

Mosaic Trisomy 9 in a Male Fetus with Severe Facial Abnormality and Genital Hypoplasia

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ABSTRACT Fetal trisomy 9 is a rare chromosomal abnormality, which was difficult to diagnose in the prenatal period. Here is reported a case of mosaic trisomy 9 fetus, prenatally detected by ultrasound examinations in the second trimester and confirmed by karyotyping from amniocentesis and cordocentesis. The fetus presented multiple malformations, especially facial deformity, polycystic kidney disease and genital hypoplasia, which were rare in previous literature.

INTRODUCTION

Trisomy 9 is one of the relatively uncommon chromosomal disorders, in which the entire 9th chromosome appears three times rather than twice normally in cells of the body. It may be present in one of the three ways: nonmosaic complete trisomy 9 (an entire extra chromosome 9 is present in all cells), mosaic trisomy 9 (presence of trisomic and disomic cells in a variable proportion), and partial trisomy 9 (trisomy for only a part of chromosome 9). Trisomy 9 and mosaic trisomy 9 syndromes were first described by Feingold and Atkins (1973) and Haslam et al. (1973), respectively. Mosaic trisomy 9 is considered to be a rare chromosomal abnormality with limited survival and manifest multiple anomalies. The features commonly associated with trisomy 9 are well documented, including growth retardation, congenital mental retardation, facial deformity, skeletal abnormalities (Akatuska et al. 1979) and congenital heart disease. Here we described a case of a male fetus with mosaic trisomy 9 confirmed by karyotyping from amniocentesis and cordocentesis with multiple malformations, especially severe facial deformity, polycystic kidney disease and genital hypoplasia.

CASE REPORT

A 25-year-old, non-consanguineous, Chinese woman was referred to our department because

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of positive biochemical screening for trisomy 18 in the second trimester. So far, she received only one ultrasound at 8+2 weeks of gestation and there was no abnormal finding. Her obstetric, medical and social histories were unremarkable. After learning about the risk of amniocentesis, she refused invasive prenatal diagnosis. Sonographic examination at 24 weeks' gestation demonstrated multiple abnormal findings including fetal severe cheilopalatognathus, lobar holoprosencephaly, hydronephrosis of the left kidney and dilatation of left ureter, the right polycystic kidney disease, and oligohydramnios. The researchers advised her once again to receive amniocentesis and she was agreed at last. Karyotyping from cultured amniotic fluid cells at 25 weeks revealed mosaic trisomy 9 according to the analysis of the chromosome karyotypes 46,XY[27]/47,XY,+9[23]. Further transabdominal cordocentesis confirmed it (46,XY[61]/47,XY,+9[39]). The couple's karyotype was normal.

On parental request, the pregnancy was terminated at 30 weeks' gestation and a malformed fetus was delivered smaller than gestational age with regard to weight and length at birth. The fetus present: male, the weight of 1350g and a length of 32cm. Multiple facial abnormality (Fig. 1) was noted to have orbital hypertelorism, flat nasal bridge, severe midline cheilopalatognathus, low-set and malformed ears, webbed neck. Genital hypoplasia (Fig. 2) was noticeable. The parents agreed to received fetal autopsy and donate the dead fetus for medical research, which had been adopted by hospital ethics committee. Fetal autopsy revealed some malformations including fetal lobar holoprosencephaly, hydronephrosis of the

left kidney and dilatation of left ureter, the right polycystic kidney disease and a small ventricular septal defect. Specimens for karyotyping from the fetal and the placental tissues were, 32% (16/50) in the skin, 14% (7/50) in the kidney, 12% (6/50) in the liver, 4% (2/50) in the lung, and 86% (43/50) in the placenta.

DISCUSSION

Mosaic trisomy 9 is a rare chromosomal abnormality prenatally diagnosed in second or third trimester pregnancy fetus. The features commonly associated with mosaic trisomy 9 include facial characteristics such as microcephaly, dolichocephaly, prominent occiput, small and up-slanting palpebral fissures, deep-set eyes, a large bulbous nose, low-set and malformed ears and micrognathia. The present case differs from those commonly reported presented with orbital hypertelorism, flat nasal bridge, severe midline cheilopalatognathus,

webbed neck and lobar holopro-sencephaly. Among craniofacial abnormalities found in association with chromosome 9 severe midline anomaly has been documented in one case of trisomy 9 mosaic (Gerard-Blanluet et al. 2002). In that report, the child had triangular face, deeply set eyes with short palpebral fissures, flat face with maxillary hypoplasia, small mouth and short philtrum, micrognathia and low-set posteriorly angulated ears, single nostril and hypotelorism. Our case had also severe midline facial abnormality, such as severe midline cheilopalatognathus and lobar holoprosencephaly. This mosaic trisomy 9 fetus in our report, mimicking trisomy 13 on craniofacial abnormalities. A case of nonmosaic trisomy 9 fetus was reported (Nakagawa et al. 2006), mimicking trisomy 13 on sonographic findings including brachycephaly, Dandy-Walker malformation, hypotelorism, hypo-plastic nose, micrognathia, and midline cleft lip. Genitourinary malformations were uncommonly found

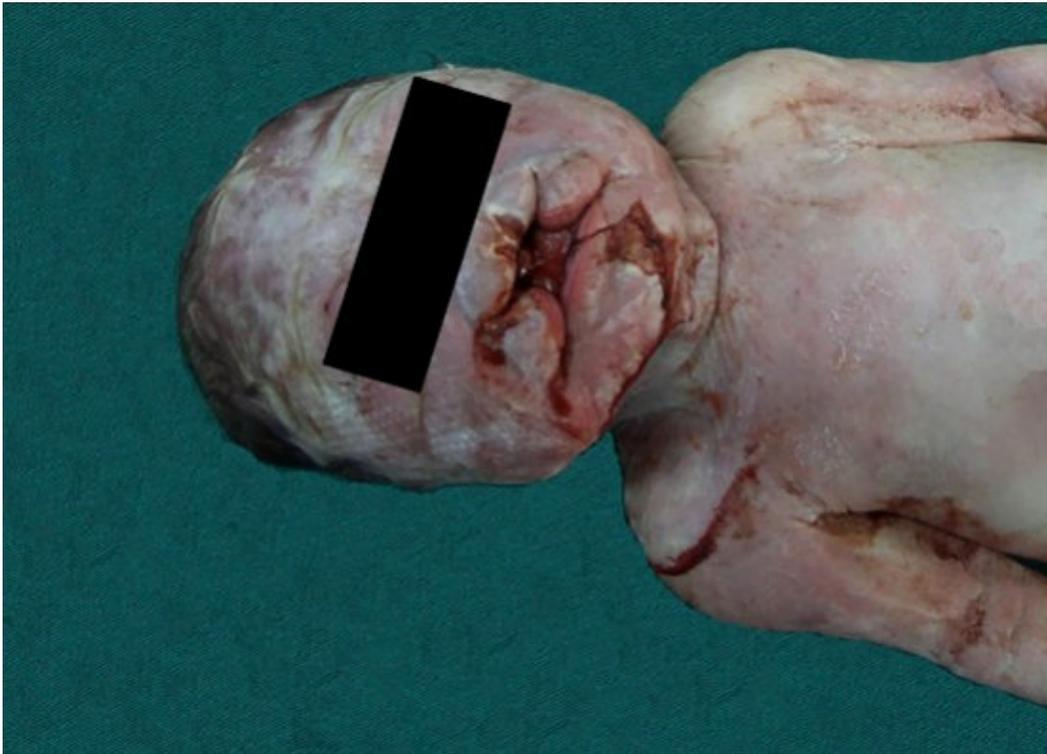


Fig.1. Face with orbital hypertelorism, flat nasal bridge, severe midline cheilopalatognathus, low-set and malformed ears, webbed neck



Fig.2. Genital hypoplasia

in association with mosaic trisomy 9. There were hydronephrosis and microkidneys reported (Takahashi et al. 2010) in trisomy 9 mosaicism. However, polycystic kidney disease and genital hypoplasia associated with mosaic trisomy 9 were rare in previous literature. The severity of the malformations of trisomy 9 mosaicism appears to be related to the proportion of trisomic cells in the total population (Sutherland et al. 1976). In the present case, the levels of trisomy 9 in the cells of various tissues were, 32% (16/50) in the skin, 14% (7/50) in the kidney, 12% (6/50) in the liver, 4% (2/50) in the lung, and 86% (43/50) in the placenta. A study (Kosaki et al. 2006) may speculate that programmed cell death (apoptosis) of the trisomic cells or selective survival (growth advantage) of the normal cells might have occurred at different levels among the various tissues. In contrast, also the scholar (Diaz-Mares et al. 1990) reported no clear relationship between the frequency of trisomic cells and the severity of the abnormalities observed.

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