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Mosaic Partial Trisomy of Chromosome 5 (q33-q ter) Associated with Fetal Polycystic Kidneys

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Abstract. A case of de novo mosaic partial trisomy of chromosome 5 (q33-q ter) in a stillborn male fetus with bilateral polycystic kidneys, and atrial septal defect, is reported. Fetal cord blood sampling was carried out at 25 weeks of gestation because of bilateral polycystic kidneys with severe oligohydramnios observed on ultrasound examination of the fetus. The family history was notable for the presence of similar phenotypic abnormality in the mother and sibling. However, no chromosomal abnormality was detected in other family members. Significance of this rare chromosomal abnormality and its association with congenital malformations in the fetus and in the family is being discussed.

Key words: Chromosome 5, Dup(5q) syndrome, Renal anomalies

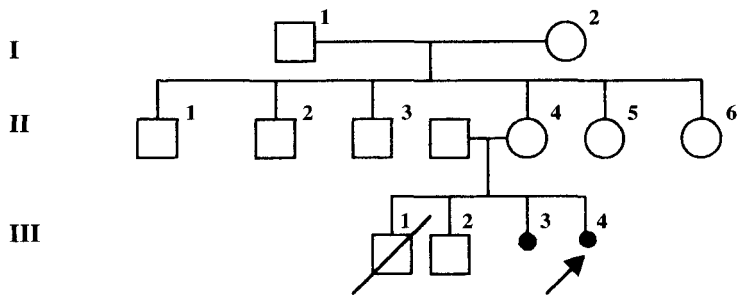
INTRODUCTION

The phenotypic similarities in patients with apparently identical structural anomalies are important in establishing karyotype-phenotype correlations for particular trisomies and monosomies. Partial 5q duplications have been reported involving different chromosomal segments [3, 4, 5, 8]. No clearcut clinical syndrome emerges from these reports. However, in cord blood, trisomy 5q mosaicism has not been reported with polycystic kidneys in the fetus.

In our report, several members of the family had cardiac and renal abnormalities. Cordocentesis performed in view of fetal polycystic kidneys showed 46, XY/46, XY dup 5(q 33-qter). Chromosomal analysis subsequently done on the parents and the surviving sibling were normal. We discuss the significance of this isolated chromosomal abnormality in the light of this family history.

CASE REPORT

A 28-year-old gravida 4, para 3 with previous bad obstetric history was booked at 20 weeks of gestation for antenatal care at the All India Institute of Medical Sciences. She was a known case of atrioseptal defect with solitary kidney. In her obstetric history, she had one early neonatal death and one stillbirth, with only one living issue (Fig. 1). In her first pregnancy, she did not have any antenatal checkup till 38 weeks of gestation. At this period of gestation, she was diagnosed to have breech presentation for which elective lower segment cesarean section was done. Ultrasonography of the fetus was not done during this pregnancy. Baby's Apgar score was 6/10 at birth. He died two days after birth. In her second pregnancy, she was booked with us. She had an uneventful pregnancy and delivered a male baby vaginally, who is alive and healthy. She was again booked with us in her third pregnancy. Level II ultrasound done at 20 weeks of gestation revealed severe oligohydramnios and fetal bilateral polycystic kidneys. Amnioinfusion and cordocentesis done at 26 weeks of gestation revealed 46, XX karyotype. Baby had intrauterine death (IUD) at 32 weeks. Autopsy was refused by parents. In the present pregnancy, patient again was found to have severe oligohydramnios with bilateral polycystic kidney disease on ultrasonography (Fig. 2). Fetal echo detected atrial septal defect. Cytogenetic evaluation was carried out from the cord blood sample of the fetus at 25 weeks of gestation. Lymphocyte cultures were initiated using standard methods and chromosome preparations were made. Cytogenetic analysis was carried out using trypsin G-banding and the chromosomes were evaluated at approximately 400 band level. Karyotypic analysis of cord blood showed the presence of an extra material on the long arm of chromosome 5 in 25% of metaphases analysed. Rest of the metaphases had normal chromosome complement. The karyotype of the fetus was interpreted as 46, XY/46, XY



II - 4: Patient's mother with solitary kidney and atrial septal defect.
III - 1: Early neonatal death.
III - 2: Alive and healthy.
III - 3: Intrauterine death at 32 weeks of gestation. Fetus had 46,XX karyotype.
III - 4: Index case with partial dup 5(q33-qter), had intrauterine death at 32 weeks of gestation.

Fig. 1 - Pedigree.

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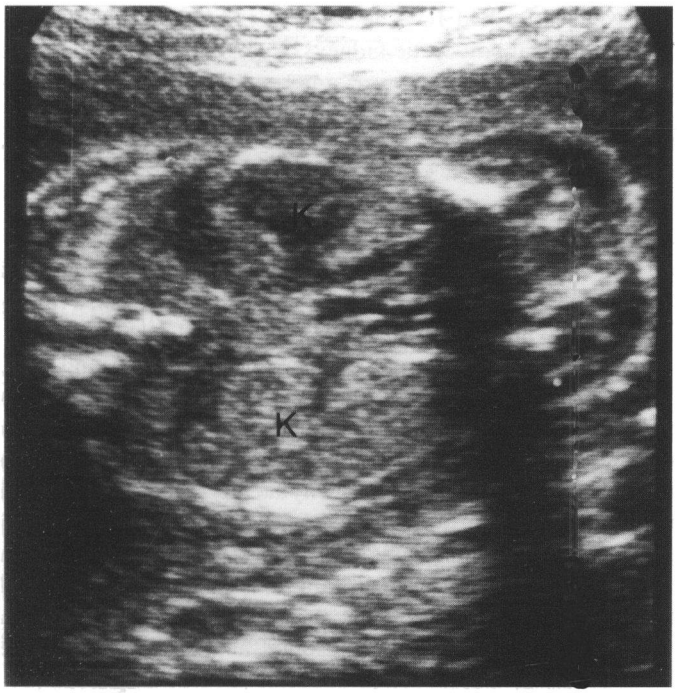

Fig. 2 - Ultrasound picture of fetal abdomen showing polycistic kidneys.

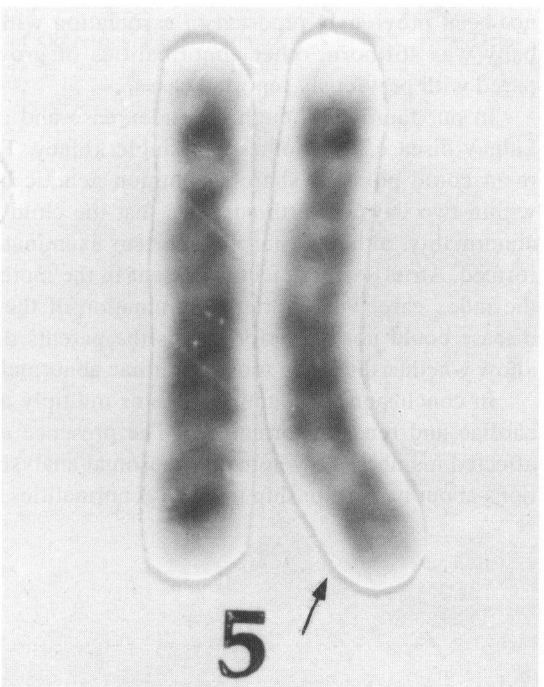

Fig. 3 - Partial karyotype of the fetus showing a normal chromosome 5 and dup(q33-qter), marked with an arrow.

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dup 5(q33-qter) (Fig. 3). This baby too had IUD at 32 weeks. Autopsy of the baby revealed atrial septal defect with bilateral polycystic kidneys. Cytogenetic analysis of the peripheral blood lymphocytes from the parents showed a normal chromosome complement.

DISCUSSION

Partial 5q duplication involving different chromosomal segments have been reported earlier in the literature. Rodewald [7] described three specific subgroups with 5q duplication. Patients in subgroup A with dup (5)(ql 1-q22) have psychomotor retardation, musculoskeletal abnormalities, facial anomalies, growth retardation and thin, tapering fingers. Those in group B with dup (5)(q31-q ter), (q32-q ter) or (q33-q ter) have severe psychomotor retardation and intrauterine growth retardation along with brachydactyly, microcephaly and facial abnormalities. Group C patients with dup (5)(q34-q ter) have mild mental retardation, obesity, brachydactyly, microcephaly and facial abnormalities. Curry et al [2] had earlier reported four cases of dup (5)(q34-q ter) and described a distinct clinical syndrome. Passarge [7] described three cases with dup (5)(q33-q ter) whose features corresponded with the Group B patients described above. However, in all the above reports, the babies were born alive and lived from months to years and the diagnosis of particular chromosomal abnormality was made only after birth. In contrast, in our case, chromosomal abnormality was diagnosed prenatally and the baby had an IUD. Although patients with dup 5(q11-15) have been reported to have renal and urinary tract abnormalities [1, 5, 8, 9], these anomalies have not been previously reported in association with dup 5(q33-q ter). In our case, as the baby was stillborn, other abnormalities of growth and development cannot be compared with previously reported cases.

In our family, although the index case and one sibling had documented polycystic kidney disease, the mother had single kidney. These abnormalities of kidney development could possibly share a common genetic basis. The fact that the first born died within two days of birth suggests that the child too might have had serious congenital abnormality, although no post-mortem examination or chromosomal analysis was performed. Atrial septal defect is present in the mother and was detected on post-mortem in the index case. Post-mortem examination of the previous baby with polycystic kidney disease could not be performed as the parents did not give consent. Hence, we do not know whether that baby too had cardiac abnormality.

In conclusion, our family contains multiply affected members with combinations of cardiac and renal abnormalities. The presence of dup 5(q 33-qter) in only one of the affected members on whom chromosomal analysis was performed raises intriguing questions about its relationship to these abnormalities.

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