# 115

**Familial Report of Duplication 9p Syndrome.** S.L. Wenger, V. Borsa, C.D. Holt, M. Hummel, M. Mullett. West Virginia University, Morgantown, West Virginia.

Duplication 9p syndrome is a clinically well described syndrome characterized by growth retardation, developmental delay, skeletal malformations and craniofacial anomalies. We report a family starting with a male infant born by c-section at 39 weeks gestation to a 38 yo G6 P 4-0-1-4. The pregnancy was remarkable for an abnormal MSAFP placing the pregnancy at a 1:17 risk for Down Syndrome. The parents refused amniocentesis after receiving genetic counseling. At 35 weeks gestation a fetal ultrasound demonstrated mild polyhydraminos, borderline hydrocephalus, and a unilateral right pyelectasis along with a proximal hydroureter. The patient had an unremarkable delivery at an outside institution with Apgars of 9 and 10. Birth weight was 4790g (>95%). Ten hours post delivery the patient began to develop significant lymphedema of the right lower extremity which is what brought him to our attention. On presentation the patient appeared with bitemporal narrowing, short palpebral fissures, and small deep set eyes. The right extremity showed significant edema involving the foot extending to the distal portion of the thigh. An x-ray of the extremity showed no fracture. A cat scan of the head demonstrated diffuse cerebral volume loss with a slightly prominent left ventricle when compared to the right. A small left subdural hygroma was also noted. A cardiac echocardiogram and a renal ultrasound were both normal. Cytogenetic study on peripheral blood lymphocytes revealed additional material on 9p. A FISH paint for chromosome 9 indicated that the extra material was duplication of 9. The G-banding pattern suggested duplication of 9p13p22. Peripheral blood was obtained from both parents and an identical karyotype was found in the mother. The mother was noted to have similar phenotypic features to the proband, namely short palpebral fissures and small deep set eyes. The mother reported having a learning disability as a child completing only a 9$^{th}$ grade education. Further family history showed the mother to have three other children all with another partner ages 11, 16, and 19 years of age. All 3 half siblings to the proband are reported as "slow". These siblings are currently being worked up cytogenetically. Since first described in 1970, more than 100 cases have been reported with a duplication involving various size segments of the 9p chromosome. Familial cases have been reported with much less frequency. The clinical features and cytogenetic findings as compared to previous reported cases will be presented.

# 116

Proximal 6q deletion phenotype: findings in de novo interstitial deletion 6q14.1q15. B.J. White[1], A.T. Schwartz[2], S.W. Levin[3], E.J. Coll[3], A. Anguiano[1], S. Wang[1] and X.-J. Yang[1]. [1]Dept. Cytogenetics, Quest Diagnostics, Inc., San Juan Capistrano, CA, [2]Dept. Pediatrics, National Naval Medical Center, Bethesda, MD, and [3]Dept. Pediatrics, Walter Reed Army Medical Center, Wash. D.C.

The phenotype associated with proximal interstitial 6q deletions has been described (Turleau, et al., 1988; Valtat, et al., 1992; Gershoni-Baruch, et al., 1996; Kumar, et al., 1997). Recurrent proximal interstitial breakpoints 6q11-q25 and terminal deletion breakpoint 6q25 were noted (F. Hecht and B.K. Hecht, 1992), and a distinct proximal deletion syndrome was suggested. In this report, we present a new case of proximal 6q deletion supporting this proposal: Birth weight was 5lb, 15oz after a 41wk pregnancy of a 19 year-old mother complicated by fetal hydronephrosis and oligohydramnios; a nuchal cord was noted at vaginal delivery. Neonatal problems included respiratory distress, a posterior urethral valve with bilateral hydronephrosis, and inguinal hernias which were later repaired. Delayed development was evident at 6mos, when auditory and ophthalmologic exams and routine karyotype were normal. At age 3yrs, he was evaluated for self-mutilation, temper tantrums, nocturnal hyperactivity, and lack of speech development. On exam, height was 10$^{th}$, weight 25$^{th}$, and OFC 50$^{th}$ centile. Facies were notable for a high forehead, short palpebral fissures, broad nose with flat nasal bridge, anteverted nares, mid-face hypoplasia, and thin upper lip. A bifid uvula, prominent and cupped ears, and syndactyly of right 3$^{rd}$-4$^{th}$ toes were present; sensory and motor exam were normal. Metabolic screening, fragile X DNA, and cranial MRI were normal. A repeat karyotype at 550 bands revealed 46,XY,del(6)(q14.1q15), and FISH with chromosome 6 painting probe revealed uniform hybridization of only both chromosomes 6, confirming the deleted region was not inserted into another chromosome; both parental karyotypes were normal.

Our patient shares several recurring major features of a syndrome associated with other 6q interstitial deletions with proximal breakpoints 6q13q15 and 6q14 or q15q16: mental impairment, typical dysmorphic facies with short palpebral fissures and thin upper lip, and inguinal hernias. In other reports, umbilical hernias were also typical. In our case, urinary tract anomalies were evident prior to birth, a post-natal finding in other cases. A clinical diagnosis of proximal 6q deletion syndrome should be considered and attention paid to that region in cytogenetic screening when these major features are present in developmentally delayed children with negative fragile X and metabolic studies.

# 117

**Tetraploidy in Prenatal Diagnosis:"culture artifact" or clinical diagnosis?** E.J.T. Winsor[1,3], D. Chitayat[1,3] M.B. Skidmore.[2,3] [1]Toronto General Hospital, University Health Network, [2]Sunnybrook and Women's College Hospital, [3]University of Toronto, ON, Canada.

In routine analysis of cultured CVS and amniotic fluid (AF) a few tetraploid cells are almost always observed. However, they are usually assumed to be due to culture artifact and are rarely documented in the laboratory report. In some CVS studies tetraploidy has retrospectively been reported as a "false positive" result. We present two cases which document the difficulty in interpreting tetraploidy.

Case 1: AF was obtained at 40 weeks gestation from a fetus with multiple congenital anomalies. Interphase FISH analysis using probes for 13,18,21,X and Y was consistent with tetraploidy. Routine G banded analysis of cultured AF and fetal skin following delivery revealed only tetraploid metaphases. Congenital abnormalities in the infant were consistent with those previously reported in the literature.

Case 2: CVS was performed at 12 weeks because of maternal age 39 and increased nuchal thickening. All 15 cells from long term culture were tetraploid while 5 cells from short term/direct preparation had a normal 46,XY karyotype. No tetraploid cells were found in cord blood following delivery while 4/30 metaphases from cultured umbilical cord were tetraploid. The infant's only congenital abnormality was a bicuspid dysplastic aortic valve with mild aortic stenosis.

Conclusion: The clinical significance of mosaic and nonmosaic tetraploidy appears to be at least in part related to the type of tissue analyzed. The presence of nonmosaic tetraploid cells in uncultured amniotic fluid by interphase FISH appears to be a strong indicator of fetal abnormality. Mosaic diploidy/tetraploidy in CVS and cultured fibroblasts is of uncertain clinical significance.

# 118

Partial Monosomy 12p and Ring Chromosome 12 Mosaicism in a Male with Developmental Delay and Mild Dysmorphism. H.A. Yee[1], J.E. Chernos[1], P.M. Veale[2], M.E. Clarke[2], G.E. Graham[1]. Departments of Medical Genetics[1] and Pediatrics[2], University of Calgary and Alberta Children's Hospital, Calgary, Alberta, CANADA.

An eleven month old male referred for developmental delay and mild dysmorphism was found to be mosaic for two cell lines with a G-banded karyotype of mos 46,XY, del(12)(p12.2) / 47,XY, del(12)(p12.2), +r. Both cell lines were monosomic for 12p and 18% of peripheral lymphocytes and 44% of skin fibroblasts both had a supernumerary ring chromosome. The ring was shown to be derived from chromosome 12 using FISH with centromeric probes (cep12, Vysis Inc.), and was significantly smaller than the 12p deletion. Parental karyotypes were normal. Dysmorphic features included macrocephaly, prominent forehead, mild telecanthus, midface hypoplasia, narrow ear canals, small hands and feet, and small phallus with normal testicles. At 11 months of age, the proband was estimated to have gross motor, fine motor and language skills that were equivalent to 7-8 month, 5-6 month and 6-7 month levels, respectively. This patient represents a de novo and unique presentation of partial monosomy 12p with mosaicism of ring chromsome 12.