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Trisomy 9 syndrome in a neonate with unusual features

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ABSTRACT

Aim of the Work: To report a newborn infant with multiple congenital anomalies and apparent complete trisomy 9 in the blood. Review will be included.
Methods: Clinical examination, TORCH screening, echocardiography, skeletal survey, ultrasound head and abdomen were done. In addition chromosomal analysis of a peripheral blood sample using GTG, CBG banding and FISH techniques were employed.
Results: Multiple congenital anomalies including craniofacial features, central nervous, cardiovascular, skeletal, gastric and urogenital systems because of chromosomal abnormality which indicated: 47, XY, inv (9) (p12;q13) + inv (9) (p12;q13) mat.
Conclusion: Our case could be a new case of apparently complete trisomy 9 syndrome with unusual findings.

Key Words:

Trisomy 9, congenital anomalies, karyotype, FISH

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INTRODUCTION

Trisomy 9 is an uncommon chromosome abnormality which can occur in a mosaic or non-mosaic state and presents with a distinct clinical picture. In 1973, trisomy 9 syndrome was first reported in a newborn male with multiple congenital anomalies[1]. It is a relatively a rare chromosomal abnormality because most of affected pregnancies result in 1st trimester spontaneous abortions[2]. Trisomy 9 syndrome, in mosaic and non-mosaic forms, shows abnormalities that seen both in trisomy 9p and 9q syndromes. However, cystic malformations of CNS are not seen either in trisomy 9 p or in 9q[3]. The common features are 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[4]. Early death is common as only 25% lived beyond one week.[5]

CASE REPORT

The proband was the only live birth child born to related healthy parents. The mother required progesterone injections during first two months of pregnancy because of previous twice spontaneous abortions. Fetal ultrasounds detected intrauterine growth retardation and oligohydramnios. The delivery was performed by cesarean section at 35 weeks of gestation due to fetal distress. Apgar scores were, 2, 5 at five and ten minute, respectively. Only one umbilical artery was found. He was small for gestational age with birth weight 1.250 kg (< 5th centile), length 37cm (< 5th centile) and head circumference 36cm (at < 75th centile). Our case presented with abnormal shape of the skull, with wide separated sutures and fontanels, low set malformed posterioly rotated ears, broad nasal base with prominant tip, narrow deep set eyes, high arched cleft palate and micrognathia. In addition cardiac defect, simian creases, talipes equinovarus, anal atresia were detected. The external genitalia were ambiguous where Small phallus and no palpaple gonads were detected. He survived only for 4 hours after birth.

TORCH screening was negative. Abdominal ultrasound showed hypoplastic kidneys (Rt.: 2.7x1.1cm and Lt.: 2.6X1.2) while the urinary bladder could not be visualized. Echocardiography showed VSD and ASD. Ultrasound head (Fig. 1) detected hydrocephalus, ventricular cyst, small cysts in hemispheric fissures and macrogyra. Chromosomal analysis was performed on lymphocytes using GTG and CBG banding (Figs. 2&3) revealed: 47, XY, inv (9) (p12; q13), + inv (9) (p12; q13). Subsequently, fluorescence in situ hybridization (FISH) technique was applied on metaphase spreads and nuclei using whole chromosome WCP9 and telomeric probes specific for 9p/9q and LSI9p21/CEP9. In addition LSI bcr (22q11)/abl (9q34) were used to exclude iso chromosome 9 phenomena. All confirmed delineation of three copies of normal size chromosome 9. The mother's Karyotype was 46, XX, inv (9) (p12; q13) while the father's was 46, XY.

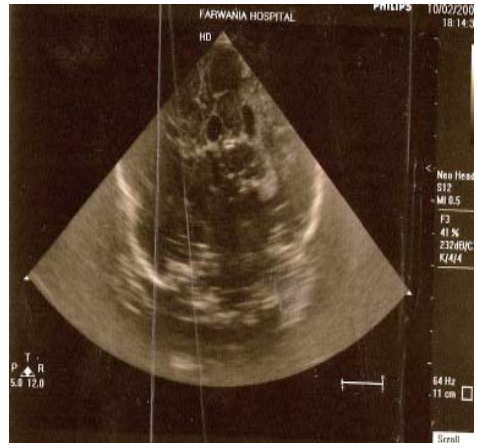

Fig. 1: U/S head showed cystic malformations in CNS.

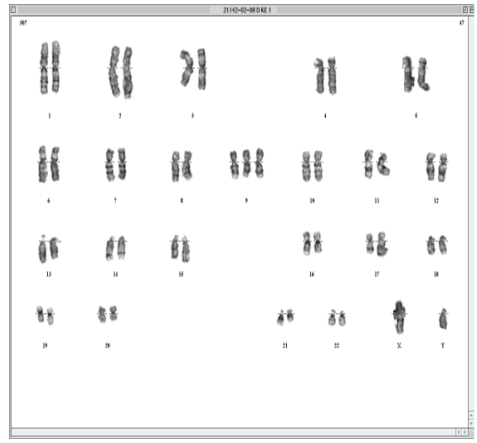

Fig. 2: GTG banding showing 47, XY, inv (9) (p12; q13) + inv (9) (p12; q13).

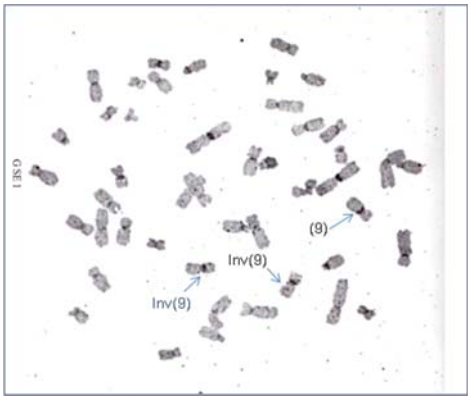

Fig. 3: C- banding showing 47, XY, inv (9qh) + inv (9qh).

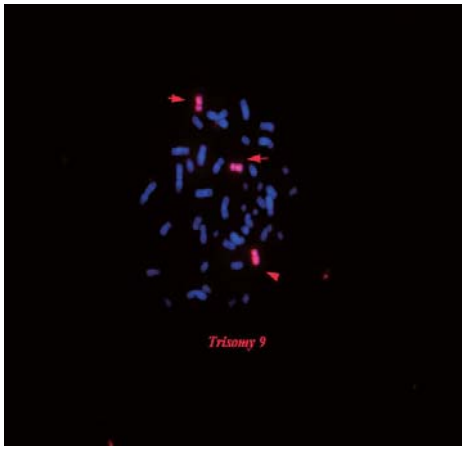

Fig. 4: FISH results showing 3 copies of normal chromosome 9 using WCP9 [VYSIS].

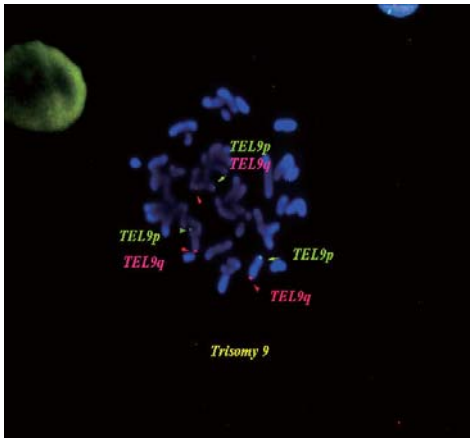

Fig. 5: FISH result showing presence of three copies of each telomeric 9 locus.

DISCUSSION

We report on a case of apparently complete trisomy 9 in a newborn who died shortly after birth. It showed the clinical phenotypes overlapping that reported in mosaic and nonmosaic forms[3,4,6,7]. Our case showed unusual charactristics such as anal atresia and macrogyra and cysts in the ventricles and hemispheric fissures. Short distance between the anus and vulva and absence of the circular muscle around the anus were reported[3]. Hydrocephalus, lobar holoprocencephaly, Dandy-Walker malformation, subarachnoid cysts were reported as intracranial anomalies[8,9]. The external genitalia of our case was ambiguous to the extent that the sex determination was identified only after the result of Karyotype. However, hypoplastic genitalia, hypospadius, micropenis and cryptorchidism were previously recorded in trisomy 9 syndrome[9-11]. Moreover, sex reversal in a patient with trisomy 9 mosaicism was reported.[12]

The term complete trisomy 9 relied on the results of the cytogenetic analysis of 100 metaphases in peripheral blood sample which was confirmed by FISH study. Since one type of tissue was examined, mosaicism was raised. Eduardo et al.[13] suggested that trisomy 9 may be viable only in the mosaic state. Cytogenetic study revealed that the extra copy of chromosome 9 is inverted (9) (p12; q13qh) and of maternal origin. It is well known that the pericentric inversion of chromosome 9 is a polymorphic variation estimated to be 1 to 3% in the normal human population[14]. Although the significance of this chromosome rearrangement is uncertain, it has been associated with repeated spontaneous abortions, infertility and congenital

anomalies[15,16]. Also, the assumption that it increases the chance for non disjunction could explain the bad obstetric history of the mother[17]. It is important to be aware of trisomy 9 syndrome prenatally when multiple congenital anomalies characteristic of trisomy 9 detected. Also, cytogenetic study of cell cultures derived from different tissues is recommended for accurate diagnosis and future genetic counseling.

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