



# Risperidone Treatment May Benefit Childhood Disintegrative Disorder: Presentation of Two Cases

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**ÖZET:** Risperidon tedavisi çocukluğun dezintegratif bozukluğunda yararlı olabilir. İki olgu sunumu

Çocukluğun dezintegratif bozukluğu, yaşamın ilk 2 yılında sözel ve sözel olmayan iletişim, sosyal etkileşim becerileri, oyun, mesane ve barsak kontrolü ile motor davranış alanlarında normal gelişimi takiben 2-10 yaşları arasında yukarıda belirtilen alanların en az ikisinde gerileme gözlenen nöropsikiyatrik bir sendromdur. Çocukluğun dezintegratif bozukluğunun oldukça seyrek olduğu kabul edilmekte ve gerçek nedeni halen bilinmemektedir. Çocukluğun dezintegratif bozukluğu olan olgular özellikle başlangıç evrelerinde farklı birçok hastalığı taklit ederek tanıda güçlük yaratmaktadır. Bu nedenle daha fazla klinik olgunun sunulması, bozukluğun farklı ortamlarda ortaya çıkış tarzlarını anlamaya yardım edecektir. Literatürde çocukluğun dezintegratif bozukluğu ile ilgili çalışmalar az sayıdadır. Bu yazıda çocukluğun dezintegratif bozukluğu olan iki olgunun risperidon ile tedavisinin sunulması amaçlanmıştır. İlk olgu dört yaşında irritabilite, karşı gelme ve aşırı hareketlilik yakınmalarıyla başlayan ve sonrasında dil gelişiminde gerileme, barsak ve mesane kontrolü ve sosyal etkileşim becerilerinde gerilemesi olan bir çocuktur. İkinci olgu ise dört yaş iki aylıkken dil gelişiminde gerileme ve davranış sorunlarıyla başlayan ve benzer şekilde dil gelişiminde gerileme, barsak ve mesane kontrolünde zayıflık ve sosyal etkileşim becerilerinde azalma olan bir çocuktur. Her iki olguda da davranış sorunlarına yönelik risperidon tedavisi başlanmış ve fayda sağlanmıştır.

**Anahtar sözcükler:** Çocukluğun dezintegratif bozukluğu, risperidon, yaygın gelişimsel bozukluk

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**ABSTRACT:** Risperidone treatment may benefit childhood disintegrative disorder: presentation of two cases

Childhood disintegrative disorder is a neuropsychiatric syndrome characterized by normal development of verbal and nonverbal communication skills, social interaction, play, bladder and bowel control and motor behavior at least in the first two years, followed by regression between 2-10 years of age in two or more of the abovementioned developmental areas. Childhood disintegrative disorder is accepted to be very rare and the exact nature is still unknown. The cases of childhood disintegrative disorder mimic various disorders, especially at initial stages may confuse clinicians to diagnose. Therefore presentation of further clinical cases will assist clinicians to manage in the characterization of the disorder in different settings. Studies related to childhood disintegrative disorder are rare in literature. The purpose of this paper is to present the pharmacological intervention of two cases of childhood disintegrative disorder with risperidone. The first case was characterized by an onset of irritability, defiance and hyperactivity at age of four years, later followed by regression in language, bowel and bladder control and social interaction skills. The second case was a child in which the disorder started with regression in language as well as behavior disturbance at four years two months of age, and then language regression, poor bowel and bladder control and decline in social interaction skills were noticed. Risperidone was used as a pharmacological agent in both cases to control behavioral problems and benefit was achieved.

**Key words:** Childhood disintegrative disorder, risperidone, pervasive developmental disorder

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## INTRODUCTION

Childhood disintegrative disorder (CDD) is one of the pervasive developmental disorders (PDD) which is characterized by normal development of verbal and nonverbal communication skills, social interaction and play, bowel and bladder control and motor skills in the first two years of life, followed by regression between 2-10 years of age in at least two of the above mentioned developmental areas. CDD is accepted to be very rare and the exact nature is still unknown (1,2). The clinical evaluation is currently accepted as the gold standard of diagnosis (2). The cases mimic various other disorders,

especially at the beginning stages and may confuse clinicians (3). Further studies will assist clinicians on how to manage CDD in different settings.

Studies related to CDD are rare in Turkey (4,5). Hence, there are no pharmacologic interventions that specifically target the core deficits of the CDD profile. However, some progress has been made in ameliorating the behavioral symptoms associated with CDD by using antipsychotics (2-5).

Although the key components of treatment are educational and behavioral therapies in PDD (6), pharmacological treatment may be considered as an option when maladaptive behaviors continue to exist (7).

Atypical antipsychotic medications are suggested to use for hyperactivity, attention problems (8), aggressive and self-injurious behaviors (9) in PDD. Among atypical antipsychotic (AA) medications, risperidone is the best studied medication in treatment of behavioral symptoms associated with PDD (7). Risperidone is also the only AA with FDA approval since 2006 for behavioral symptoms in PDD. In addition, risperidone has been shown to safely and effectively reduce behavioral symptoms in PDD in several double-blind and open label studies (7).

The purpose of this paper is to discuss pharmacological treatment with risperidone of two cases with CDD. Risperidone is usually known to be safe and effective in behavioral control of children with pervasive developmental disorders, however reports of its use in CDD management are rare (10).

## CASE 1

Patient was a 5 year 9 months old boy who presented with complaints of language regression and hyperactivity. The disorder started with irritability, hyperactivity and defiance, which lasted nearly all day, when he was four years old. Language regression, loss of bowel and bladder control emerged later. He was a normal developing child with his language skills that started to speak with words at first year and sentences when he was two and a half years old. He had no problem in expressive language skills until he was four years old. The language regression culminated in complete loss of speech, with the child becoming essentially mute when he turned four years old. Nonverbal interaction, social interaction, playing ability and ability to interact within his surrounding also suffered. Stereotypical behaviors and unusual interests emerged later. The parents have no remembrance of the exact timeline of when the deteriorations start. They indicate that he was able to walk when he was one years old and he gained sphincter control when he was three years old. There was no significant family history for both maternal and paternal side.

At the initial mental status examination conducted in May 2008, he was uncooperative and unresponsive to environment. No eye contact could be elicited. Frustration tolerance was reduced. Speech was very limited with immediate echolalia. Motor activity was increased with occasional stereotypical behavior and mannerisms. Sleep

onset was delayed and total sleep time only averaged 6 hours per night while appetite was reduced due to food fads. He lost 3 kilograms in 6 months. Pediatric and neurological examinations were within normal limits. Electroencephalogram (EEG), Magnetic Resonance Imaging (MRI), biochemical, hematologic parameters and metabolic screening tests were all within normal limits. EEG and neurological examination results were used to rule out Landau-Kleffner syndrome. Biochemical, hematological and metabolic diagnostic tests were used to rule out neurocognitive regression in childhood due to metabolic, infectious and mitochondrial etiologies.

The general development of the child was measured by Ankara Development Screening Inventory. The scores were on par with 2 years to 2 years 3 months age equivalency (11). Evaluation with the Childhood Autism Rating Scale (CARS) revealed a score of 44, which corresponds to severe autistic symptoms (12). The choice for management after the initial examination was risperidone with a dose of 0.25 mg/day for a week and increased dosage to 0.50 mg/day for hyperactivity, opposition and irritability. Speech therapy was also commenced. No side effect related to risperidone was reported by the parents and none was observed. Parents were informed about disorder, management and prognosis. In the second evaluation conducted two months after, hyperactivity, opposition and aggression were reduced and compliance to rules improved. Bowel and bladder control, social interaction improved moderately, interest in surroundings improved slightly and stereotypical behaviors, and unusual interests reduced moderately. Evaluation with CARS in the second interview revealed a score of 23 which was below the cut-off score for that scale. It was determined that the relation to others, affective reactions, fear or nervousness and verbal interaction subscales were the most improved. Initially, the focused of therapy was on speech and social interaction. While there were improvements observed in various other domains and that parents' reported slight improvements in irritability and hyperactivity, most of the improvements, especially after the first two weeks of treatment were deemed especially to be due to pharmacological intervention.

## CASE 2

Patient was a 4 years and 5 months 5 year 9 months

old boy who presented with the complaints of regression in speech and behaviors. The complaints started three months prior to the clinical visit, initially with anxiety and decrease in the number of words. Disorganized speech, immediate echolalia and loss of bowel and bladder control occurred a month before the first clinical visit. Spontaneous crying spells, loss of interest in play and in surroundings, reduced social and non verbal interaction were added to the initial complaints. Stereotypical behaviors and interests were also present during the clinical observation. Motor developmental milestones were within normal limits before the onset of complaints with language regression. He started to speak with words at 14<sup>th</sup> month and sentences when he was two and a half years old. There was no significant family history for both maternal and paternal side.

He was uncooperative and unresponsive to the environment during the initial mental status examination conducted in July 2008. He has no eye contact and his speech was very limited. Reportedly his sleep onset was delayed and that total sleep time only averaged 4 hours per night while appetite was reduced due to food fads. He was interested in eating macaroni only for the past 4 weeks and was forced to swallow a few morsels of other foodstuff per meal. He lost 2 kilograms in the month preceding the examination. Pediatric and neurological examinations were within normal limits. EEG, MRI, biochemical, hematologic parameters and metabolic screening tests were all within normal limits. EEG and neurological exam results were used to rule out Landau-Kleffner syndrome. Biochemical, hematological and metabolic diagnostic tests were used to rule out neurocognitive regression in childhood due to metabolic, infectious and mitochondrial etiologies.

Ankara Development Screening Inventory showed that the general development was on par with 1 year to 18 months (11). Evaluation with the CARS revealed a score of 55 which denoted severe autistic symptoms (12). Risperidone 0.25 mg/day was started after the initial examination for hyperactivity, stereotypical behaviors and interests and anxiety and the child was referred for speech therapy. There were no side effects related to risperidone use was reported by the parents and none was observed. Parents were informed about disorder, treatment and prognosis. During the second evaluation conducted three months following the initial visit, hyperactivity and

stereotypical behaviors and interests were found to be reduced moderately. Anxiety and social interaction were noted to improve significantly. Evaluation with CARS in the second interview revealed a score of 28, which was below cut-off for that test (12). The subscales of relation to others, affective reactions and fear or nervousness were the most improved behaviors. Because of the facts that the parents of this child could arrange commencement of the speech therapy only two months after the initial examination due his family's request, the therapy focused on speech and social interaction, while improvements were observed in various other domains and that parents reported improvements in hyperactivity and anxiety before the commencement of second session, after four weeks of treatment, the improvements were deemed especially to be due to pharmacological intervention.

## DISCUSSION

Two cases of CDD from a tertiary medical center treated with risperidone were presented in this paper. The initial predominance of irritability and anxiety in our patients is similar to that reported in the literature (2,5). Later, the clinical progression involved loss of previously normal higher cognitive functions, bowel and bladder control and social interaction and these are also concurrent with previous findings (13).

It is known that over 25% of patients with autism have elevated serotonin levels. This abnormality is not specific and is also observed in many other diseases. Seizure activity is also known to increase serotonin levels in brain tissue. Serotonin is important in that it is involved in early neurogenesis. Altered serotonin modulation of the thalamocortical connectivity during development may possibly explain the abnormal sensory perceptions in patients with autistic regression and perhaps in some patients with CDD (14). We posit that the effect of atypical antipsychotics on CDD might be due to their serotonin antagonism in conjunction with dopamine. It is also possible that abnormalities in serotonin metabolism may identify a subgroup within CDD which may respond to treatment with atypical antipsychotics. Further studies are deemed to be necessary to clarify this hypothesis (14).

Irritability and anxiety which were determined in the initial stage of two cases presented here are very important for both diagnosis and differential diagnosis. It

was reported that a global anxiety and irritability preceded rapid regression in a subgroup of patients with CDD similar to those presented by us and those features may help in differential diagnosis from other pervasive developmental disorders (2).

As it is suggested to use AA for both hyperactivity (8) and aggressive and self-injurious behaviors (9) in patients with PDD, it was reasonable to prescribe AA medication for our patients. Since risperidone was approved by FDA and data supporting risperidone in PDD is more than other AA, it is generally the first choice for behavioral symptoms. Though Shea and colleagues (15) reported that their sample of patients with pervasive developmental disorders responded favorably to a risperidone dose of 0.04 mg/ kg/ day, the dose for used for our patients were 0.03 and 0.02 mg/ kg/ day; respectively. The lower dose may also explain the lack of adverse effects in our patients, though a longer period of follow-up is necessary both to illustrate the course of CDD and to evaluate side effects related to risperidone.

As for other AA, quetiapine does not seem to be

effective in PDD, which may be due to its fast disassociation at dopamine receptors. The use of olanzapine in CDD is limited to a letter (3). There is only a small amount of data for ziprasidone and aripiprazole but these data are promising. According to these reports ziprasidone and aripiprazole did not cause weight gain, and some patients lost weight while receiving these medications. The use of clozapine is limited because of its incidence of agranulocytosis and its potential for lowering the seizure threshold. It is also known that risperidone, olanzapine, and quetiapine all cause to significant weight gain, with weight gain being slightly greater with olanzapine. The clinicians should also be aware of risk for metabolic syndrome which is characterized by hyperglycemia and dyslipidemia while using AA (16).

The main limitation of this case report is that the long term results of pharmacotherapy have not been evaluated and therefore are not reported.

Considering all of these, it can be said that there is a need for more research in the areas of the biology, course and outcome of CDD, as advocated by previous studies.

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