TITLE

Trisomy 9 Syndrome in an Infant with Ambiguous Genitalia

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OBJECTIVES

•The 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 are 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 ultrasounds 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 palpaple gonads in scrotom was detected. He haD perinoscerotal hypospadiasis (Figure 1). Laboratory tests, such as DHEAS (Dihydroepiandrostrone, 17OHP (Hydroxy progesterone), Andrestandione, sodium, potassium, cortiso l, ACTH were all normal. In HCG (Human Chorionic Gonadotropin) test, testosterone and dihydrotestostrone were increased after test (Testosterone and dyhydrotestostrone before test were 0.06 ng/ml and 22 pg/dl respectively, respectively; after test testosterone and dyhydrotestostrone were 5.5 ng/ml and 63 pg/ml, respectively). Echocardiography revealed VSD (venticular 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 father's was 46, XY.

Discussion

•In this study, a case with ambiguous genitalia was presented that the sex determination after the chromosomal analysis revealed 46 XY, trisomy 9 inv(p12,q13). The chance of structural abnormalities of autosomes or sex chromosomes in new born infants is about 0.5% (11). The most common and known chromosomal abnormality are trisomy 21 and the fragile X syndromes (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 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 include hypospadias, micropenis and cryptorchidism were previously reported in trisomy 9inv (p12,q13) (14,15,17). The presented case here had also genital ambiguity such as micropenis, hypospadias, and bifid scrotum.

•Trisomy 9 syndrome 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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