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Williams syndrome : analysis by R-bands, G-bands and fluorescent *in situ* hybridyzation techniques. D.Bérubé and R. Gagné. Centre Hospitalier Universitaire de Québec, Pavillon CHUL, Québec, Canada.

Williams syndrome occurs with a frequency of 1 in 20,000. Clinical features of this syndrome include short stature,mental handicap, cardiac malformatons and a characteristic facies. Many patients are sporadic but autosomal dominant inheritance ia apparent in some families. Moreover, in many patients, chromosomal abnormalities are present. Williams syndrome belongs to a group of microdeletion syndromes meaning that in the vast majority of cases, the deletion is located on the long arm of chromosome 7 and it is visible on chromosomes only using molecular cytogenetic. In this study, we wanted to show that the deletion is visible by routine chromosome analysis in a significative number of cases. For this study, we have reviewed and reanalysed our cases of Williams syndrome by R-bands routine cytogenetic technique and proved by fluorescent in situ hybridyzation. The data obtained in this study showed 25% of cytogenetic deletion with R-bands routine cytogenetic analysis. We know that all cases with a microdeletion are put in evidence with in situ hybridyzation with Elastine probe located in chromosome 7q11.2, the region of Williams syndrome.We compare our cytogenetic results with other centres in Quebec working with G-bands cytogenetic routine analysis, they never see the deletion with their cytogenetic routine analysis. We can conclude that the use of R-bands is probably helpful revealing a chromosomal deletion in some cases of Williams syndrome. Up now, these patients do not show a different phenotype or behavior when they are compared with those ones they do not have the chromosomal deletion.

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Prenatal phenotype of 48, XXYY with elevated MSAFP. S.M. Carter[1], P.A. Levy[2], V. Pulijaal[1], S.J. Gross[1]. Montefiore Medical Center, [1]Dept. of Obstetrics and Gynecology, and [2]Dept. of Pediatrics, Bronx, N.Y.

Elevated maternal serum alpha-fetoprotein (MSAFP) has long been associated with fetal abnormalities such as open neural tube defects, ventral wall defects, and cystic hygromas. The need for amniocentesis following a normal ultrasound has been debated because variability in ultrasound quality is vast. From several studies the incidence of fetal aneuploidy ranges from 0.6-1%, the incidence of all chromosomal abnormalities in women age 36 undergoing amniocentesis. We believe that providers should offer amniocentesis to women who have elevated MSAFP and a normal ultrasound since the quality of ultrasound varies widely.

SD a $G_2 P_{1001}$ 32 year old Guyanese female, was seen for genetic counseling and amniocentesis at 19 weeks for elevated MSAFP (3.19MoM). Ultrasound performed a few days prior did not note any fetal abnormalities. Family history revealed the patient's brother had isolated polydactyly, a common malformation. She declined the procedure because of the risk of a miscarriage. An anatomic exam at 21 weeks revealed bilateral clubfeet and possible left-hand postaxial polydactyly. The patient declined amniocentesis again and missed an appointment for fetal echocardiography.

The baby was born premature, at 29 weeks gestation by cesarian section. This was the second child born to these non-consanguineous parents. Birth weight was 1155 gms (25^{th}%ile), length 37.5 cm (25^{th}-50^{th}%ile), and head circumference was 27.5 cm (50^{th} - 75^{th}%ile). Physical exam revealed minimal facial dysmorphic features including: hypertrichosis-especially of the forehead, relatively small eyes, lowset ears with malformed pinnae, and a prominent nasal bridge. Other notable findings included: normal male genitalia (with slight chordee), sacral dimple, long slender fingers, prominent convex nails and bilateral clubfeet (equinus varus). Chromosomal testing revealed a 48 XXYY karyotype, which may have originated from consecutive meiotic non-dysjunction during paternal gametogenesis.

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A possible centromeric 21/22 translocation as an alternative cause of nondisjunction in trisomy 21. V del Castillo, S. Ramos, B. Molina, S. Frías. Instituto Nacional de Pediatría. México,D.F.

Two cases with normal karyotype and an additional signal in chromosome 22 with the 13/21 alpha satellite DNA probe have been reported in the literature. In both, one of the parents had the same marker, so an inherited polymorphism was considered. Here we describe another family case which is the first related to aneuploidy.

The patient is a 16 month old boy with Down syndrome, he is the second product of young non consanguineous parents, there is family history of a paternal cousin who was a malformed stillbirth. The G banding karyotype was 47,XY+21 and FISH with centromeric 13/21 probe showed 6 signals instead of 5. Cytogenetics analysis with G and C bands and dual FISH with 13/21 and 14/22 probes evidenced that the extra signal was in a chromosome 22, which was inherited from the father because he revealed 5 marks with the 13/21 probe and 4 with the 14/22.

This rearrangement could be explained by an inherited polymorphism, cross-hybridization or a translocation between the centromeric region of chromosomes 21 and 22. In this case, the father could be a new mutation or the product of an adyacent 1 segregation inherited from an ancestor, without an abnormal phenotype but with the risk of nondisjunction during the pairing at meiosis. In order to prove this hypothesis for genetic counseling, it is necessary to establish the parental origin of the patient's extra chromosome 21, determine the frequency of nondisjunction in the father's semen by FISH analysis and complete cytogenetic studies in other paternal relatives.

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Human 27-kDa heat shock protein (hsp27) gene family: chromosomal band assignments and possible involvement in Williams syndrome deletion. T.R. Dennis[1], P.A. Spallone[1], E. Hickey[2], L.A. Weber[2], C.A. Morris[3], and A.D. Stock[1]. [1]Department of Pathology, Laboratory of Molecular Cytogenetics, University of Nevada School of Medicine, Reno, Nevada, [2]Department of Biology, Reno, NV and [3]Department of Pediatrics, Las Vegas, NV.

The 27-kDa human heat shock protein (hsp27) is expressed in a wide variety of tissues in the absence of stress and is thought to regulate actin filament dynamics. Three related human hsp27 sequences had been previously mapped to chromosomes 3, 9, and X (McGuire et al., 1989). We have used fluorescent *in situ* hybridization (FISH) to correct and refine the map position of the transcribed hsp27 gene to chromosome 7, band 7q11.23 and its two pseudogenes to chromosome bands 9q21 and Xp11.2. Band 7q11.23 is the site of a deletion associated with Williams syndrome (WS), a congenital developmental disorder involving the vascular, connective tissue, and central nervous systems. We performed FISH mapping of hsp27 DNA to the chromosomes of four WS patients and found that in the majority of cells (77%), a bright signal was found on only one chromosome 7 at band 7q11.23. These results may indicate that the WS deletion includes the gene for the 27-kDa heat shock protein. However, in a small proportion of cells, a second, less intense signal was found on the other chromosome 7. We have interpreted these second weak signals as cross-hybridization due to the repeated DNA sequences (Alu sequences) known to reside within the introns and the flanking regions of this gene. Southern hybridization analysis is currently being performed to substantiate these findings in WS patient DNAs.

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