Case Report

Dandy-Walker malformations in a case of partial trisomy 9p (p12.1→pter) due to maternal translocation t(9;12)(p12.1;p13.3)

Babu Rao Vundinti, Lily Kerketta, Seema Korgaonkar, Kanjaksha Ghosh
Institute of Immunohematology (ICMR), 13th Floor, New Multistoried Building, K.E.M Hospital Campus, Parel, Mumbai - 400 012, India

We describe a five-year-old proband presented with Dandy-Walker malformations, right microopthalmia, hamstring contractures, undescended testis with absence of testis in right scrotum in addition to typical trisomy 9p clinical features. Routine cytogenetic studies with GTG - banding showed 46,XY,der(12)t(9;12) (p12;q13.3),mat karyotype (trisomy 9p). Chromosomal analysis of the father was normal and phenotypically normal mother had 46,XX,t(9;12)(p12;q13) karyotype. Fluorescence *in situ* hybridization analysis with single copy probes bA5OIA2 (9p11.2), bA562M8 (12p12.1) and centromere probes (9) showed break point at 9p12.1 region. The gene dosage effect of Chromosome 9p along with environmental factors might be associated with Dandy- Walker malformations in the patient.

Key words: Balanced translocation, Dandy-Walker malformations, genetic counseling, growth retardation, micropthalmia, partial trisomy 9p.

Introduction

Structural chromosomal abnormalities in children originating from balanced chromosomal aberrations in either parents most of the cases causes mental retardation and congenital malformation.[1] Trisomy 9p is a well-described chromosomal aberration associated with mental and growth retardation.[2] Dandy-Walker malformations is estimated to occur in one in 25000-35000 pregnancies. Chromosomal aberrations, Mendelian mutations and environmental factors have been reported to be associated with the Dandy-Walker malformations.[3] We report a Dandy- Walker malformations in a boy with partial trisomy 9p12.1- pter due to maternal balanced translocation t(9;12) (p12.1;p13.3).

Case Report

The proband, a five-year-old boy born to non-consanguineous parents, referred for chromosomal analysis because of dysmorphic features and developmental delay. The father was 32 years old and the mother was 28 years old. During pregnancy the mother had hypermesis and was treated with medicines. Mother delivered at full term by low vaccum application, indicated short cord with occipito transverse presentation. The child born with low birth weight (1.940 kg) and developed neonatal jaundice on the second day of life for which he was given phototherapy. Developmental milestones were delayed from birth and attained head holding five to six months, babbling was 10-11 months. The child had poor weight gain and frequent upper respiration tract infection. The child had Dandy-Walker malformations with hydrocephalus and operated at the age of 3 years. The proband height was 90 cm, weight 9 kg, head circumference 48.5 cm. The total palm length 10 cms, middle finger length 5 cm, total fingure length 5.4 cm, outer canthal distance 10 cm, inter canthal distance 13 cm and inter papillary distance was 6.5 cms. The upper and lower body segments measurements were 50 cm and 40 cm respectively. On examination the proband had short stature, microcephaly, low set anteriorly slanted large ears, clinodactly, right micropthalmia, both hamstrings were in contractures congenital talpio-equenovanis, epicanthic folds, hypertolerism, high arched palate, bilateral simian crease, rocker bottom feet, undescended testes with the absence of testis in right scotum. The child had mental retardation and bilateral

Address for Correspondence: V. Babu Rao, Institute of Immunohematology (ICMR), 13th floor, New Multistoried Building, K.E.M Hospital Campus, Parel, Mumbai - 400012, India. E-mail: vbaburao@hotmail.com

conductive hearing loss. The ultrasonography abdomen revealed normal liver gall bladder, spleen and absence of pancreas.

Cytogenetics

Chromosome preparations obtained from peripheral blood lymphocyte cultures were subjected to GTG banding. Chromosomal analysis of proband revealed 46 chromosomes, with an additional chromosomal segment on the short arm of Chromosome 12 with a 46,XY,der(12)t(9;12)(p12.1;p13.3),mat karyotype. Father was cytogenetically normal and mother was carrier of reciprocal translocation involving Chromosomes 9 and 12 [Figure 1]. The translocation was observed in all metaphases analysed.

Fluorescence *in situ* hybridization (FISH) was carried out using centromere probe for Chromosome 9 and locus specific probes 9p11.2(bA5OIA2) and 9p12.1(bA562M8). By combining GTG - banding and FISH results, the patient was found to have the karyotype 46,XY,der(12),t(9;12)(p12.1;p13.3),mat and mother was a carrier of reciprocal translocation, t(9;12)(p12;p13.3). The proband had two normal 9 chromsomes and a derivative 12 with an extra segment of Chromosomes 9 from mother and normal Chromosome 12 from father. Hence the proband was trisomic for 9p12.1 → pter region [Figure 2a and b].

Discussion

The trisomy 9p associated with distinct clinical manifestations include psychomoter and growth retardation, hypotonia, strabismus, myopia, a short neck, microcephaly, barachycephaly, hypertolerism, antimongoloid slant of palpebral fissures a globulous large nose, a large mouth with down turned corners, poorly lobulated ears, small hands and feet, clinodactyly and and branchymesophalangy of little fingers.[2] The clinical features especially the facial and hand anomalies are common in partial trisomy 9p despite variation in size of the duplications.[4,5] The less frequently observed clinical features in trisomy 9p are congenital heart defects, facial clefts, hydrocephalus, hydronephrosis, umbilical hernias and hypospadias.[1] In our case in addition

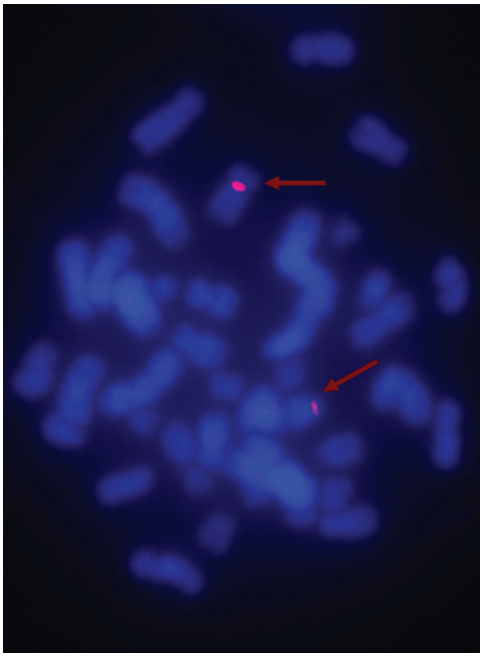

Figure 2a: FISH with centromere probe for Chromosome 9 showing deleted p arm on Chromosome 9 in mother

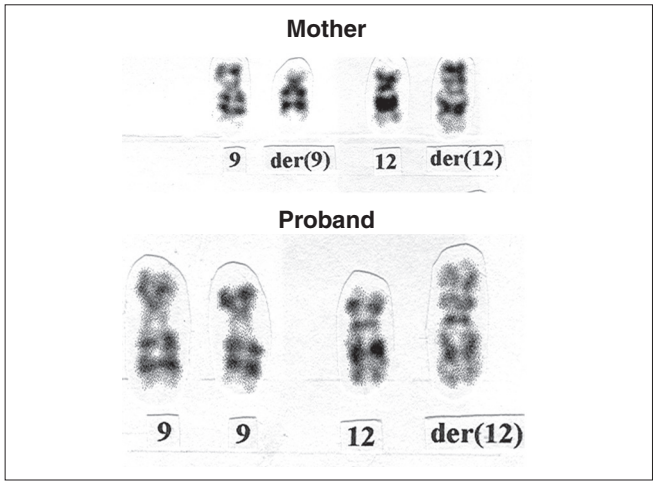

Figure 1: Partal karyotype showing t(9;12) in mother and partial trisomy on 9p in proband

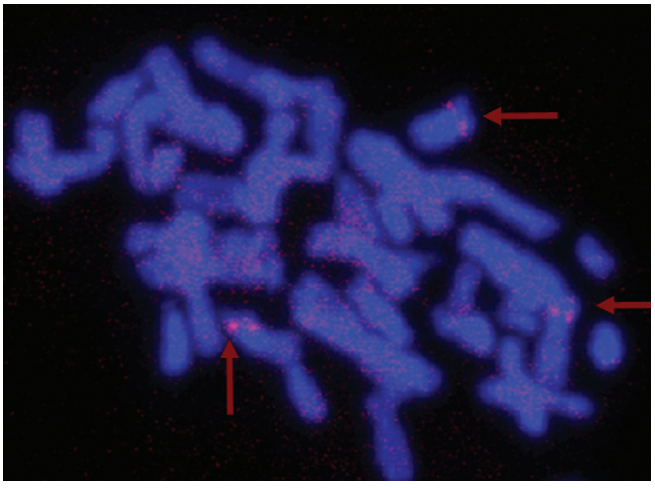

Figure 2b: FISH showing three red signals for 9p12.1 (trisomy) region in proband

to typical trisomy 9p clinical features such as growth retardation, mental retardation the proband had additional clinical features; Dandy-Walker malformations, right micropthalmia, hamstring contractures, undescended testis with the absence of testis in right scrotum.

The frequency of chromosomal abnormalities in the Dandy-Walker malformations ranges from 14.5% to 46% and common chromosomal abnormalities reported to be trisomy 13, 18 and triploidy.[6,7] The bilateral ventriculomegaly and an enlarged cistern magna reported in fetus with partial trisomy 9 (pter → q22) and partial trisomy 21(q22.3- qter).[8] vonKaisenberg *et al*[9] reported a Dandy-Walker malformation and hypoplasia of the cerebellar vermis in a fetus with partial trisomy 9 and 7. Recently partial trisomy 9p (p 11.2 → pter) reported in a fetus with Dandy-Walker malformation and it was suggested that the 9 pter → 11.2 region critical for the development of Dandy-Walkermalformation and ventriculomegaly.[10] In our case absence of 9 p 11.2 region on der(9) chromosome does not prevent a Dandy-Walker phenotype. Hence the gene dosage effect of Chromosome 9 along with environmental factors may be associated with the central nervous system in patients with partial or complete trisomy 9. As the Dandy-Walker malformation is a complex disease, the chromosomal analysis is important in patients and parents to understand the carrier status and for the appropriate genetic counseling.

References

1. Shinzel A. Catalogue of unbalanced chromosome aberrations in man. de Gruyter: Berlin; 1983;844-8: 46.
2. Wilson GN, Raj A, Baker D. The phenotypic and cytogenetic spectrum of partial trisomy 9. Am J Med Genet 1985;20:277-82.
3. Murray JC, Johnson JA, Bird TD. Dandy-Walker malformation: Etiologic heterogeneity and empiric recurrence risks. Clin Genet 1985;28:272-83.
4. Motegi T, Watanase K, Nakamura N, Hasegawa T, Yanagawa Y. *De novo* tandem duplication 9p (p12 → p24) with normal GALT activity in red cells. J Med Genet 1985;22:64-6.
5. Tsezou A, Kitsiou S, Gaua A, Petersen MB, Karadima G, Syrrou M, *et al*. Molecular cytogenetic characterization and origin of two *de novo* duplication 9p cases. Am J Med Genet 2000;91:102-6.
6. Conford E, Twining P. The Dandy-Walker syndrome: The value of antenatal diagnosis. Clin Radiol 1992;45:172-4.
7. Ecker JL, Shipp TD, Bromley B, Benacerraf B. The sonographic diagnosis of Dandy-Walker and Dandy-Walker variant: Associated findings and outcomes. Prenat Diagn 2000;20:328-32.
8. Chen CP, Shin JC. Prenatal diagnosis of bilateral ventriculomegaly and an enlarged cisternea magna in a fetus with partial trisomy 9 partial 21. Prenat Diagn 1999;19:1175-80.
9. von Kaisenberg CS, Calibe A, Krams M, Hackeloers BJ, Jonat W. Absence of 9q 22 - 9q ter in trisomy 9 and does not prevent a Dandy Walker phenotype. Am J Med Genet 2000;95:425-8.
10. Chen JP, Chang TY, Shin JC, Lin SP, Lin CJ, Wang W, *et al*. Prenatal diagnosis of the Dandy Walker malformation and ventriculomegaly associated with partial trisomy 9p and 12p deletion. Prenat Diagn 2002;22:1063-6.

Source of Support: Nil, **Conflict of Interest:** None declared.