

SHORT COMMUNICATION

Karyotype analysis in children with idiopathic intellectual disability

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ABSTRACT

Intellectual disability (ID) is a heterogeneous condition, affecting 1–3% of general population. In this study, karyotype analysis was performed in 33 children with idiopathic ID in a hospital with limited laboratory facilities to determine the value of karyotype analysis as a first step test in children with idiopathic ID. Thirty-three patients with idiopathic ID were included in the study. Giemsa-trypsin-Leishman (GTL) banding karyotype resolution at a standard resolution of 550 bands was performed to determine whether the patients had microdeletion/microduplication by using of conventional karyotype analysis. Of 33 children, seven (21.2%) showed various chromosomal changes. Polymorphisms including 46,XX,1qh+; 46,XX,1qh+,1qh+; 46,X,add(Y),q12; 46,XY,21ps+ and 46,XX,1qh+ were diagnosed in five children. Inversion [46,XY,inv9(p12q13)] and inversion and polymorphisms [46,XY,inv9(p12q13),13ps+] were diagnosed in two children, respectively. We believe that inv(9)(p12q13) is a benign variant. In conclusion, our findings showed that the karyotype analysis was not helpful to determine

etiology in children with idiopathic ID, probably because of the low patient number in our study.

KEYWORDS

Idiopathic intellectual disability; Chromosomal analysis; Child

INTRODUCTION

Intellectual disability (ID) is a heterogeneous condition, affecting 1–3% of general population [1]. Based on the evidence to date, a standard karyotype, fragile X molecular genetic testing, array comparative genomic hybridisation (aCGH) and neuroimaging are performed in patients in whom an etiologic diagnosis is not suspected after the history and physical examinations. However, one can expect rapid changes in the microarray technology in the near future [2].

In the present study, karyotype analysis was performed in 33 children with idiopathic ID in a hospital with limited laboratory facilities to determine the value of karyotype analysis as a first step test in children with idiopathic ID.

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MATERIALS AND METHODS

This study has been performed at Yüzüncü Yıl University, Faculty of Medicine, Department of Pediatric Neurology, Turkey. Thirty-three children with idiopathic ID, who had not major dysmorphic signs, or an underlying neurological or metabolic disorder leading to ID, were included in the study.

The patients' demographical data were noted and a detailed physical examination was performed in all the patients. Porteus Labirents test for performance intelligence quotient (IQ) and Kent EGY test for verbal performance IQ were used in patients over 6 years. IQ was predicted based on clinical observations and information taken from parents in younger than 6 years and non-cooperative patients. In order to detect etiology of ID, serum thyroid function tests, tandem-mass spectrometry and cranial magnetic resonance imaging were performed in all the patients. Urinary organic acid analysis, urinary-blood amino acid levels, investigations for TORCH infections and cranial computerised tomography were examined in required patients. Giemsa-trypsin-Leishman (GTL) banding karyotype resolution at a standard resolution of 550 bands was performed to determine whether the patients had microdeletion/microduplication by using conventional karyotype analysis. The study was approved by Ethics Committee of Erciyes University Faculty of Medicine. A written consent was received from the patients' parents.

RESULTS

Of 33 patients, 21 (63.6%) were males and 12 (36.4%) were females. Male/female ratio was 1.75. The mean age of patients was 4.25 ± 2.47 years (2.5–17 years). There was consanguinity between the parents of 10 (30.3%) patients. Three (9.0%) patients had severe ID, 15 (45.5%) had moderate ID and another 15 had mild ID. In addition to ID, 12 (36.3%) patients had epilepsy and motor retardation, 9 (27.2%) had motor retardation and 9 (27.2%) had epilepsy. No additional disorder was detected in the remaining three (9.0%) patients.

Of 33 children, seven (21.2%) showed various chromosomal changes. Polymorphisms including 46,XX,1qh+; 46,XX,1qh+,1qh+; 46,X,add(Y),q12; 46,XY,21ps+ and 46,XX,1qh+

were diagnosed in five children. Inversion [46,XY,inv9(p12q13)] and inversion and polymorphisms [46,XY,inv9(p12q13),13ps+] were diagnosed in two (6.0%) children, respectively.

DISCUSSION

Genetic causes of ID are highly heterogeneous, including large chromosomal abnormalities, submicroscopic copy number variants and monogenic forms due to pathogenic variants in single genes. The monogenic forms are classified based on inheritance mode to X linked, autosomal dominant and autosomal recessive ID. Close relation of the parents, double cousin or uncle-niece unions makes ID three to four times more common than in children of unrelated parents [3]. In our study, 10 (30.3%) patients who had consanguinity between the parents have the possibility of autosomal recessive ID. The high percentage of epilepsy associated with ID (36%) also supports the monogenic background.

Microarray testing is diagnostic on average in 7.8% (Class III) and G-banded karyotyping is abnormal in at least 4% (Class II and III) in patients with ID [4]. Nonetheless, microdeletion and microduplication syndromes associated with autism, developmental delay and/or multiple congenital anomalies are not detected with a karyotype [5]. In our study, we used G-banded karyotyping. Unfortunately, we could not analysed aCGH or fluorescent *in situ* hybridisation for subtelomeric imbalances in our patients, because of lack of laboratory facilities. This is one of the limitations in our study.

Polymorphisms are found in a rate of up to 8% in the general population. The most frequent one is inv(9). In routine cytogenetics, they are referred as heterochromatic variants or heteromorphisms [6,7]. These heteromorphisms or heterochromatic variants can include 9qh+, 9cen+, 9ph+, 9ph- and inv(9)(p11q13) [6]. Çöp et al. [8] evaluated 96 children with autism spectrum disorders for genetic testing. They found abnormalities on karyotype in 9.7% patients including inv(9)(p12q13) in a 24-month-old boy without dysmorphic features [8]. Sobreira et al. [9] described a 9-year-old girl with pseudoaminopterin syndrome, including multiple congenital malformations, who has a karyotype

of 46,XX, with an inv(9)(p12q13) polymorphism. Malinverni et al. [7] reported a simple pericentric inversion of chromosome 9 [46,XX,inv(9)(p12q13)] in a patient with facial dysmorphism, language and neurodevelopmental delay and ID. Molecular cytogenetics showed an unusual, rearranged chromosome 9, der(9)(pter→p11.2::q21.11→q12::p11.2→p13.2::q12→p11.2::q21.11→qter) [6]. In our series, various polymorphisms and inv(9)(p12q13) were diagnosed in five and two children, respectively. Based on the literature data, inv(9)(p12q13) can be correlated to the patients' phenotype; however, we think that inv(9)(p12q13) is a benign variant. We did not detect any positive result. We think that this is due to the small number of our patients, which is the second limitation of our study.

CONCLUSION

Our findings showed that the karyotype analysis was not helpful to determine etiology in children with idiopathic ID probably because of the small number of patients in our study. Although we did not detect any positive result in the present study, we still think that karyotype analysis should be performed in children with idiopathic ID as the first step test in medical centres with limited laboratory facilities.

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CONFLICT OF INTEREST

There are no conflicts of interest.

ETHICS

The study was approved by Ethics Committee of Clinical Research of Erciyes University Faculty

of Medicine (Date: 20.09.2011; References number: 2011/11).

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