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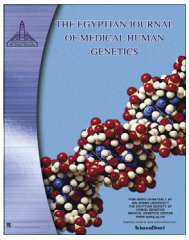

ORIGINAL ARTICLE

Chromosomal abnormalities and autism

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KEYWORDS

Autism;
Chromosomal abnormality;
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Abstract *Background:* Autism is a neurodevelopmental disorder characterized by clinical, etiologic and genetic heterogeneity. Many surveys revealed cytogenetically visible chromosomal abnormalities in 7.4% of autistic patients documented as well as several submicroscopic variants. This study had been conducted to identify some aspects that might be involved in the pathogenesis of autism which is necessary for offering proper genetic counseling to families of autistic patients and their role in the prenatal diagnosis of autism.

Methods: This cross sectional study was conducted at the Child Psychiatry Clinic, Pediatric Hospital, Ain Shams University on 30 autistic patients who were subjected to the following tools: Confirmation of diagnosis using DSM-IV-TR criteria, IQ assessment using Stanford-Binet intelligence scale and assessment of severity of autistic symptoms using childhood autism rating scale (CARS). Full clinical examination, neurological examination, EEG, audiological assessment were also done. High resolution karyotyping was done for detection of numerical or structural chromosomal abnormalities as deletion, duplication, translocation of chromosomes.

Results: All the results of cytogenetic analysis were normal with no detectable numerical or structural chromosomal abnormalities. Males are affected more than females, only one case had history of drug intake (progestin), two cases had history of anti-D injection and two cases had history of diabetes mellitus during pregnancy. Four cases had history of respiratory distress and seven cases had history of jaundice. Two cases had history of generalized tonic clonic convulsion and four cases had history of EEG abnormalities. Fifteen cases of our autistic patients had mild mental retardation and six cases had moderate mental retardation.

Conclusion: Chromosomal abnormalities were not detected in the studied autistic children, and so the relation between the genetics and autism still needs further work up with different study methods and techniques.

1. Introduction

Autism is a syndrome characterized by impairment in social communication, repetitive behavior, abnormal movement

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and sensory dysfunction [1]. It is currently estimated that 3–6 children out of every 1000 worldwide have autism with three to four fold higher incidence in males than in females [2]. Autism is a neuro-developmental disorder characterized by clinical, etiologic and genetic heterogeneity, it is often associated with other conditions such as disorders of the CNS (tuberous sclerosis), developmental delay, attention deficit, epilepsy, anxiety and mood disorders [3]. Many surveys revealed cytogenetically visible chromosomal anomalies in 7.4% of autistic patients, among the most consistent cytogenetic findings are fragile-x and duplication of maternal chromosome 15q11–13 [4].

Environmental component is another important aspect of research in autism. Environmental factors such as mercury and radiation have been proposed as possible causes of autism [5]. Several studies provided strong evidence against the hypotheses that MMR vaccination causes autism [6]. The causes of autism are still unclear, although results from twin and family studies provide evidence for strong genetic contribution, with the probability of multiple genetic loci involved [7].

Despite significant research on prenatal, natal, neonatal and other risk factors in autism, the causal nature of these associations is still disputed due to several current methodological limitations of studies [8].

2. Patients and methods

The present study enrolled 30 cases with autism diagnosed with DSM-IV-TR criteria [9,10]. The patients were 23 males (76.7%) and 7 females (23.3%). Their age ranged from 2 to 9 years. They were recruited from the psychiatric clinic, pediatric hospital, Ain Shams University.

All cases were subjected to the following:

1. Detailed history taking with special emphasis on, onset, course, age, sex and consanguinity of the patients.
   - Antenatal history included history of threatened abortion, chronic illness as diabetes mellitus and hypertension, medications as antiepileptics, antithyroid, and progestin, and anti-D injection.
   - Natal and postnatal history including, gestational age, complications during delivery, history of prematurity, perinatal problems and postnatal course especially occurrence of neonatal hypoxia, respiratory distress and jaundice.
   - Developmental assessment included both motor and mental development: age of sitting without support, walking unassisted, first spoken word, combining words, accurate details of cognitive abilities, gross and fine motor functions and history of vaccination.
   - Past history including: major childhood illnesses, history of allergy and gastrointestinal disorders as diarrhea or constipation.
   - Family history for any similar condition, any genetic disease or other psychological or mental disorders in the family.
2. Through clinical examination
   - Laying stress on neurological examination.
3. Psychiatric evaluation:
   - Confirmation of diagnosis using DSM-IV-TR criteria of autism i.e., impairment in language, social skills and restricted stereotyped interests or activity.
   - Assessment of intelligence quotient (IQ) using Stanford-Binet intelligence scale (1986) [11], which is used to measure the cognitive abilities of children aging from 2 to 16 years. Abnormal intellectual function is diagnosed when IQ is below 70.
   - Assessment of severity of autistic symptoms using childhood autism rating scale (CARS) [12], which rates the child from one to four in each of fifteen areas (relating to people, emotional response, imitation, body use, object use, listening response, fear or nervousness, verbal and non verbal communication, activity level, consistency of intellectual response, adaptation to change, visual response, taste, smell, touch response and general impression).
4. Genetic evaluation:
   - Pedigree of family of autistic patients.
   - Cytogenetic analysis by high resolution banding techniques [13] which have facilitated the identification of chromosomes and major structural abnormalities by examining chromosomes with more number of bands by obtaining prophase and prometaphase chromosomes which are less condensed. High resolution banding facilitates better karyotyping analysis and more precise designation of breakpoints and subtle chromosome abnormalities [13]. Prophase and prometaphase cells can be obtained by harvesting the cultures without metaphase block, or by reducing the concentration of the blocking agent (colcemid) and the duration of treatment. An alternative approach is to accumulate the maximum number of cells at a particular stage of the mitotic cell cycle and release them synchronously to capture the early stages of mitosis, prophase and prometaphase. This approach with a brief exposure to low concentration of colcemid, is employed to obtain considerably long chromosomes.

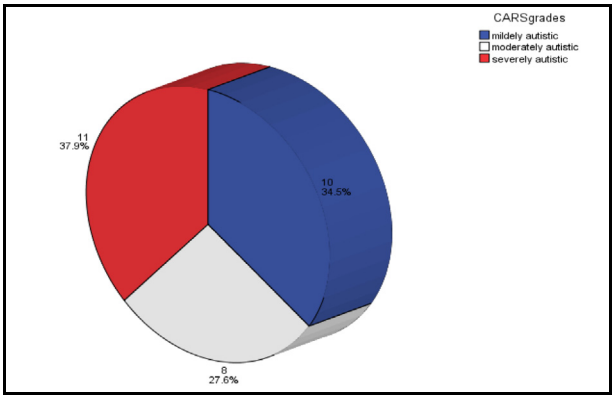

Figure 1 Degree of autism according to CARS in autistic patients.

3. Results

The present study included 30 cases with autism diagnosed with DSM-IV-TR criteria [9,10]. The patients were 23 males