SHORT COMMUNICATION

CASE REPORT: UNIPARENTAL DISOMY 16 IN ASSOCIATION WITH CONGENITAL HEART DISEASE

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SUMMARY

Uniparental disomy (UPD) is the inheritance of both copies of a given chromosome from the same parent (Warburton, 1988; Anon., 1991). The exact disease associations of UPD of individual chromosomes have yet to be fully elucidated and the question of whether UPD of some chromosomes may be regarded as a benign finding remains unanswered. We report an infant with uniparental maternal disomy 16, the only such infant identified at King’s College Hospital. The infant had intrauterine growth retardation and minor congenital heart disease.

KEY WORDS: confined placental mosaicism; prenatal diagnosis; uniparental disomy

CASE REPORT

A 38-year-old woman conceived spontaneously after several years of secondary infertility. She had a regular menstrual cycle of 28 days and was certain of the date of her last menstrual period. Maternal serum biochemistry screening after 16 weeks of amenorrhoea suggested a very high risk of trisomy 21. Ultrasound examination, however, suggested that the fetal measurements were compatible with 13 rather than 16 weeks’ gestation and this was thought to be the most likely explanation for the abnormal biochemical results. Fetal karyotyping was requested by the parents, which was carried out by chorionic villus sampling (CVS). CVS analysis was performed in both cytotrophoblast and mesenchyme culture. This revealed 100 per cent trisomy 16 in 18 cells by direct and culture analysis, so an amniocentesis was performed on the suspicion of confined placental mosaicism (CPM). Cytogenetic analysis of 25 fetal cells so obtained and 25 fetal cells from fetal blood follow-up revealed a normal female karyotype, but DNA studies demonstrated maternal UPD16. Three loci were examined. D16S99 (16p12.1–p11.2) was uninformative. At D16S89 (16p12.1–p11.2), a microsatellite repeat analysed by polymerase chain reaction (PCR), both the mother and the father were heterozygotes with no sharing of alleles. The fetus had inherited both maternal alleles. Similarly, at D16S7 (16q24), a variable number tandem repeat analysed by Southern blotting, both the mother and the father were heterozygotes with no allele sharing and the fetus had inherited both maternal alleles. These data indicate uniparental heterodisomy for chromosome 16 at the two loci studied.

In view of the association of this condition with fetal growth retardation, serial ultrasound examinations were carried out, which demonstrated a
normal growth velocity and fetal biophysical profile until 31 weeks' gestation, when the amniotic fluid volume was decreased. At 33 weeks, there was diminished fetal movement and decreased fetal growth velocity. Although cardiotocography demonstrated normal fetal heart rate patterns, in view of the maternal subfertility and uncertain fetal prognosis of this condition, it was decided to undertake elective delivery. A live female infant was delivered by Caesarean section with Apgar scores of 8 at 1 min and 9 at 5 min. Her birth weight was 1790 g, which is just above the tenth centile for 33 weeks' gestation, but well below the third centile for 36 weeks' gestation. The gestational age was estimated by Dubowitz scoring to be 37 ± 2 weeks, which agreed with maternal dates, and a diagnosis of intrauterine growth retardation was made. Examination on days 1 and 3 of life revealed no abnormality. However, on day 4, she was noted to be jaundiced and to have a loud systolic murmur with no evidence of cardiopulmonary compromise. She received phototherapy for 24 h (maximum serum bilirubin of 298 μmol/l). Chest radiograph and electrocardiogram were normal. However, the echocardiogram showed a secundum atrial septal defect with significant left to right shunt, a small perimembranous ventricular septal defect with minor left to right shunt, and a hypertrophied, dilated right ventricle suggesting pulmonary hypertension. Subsequent echocardiograms have shown improvement and she remains otherwise well at 6 months of age. Maternal UPD16 has been subsequently confirmed by investigation of peripheral blood lymphocytes.

**DISCUSSION**

The understanding of CPM has been increasing since the advent of CVS. In women who have undergone CVS, the incidence ranges between 1 and 2.5 per cent in various studies (Wolstenholme et al., 1994; Breed et al., 1991; Leschot et al., 1987; Schwinger et al., 1989), but the incidence in the general population is unknown. CPM has been associated with obstetric complications including intrauterine death and intrauterine growth retardation (Leschot et al., 1987; Johnson et al., 1990; Kalousek et al., 1991), but other studies (Johnson et al., 1990; Schwinger et al., 1989; Leschot and Wolf, 1991; Roland et al., 1994) have failed to demonstrate an adverse pregnancy outcome.

The loss of one of the copies of the trisomic chromosome to result in a disomic embryo and CPM would be predicted to result in UPD in one-third of cases. When the trisomy occurs at meiosis I following normal recombination, a combination of iso- and heterodisomy of the maternal chromosome 16 copies will be seen in the eventual UPD offspring.

Eleven pregnancies exhibiting UPD 16 have been reported in the literature (Kalousek and Barrett, 1994; Wolstenholme, 1995; Whiteford et al., 1995). All but one were associated with moderate to severe uteroplacental dysfunction and early fetal growth retardation. Of those 11 cases, the majority were heterodisomic for those markers studied, with two being reported as maternal isodisomy (Sutcliffe et al., 1993; Whiteford et al., 1995). Half of the reported maternal UPD16 infants have had documented structural abnormalities. One of these fetuses and two of the live births had an imperforate anus; another had talipes (Vaughan et al., 1994; Sutcliffe et al., 1993). The present infant was growth-retarded and had minor congenital heart disease. Although congenital heart disease is a relatively common sporadic finding, especially in association with chromosomal abnormalities, an infant having congenital heart disease (an atrioventricular canal defect) in association with this condition has only been reported once (Whiteford et al., 1995).

The study has not ruled out the possibility that the infant presented here is not a mosaic trisomy 16. Only amniocytes and lymphocytes have been studied in the baby in our report; both were only in UPD16, with no evidence of mosaicism.

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**REFERENCES**


