q23)* family.

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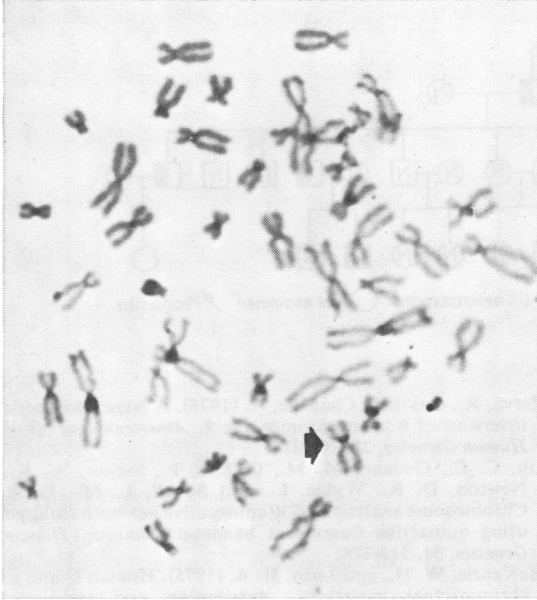


Fig. 3 C-banded metaphase showing *inv(11)(p11q11)* (arrow).

family. Neither a duplication-deficiency recombinant chromosome, nor a derivative of more complex chromosomal rearrangements appears likely. Hence we regard this inversion as established. By contrast, it may be a matter of definition whether the *inv(11)(p11q11)* is an inversion or merely a variant since it is detectable by one banding technique only (C-banding).

A comparable situation pertains to the brightly fluorescent Q-band variant near the centromere in chromosome 3. Soudek *et al.* (1974) described the

marker chromosome as an *inv(3)(p13q12)* when the brightest fluorescence was on the short-arm side of the centromere. Lin *et al.* (1976) described a similar marker as a 'reallocation of a variable band between the area of p11 and q11 of chromosome 3' and did not consider it a structural chromosome aberration. The Paris Conference (1971) listed the centric region of chromosome 3 as 'variable' by Q-banding. Similar definitions were not outlined for C-banding at the Paris Conference, but variants, particularly of the secondary constrictions and some darkly staining areas in non-centromeric regions, are well known (Craig-Holmes *et al.*, 1973; Carnevale *et al.*, 1976).

To the best of our knowledge the C-band in chromosome 11 has not been reported as located elsewhere than at the centromere itself. McKenzie and Lubs (1975) classified the C-band of chromosome 11 as the second largest in group C. In a survey of 376 neonates Müller *et al.* (1975) found large C-band variants in 13% of chromosome 11s.

It might perhaps be argued that an abnormal location of a band within a variant region is not an inversion unless there is evidence of meiotic crossing over within the inverted segment, yielding unbalanced recombinants in the offspring. But if this were so, several clear-cut human inversions would not meet the criteria (*cf.* Moorhead, 1976).

We, therefore, tentatively define the abnormal chromosome as a pericentric *inv(11)(p11q11)* because it is not merely a size variant of the C-band. However, we recognise that it may be a matter for discussion whether it should be defined as a location variant instead.

The clinical significance of both inversions described appears to be negligible or at least questionable. This is in line with previous findings for other inversions found in this laboratory (de la Chapelle

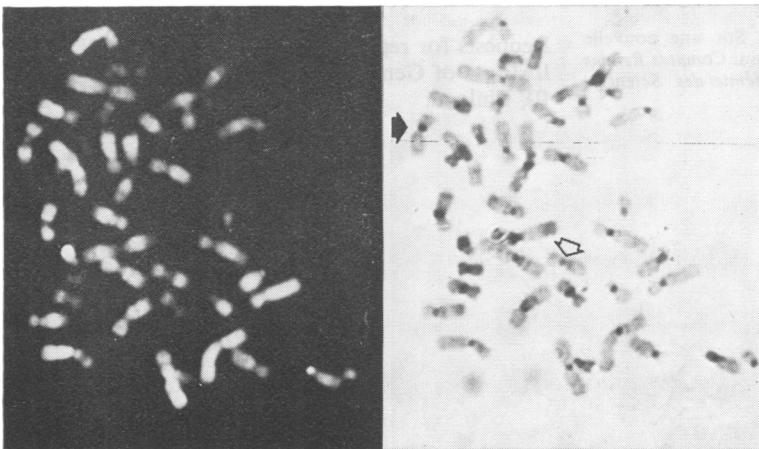


Fig. 4 Partial metaphase stained successively with the Q- and C-banding methods. The normal chromosome 11 is indicated by an open arrow and the *inv(11)(p11q11)* chromosome by a closed one.

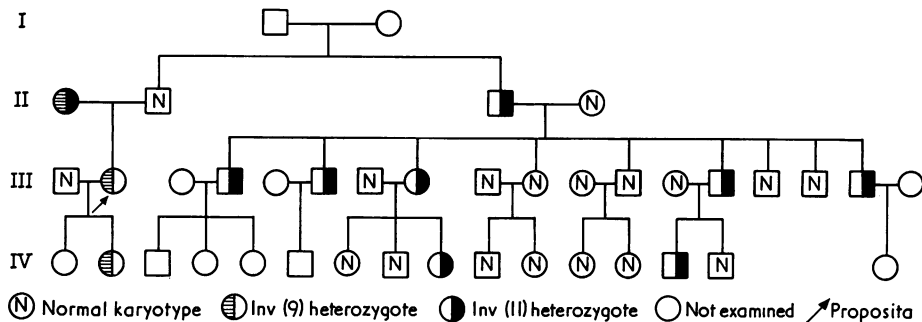


Fig. 5 Pedigree of the *inv(11)(p11q11)* family.

*et al.*, 1974; Herva and de la Chapelle, 1976) and in several others as well (Moorhead, 1976).

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