CYTOGENETIC STUDIES AMONG MENTALLY RETARDED CHILDREN ATTENDING TO SPECIAL CLASSES OF MEBARAM IN ANTALYA PROVINCE

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ABSTRACT

Objective: The aim of this study was to investigate chromosomal abnormalities among mentally retarded children attending special classes at Antalya Guide and Research Center (MEBARAM).

Methods: One hundred and fifty-one children having different IQ and ages attending special classes of MEBARAM were screened for chromosomal abnormalities using cytogenetic techniques.

Results: The significant chromosomal abnormalities have been found as both major (3.97%) and heteromorphic (11.25%). The major chromosomal abnormalities were 46,Y, fra(X) (q27.3), 46,X, fra(X) (q27.3) with fra (3) (p14) and fra(16) (q23), 46,Y, fra(X) (p22), 46,XY, fra(8) (q22), and two cases 47,XX+21. Seventeen out of 151 children had different types of heterochromatic chromosomal abnormalities (1qh+, 10qh+, 15ph+, 16qh+, 21ph+, 22pss, Yqh+, Yqh-) and two had pericentric inversion of chromosome 9.

Conclusion: We suggest that children with learning difficulties should be screened for chromosomal abnormalities. Families with incidences of a child having fra (x) (q 27.3) and trisomy 21 chromosomal abnormalities should be quided towards prenatal diagnosis with genetic counseling.

Key Words: Mental retardation, Chromosome abnormalities, fra (X) (q27.3), Trisomy 21, Heteromorphism.

INTRODUCTION

Mental retardation (MR) frequency seems to be increased in school children because it is more easily recognized through learning difficulties (1). MR is affected by multifactorial features, inborn errors of metabolism, consanguinity, social-economic-cultural differences and chromosomal abnormalities. MR is divided into different classes. The major class is mild mental retardation with subnormal IQ's (intelligence quotient) (1). Lamont et al. have found significant chromosome abnormalities in nine out of 166 mild mentally handicapped children (2). Turner et al. reported fragile X chromosomes in five out of 72 mildly retarded girls (3). Thake et al. have brought out chromosome abnormalities as both major and heteromorphic in children at school with mild mental retardation (4). The aim of the present study was to define the chromosomal abnormalities on the mentally retarded children attending fourteen special classes at Antalya Guide and Research Center.

MATERIALS AND METHODS

Chromosome studies were done on 151 mentally retarded children attending fourteen special classes at Antalya Guide and Research Center (MEBARAM). There were 94 boys and 57 girls, with ages ranging from 7 to 13 years. The IQ levels of the children determined by Stanford-Binet Testing (5) by MEBARAM varied from profound to borderline. (IQ 20-75). Venous blood samples were obtained with the written permission of their parents. Chromosome analyses were performed on peripheral lymphocytes, cultured for 72 hours in tissue culture medium 199 supplemented with 5% fetal calf serum (FCS) and methotrexate (MTX, 10^{-7} M, final concentration) inducing the fragile sites of X chromosome. The chromosomes were banded by modified G-banding, C-banding and NOR technique (6). The C-banding and NOR were applied to slides according to results of G-banding. Ten metaphases were examined for structural chromosomal anomalies. However, for males and females, at least 100 and 200 cells were analyzed for fragile X chromosome and mosaic rearrangement after G-banding, respectively.

RESULTS

Chromosome studies on all of 151 specimens were performed at the first culture. Whereas, non-specific chromosomal breakages were detected on the slides of four students, at primary cultures but these breakages did not appear after further culturing. Both major (3.97%) and heteromorphic (11.25%) chromosomal abnormalities were found in the six and seventeen out of 151 children, respectively (Table I,II). Major chromosomal abnormalities (a total of six) were 46,Y, fra(X) (q27.3), 46,X,fra(X) (q27.3) with fra(3) (p14) and fra(16) (q23), 46,Y, fra(X) (p22), 46,XY, fra(8) (q22), and two cases 47,XX, +21 (Table I).

Table I. Chromosomal etiology of mental retardation determined to be either Down syndrome or fragile X syndrome in 4 out of 151 mildly mentally retarded children.

Case	Sex	Age	IQ	Cell(n)	Medium	Finding	Frequency %
RLD	M	8	50	100	Med 199+MTX	Fra(X) (p22)	2
ST	M	8	38	100	Med 199+MTX	Fra(X) (q27.3)	16
SK	F	8	53	200	Med 199+MTX	Fra(X) (q27.3)	2
						Fra(3) (q14)	6
						Fra(16) (q23)	6
MI	M	11	45	100	Med 199+MTX	Fra(8) (q22)	18
ÖB	F	7	31	100	Med 199+MTX	47,XX,+21	100
SB	F	11	35	100	Med 199+MTX	47,XX,+21	100

Table II. Distribution of variants and heteromorphisms among 151 mildly retarded children.

				Applied Cytogenetic Methods			
Case	Sex	Age	IQ	GTG	CBG	NOR	Findings
MÖ	M	7	58	+	+	-	46,XY,inv(9) (p11;q13)
AS	F	11	54	+	+	-	46,XX,inv(9) (p11;q13)
SK	M	12	-	+	+	-	46,XY,10qh+
HB	M	7	64	+	+	+	46,XY,15ph+
ZÖ	M	8	47	+	+	-	46,XY,16qh+
AI	M	7	75	+	+	-	46,XY,1qh+
YG	F	8	48	+	+	-	46,XY,16qh+
SÇ	F	9	57	+	+	-	46,XX,16qh+
MY	M	8	-	+	+	+	46,XY,21ps+
ZU	M	8	68	+	+	+	46,XY,21ps+
GB	F	7	45	+	+	+	46,XX,21ph+
VG	M	8	45	+	+	+	46,XY,22pss
MY	M	8	49	+	+	-	46,X(Y)qh+
İU	M	7	48	+	+	-	46,X(Y)qh+
MM	M	7	57	+	+	-	46,X(Y)qh+
ÖG	M	7	68	+	+	-	46,X(Y)qh-
RG	M	9	63	+	+	-	46,X(Y)qh-

DISCUSSION

The chromosomal etiology of mental retardation is very complex and the mild class of mental retardation has been observed in children without abnormal clinical features, therefore, chromosomal investigation is usually not considered for these children by pediatricians. We have performed cytogenetic analysis on 151 students who were 7-13 years old and have IQ levels profound-borderline (IQ 20-75) determined by MEBARAM. The chromosomal analysis of these children revealed both major (3,97 %) and

heteromorphic (11.23%) chromosomal abnormalities. A male student (S.T) who was carrying fra(X) (q27.3) had an IQ of 38, while two girls had Down syndrome whose mental retardation was severe enough to allow reliable intelligence testing. However, other children whose chromosomal abnormalities fell in within the range of mild intelligence-IQ 45-75 (Table I,II). It has been understood that both severe and mild mental retarded children were present in these classes. Czeizel et al. found the chromosomal abnormalities of children attending a special school to be 5.3 percent. They could not find any student carrying fragile X chromosome (7). However, our results, showed that the prevalences of both (fra X) carriers and Down syndromes are I and 2 percent, respectively. Whereas, Gustavson et al. suggested that the prevalence of fragile X carriers with mild mental retardation was 2,9 % (8), Lüleci et al. reported that 8 out of 50 mentally retarded children had chromosomal abnormalities, 4 out of 8 had fragile X chromosome (9), and this was higher than the value we obtained in our study. Tharapel and Summit have reported that no significant differences in frequencies of heteromorphisms were noted between 200 hundred mentally retarded patients and 200 hundred controls (10). Also Funderburk et al. had found no correlation between IQ and satellite size in mentally retarded and psychiatricly disordered children (11). Although 17(11.25%) out of 151 children had different types of heterochromatic chromosomal abnormalities (Table II), there was no significant correlation between heteromorphism and mental retardation. We suggest that children with learning difficulties should be screened for chromosomal abnormalities. The families having a child with fra(X) (q27.3) and trisomy 21 chromosomal abnormalities should be directed for prenatal diagnosis with genetic counseling.

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