106

Mosaicism for a small supernumerary chromosome 22 associated with dysmorphic features and early onset dementia. U.Tantravahi[1], D.Abuelo[2] and S.J. Patrick-MacKinnon.[3] [1] Women and Infants Hospital, Brown University, RI,[2] Rhode Island Hospital, Brown University, RI, [3] Bristol Neurology Services, RI.

A 46 -year old female was referred to the neurologist by her optometrist for a right homonymous superior field defect. As an infant, she was diagnosed as having multiple congenital abnormalities that included micrognathia which required several jaw surgeries, multiple ear tags as well as problems with rectal weakness which required surgery. She also indicated that for a couple of years she has been experiencing poor memory. On physical examination, she was noted to have a long narrow face with downward slanting palpebral fissures, a small jaw and mild scoliosis. Her mental status was within normal limits to language, comprehension and repetition. Neuropsychology testing revealed impaired psychomotor ability, reduced executive functioning and border- line visual memory. A neuro-ophthalmologist confirmed the diagnosis of right homonymous superior quadranopsia probably due to a congenitally smaller or dysplastic left occipital lobe. A SPECT scan showed decreased activity in the right temporal and bilateral superior parietal lobes consistent for the early stages of Alzheimer's disease.

Peripheral blood chromosome analysis revealed a mosaic karyotype, 47,XX+mar[3]/46,XX[17]. The marker chromosome was identified using whole chromosome paint probes and FISH analysis to be derived from chromosome 22. Some of the phenotypic features seen in this patient are similar to that of the Cat-eye syndrome which also has a supernumerary chromosome derived from chromosome 22. In addition, our patient seems to have symptoms of early onset dementia. It is not clear whether this is associated with the marker chromosome 22.

107

Vanishing twin due to an apparent genomic imbalance. R.S. Verma[1,2], M.J. Macera[1] and E.S. Bronstein[2,3]. [1]Institute of Molecular Biology and Genetics, Brooklyn, NY, [2]SUNY Health Science Center at Brooklyn, N.Y. and [3]Coney Island Hospital, Brooklyn, NY.

The disappearance of one or more gestational rings on repeated ultrasonic examination during the 1st trimester have led to the vanishing twin phenomenon. In recent years, the concept of vanishing twins has gained much attention during genetic amniocentesis. A couple was initially referred to us because of a high incidence of fetal loss. They later conceived with a twin pregnancy, however, one of the twins was lost at 7 weeks of gestation while the other one is a normal, 46,XX female. The couple experienced three more successive fetal losses and was referred for cytogenetic evaluation. Cytogenetic findings with GTG- and FISH- techniques revealed a balanced translocation between chromosomes 9 and 11 in the father i.e. 46,XY,t(9;11)(p22;q22). ish 46,XY,t(9;11)(p22;q22)(wcp9+;wcp11+) while the mother is cytogenetically normal, 46XX. It is obvious that the vanished twin was cytogenetical abnormal with an unbalanced karyotype. The couple is religious and do not wish to go through an amniocentesis but want to have at least 10 more children. All options were explained to them. Their Rabbi suggested that they are only allowed a non-invasive procedure that must occur prior to five weeks of pregnancy. At present, the technology allowing enough maternal cells of fetal origin to be captured at such an early stage has not been perfected. The genetic and social aspects of vanishing twins is presented.

108

A rare interstitial deletion (2)(p11.2p13) in a child with pericentric inversion (2)(p11.2q13) of paternal origin.

BJ White[1], FL Lacbawan[2], A Anguiano[1], D Rigdon[3], K Ball[3], G Bromage[3], XJ Yang[1], M DiFazio[4], and SW Levin[4].
[1]Quest Diagnostics, San Juan Capistrano, CA, [2]NIH, Bethesda, MD, [3]USAF, Keesler AFB, MS, [4]Walter Reed AMC, Washington, DC.

An unbalanced 46,XY,der(2)del(2)(p11.2p13)inv(2)(p11.2q13) karyotype was found in a phenotypically abnormal child. A de novo interstitial deletion resulting in loss of band 2p12 was present on a chromosome 2 with an inv(2)(p11.2q13) inherited from the father. The inv(2) is generally considered a benign familial variant without significant reproductive consequences. However, our findings led us to consider a previously proposed mechanism of unequal meiotic crossing over at the base of a parental inversion loop, which could lead to either duplication or deletion of a segment adjacent to the inverted region in offspring. This phenomenon has been reported in association with inversions of chromosomes 7, 13, 15 and 17 and may explain origin of the deletion in our case. Alternatively, repetitive sequences might be present around such inversions which could predispose to de novo deletions independently of the inversion.

Although the mechanism of origin of the deletion in our proband cannot be proven, our review of similar imbalances with other inversions and the findings in the family described in this report suggest there could be a small risk for a related imbalance in offspring of couples with an inv(2)(p11q13). Further monitoring of pregnancy outcome in families with the inversion should be considered. However, at this point, it seems premature to recommend prenatal diagnosis for all couples in this situation.

For del(2)(p11.2p13), which is rare, an emerging phenotype is proposed. Our patient shared several features with four previously published cases, namely a broad nasal bridge, abnormal ears, highly-arched palate, psychomotor retardation, and micrognathia. However, our patient also had sensorineural hearing loss and significant hypotonia which have not been previously reported.

109

Two patients with mosaic trisomy ring 20. Doing the right test for the wrong reasons.

M.S. Williams[1], K.D. Josephson[2], F.S. Edelman[3], G.S. Sekhon[4], S. Scheib-Wixted[4].
[1]Gundersen-Lutheran Medical Center, La Crosse, WI; [2]La Crosse Regional Genetic Services, La Crosse, WI; [3]Physicians Plus Medical Group, Madison, WI; [4]University of Wisconsin-Madison, Waisman Center, Madison, WI.

We report two patients with mosaic trisomy ring 20. The first patient was a 16 yo referred for possible Cohen syndrome because of obesity, learning disabilities and speech delay. Additionally, he had a history of Tetralogy of Fallot, myopia, small posterior subcapsular cataracts and dysmophic features inconsistent with the referring diagnosis. Chromosome analysis was performed looking for 22q deletion (given the conotruncal heart lesion). Karyotype was 47,XY,+r[6]/46,XY[24].ish r(20)(p?q?)(D20Z1+),22q11.2(D22S75x2). The second patient was a 10 month old with developmental delay and hypotonia. Additional features included small penis, a broad face and small hands and feet. Chromosome analysis was performed looking for 15q deletion. Karyotype was 47,XY,+mar[35]/46,XY[45].ish 15q11-q13(SNRPNx2; D15S10x2).ish r(20)(p11.2q11.2)(coatasome 20+).

Only three other cases of mosaic trisomy ring 20 have been reported in the medical literature. Only one has been molecularly characterized. A consistent phenotype has not been seen, which likely reflects differences in the genetic material present in the ring, as well as the level of mosaicism present. Comparison with the 3 reported cases as well as with other cases of mosaic trisomy 20p and 20q will be presented. These cases also point out a potential pitfall in that exclusive utilization of molecular cytogenetic techniques for specific syndromic diagnosis would have led to missed diagnoses in both of our patients. Molecular cytogenetics should continue to be use as a complement to standard high resolution cytogenetic analysis.