103

Molecular and cytogenetic analysis of Y;1 familial translocation
J.W. Kim[1], I.S. Kang[2], S.A. Nam[1], Y.M. Kim[1], Y.S. Lee[3] and S.Y. Park[1] [1]Laboratory of Medical Genetic, [2]Obstetrics and Gynecology, [3]Urology, Samsung Cheil Hospital & Women's Healthcare Center, Seoul, Korea.

A balanced reciprocal translocation t(Y;1)(q12;q21) was found in an azoospermic male. Using the testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI), the patient had a boy who was found to have the same translocation. They were revealed to have a balanced reciprocal translocation by G-, C-, R- and high resolution banding. Fluorescence in situ hybridiation (FISH) with the probe chromosome Yq heterochromatin and C-banding were confirmed that the breakpoint is in Yq12 heterochromatic region. It was known that deletion of the AZF region of the Y chromosome is most frequent molecularly defined cause of spermatogenic failure. Especially the DAZ (deleted in azoospermia) gene is expressed exclusively in the human male germ line, and is frequently microdeleted in azoospermic men. To detect the small deletion in AZF gene, we studied on seven loci (sY84, 129, 134, 156, 254, 255, 269) including 3 DAZ regions. Also three loci (SRY, DYZ3, DYZ1) on the short arm, centromere and long arm respectively were amplified. Microdeletion of 10 loci was not detected in infertile male and his son. The results indicate that the infertility of this patient could be due to alteration of the sequence order of Y chromosme or to a disturbance of X chromosome inactivation as a result of the proximity to the autosomal portion.

104

Chromosomal nosology in referred populations. S.M. Kleyman, V. Mizhiritskaya, M.J. Macera and R.S. Verma. Division of Molecular Medicine and Genetics, Wyckoff Heights Medical Center, Brooklyn-New York Hospital/Weill Medical College of Cornell University, New York, Institute of Molecular Biology and Genetics and SUNY Health Science Center at Brooklyn, NY.

Specific chromosomal abnormality are related to over 70 clinical syndromes representing 0.5-0.7 percent in live births. For the past three years, we were referred 986 individuals with various clinical problems including: congenital malformation, mental retardation, neurodevelopmental disability, infertility, sexual differentiation (male), hermaphroditism, defect in pubertal development and miscarriage etc. There were 125 (12.7%) individuals that were found to have a variety of chromosomal abnormalities. Most of the cases were referred to rule out Down syndrome. Various types of chromosomal abnormalities producing recognizable syndromes were identified, however, none of them was clinically identified prior to chromosomal abnormalities. Utmost caution should be exercised when relating specific clinical features with chromosomal segments. Patients with complex chromosomal abnormalities were further evaluated using loci and whole chromosome painting probes. Clustering of breaks on various chromosomes are being tabulated and their clinical significance with respect to the chromosomal pathology is presented.

105

Smith-Magenis Syndrome Diagnosed at Birth. C. Lozzio, T. Ryan, E. Bamberger, E. Holland, and W. Carter Univ. of Tennessee Developmental and Genetic Center, Knoxville

Most cases of Smith-Magenis Syndrome are diagnosed in children with self-destructive behaviors, disturbed sleep patterns, dysmorphic features, speech delay, and mental retardation. We report the detection of an interstitial deletion of the short arm of chromosome 17 at band p11.2 in a newborn infant with mild dysmorphic features. She was born at 39 gestational weeks and chromosome analysis was performed within the first 24 hours after birth due to the findings of prominent forehead, mild midface hypoplasia, small nose, and anteverted nostrils. Cytogenetic analyses in metaphases (450 bands) and prometaphases (750 bands) revealed the presence of an interstitial deletion 17p11.2. The microdeletion for the Smith-Magenis region was confirmed with fluorescence "in situ" hybridization (FISH) studies using the dual color Vysis probe and the ONCOR probe. Chromosome studies and FISH studies are pending on the parents. The diagnosis of an interstitial deletion 17p11.2 in a newborn infant offers the opportunity to provide early intervention and behavior management of the severe developmental and behavioral symptoms described in this syndrome. It also raises the question on whether or not this microdeletion may be present in children with dysmorphic features who are not diagnosed because they have milder clinical manifestations of this syndrome.

106

Chromosome analysis of spermatozoa extracted from testes of men with non-obstructive azoospermia. R.H. Martin[1,2], Calvin Greene[3], Alfred Rademaker[4], Leona Barclay[2], Evelyn Ko[2], Judy Chernos.[2] [1]Department of Medical Genetics, Faculty of Medicine, University of Calgary, [2]Department of Genetics, Alberta Children's Hospital, Calgary, Alberta, Canada, [3]Department of Obstetrics and Gynecology, Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada, [4]Cancer Center Biometry section, Northwestern University, Chicago, Illinois, USA.

Infertile men with azoospermia now have the possibility of fathering a pregnancy by testicular sperm extraction combined with intracytoplasmic sperm injection. However, there are concerns about the risk of chromosomal abnormalities in their sperm. We have studied aneuploidy frequencies for chromosomes 13, 21, X and Y by multicolour fluorescence in situ hybridization (FISH) analysis in testicular spermatozoa extracted from three men with nonobstructive azoospermia. The men were 34-37 years of age and had normal FSH levels and normal 46,XY somatic karyotypes. A total of 3324 spermatozoa were analyzed. The infertile patients had an elevated frequency of disomy for chromosomes 13, 21, XY disomy compared to controls but none of these reached statistical significance. Also there was no significant difference in the sex ratio or the frequency of diploidy in azoospermic patients compared to normal control donors. This first report on chromosomal aneuploidy in spermatozoa extracted from testes of patients with nonobstructive azoospermia suggests that some azoospermic men do not have a substantially increased risk of chromosomally abnormal spermatozoa.