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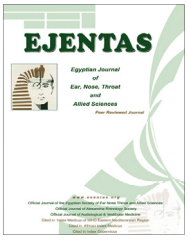

ORIGINAL ARTICLE

Plasma level of transforming growth factor β 1 in children with autism spectrum disorder

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KEYWORDS

Autism;
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Abstract *Background:* Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders characterized by pervasive abnormalities in social interaction and communication, and repetitive and restricted behavioral patterns and interests. ASD include autistic disorder, Asperger's disorder, pervasive developmental disorder not otherwise specific and childhood disintegrative disorders.

Objectives: To detect plasma level of transforming growth factor beta 1 (TGFβl) in children with ASD and to find out correlation between the plasma level of TGFβ1 and severity of ASD.

Patients and methods: Our study included 30 patients with autistic spectrum disorder (ASD) diagnosed on the basis of criteria of autistic spectrum disorders as defined in Diagnostic and Statistical Manual of Mental Disorders fourth edition text revised (DSM-IV) (TR). They were 26 males and 4 females, their ages ranged from 3 years to 13 years. Thirty apparently healthy sex and age matched children served as controls (22 males and 8 females). They were subjected to full history taking, clinical examination and severity rating using Child Autistic Rating Scale of Children (CARS) and Diagnostic and Statistical Manual of Mental Disorders fourth edition text revised (DSM-IV) (TR).

Results: Our study revealed: (a) sex distribution among the patient group with male/female ratio 6.5:1; (b) mean value of maternal age was significantly higher among patients than controls; (c) about 50% of patients had a history of prenatal complication; (d) the patient group shows lower plasma level of TGFβ1 compared to the control group.

Conclusion: There may be an important role for the immune system in autism spectrum disorders that may have profound implications for diagnosis and treatment of this disorder. A negative correlation was found between severities of ASD and TGFβ1 plasma level.

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1. Introduction

Autistic spectrum disorder is a complex developmental disorder with social and communication dysfunction at its core. Autistic spectrum disorders are a wide spectrum of conditions having a common triad of impairments. Deficits include those in social communication, social interaction and social imagination. It first gives signs during early childhood. Impairments result from maturation-related changes in various systems of the brain.[1]

The prevalence of ASD has increased substantially over the last decade rising from 5 to 60/10,000.[2] The male to female ratio is three or four to one, but when it occurs in females it is more severe.[3] The exact etiology of autism and ASD remains unknown, it is likely to result from a complex combination of environmental, immunological and genetic factors. Strong genetic links have been shown for cases with Tuberous sclerosis, Fragile X, neurofibromatosis, and chromosomal abnormalities.[4,5]

There is growing awareness of an immunological involvement in children with ASD. Evidence of immune dysregulation has been observed in some individuals with ASD including increase levels of pro-inflammatory cytokines in brain tissue, CSF and plasma and increased production of pro-inflammatory cytokines by peripheral blood mononuclear cell culture when compared to typically developing control.[6–8] The regulatory immune response is also critical in the down-regulation of the inflammatory immune response following infection, thus limiting potential tissue damage. Immunosuppressive cytokines such as transforming growth factor beta 1 (TGFβ1) are critical for immune homeostasis, important in induction of unresponsiveness in activated T cell.[9,10]

There are several studies that demonstrate an alteration or dysregulation of immune response in autism compared with matched controls.[7,11–13] Altered TGFβ1 levels have been observed in brain specimens of subjects with autism.[8] Another study revealed decreased plasma TGFβ1 in adults with autism.[14]

This work was designed to evaluate patients with autistic disorders through detailed history and rating their severity using CARS, together with detection of the plasma level of TGFβ1, in order to find out if it is altered in ASD thus it can help in understanding the nature of the problem and it may be used as an early marker in diagnosis.

2. Subjects and methods

2.1. Subjects

The study sample was composed of 30 children suffering from autism spectrum disorders (ASDs), attending outpatient clinic of Pediatric Neuropsychiatry and Phoniatrics of Tanta University Hospital.

2.2. Inclusion criteria

1- Age range of 3–13 years.
2- Children diagnosed by using Diagnostic and Statistical Manual of Mental Disorders fourth edition text revised (DSM-IV) (TR) and Child Autistic Rating Scale of Children (CARS).

2.3. Exclusion criteria

1- Other mental or neurobehavioral disorders.
2- Chronic diseases or infections.
3- Medications modulating immunity.
4- Immune deficiency states.

The control group was composed of 30 clinically healthy properly matched children (22 males and 8 females), their ages ranged from 3 to 13 years. None of them had a history of chronic illness. Their total score fell in the range of 15–29 according to CARS.

2.4. Ethical issues

A formal written consent of parents or guardians was taken separately after explanation and assurance that the procedure will not harm patient or delay his improvement.

All participants' names were hidden and replaced by code number to maintain privacy of the participant.

2.5. Methods

All children in this study were subjected to the following:

1- Full history taking especially developmental history and prenatal complications.
2- Physical examination and especially neurological examination.
3- Cognitive age (mental age) using Stanford Bine intelligence scale (1960) or the non-verbal intelligence test of Snijder Oomen (1979) to exclude other mental or neurobehavioral disorders.[15]
4- Psychometric study using:
   - Diagnostic and Statistical Manual of Mental Disorders fourth edition text revised (DSM-IV) (TR).[1]
   - Child Autistic Rating Scale (CARS).[16]
5- Laboratory detection of plasma level of transforming growth factor beta 1 (TGFβ1) by ELISA.[13]

2.6. Child Autistic Rating Scale (CARS)

The child is considered non-autistic when his/her total score falls in the range of 15–29, mildly–moderately autistic when the total score falls in the range of 30–36 and severely autistic when the total score falls in the range of 36–60.

2.7. Monitoring of the data

Data were recalled in a confidential manner and the privacy of all patients was maintained.

2.8. Duration of the study

The study duration was 15 months.