Pericentric Inversion of Chromosome 9 in an Infant With Ambiguous Genitalia

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Abstract- Pericentric inversion of Chromosome 9 is one of the most common chromosomal abnormalities, which could be associated with various manifestations in some cases. Herein, a patient is presented with ambiguous genitalia that karyotyping revealed pericentric inversion of Chromosome 9 (p12,q13). Pericentric inversion of Chromosome 9 could be considered in the list of differential diagnosis of those with ambiguous genitalia, while chromosomal karyotype and culture could be recommended in children with ambiguous genitalia.

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Keywords: Pericentric inversion of chromosome 9; Chromosomal structural abnormalities; Ambiguous genitalia

Introduction

Pericentric inversion of Chromosome 9 is the most common abnormality of human chromosomal after trisomy 21 and fragile x (1), which is estimated to be seen up to 1-3 percent in general population (1-4). Although this chromosomal abnormality might not lead to any clinical presentation in the most cases (5), several signs and symptoms have already been reported in some cases such as infertility, recurrent miscarriage, unusual features and multiple congenital anomalies (1,6-9). The clinical attribute of this syndrome is growth and mental retardation, microcephaly, low-set ears, upward-slanted eyes, wide sutures and fontanelles, broad nose, congenital heart defects, micrognathia, enophthalmos or microphthalmos, abnormal brain, skeletal and urogenital abnormalities and external genitalia ambiguous (8,10).

Case Report

The patient is a 4-month boy who was referred to the Children's Medical Center, the Pediatrics Center of Excellence in Iran, because of ambiguous genitalia. There was no problem in mother pregnancy, while the fetal ultrasound was also normal during pregnancy. Birth weight was 3200 gram, length 49 cm, and head circumference was 34 cm. He has normal growth and development. On physical examination, the external genitalia was ambiguous. There was small phallus, while palpable gonads in scrotum were detected. He haD perinoscerotal hypospadias (Figure 1).

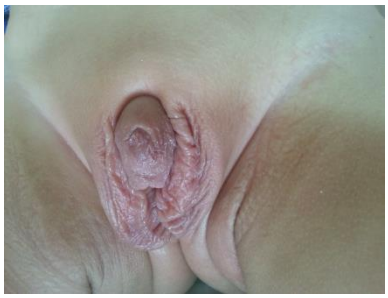

Figure 1. Perinoscerotal hypospadias in the patient with pericentric inversion of Chromosome 9

Laboratory tests, such as DHEAS (Dehydroepiandrosterone, 17OHP (Hydroxyprogesterone), Andrestandione, sodium, potassium, cortisol, ACTH were all normal. In HCG (Human Chorionic Gonadotropin) test, testosterone and dihydrotestosterone were increased after the test

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(Testosterone and dihydrotestosterone before tests were 0.06 ng/ml and 22 pg/dl respectively, respectively; after test testosterone and dihydrotestosterone were 5.5 ng/ml and 63 pg/ml, respectively). Echocardiography revealed VSD (ventricular septal defect) with 5 mm diameter. Sonography of brain and kidney were normal. Karyotype was performed which showed 46, XY, inv (9) (p12,q13) (Figure 2). His mother's Karyotype was 46, XX, inv (9) (p12,q13), while the fathers was 46, XY.

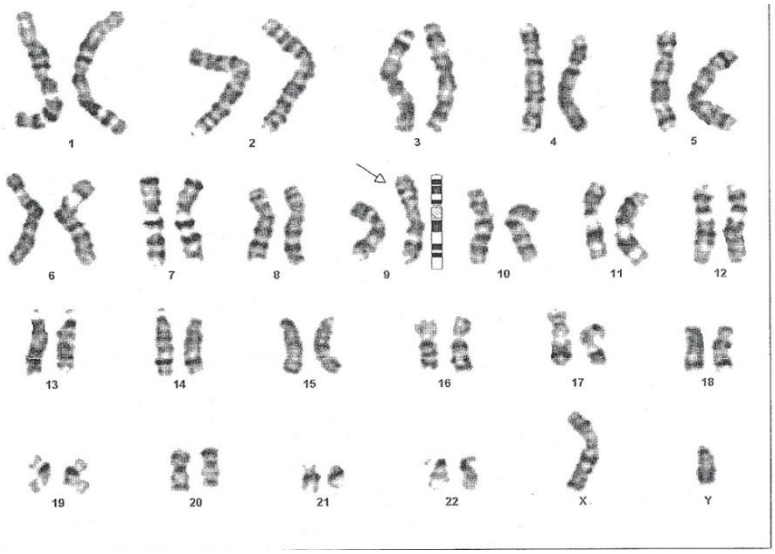

Figure 2. Karyotype of the patient showing 46, XY, inv (9) (p12; q13)

Discussion

In this study, a case with ambiguous genitalia was presented that the sex determination after the chromosomal analysis revealed 46 XY, pericentric inversion of Chromosome 9 (p12,q13). The chance of structural abnormalities of autosomes or sex chromosomes in newborn infants is about 0.5% (11). The most common and known chromosomal abnormalities is trisomy 21 and the fragile X syndrome (1). Pericentric inversions could be occurred in all chromosomes, except chromosome 20 (6). It seems that the chromosome 9 is susceptible to breakage, and this could be the reason that inversion 9 could occur commonly (12). The incidence of inv (9) is higher in females fetuses than males fetuses (7:1) (9). Inv (9) could be associated with different clinical conditions such as children with dysmorphic features and with repeated spontaneous abortions. Previous reported showed that inv (9) was detected in patients with various congenital anomalies such as in the central nervous system, heart, and kidney (1,9,13-16), but our patient just had VSD with diameter 5 mm in echocardiography (13-17). Inv (9) in children is associated with dysmorphic features and some symptoms such as growth and mental retardation, low-set malformed ears, microcephaly, wide sutures and fontanelles, upward-slanted eyes, small palpebral fissures, enophthalmos or microphthalmos, broad nose with bulbous tip, micrognathia, abnormal brain, congenital heart defects, skeletal and urogenital abnormalities (6,18). However our case had got normal features (1,13). Abnormal ambiguity includes hypospadias, micropenis and cryptorchidism were previously reported in pericentric inversion of Chromosome 9, inv (p12,q13) (14,15,17). The presented case here had also genital ambiguity such as micropenis, hypospadias, and bifid scrotum.

Pericentric inversion of Chromosome 9 could be considered in the list of differential diagnosis of those with ambiguous genitalia. Chromosomal karyotype and culture could be recommended in children with ambiguous genitalia, while parental chromosomal analysis is necessary for genetic counseling.

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