LETTER TO THE EDITOR

PRENATAL DIAGNOSIS OF SATELLITED 21q DERIVED FROM PERICENTRIC INVERSION INVOLVING THE SATELLITE STALK REGION AND TERMINAL 21q

BY C.-P. CHEN [1,2,3,4,5,6], F.-J. TSAI [4,7], C.-C. LEE [1], W.-L. CHEN [1], C.-W. PAN [1], P.-C. WU [1] AND W. WANG [2,8]

A 29-year-old primigravid woman was referred for amniocentesis at 33 weeks of gestation because of an obstetric history of small for gestational age. Her husband was 30 years of age. The woman and her husband were normal and healthy. There was no family history of congenital malformations. Prenatal ultrasound revealed a biparietal diameter of 7.79 cm and a femur length of 6.27 cm equivalent to 33 weeks, and internal organs were unremarkable. Magnetic resonance imaging (MRI) revealed normal brain volume and no structural abnormalities. Elective amniocentesis was performed due to maternal anxiety. Cytogenetic analysis of cultured amniocytes showed an aberrant chromosome 21 (Fig. 1). Karyotyping of the parental blood lymphocytes identified the same aberrant chromosome 21 in the father. The maternal karyotype was normal. Standard Ag-nucleolus organizer region (NOR) staining showed two NORs on the aberrant chromosome 21 with one NOR on the region of the short arm and the other ectopic NOR on the terminal region of 21q (Fig. 2). Fluorescent *in situ* hybridization (FISH) study using the 21q telomeric probe showed two 21q telomeric probe signals on the aberrant chromosome 21 with one signal on the tip of the short arm and the other signal on distal 21q (Fig. 3). The aberrant chromosome 21 thus was derived from a pericentric inversion in which breakage and reunion had occurred at the satellite stalk region of chromosome 21p and the terminal region of chromosome 21q (Fig. 4). The karyotype of the fetus was 46,XX,inv(21)(p13q22.3)pat. A female baby was delivered uneventfully at 39 weeks of gestation with a body weight of 2,900 g. When examined at 4 years of age, she was normal and healthy with no phenotypic consequence.

A satellited acrocentric chromosome results from translocation of the genetic material involving NOR of an acrocentric chromosome short arm onto the tip of the long arm of an acrocentric chromosome (3). A satellited non-acrocentric chromosome results from translocation

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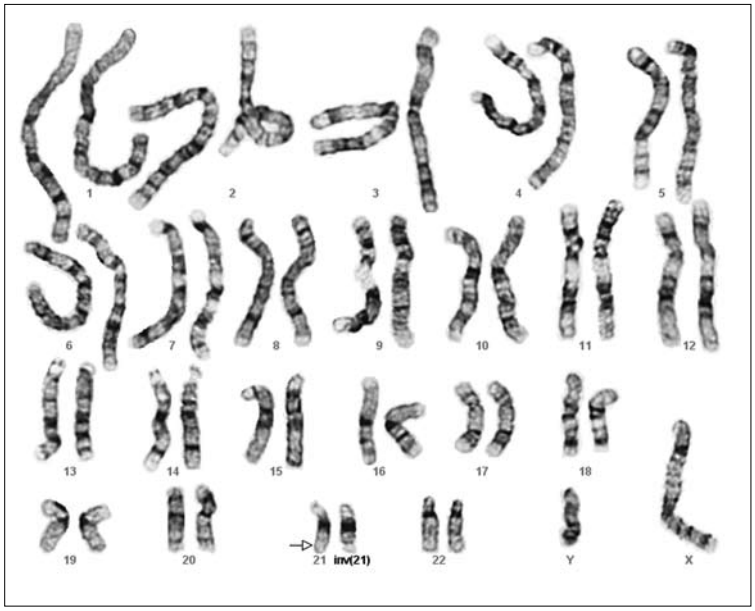

Figure 1: G-band chromosome preparation shows a normal chromosome 21 (arrow) and an aberrant chromosome 21 [inv(21)].

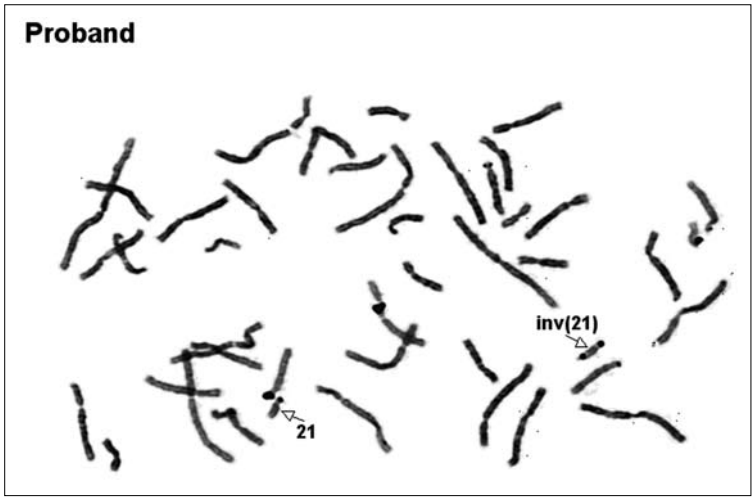

Figure 2: Ag-NOR staining of the chromosome preparation shows two NORs on the aberrant chromosome 21 [inv(21)] and one NOR on the normal chromosome 21.

of the genetic material involving NOR of an acrocentric chromosome short arm onto a non-acrocentric chromosome (1-2). The NOR can be translocated either to a terminal region or to an interstitial region of another chromosome resulting in a terminal NOR or an interstitial NOR. Prenatal diagnosis of a terminal NOR in a satellited non-acrocentric chromosome has been well described (1, 4). However, prenatal diagnosis of a satellited acrocentric chromosome is very uncommon. The most common satellited non-acrocentric chromosome is the satel-

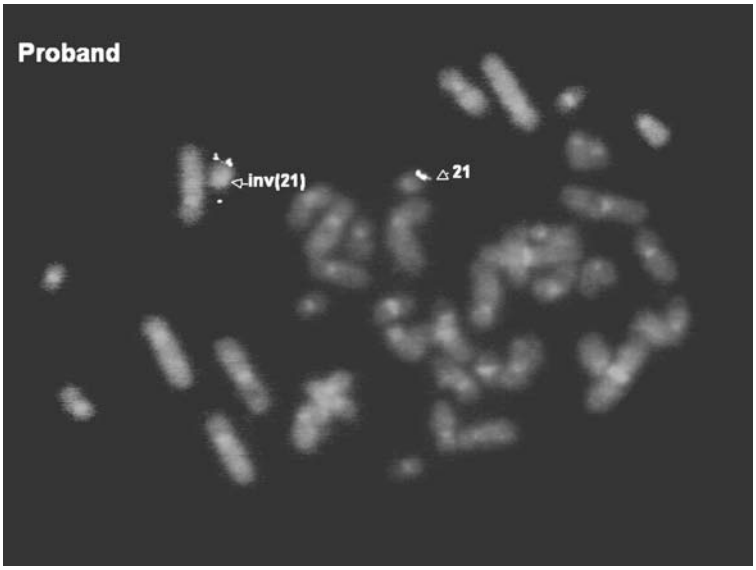

Figure 3: Fluorescent *in situ* hybridization (FISH) using a 21q telomeric probe (spectrum red), TelVysion™ 21qSO (Vysis, Downers Grove, IL, USA) shows two signals on the aberrant chromosome 21 [inv(21)] and one signal on the normal chromosome 21.

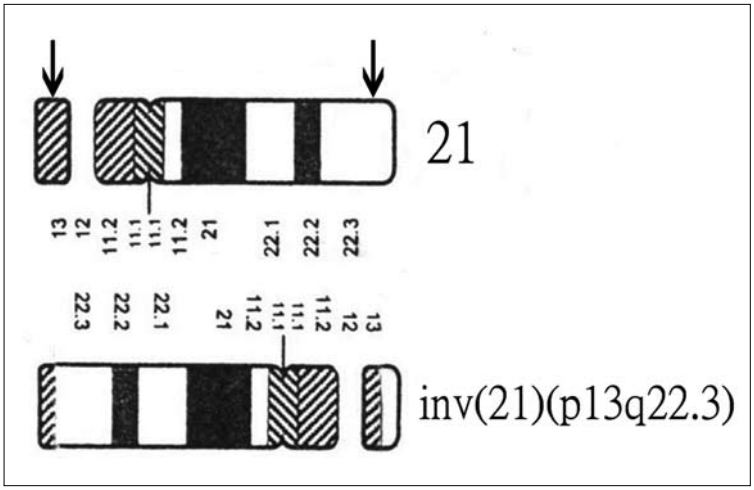

Figure 4: Diagrammatic representation of an inv(21)(p13q22.3)pat pericentric inversion heterozygote. Arrows indicate the points of breakage and reunion.

lited Yqh chromosome derived from a translocation between Yq12 heterochromatin and either 15p or 22p (5, 7). Carriers of an interstitially ectopic NOR chromosome are likely to exhibit no phenotypic effects (2). Norris *et al*. (6) reported interstitially ectopic NORs in Yq and 22q in two healthy cases. Chen *et al*. (2) reported prenatal diagnosis of interstitially satellited 6p derived from paternal balanced translocation of t(6;14)(p22;p12) with no phenotypic consequence.

The NOR translocation can be pathogenic due to a cryptic deletion from *de novo* rearrangement or from malsegregation of a familial balanced translocation (1, 3). Chen *et al*. (1) reported inherited satellited 4p with

a karyotype of 46,XX,der(4)t(4;15)(p16;p11.1)mat, a distal 4p deletion and Wolf-Hirschhorn syndrome in a malformed infant. Chen *et al*. (1) also reported inherited satellited Xq and a karyotype of 46,XqsY in a mentally retarded boy with a distal Xq deletion. Chen *et al*. (3) reported *de novo* satellited 21q with a distal 21q deletion, corpus callosum dysgenesis, colpocephaly, a concealed penis, congenital heart defects and developmental delay in a 3-year-old boy. In order to rule out the possibility of a cryptic deletion, prenatal diagnosis of a satellited chromosome should include genetic counseling with a proper evaluation of family members, Ag-NOR staining, a high-resolution banding, FISH using probes at the critical breakpoints, and molecular analysis such as array-comparative genomic hybridization and polymorphic DNA markers especially in *de novo* cases.

We have presented a very rare case of inherited satellited 21q detected prenatally due to maternal anxiety. The present case provides evidence that an ectopic terminal NOR in an acrocentric chromosome can be derived from a familial balanced pericentric inversion involving the satellite stalk region and the terminal region of the long arm with no phenotypic consequence.

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