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A case of inverted insertion assessed by R and G banding

SUMMARY Cytogenetic studies in a 2-year-old boy referred to our laboratory for developmental delay showed an unusual karyotype with a three break rearrangement. R and G banding were both necessary to determine the exact nature of the rearrangement which is described as 46, XY, inv ins(16;3)(q22;p26p13). Several features coincide with the reported description of another patient where 3p26 was missing, and the coincidence is explained as a position effect.

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The proband was the third of three sibs. His parents were healthy and were 26 years old at the time of his birth. His elder brother and sister were aged 3 and 1 at the time. They both have a history of febrile convulsions. Family history is otherwise unremarkable.

The patient was born by breech delivery after 35 weeks' gestation. Birthweight was 1·39 kg, length 40·6 cm, and head circumference 30·5 cm. The patient spent 2 months in the Special Care Baby Unit. He had mild hyaline membrane disease and jaundice. A right-sided inguinal hernia was repaired at 3 months.

During his first year of life he had numerous admissions to hospital because of recurrent respiratory infections. He also had seborrhoeic dermatitis and his development was retarded. X-ray showed only spina bifida of S1. Both little fingers were inwardly curved.

The patient was reassessed at 2 years of age when he showed psychomotor retardation of approximately 6 months. He was able to walk and run with a broad based gait and his vocabulary consisted of 6 to 10 words. His height (75 cm) and weight (10 kg) were less than the 3rd centile. His head circumference was 49·5 cm (50th to 75th centile).

Physical examination showed the following: visible veins over the skull, arched eyebrows, slight mongoloid slant to the eyes, epicantic folds, broad nasal bridge, long philtrum, low set ears, and notched teeth. He also had divarication of the recti and partial syndactyly of toes 2 and 3. His seborrhoeic dermatitis was still present. He had had persistent lymphadenopathy in the left posterior cervical triangle for over 12 months. Neurological examination was normal. A cytogenetic investigation was undertaken at this stage.

Cytogenetic studies and discussion

Chromosomes were studied in peripheral leucocyte cultures from the three sibs and their parents. R and G banding were performed in all. Only the index patient showed abnormal chromosomes. All his cells showed insertion of nearly the whole short arm of chromosome 3 into the median region of the
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The long arm of chromosome 16 (fig 1). This produced a new B-like chromosome, which was the one carrying the insertion, and a new D-like chromosome, while one chromosome 3 and one 16 were missing.

Both R and G banded cells showed that the extra D-like chromosome was the segment 3p13→3qter (fig 2a, b). The short arm and the proximal part of the long arm of the chromosome carrying the insertion were identified as 16pter→16q21 by both techniques. R banding was particularly useful in identifying the distal bands of the rearranged chromosome as segment 16q22→16qter (fig 2c). Unfortunately, the R banding pattern of the inserted segment 3p24→3p13 is nearly symmetrical, and therefore it could not be established with this technique alone whether the insertion is direct or inverted. However, the G banding pattern of that segment is not symmetrical, since bands 3p22 and 3p24 are very close and often fused, giving a dark band wider than 3p14. Fig 2d, made by rearranging the standard chromosomes, indicates the suggested breakpoints and shows that the insertion is inverted. The wide dark band in the distal segment of the rearranged chromosome can be resolved in some cells (fig 1) as 3p14 plus 16q23.

It could be relevant to establish the type of insertion in this case, where the patient is in general good health and the segment involved in the insertion is long (3.5% of the length of the karyotype). Fig 3 shows why. In the event of meiosis in this patient, a cross over in the inserted segment could be expected and the resulting products would be different, depending on whether the insertion is direct or inverted. If it is inverted, as in the present case, dicentrics and acentric fragments would be produced, causing the resulting gametes to be severely unbalanced (fig 3 top), whereas in the case of a direct insertion (fig 3 bottom) the imbalance would be less severe.

Since the first report by Rethoré et al of a chromosomal insertion in humans involving three breakpoints, about a dozen cases have been described, most of them discussed by Toomey et al and Chudley et al. The frequency of these three break events has been estimated as 1/10 of other two break rearrangements, that is, 1 in 5000 newborn infants or less. In our case, a deletion of the distal part of band 3p26 has to be postulated, since disruption of the telomere is required for rejoicing to take place, but it cannot be clearly demonstrated in our banded cells. Band 3p26 is clearly seen in fig

FIG 1  G banded karyotype of proband: 46,X,Y,inv ins(16;3)(q22;p26p13).
FIG 2 Partial karyotypes of the proband showing the newly formed chromosomes and the normal 3 and 16. (a) R banded, (b) G banded, showing that 3p26 has been preserved after the insertion, (c) R banded, showing that the distal bands in the chromosome carrying the insertion are 16q22→16pter, (d) diagrammatic representation of the rearrangement.1

FIG 3 Result of crossing over in inserted segment when insertion is inverted (top), and when it is direct (bottom).

2b. The clinical picture of our patient, hardly the result of such a minute deletion, bears some resemblance to the case reported by Verjaal and De Nef,5 a case of pure deletion of segment 3pter→3p25. Even though the patients are not identical, they have in common psychomotor retardation, epicanthic folds, low set ears, micrognathia, inwardly curved fifth finger, slight mongoloid slant of the eyes, arched eyebrows, and partial syndactyly of the second and third toes. In the case reported here the distal segment of 3p is now brought into contact with the heterochromatic block 16qh, which suggests that the clinical picture might be in this case the result of the deficient expression of information contained in the 3pter region because of a position effect.

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Familial pericentric inversion of chromosome 11 detected prenatally

SUMMARY A pericentric inv(11)(p12q25) was detected by prenatal diagnosis and subsequently found in four other family members. There was no apparent evidence of clinical consequences caused by this inversion.

With the advent of banding, pericentric inversions have now been described for the majority of human chromosomes.1 The most common inversion is a pericentric inversion of chromosome 9, which occurs in approximately 1 to 1.5% of the population.2 3 Inversions of chromosome 11 are rarely seen, for generally this chromosome appears to be relatively stable. To our knowledge, there have been four cases of pericentric inversion of chromosomes 11, each having different breakpoints.4-6 This report describes a case of inv(11)(p12q25) that was shown to be present in two generations.

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The proband, a 37-year-old Caucasian, gravida 4, para 3, and her 38-year-old spouse were referred for genetic counselling and prenatal diagnosis because of advanced maternal age. The pedigree is shown in fig 1. There was no known family history of consanguinity, spontaneous abortions, or perinatal

![Pedigree of the family.](Image)

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![Partial karyotypes of (a) father, (b) fetus, and (c-e) sibs showing the pericentric inversion of chromosome 11.](Image)
A case of inverted insertion assessed by R and G banding

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