Biamnial alpha fetoprotein concentration in twins, one with multiple malformations

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SUMMARY In the 18th week of pregnancy in a 22 year old patient, twins were diagnosed by ultrasound. It was found that one twin had an abnormal skull outline and an echo-free area covered by a thin membrane in the region of the abdomen. The second embryo showed no sign of malformation. Amniocentesis was performed and the AFP in both samples of amniotic fluid were in the pathological range. Our own observations with indirect immunofluorescence confirmed that one twin with defects leading to abnormally high AFP levels can cause pathological AFP levels in the amniotic sac of a healthy twin.

In the case of biamnial twins amniocentesis for antenatal diagnosis has to be carried out on both amniotic sacs. The sac which is punctured first is marked with colouring fluid to facilitate identification. The case we report deals with twins, one of which was completely healthy, while the other had multiple malformations. The AFP concentration in both amniotic sacs, including that of the healthy child, was far above normal.

Case report

The 22 year old patient had no family history of genetic disorders. Two years before this pregnancy she had given birth to a healthy child, birth weight 4270 g and length 54 cm. The last menstrual period was on 10.3.80. By the 18th week of pregnancy the patient had gained 10 kg. However, she did not show any symptoms of toxæmia and the results of a glucose tolerance test were normal. In the 18th week twins were diagnosed by ultrasound. It was found

that one twin had an abnormal skull outline and an echo-free area covered by a thin membrane in the region of the abdomen.

In the 19th week of pregnancy both amniotic sacs were punctured. In each case 10 ml of light yellow, clear amniotic fluid were extracted. The amniotic sac which was punctured first was marked with Indigo Carmine. As well as the AFP determination, chromosome analysis was carried out which showed a karyotype of 46, XY for both twins. The AFP of the amniotic fluid of the malformed child was 32.6 mg/100 ml and that of the apparently normal child 18.3 mg/100 ml. For personal reasons the patient refused further medical help and only returned to hospital in the 30th week of pregnancy when she was having contractions. In spite of induction, the patient gave birth 2 days later to a 1370 g boy with no outward signs of abnormality. The second twin, a 1000 g boy, length 31 cm, was stillborn and had multiple malformations including microcephaly, slight indentations instead of eyes, ears, and nasal passages, holocardius, phocomelia on the right side and amelia on the left, agenesis of the liver, absent spleen, malrotation of the intestines, and a parchment thin hernia of the abdominal wall filled with the small intestine (figs 1 and 2).

Discussion

In spite of the high molecular structure of AFP it appears to be able to pass through the amnion. This is made possible by the ultrastructure of the amniotic epithelium, which to a large extent allows circulation of the amniotic fluid including dissolved matter extracellularly. The basis for this is the large number of broad, heavily segmented, intercellular canals which pervade the amniotic epithelium.¹ This special intercellular permeability is also improved by the complete absence of ridges and a basal membrane

FIG 1 *The malformed twin immediately after delivery.*

FIG 2 *X-ray of the malformed twin.*

FIG 3 *AFP immunofluorescence of amniotic epithelium.*

which allows macromolecular compounds to pass.² The high level of permeability of the intercellular framework is shown by various studies; for example, longer washing of fixed samples of amniotic membrane incubated with Ferritine leads to a significant outflow of Ferritine from the amniotic intercellular canals into the buffer solution used for washing.

Our own observations with indirect immunofluorescence proved the presence of AFP in the amnion and therefore the passage of AFP through the intercellular canals (fig 3). Therefore, exchange of AFP between biamnial twins can be assumed.

The transamniotic-uterine passage of AFP is doubtful, however, not only because of the different concentration maxima in the maternal and fetal section,³ but also because of the different micro-heterogeneity of maternal and fetal AFP.⁴

Nevertheless, one can summarise the clinical consequences of our observations as follows: one twin with defects leading to abnormally high AFP levels can cause pathological AFP levels in the amniotic sac of a healthy twin.

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A familial insertion involving an active nucleolar organiser within chromosome 12

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SUMMARY As far as the authors are aware this is the first report of the insertion of an active NOR into a non-acrocentric chromosome, although a simple translocation involving an active NOR has been previously recorded. More specifically, this case involves the non-reciprocal translocation of the centromere and stalk of an acrocentric into 12p, generating an apparently stable dicentric chromosome. The insertion is seen in three generations and may be relatively genetically benign. The abnormality is fully described by G and sequential C banding, DA/DAPI fluorescence, kinetochore staining, and Ag-NOR staining, and the findings are discussed in the light of the limited published reports of insertion in man.

In man, simple translocations are fairly common two break rearrangements, as are pericentric and paracentric inversions. In total, two break rearrangements occur at a frequency of about 1 in 500 newborns.¹ Insertions are normally considered to be three break events and are much rarer in man. In *Drosophila*, insertions can be artificially induced but are at least ten times less frequent than translocations. A similar situation is found in the mouse.²

Since the first unambiguous report of a human insertion,³ insertions have been reported either between^{4–13} or within^{14–15} chromosomes. Therefore, with the exception of a few presumptive insertions reported in the pre-banding era, the authors are aware of only 13 documented cases in humans. The

rarity of such non-reciprocal rearrangements in man is further emphasised by the fact that the International Repository of Chromosome Anomalies¹⁶ lists details of only 17 insertions from a grand total of 12 384 chromosome abnormalities, each of which is rare in its own right.

Although a non-acrocentric with an active NOR resulting from a simple, two break translocation has been previously reported,¹⁷ we describe here what we believe to be the first report of a three break rearrangement which involves the insertion of active nucleolar organiser material into 12p. It has segregated uneventfully in three generations and therefore may be genetically benign.

Case report

A male infant was delivered to a 23 year old woman at 38 weeks' gestation after an uneventful pregnancy. The baby was heavy for dates weighing 4300 g and measured 55 cm from heel to crown with a head circumference of 35.2 cm. Physical examination revealed a baby with an asymmetrical face, slightly low set ears, a left simian crease, a short neck, widely spaced nipples, and a slight mongoloid slant to the eyes. A systolic murmur was noted at the left sternal edge and an echocardiogram suggested that this might be due to a small atrial septal defect. The baby's hospital stay was relatively uncomplicated and, despite being heavy for dates, he was not hypoglycaemic, but developed jaundice requiring phototherapy. In view of the chromosome analysis, clinical examination was repeated 3 weeks later. The baby had only mild mongoloid features, normal tone, and the cardiac murmur was no longer apparent. Developmental assessment at 9 months was normal.

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