A newborn proband with der (15) and maternal karyotype 46,XX, der (15) t(9; 15) with a bad obstetric history.

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Abstract: We report a newborn propositus with multiple congenital anomalies and with an abnormal karyotype 46, XY, der (15). The mother presented with a previous history of a stillbirth. Chromosomal analysis of the phenotypically normal parents was done to ascertain the origin of abnormal chromosome and for genetic counseling. Karyotype of the mother showed a reciprocal translocation i.e. 46, XX, der (15) t (9q; 15q) while that of father was found to be normal karyotype of 46, XY. The significance of chromosomal analysis in newborn with congenital anomalies is discussed.

Key words: Proband der (15), maternal t (9; 15), multiple congenital anomalies, newborn.

Introduction:
Couples with history of multiple miscarriages or stillbirths are at a risk for carrying a balanced translocation since these carriers may produce unbalanced gametes, Shaffer et al (1996). Trappe et al (2002) reported a case of familial translocation with recurrent abortion. These small imbalances may lead to offsprings with multiple congenital anomalies. Celep et al (2001) reported an unbalanced t (4; 15) by molecular studies (Fluorescence in-situ hybridization, FISH) in a child with multiple congenital malformations. The present report suggested the importance of cytogenetic analysis in a child with multiple congenital abnormalities in phenotypic normal parents with a previous bad obstetric history of the mother.

Case Report:
A newborn proband with multiple congenital anomalies of hydrocephalus, short neck, flat bridge of nose and cleft palate was investigated for cytogenetic analysis. Previous maternal obstetric history reveals a stillbirth at 32 weeks of gestation. The cause of stillbirth and status of the child was not known. The prenatal radiographic study of the second issue (Proband) at 30 weeks of gestation showed hydrocephalus with polyhydraminos. The pregnancy was terminated at 34 weeks of gestation. The newborn was weighing 1.34 kg, which was less for the gestational age and survived for 15 days. Chromosomal analysis from the peripheral blood of newborn was performed according to the standard cytogenetic methods using G- banding technique. On history, because the parents revealed that they had a stillbirth in the previous pregnancy, so, to know the origin of the abnormal chromosome in the newborn i.e. whether de novo or inherited paternally, the chromosomal analysis of both the parents were also done.

Result:
The karyotype of the newborn showed, 46, XY, der (15) [Figure 2]. The chromosomal study of phenotypically normal couple was also done. The mother showed a karyotype of 46, XX, der (15) t (9q; 15q) [Figure 1] while father had a normal karyotype of 46, XY. The karyotype of the mother using G-band technique confirmed a reciprocal balanced translocation between chromosome 9 and 15.

Discussion:
The overall incidence of chromosomal abnormalities in a newborn has been found to be 1:160 births, Thompson and Thompson (1991). Balanced rearrangements are rarely identified clinically unless a carrier with an unbalanced chromosome gives birth to an abnormal child as in the present study. In such cases chromosomal analysis of the couple can help in knowing the origin of the abnormal chromosome. Unbalanced rearrangements are likely to come to clinical attention for unusual conditions like dysmorphism and delayed physical and mental development or multiple congenital anomalies. Studies conducted by Sachs et al (1985) on 500 couples with recurrent abortions revealed abnormal karyotype in 50 couples (10%). In 20 cases the translocations were reciprocal and mainly maternal. A familial chromosomal translocation t (6q; 7q) with habitual abortions was described by Zhang et al (1989) with no phenotypical abnormality in the carriers. Similar familial translocation t (10; 21) (q22; q22) was observed by Delicado et al (1979) in a family with several miscarriages and two siblings with multiple congenital malformations. In a recent report, Hou (2003) presented a rare disorder in a boy with developmental delay and multiple anomalies. The karyotype was consistent with der (22). Kadir et al (1997) did prenatal detection by cordocentesis at 27 weeks of a fetus with maternal balanced translocation and he found the fetus to have der (22).

In the present study though the couple was phenotypically normal but they had a congenitally malformed child and the mother had a previous bad obstetric history. The chromosomal analysis of the proband showed der (15). The maternal karyotype was 46, XX, der (15), t (9q; 15q) and the father had a normal karyotype, 46, XY. This analysis was done to determine...
Fig. 1: Karyotype of mother showing balanced translocation involving chromosome 9 and 15 (arrows) i.e. 46, XX, der (15), t(9q; 15q).

Fig. 2: Karyotype of proband 46, XY, der (15) (Arrow indicates der (15)).
the origin of the derived chromosome, der (15) in the newborn, whether it was de novo in origin or parenterally inherited. In the proband the der(15) has been inherited from the mother because the father had a normal karyotype. In the newborn the der (15) could have produced genetic imbalance leading to partial trisomy 9q, which might have resulted in multiple congenital anomalies in the proband. The maternal translocation might have lead to formation of imbalanced ova, which might be resulted in stillbirth in the first pregnancy and congenitally abnormal child in second. Thus in such a case where the mother having a genotype of 46, XX, der (15) t (9q; 15q) and father has a normal karyotype 46, XY, the chances of the couple having a normal child are only 25% and an abnormal child are 75% in subsequent pregnancies.

Clinicians should screen the parents for subtle chromosomal anomalies in cases where a child is born with multiple congenital anomalies and mother has a bad obstetric history. Family members should also be screened for carrier state and assessment, so that they can be offered genetic counseling and an opportunity for early prenatal diagnosis.

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**References:**