

Recurrent miscarriages in a couple with $t(4,8)$ and $inv(9)$

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Abstract

Nearly 60% of all first trimester spontaneous miscarriages are due to chromosomal abnormalities. The most frequent are numerical abnormalities (94%), followed by structural abnormalities(5%) and less frequently mosaicism(1%).

We report a 28 years-old couple in which an 4,8 translocation and 9 inversion has been identified during the investigation for recurrent miscarriages.They were phenotypically normal female and male. She had suffered four miscarriages in 7 years but no cytogenetic analyses had been performed in these abortuses.

In karyotyping by standard G-banding techniques of peripheral blood cultures showed 46,XY,t(4,8) and 46,XX,inv (9). The translocation was also confirmed by FISH studies.We conclude that cytogenetic analysis should be an integral part of etiological exploration in couples with recurrent abortions.

Keywords: Chromosome abnormalities, recurrent abortions ,inversion.

Introduction

Balanced structural chromosome abnormalities (abnormalities that involve the rearrangement of genetic material but no overall gain or loss, such as inversions and translocations) in parents can cause recurrent miscarriage. In couples with two or more miscarriages the incidence of these abnormalities varies between 3% and 6% (1-4). In carrier couples the products of conception can have a normal karyotype, the same balanced structural chromosome abnormality as the carrier, or an unbalanced structural chromosome abnormality. The last scenario can lead to the fetus being miscarried, a stillborn child, or a child born with major congenital defects and severe mental handicap. Current guidelines for the management of recurrent miscarriage recommend chromosome analysis in both partners (5-7). Once a structural chromosome abnormality has been detected, prenatal diagnosis in subsequent pregnancies and termination of pregnancy in the case of an unbalanced fetal karyotype is available.

To counsel carrier couples about their risk of viable offspring with unbalanced chromosomal abnormalities and their chances of having a healthy child or miscarriage we need to know the outcome in a population with similar abnormalities. Reports of reproductive outcome in carrier couples whose carrier status was ascertained after recurrent miscarriage provide information on only the first pregnancy after chromosome analysis or on the results of prenatal diagnosis in subsequent pregnancies, or they lack detailed information on reproductive outcome (8-13). The frequency of balanced chromosomal translocations in the general population is 0.3%.

The pericentric inversion of Chromosome 9 or *inv(9)* is commonly seen in normal humans and the frequency estimated to be 1 to 3% in general population (14,15,16,17).

The *inv(9)(p12q13)* also been reported in various human diseases such as couples with repeated spontaneous abortions, bad obstetric history, infertility and congenital anomalies (18,19,20).

Presentation of the case.

A 28 years-old couple in which an 4,8 translocation and 9 inversion has been identified during the investigation for recurrent miscarriages. They were phenotypically normal female and male. She had suffered four miscarriages in 7 years but no cytogenetic analyses had been performed in these abortuses.

Methods

We obtained chromosome preparations from routine peripheral blood lymphocyte cultures. At least five GTG banded metaphases (minimal 500 band level) were evaluated for couple. Karyotypes were recorded according to the recommendations of the international standing committee on human cytogenetic nomenclature 1995 (21).

Peripheral blood cultures were set up in F-10 nutrient media and with 20% fetal bovine serum. The cultures were stimulated with phytohaemagglutinin (PHA-M) and incubated for 72h at 37°C. The cultures were arrested with colchicine (10 mg/ml) at 70,5th h and treated with 0.075 M KCl. The cultures were fixed with cornoy fixative (methanol: Acetic acid, 3:1). The chromosomes were prepared on prechilled slides and stored for three days at room temperature for ageing of the slides. The chromosome preparations were subjected to GTG-banding using standard procedure. Briefly, the slides treated with trypsin-EDTA in Sorensen's buffer for 30 seconds and stained with giemsa

stain. At least 30 well-spread and banded metaphases were analyzed under microscope and karyotyped according to ISCN 2000.

Discussion

Chromosome 9 represents with the highest degree of morphological variations. The mechanisms of origin of inversions 9 are highly complex (22).

The risk of viable offspring with chromosomal abnormalities was low in carrier couples whose carrier status was ascertained after two or more miscarriages. Their chances of having a healthy child were as high as non-carrier couples, despite a higher risk of a subsequent miscarriage.

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Legends to Figures

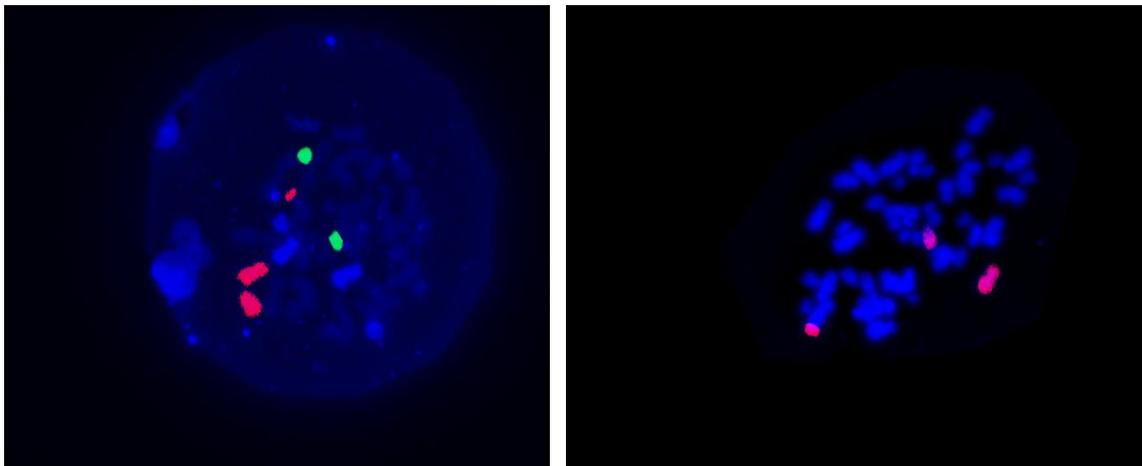


Figure 1. FISH image with whole chromosome painting for chromosome 4(red)

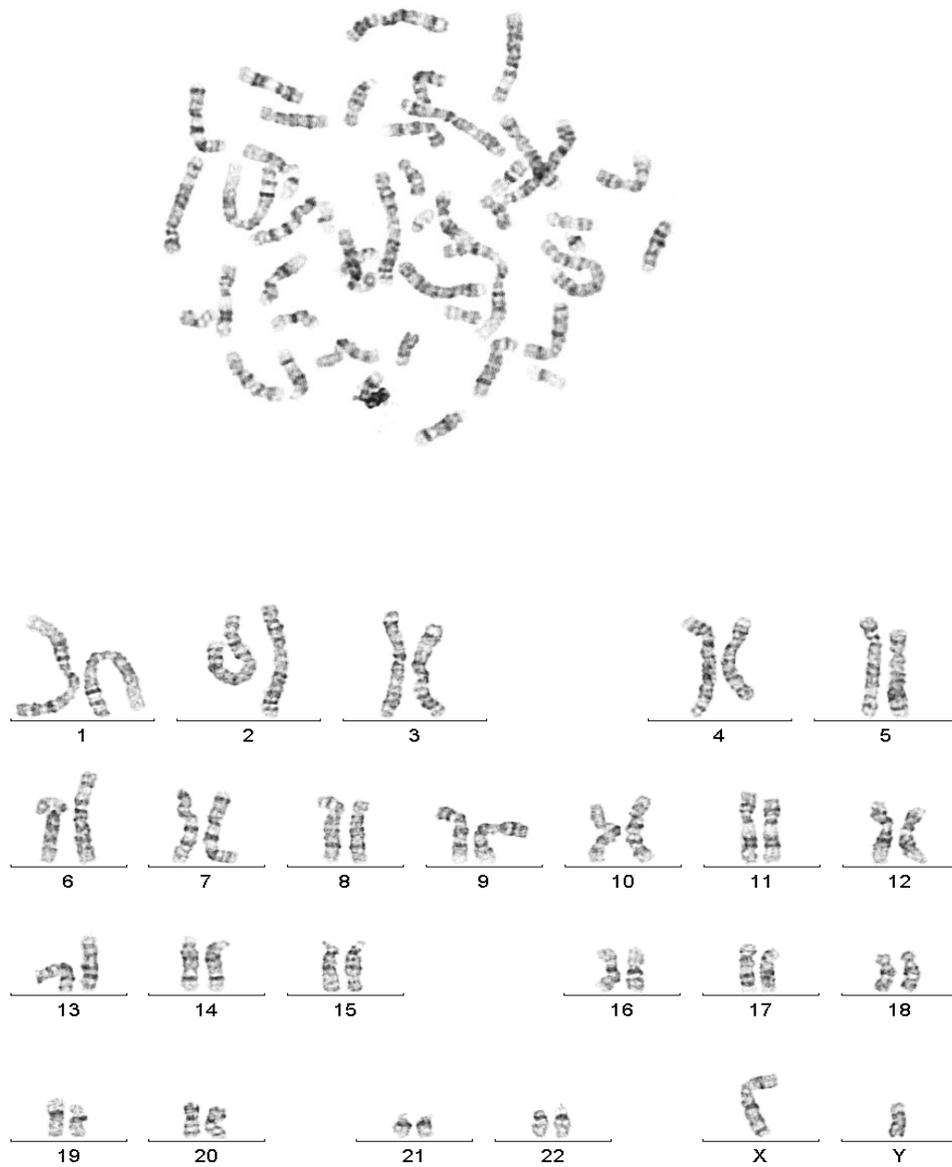


Figure 2. 46, XY, der(4;8)(4pter→4q35::8pter→p21)del(8)(:p21→qter)

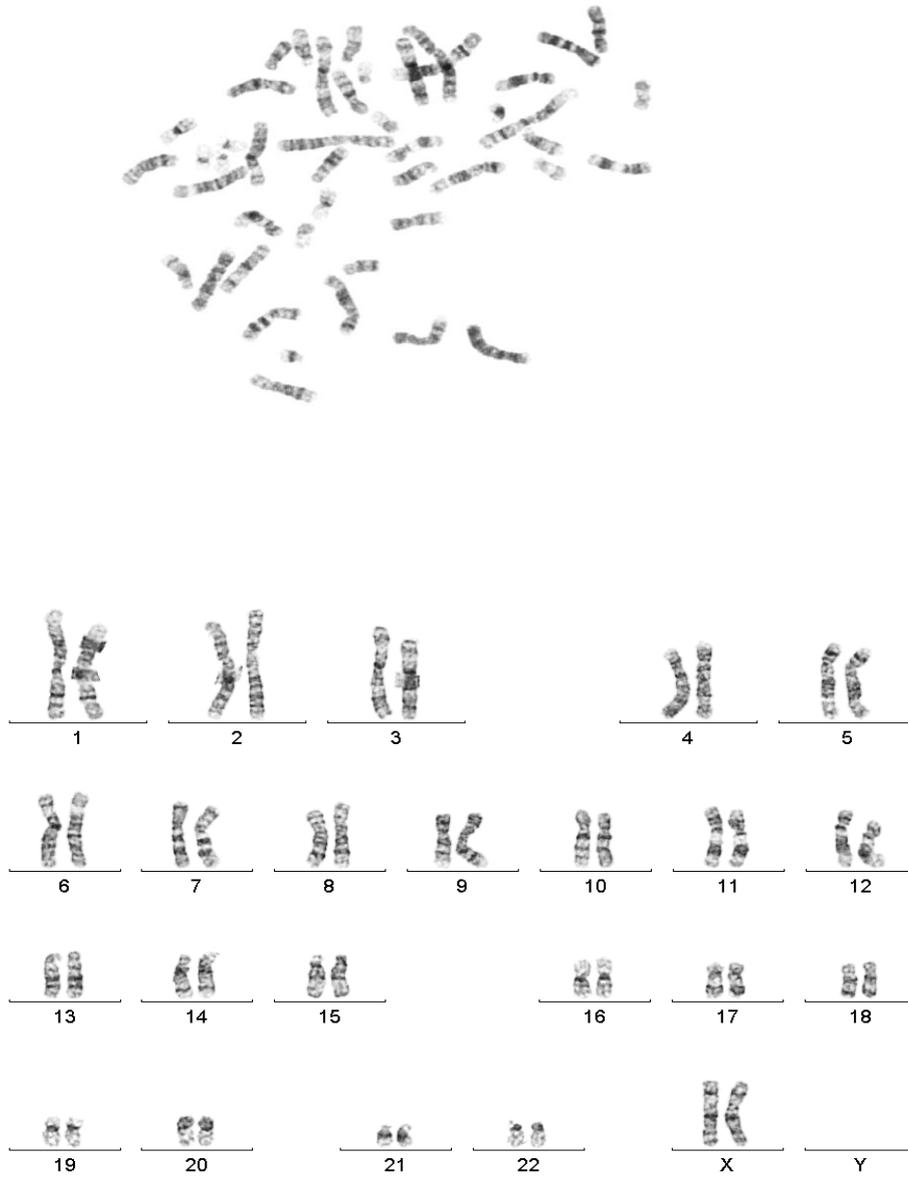


Figure 3. 46, XX, inv(9)(p13q13)