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CASE REPORT

Cri du Chat Syndrome Coexistent with Autism Spectrum Disorder: A Case Report

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ABSTRACT

Background: Cri du chat syndrome is characterized by significant impairment in expressive language skills, and impairment of the recipient language. This syndrome is caused by a deletion in the short arm of chromosome 5. Behavioral features associated with syndrome include hyperactivity, self-injurious, aggressive, and stereotyped behaviors. Autism Spectrum Disorders (ASD) is a serious neuropsychiatric disorder characterized by impairments in social interaction and communication, restricted and stereotyped behavioral patterns.

Case Report: Two year and four month old male case presented with complaints of unsteady walking, short time eye contact, speech delay, repetitive behaviors like wing flap, excessive interest in rotating objects. In addition to these, we recognized hypertelorism, broad nasal root, micrognathia, and microcephaly in the physical examination. His walking was ataxic. In psychiatric evaluation, we found that his social communication and interaction were limited. We started follow-up and treatment with ASD diagnosis. In the chromosome analysis examination; 46, XY, del (5) (p15) and Cri du Chat syndrome was diagnosed.

Conclusion: The relationship between autism spectrum disorders and genetic diseases is still one of the mysteries. This case report presents a case of Cri du Chat syndrome and ASD in order to shed light on this relationship.

Keywords: Autism, cri du chat syndrome

INTRODUCTION

Cri Du Chat syndrome (CdCS) is a gene disorder caused by partial interstitial deletion of the 5p chromosome. The incidence of CdCS is between 1/15,000 and 1/50,000. In a sample with intellectual disability, the prevalence may rise to 1/350. The ratio of girls to boys is 4/3. Significant clinical features of CdCS include microcephaly, round face, hypertelorism, micrognathia, epicentral folding, hypotony, marked nasal bridge. This syndrome is characterized by severe and profound intellectual impairment, with fewer impairments in the recipient language, and significant impairments in expressive language skills. In addition, affected infants may experience a cat-like monochromatic crying, in a diagnostic fashion, with a high-pitched cry (1,2). Behaviors associated with CdCS include self-stimulatory/ repetitive behaviors, self-injurious behavior, aggression, temper tantrums, hyperactivity, poor concentration/ distractibility, and impulsivity (3) .

The clinical appearance of individuals with deletion of 5p may vary. The high level of phenotypic variability is associated with the gene content of the monosomal region and the deletion size, which can vary mainly between 5 and 40 Mb. It has been reported that the degree of cognition and deterioration in the phenotype is associated with larger deletions (4). Many genes over 5p, such as semaphorin 5A (SEMA5A), deltacetin

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(CTNND2) and human telomerase reverse transcriptase (TERT) have been associated with ASD, mental retardation, schizophrenia or impaired fetal development (4).

Autism spectrum disorders (ASD) are part of childhood neurodevelopmental disorders. Symptoms start in early childhood, the social communicative field is a disorder characterized by significant deficits and limited, repetitive behaviors and interests (5).

The association between autism spectrum disorder (ASD) and genetic disorders has recently become a source of great interest and debate within the behavioral phenotype and autism literatures. A large number of genetic syndromes have been reported to show a degree of association with ASD that is higher than expected (i.e., Tuberous Sclerosis Complex, William's synrome, Fragile X, Rett's disorder, Cohen, Down, and Cornelia de Lange syndromes) (3).

Actually ASD symptoms are not strongly associated with CdCS (6). In 2011, Claro et. al examined whether the fatigue level of children diagnosed with cri du chat syndrome was associated with the expression of autistic symptoms. Sixty-nine children with Cri du Chat syndrome were compared with 47 children with moderate to severe intellectual disabilities who did not differ on intellectual severity. The findings suggest that children with high levels of fatigue, regardless of diagnosis, are more likely to exhibit autistic symptoms compared with children who have low levels of fatigue. However, it was the children from the comparison group and who presented with high fatigue levels that conferred the greatest vulnerability to the expression of autistic symptoms. ASD symptoms were less severe in individuals with CdCS than in a matched control group (7). In addition, several studies report a relative strength in non-verbal communication and social interaction skills among CdCS individuals (8,9). It is not clear whether the reported strengths in social interaction skills remain stable over time or whether these areas of behavior demonstrate changes with age (3). On the other hand , another study reported that about half of the 27 children with CdCS had problems with their friends' relationships (9). A recent study identified approximately 40% of children and young adolescents with cri du chat syndrome as fulfilling criteria for autism using the Autism Diagnostic Observation Schedule (6).

The similarity of some of the symptoms of genetic syndromes with ASD and mental retardation makes it difficult to establish a definite diagnosis. Many of these genetic syndromes, which have complex communication, behavioral, emotional and physical problems, can be overlooked, and these individuals only receive ASD diagnosis or vice versa. The possibility of a double diagnosis is not assessed. Therefore, cases with better clinical status can be neglected with specific interventions (6).

It should be kept in mind that a person with a genetic syndrome has similar characteristics to those who have ASD recognition and may benefit from similar educational and other interventions. For this reason, it is important to identify syndromes in which the likelihood of autistic-like behaviors is increasing (6).

CASE PRESENTATION

A two-year, four-month-old male was brought to the Ankara University School of Medicine Child and Adolescent Psychiatry Department because of "unbalanced gait, brief eye contact, delayed speech, repetitive behaviors like flapping wings by his family.

From the story, he was born on the 38 weeks 4 days of pregnancy, with a birth weight of 3,670 gr. It was learned that he had developmental delay in many areas including language, fine-gross motor ability and social-self help areas. He had sucking problem after birth, his head was upright when he was 4 months old, he was sitting without support when he was 8 months old and started to walk at 2 years old, he said his first words at one year old. Toilet training has not been gained yet.

In the psychiatric evaluation of the child, dysmorphic facial features such as hypertelorism, broad nasal root, micrognathia, and microcephaly were evident. The child's walk was ataxic and frequently hit the surrounding furniture. It has been observed that when the child is called with a name, he does not look consistently. He has a

limited eye contact, his joined attention is very bad, he understands simple commands but does not initiate a conversation, he uses few words and can not make any sentences. It has been determined that his social interaction is limited. It was observed that there were stereotypical behaviors such as "flapping wings" in video-mediated observations and did not interact with friends in playgroups. It is learned that the imitation ability does not develop, there are stereotypical movements in the form of rotation around himself, looking for a long time to rotating objects such as a washing machine, a toy car wheel. He also had harmful behaviors (biting, hitting, hair pulling) against people around him. Due to psychiatric evaluations with DSM-5, we started follow-up and treatment with ASD diagnosis.

The developmental evaluation was made with the Ankara Developmental Screening Inventory. It was determined that general development was 18-19 months, language cognitive development 18-19 months, fine motor skills 18-19 months, rough motor skills 20-21 months, and social skills self care development 16-17 months when his age was 28 months.

The case was assessed later by the Department of Pediatric Neurology. Cranial magnetic resonance imaging (MRI) and brain-stem auditory evoked potential (BAER) results were normal. The child was evaluated by the Pediatric Metabolism Department and metabolic screening tests were also normal. In the chromosome analysis; 46, XY, del (5) (p15) structure was shown and Cri du Chat syndrome was diagnosed.

In the follow-up period, special and pre-school education were started. In the follow-up sessions child-parent interaction was observed by Crowell technique and appropriate suggestions and interventions were conducted by the clinical team. Interactive guidance in order to be set up a favorable play between child and parent was given to the family.

DISCUSSION

In this report, a case with CdCS with ASD was presented. Stereotyped behaviors, delays in language development and intellectual disabilities are frequently seen in CdCS as well as in ASD. While social interaction is at a limited level in the ASD, there is inconsistent information about social interaction in CdCS (7) . Some of the studies demostrated that social interaction is normal in individuals with CdCS (7) , on the other hand some others showed that about half of CsCS cases have problems in friend relationships (9). The abnormality of some genes on 5p, such as SEMA5A, CTNND2, elicits an autistic and cognitive phenotype (3).

When we examined the CdCS and ASD relationship, we found a few studies examining the comorbidity but the results were different according to the used evaluation tool. In Moss et al.'s study in 2008, two different tools were used: Social Communication Scale (SCQ) and Autism Diagnostic Observation Schedule (ADOS). Due to SCQ, non of the 23 CdCS had higher scores than autism cut off, but only two (8.7%) had a score that is significant for autism spectrum. On the other hand, with ADOS, 60.9% (14) were in Autism Spectrum while nine of them (39.1%) had an autism diagnosis (6). In another study conducted by the same author in 2013, 63% of cases with CdCS were rated as broad autism phenotype while 13% of the sample were diagnosed as autism (10). Experts suggest that the use of ADOS and SCQ alone for autism diagnosis is not as reliable as expected due to differences between results (6). In 2015, Cochran et al. investigated whether the severity of autism symptoms changed during age progress in CdCS patients and they found that autism and ASD remained stable across these age bands due to SCQ cut off scores (3).

In conclusion, ASD symptoms are common among genetic disorders. But, other medical problems and mental retardation that seen in genetic diseases may cause delay in a recognition of autism spectrum disorders. In addition, the answers of "are ASD and genetic disorders frequently seen together? " or "are all the symptoms are a result of genetic disorders?" are not clear yet and these answers are important to a better understand the etiology of autism and to develop appropriate treatment modalities. We suggest to keep in

mind the CdCS in children with marked dysmorphic facial appearance, motor and language delay, and autism symptoms. It is emphasized that a multidisciplinary approach is necessary in terms of diagnosis and treatment.

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