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Chromosomal Abnormalities in Idiopathic Mental Retardation Patients at a Charity Center in Hamadan, Iran

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Abstract

Background: Chromosomal aberrations are one of the most common causes of mental retardation (MR).
Objectives: In this study, in order to identify the rate of chromosomal abnormalities in idiopathic MR, 50 MR patients at a charity center in Hamadan, Iran, were investigated.
Methods: Fifty mentally retarded male patients without specific chromosomal abnormalities (e.g., Down syndrome, Fragile X syndrome, and Klinefelter syndrome) were included in the study. Standard cytogenetic techniques and high resolution GTG banding were performed on all the patients.
Results: All the patients were male, with a mean age of 37.12 years. Skeletal and facial abnormalities were found in 8% and 22% of patients, respectively. All the patients showed a moderate to severe level of mental retardation. None of the patients had numerical chromosome abnormalities. Two out of the 50 patients (4%) demonstrated structural chromosomal abnormalities. One patient had a paracentric inversion in chromosome 1, while the other had a pericentric inversion in chromosome 2.
Conclusions: The presence of structural chromosomal abnormalities (4%) in the studied MR patient population emphasizes the importance of cytogenetic investigation for all idiopathic MR patients.

Keywords: Idiopathic Mental Retardation, Chromosome Abnormality, GTG Banding

1. Background

Mental retardation is one of the most serious public health concerns worldwide due to its prevalence (ca. 2% - 3%), the limited availability of therapeutic options, and the resultant life-long implications for the affected persons, their families, and society as a whole (1-3). The severity of this mental abnormality is typically classified as either mild, intermediate, severe, or deep according to an IQ test. Although this categorization is commonly used, the American Association of Mental Retardation modified the main criteria for mental retardation in 1992 so that they are now based on an individual's disabilities when performing personal tasks such as fundamental problems in learning and skills during their daily work and defects in the skills necessary for daily activities (4-6).

Chromosomal aberrations are one of the most important causes of MR. Numerical and structural abnormalities are responsible for about 4–28% of all mental retardation, and they are found in almost 40% of severe MR and 10% of the mild type (7, 8). Since chromosomal defects are one of the main causes of mental retardation, the screening of all mentally retarded patients with regard to chromosomal abnormalities seems to be necessary (9-11). Although no approved treatment is currently available for repairing genetic defects, the correct diagnosis of the etiological sources of these defects should be considered (12).

Nowadays, the number of diagnostic strategies available for investigating the genetic causes of mental retardation has increased. In recent years, the application of novel techniques using high-resolution chromosome analysis has become more common, and the identification of most genetic defects caused by monogenic disorders has been facilitated (13, 14). However, the diagnosis of the genetic reasons for mental retardation can be finalized in just half of all patients (15).

For many people with MR, it is unclear whether a genetic cause or an unknown exogenous cause is present. This is, however, a question of major importance to the parents of individuals with MR if they wish to have more children, as well as to other members of the family. Thus, the determination of the etiology of MR could be beneficial in reducing the risk of subsequent children being born with mental abnormalities (2).

2. Objectives

Despite the high prevalence of mental retardation in some developing countries, including Iran, and the associated high economic burden on families and society, there is currently only limited information available about the possible causes of MR in Iran. Therefore, this study aimed to investigate the chromosomal abnormalities in idiopathic MR patients at a charity center in Hamadan, Iran.

3. Methods

A cytogenetic study was conducted on 50 MR patients with unknown origins who resided at a charity center for mentally and psychiatrically disabled patients in Hamadan, Iran, during 2014 and 2015. The inclusion criterion for the patients was the presence of idiopathic MR (excluding all known genetic syndromes such as Down syndrome and Klinefelter syndrome or any evidence of cerebral palsy). The patients' baseline characteristics, including medical history, presence of retardation in the family, IQ score, and facial and skeletal abnormalities, were investigated. For the cytogenetic analysis, blood samples were first collected from all the patients in sterile heparinized test tubes. The heparinized samples were then sent to the cytogenetic center at Shahid Beheshti hospital in Hamadan. Peripheral blood lymphocytes were cultured in 5 mL of RPMI 1640 (GIBCO®; Invitrogen, Paisley, Scotland, UK), supplemented with 20% (v/v) fetal bovine serum (GIBCO®; Invitrogen) and 10 μL/mL of phytohemagglutinin (PHA) (GIBCO®; Invitrogen) at 37°C. After 72 hours of incubation, 40 μL of colcemid (10 μg/mL) (GIBCO®; Invitrogen) was added to the cells. Thereafter, the cells were incubated at 37°C for about 10 minutes. Finally, the karyotype was determined in all the patients using standard techniques (16) and high resolution GTG banding.

4. Results

A total of 50 patients with idiopathic mental retardation were studied. All the patients were male, with a mean age of 37.12 $\pm$ 5.59 years (range 16 - 54 years). Additionally, the average height of the patients was 164.88 $\pm$ 9.12 cm (range 153 - 172 cm). Skeletal abnormalities were detected in 8% of patients and facial abnormalities in 22%. Whether based on either the presence or absence of a history of taking psychological medications, aggressive behaviors were not reported in any of the cases. Based on the IQ scores, all the patients had a moderate to severe level of mental retardation. The cytogenetic study showed that none of the patients had numerical chromosomal abnormalities. In this regard, two out of the 50 patients exhibited structural chromosomal abnormalities. One (31-years-old) had a paracentric inversion in chromosome 1 with a final diagnosis of 46,XY,inv(1)(pter→p34::p31→p34::p31→pter:46,XY,inv(1)(P31 P34) (Figure 1), while the other patient (35-years-old) had a pericentric inversion in chromosome 2 with a final diagnosis of 46,XY,inv2(P13q21), inv(2) (Pter→P13::q21→P13::q21→qter) (Figure 2).

5. Discussion

With a prevalence of 2% - 3% in the population, mental retardation is a heterogeneous disorder defined by an intelligence quotient (IQ) of less than 70 (1). In our study, only 4% of mentally retarded patients revealed structural chromosomal anomalies such as paracentric and pericentric inversions in chromosomes 1 and 2, while changes in the number of chromosomes were not detected in any patients. The findings of previous studies with a similar purpose exhibited wide variations, probably due to the criteria for selecting patients and the techniques applied for chromosomal assessment, for example, a cytogenetic study alone or a cytogenetic study with molecular techniques comprising fluorescent in situ hybridization (FISH) or comparative genomic hybridization (CGH). In a study conducted among a Polish mentally retarded population, the overall prevalence of abnormal karyotypes was 10.1%, whereas only 2.2% of patients had specific structural chromosomal anomalies (17). Celep and colleagues (18) showed an overall prevalence of 4.8% in 475 Turkish mentally retarded patients. In a study among Slovakian mentally retarded patients, 32% of subjects demonstrated chromosomal abnormalities (19). A similar study performed by Behjati et al. (13) in Iran showed that only 1.24% of mentally retarded patients from consanguineous marriages showed chromosomal abnormalities comprising translocation and paracentric inversions in chromosome 2, which is consistent with the findings of our study. It seems that the presence of paracentric and pericentric inversions in chromosomes 1 and 2 could be an identified chromosomal abnormality among Iranian mentally retarded patients.

In conclusion, cytogenetic investigation should be considered as the first step in the assessment of mentally retarded individuals with unknown origins. This approach can help to effectively manage the disabilities of such patients. Moreover, identifying the causes of mental retardation and studying numerical and structural chromosomal anomalies such as translocation, inversion, or deletion in these patients can prove effective for the prevention of abnormal neonates in the next generation. Additionally, due to the limited resolution power of cytogenetic assessment, which ranges from 4 to 10 mega bases, the necessity

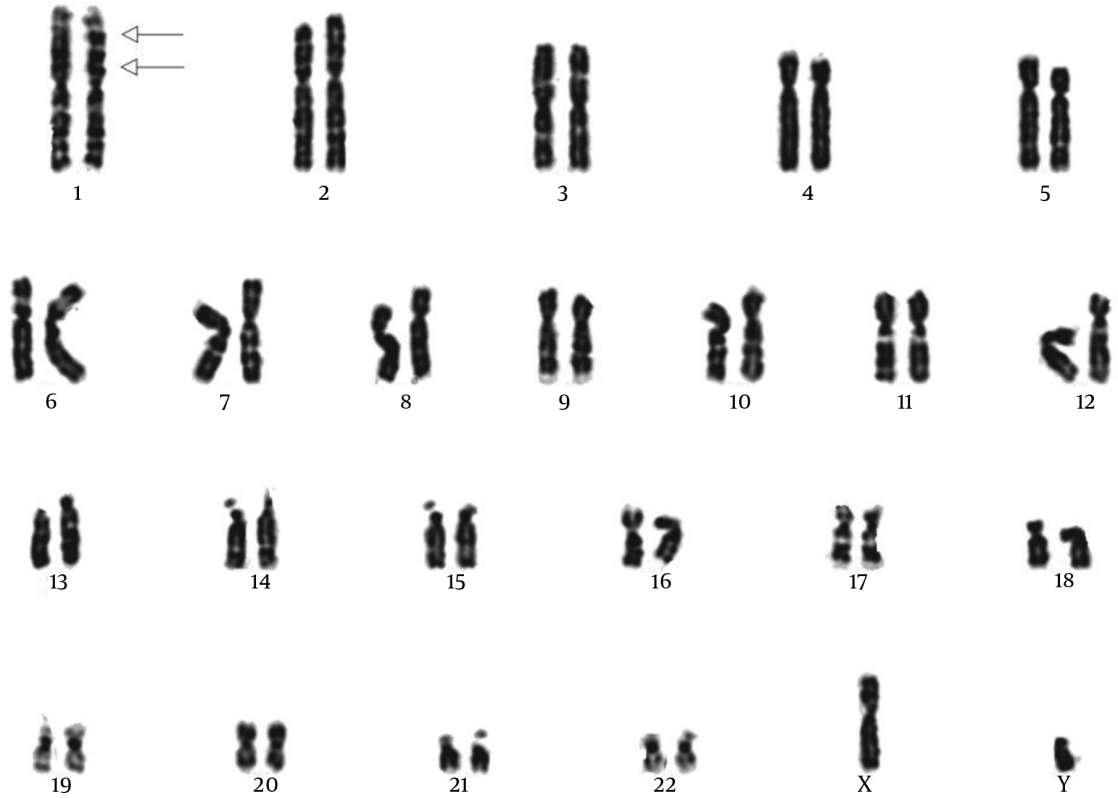

Figure 1. Paracentric Inversion in Chromosome 1 With a Final Diagnosis of 46,XY,inv(1)(pter→p34::p31→p34::p31→pter:46,XY,inv(1)(P31 P34) in a Patient With Mental Retardation

of other molecular methods such as fluorescent in situ hybridization or comparative genomic hybridization will be of importance in future studies.

Footnotes

Authors' Contribution: Katayoon Etemadi was responsible for the study design, data acquisition, and statistical analysis.

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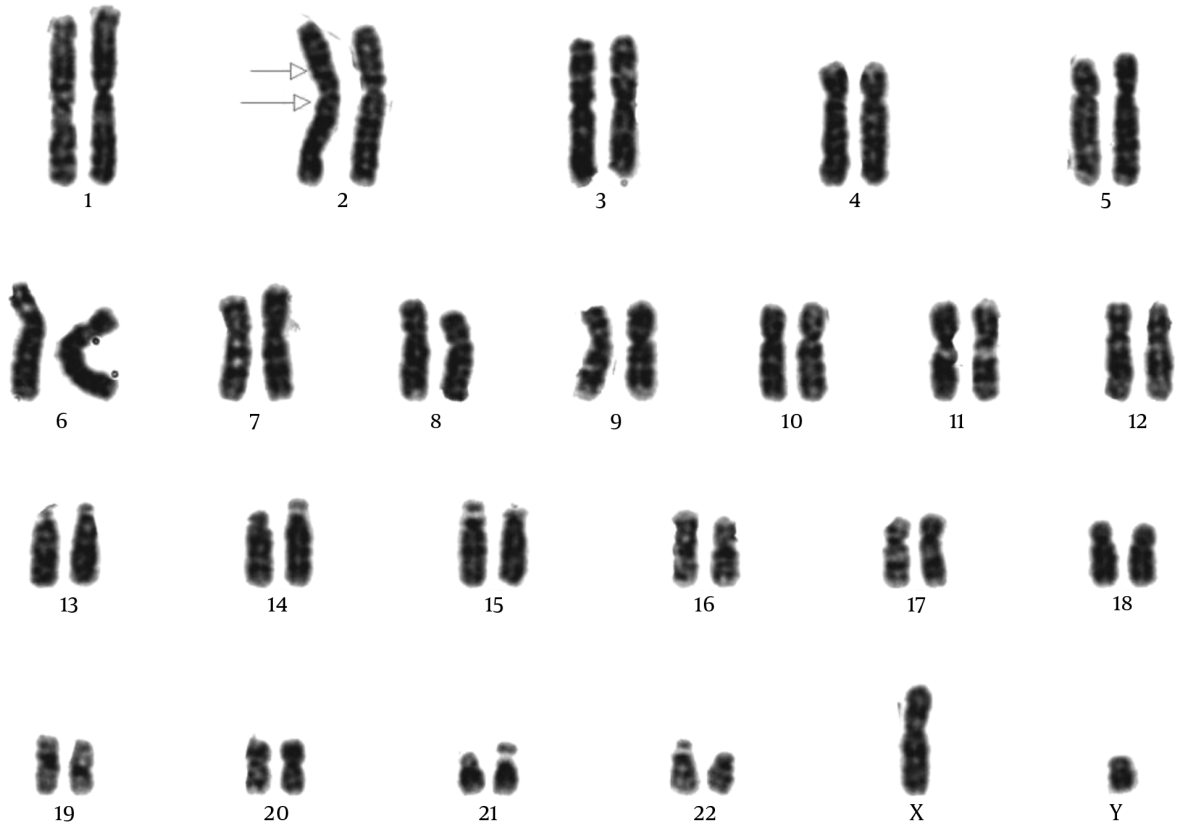

Figure 2. Pericentric Inversion in Chromosome 2 with a Final Diagnosis of 46,XY,inv2(P13q21), inv(2) (Pter→P13::q21→P13::q21→qter) in a Patient With Mental Retardation

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