

Patient with Asperger’s syndrome, with episodes of fantasizing and rocking of body, treated with aripiprazole – a case report

Maciej Dul, Krzysztof Walczewski

Dr. Joseph Babinski Specialist Hospital in Cracow

Summary

In this article, we present the case of an adult patient, whose main problem is episodes of fantasizing and rocking lasting up to 12 hours a day and completely preventing school development. The nature of the disorder in the patient is related to the sinking into fantasies, and not typical obsessions as in OCD. The patient was previously treated with drugs from the SSRI group, neuroleptics (without aripiprazole) and methylphenidate. Only methylphenidate showed some improvement; however, it made the patient feel “stiff in thinking”. The patient was hospitalized because of a suicide attempt, which, as it later turned out, was self-harm with no intention of killing himself. During hospitalization, a differential diagnosis was performed and the diagnosis of Asperger’s syndrome was made, which was accompanied by immersion in the world of one’s fantasies and stereotypical behavior. The patient was administered aripiprazole at a dose of 15 mg/d and after three weeks, a significant improvement in health was achieved, including a reduction in the duration of episodes from several hours to several dozen seconds. The drug is well tolerated by the patient. The patient was discharged from the hospital and continues his school education.

In the article, we present single case reports in which similar spectacular results were achieved in similar cases. We also describe a possible physiological explanation for this response to this drug.

Key words: Asperger’s syndrome, aripiprazole, stereotypical behaviors

Introduction

Asperger’s syndrome (sometimes called Asperger’s disorder) was defined as a disease entity relatively recently, around the mid-1980s. Cases of children with a clinical picture corresponding to this definition were very carefully described in the 1940s by the Viennese pediatrician Hans Asperger. Nevertheless, Asperger’s syndrome was officially recognized only in the fourth edition of the Diagnostic and Statistical Manual

of Mental Disorders (DSM-IV) published in 1994 and then in the International Classification of Diseases (ICD-10) in 1996.

The 'Asperger syndrome' is used to describe the mildest cases of autism, mainly related to functional disorders. The frequency of this disorder is defined as 1 in 10,000. The disorder is more common in boys (ratio to girls is 9 to 1). Like all cases of autism, it is a developmental disorder of a neurological background, whose causes are generally unknown. A genetic basis and environmental influences are postulated in the form of excessive intellectualization stimulated by parents with a simultaneous neglect of emotional development.

Typical features of Asperger's syndrome include instances of extremely strong and restricted interest, or limited repetitive stereotypical patterns of behavior, interest or activity. This is manifested in becoming immersed in particular activities or interests for a long period of time, compulsive and non-functional routine, ritual activities or stereotypical motor mannerisms [1, 2]. In addition, difficulties exist in the area of social interactions, perceiving the emotions of other people, and non-verbal communication. Contrary to autism, according to the criteria from the ICD-10, the first three years of development proceed without significant difficulties in terms of speech development, communication, interest in the environment, social interactions or adaptive behavior. The position of this disease entity has changed significantly in recent years. In the DSM-5 classification (in use since 2013), the term "pervasive developmental disorders" and disease entities belonging to it, including autistic disorder and Asperger's syndrome, were dropped and replaced with the term "autism spectrum disorder" (299.00). Moreover, the severity of the disorder was distinguished: L1-L3 as mild, moderate and severe, respectively. Asperger's syndrome is considered here as a mild autism spectrum disorder.

The latest ICD-11 classification also introduces changes by removing the term "pervasive developmental disorders" (F84) and the subcategory of Asperger's syndrome (F84.5), and introducing a separate term "neurodevelopmental disorders" (Block L1-6A0) and placing "autism spectrum disorder" (6A02) in this group. Likewise, here the term "Asperger's syndrome" is absent, but due to clinical features it can be classified under the code 6A02.0 – "Autism spectrum disorder without disorder of intellectual development and with mild or no impairment of functional language" [2-4].

The treatment of Asperger's syndrome is mainly based on educational psychotherapy, emotional expression training and improvement of social relations. Family therapy is often indicated. Additionally, attempts are made to undergo pharmacological treatment. There is no causal treatment for Asperger's syndrome. The use of pharmacotherapy is limited to symptomatic treatment. Pharmacotherapy of this type of disorder causes many problems, it is often frustrating both for the patient and the psychiatrist, and is usually based on symptomatic treatment with off-label medications. A meta-analysis of studies on the use of second-generation antipsychotic drugs – aripiprazole, olanzapine, quetiapine, risperidone and ziprasidone – in the treatment of behavioral disorders associated with autism spectrum disorders, such as irritability and aggression was carried out. The results suggest an improvement in these disorders, but the studies taken into account did not demonstrate high methodological quality [5]. Due

to the presence of negative symptoms similar to those in schizophrenia, another study used risperidone to reduce these symptoms and improvement was achieved [6]. In the treatment of accompanying hyperactivity and attention deficit disorders, studies suggest the use of methylphenidate [7]. Studies have also been carried out with oxytocin in patients with Asperger's syndrome. In one randomized trial, patients were given oxytocin to determine its effect on patients' ability to recognize emotions in other people's faces. At the same time, biological changes were observed with the use of functional magnetic resonance imaging (MRI). The results showed a positive effect of oxytocin on the ability to recognize emotions in these patients. This was associated with increased left amygdala reactivity in response to facial stimuli and increased activity in the neural network involved in social cognition [8].

The treatment process under discussion in this article concerns an adolescent with a pervasive developmental disorder of the Asperger's subtype, diagnosed during hospitalization. The main reasons for hospital treatment were: resignation tendencies, patient isolation and self-inflicted injuries. Suicides and suicidal ideations in young men are still an underrated and insufficiently recognized problem.

The main subject will be the use of an atypical neuroleptic to reduce automatic, intrusive thoughts, agreed upon and thoroughly discussed with the patient. An improvement in mood was achieved along with a higher level of cognitive and social functioning.

Clinical case

The patient is 19 years old. This is his second psychiatric hospitalization. The previous hospitalization was caused by an overdose of benzodiazepine derivatives. The patient was admitted due to self-inflicted injury to the right upper limb, without suicidal tendencies. The patient has been treated psychiatrically from the age of 16 with a diagnosis of obsessive-compulsive disorder. The patient's development in the first three years of his life was normal. The pregnancy was without complications. There were no mental disorders in the family. Until the symptoms appeared, no significant difficulties in learning at school were observed. The patient's primary complaints include body rocking and fantasizing. The content of the fantasy is about being a hero and saving the world. The swaying of the body accompanies these fantasies. In this state, the patient is focused on internal experiences and does not pay attention to the surroundings. The rocking episodes came at different times, lasted for a varying amount of time (up to 12 hours a day), and did not require the repetition of the activity a certain number of times. The onset of symptoms (walking around in a circle) was at the age of 5. Since childhood, the patient liked to focus on a specific task that filled his attention – e.g., stacking building blocks, which sometimes took hours. He has also always avoided people, feeling no need of contact.

Currently, the patient attends an extramural secondary school which he interrupted due to burdensome symptoms. Past history of drug use includes marijuana, benzodiazepine derivatives, mephedrone and methylphenidate. Currently, the patient does not meet the criteria of addiction. For three years, he was treated with many medications,

such as: sertraline 200 mg/d, valproic acid salts 1000 mg/d, sulpiride 100 mg/d, olanzapine, methylphenidate, and clomipramine. In addition to pharmacological treatment, psychotherapy was also applied. The treatment yielded no result. The patient had noted that the use of methylphenidate significantly reduced the symptoms, to the extent that once taken off this medication, he would procure the substance on his own.

During hospitalization, the patient often engaged in fantasizing and rocked his body. At the beginning, he did not cooperate, was withdrawn from contact with others, stayed in bed, and his affect was slightly reduced. Apart from the episodes of fantasizing and rocking, no disorganization of thoughts and behavior was observed. Delusions or hallucinations were not present either. The differential diagnosis included obsessive-compulsive disorder, schizophrenia, stereotypic movement disorder, Tourette's syndrome, and other tic disorders. Obsessions, according to DSM-5, understood as recurrent, experienced as intrusive and unwanted or inappropriate thoughts, impulses or images do not match the revealed experiences of the patient. As mentioned, the content of the patient's fantasies was pleasant and did not cause suffering. The patient focused on these experiences and did not pay attention to his surroundings, which suggests the presentation of an autistic attitude at that time. The swaying of the body accompanying these fantasies was not a reaction to an obsession and was not intended to alleviate the fear or avoid any dangerous event. It took the form of a motor stereotypy (repetitive, seemingly controlled, non-functional motor behavior). This behavior was not in the form of tics (sudden, rapid, repetitive, non-rhythmic motor stereotypies or vocalizations); therefore, it did not meet the criteria for tic disorders, including Tourette's syndrome. Schizophrenia was also excluded.

Psychological testing was carried out, which noted difficulties in social relations and a tendency to over-focus on selected aspects of reality, objects and situations. In the Beck Depression Inventory, the patient scored 28 points – at the level of moderate depression. The overall picture of the patient – history, description of the clinical condition and psychological examination – indicates a diagnosis of Asperger's syndrome or, in the newer classifications: mild autism spectrum disorder. Stereotypical behaviors should be considered here as accompanying the disorder, and not as a separate disease entity. Ultimately, during hospitalization, the patient was diagnosed with Asperger's syndrome and a moderate depressive episode.

Due to the lack of previous efficacy of sertraline, olanzapine, and risperidone and a clinical picture other than OCD, SSRI augmentation with antipsychotics was not initiated and it was proposed to include off-label aripiprazole at a dose of 15 mg/d. At the same time, the medications used by the patient were discontinued. After three weeks, a noticeable reduction of symptoms was achieved. The episodes were sporadic, and lasted up to 20 seconds. Moreover, the patient's mood was stabilized, and there was also a significant improvement in communication and the functioning of the patient, both in terms of daily activity and in the social dimension. The patient stated himself that he has undergone a complete metamorphosis. A further treatment plan as well as life plans were developed with the patient. Until the beginning of the new school year, the patient will be treated at a day ward. Next, he will go to Warsaw to a facility with therapy and ward teaching, in which he will be able to complete his education

in combination with the process of psychotherapy and under medical supervision. The patient is planning to take the maturity (secondary school graduation) exam, and ultimately wants to become an IT specialist.

Discussion

The essence of the presented clinical case is to differentiate the plunging into fantasies and stereotypical behaviors of the patient with intrusive thoughts or activities. A lack of a detailed differential diagnosis may lead to a misdiagnosis of schizophrenia or obsessive-compulsive disorder (OCD) in persons with Asperger's syndrome, especially if the diagnosis is carried out in adulthood. That was the case in our patient. Obsessive-compulsive disorder may occur in the course of Asperger's syndrome. People whose clinical picture is dominated by typical symptoms of OCD can benefit from the use of SSRIs or clomipramine (in accordance with the pathophysiology of this disorder associated with the serotonergic system). However, there are cases where this approach has been insufficient or ineffective. The standard action in the case of SSRI or clomipramine failure in OCD is augmentation with antipsychotic drugs – first with aripiprazole or risperidone, then with haloperidol. At subsequent levels of augmentation, attempts are also made to use other drugs such as lamotrigine, pindolol, memantine, ondasetron or pregabalin [9, 10]. Aripiprazole has been shown to be effective and well-tolerated in the treatment of OCD also in patients with autism spectrum disorder, including hyperactivity and stereotypical behavior, as shown by a recent systematic review and meta-analysis [11, 12].

Antipsychotic drugs can alleviate adjustment disorders and stereotypical behavior. Risperidone has been shown to reduce impulsivity and aggression and may have anti-autism effects [13, 14]. Thus, patients who clearly manifest autism and stereotypical behavior but do not have the typical compulsions may not respond to SSRI medications, such as the patient presented in this article [15]. This is probably due to a different pathophysiology of these symptoms, which may be related to dysregulation of the dopaminergic system. However, it should be remembered that the use of SSRIs in this group of patients may cause impulsivity, aggression and sleep disturbances, and antipsychotics may cause sedation, which may have an impact on school performance and metabolic disturbances [14]. Methylphenidate is used in the treatment of attention deficit disorders associated with Asperger's syndrome [16]. The decision to administer aripiprazole was based on the known activating effect of this medication and the regulatory properties in terms of dopaminergic neurotransmission, whose cortical weakening could explain the symptoms of the patient, especially apathy, lack of motivation, flat affect, and autistic attitude.

There is little data on the use of aripiprazole in Asperger's syndrome in adults. Several similar clinical cases have been described, in which the use of aripiprazole resulted in a spectacular improvement, especially in terms of socialization, broadening of interests and anti-autistic effect. Dratcu et al. [17] describe a patient with misdiagnosed schizophrenia, who was ultimately diagnosed with Asperger's syndrome. After three weeks of aripiprazole treatment with a gradual increase of the dose to 15mg/d,

a clear improvement was achieved. The patient started to engage in the life of the ward, became more willing to make contact, played with other patients, and also participated in occupational therapy.

Staller [18] describes the case of a 34-year-old man with Asperger's syndrome significantly impairing functioning within 20 years of the diagnosis. After administering aripiprazole, an outstanding improvement of the clinical condition took place, which was manifested through increased sociability, a reduced autistic attitude, reduced anxiety and irritability, and increased self-awareness.

Celik et al. [19] cite the case of a 15-year-old boy diagnosed with Asperger's syndrome at the age of 5, who displayed OCD symptoms and who had not undergone pharmacological treatment before. In this case, too, the use of aripiprazole improved the patient's functioning through its anti-autism effect, but also brought a substantial reduction in obsession and compulsion.

Anatomical examinations of the brains of patients diagnosed with Asperger's syndrome and healthy people using quantitative MRI have shown a reduction in the volume of the cerebral hemispheres and caudate nuclei in affected individuals. In addition, people with Asperger's syndrome have significantly less gray matter in fronto-striatal and cerebellar areas than control groups, and there are widespread differences in white matter. A significant reduction in sensorimotor gating was also found. A hypothesis was put forward that Asperger's syndrome is associated with irregularities in the fronto-striatal circuits, which leads to the malfunctioning of sensorimotor gating and, as a consequence, to the characteristic difficulties in stopping repeated thoughts and actions [20].

The above-listed anatomical changes as well as the irregularities in the functioning of the dopaminergic system related to the decrease in the amount of dopamine in the prefrontal cortex are also found in schizophrenia. A decrease in the number of neurons, morphological disorders and a decrease in the number of connections between cells due to the improper development of neural pathways, improper cell migration, or a limited production of trophic factors during fetal life is the basis for the currently adopted neurodevelopmental theory of schizophrenia, especially with its negative symptoms. The impaired functioning of NMDA receptors may cause dopaminergic disinhibition in the mesolimbic pathway, which is associated with positive symptoms, as well as the inhibition of corticopetal dopaminergic transmission, which exacerbates negative symptoms [21]. Common symptoms and the detected similarity of changes at the level of anatomy and neurotransmission suggest the existence of a relationship between schizophrenia and disorders from the autism spectrum. Aripiprazole occupies an important place among the medications currently used in psychiatry because of its unique mechanism as a partial dopaminergic agonist, and the effect of this medication on 5-HT_{2A} and 5-HT_{1A} receptors, resulting in an increase of this neurotransmitter in the structures of prefrontal cortex and the balancing of its activity in schizophrenia and probably also in autism spectrum disorders. Regulating the level of dopamine in the brain may therefore explain the effectiveness of aripiprazole in both diagnoses. In addition, the literature features research concerning attenuating impulsiveness in people overusing and addicted to psychoactive drugs, which can restrict the consumption of alcohol or other psychoactive substances and is probably linked to the stabilizing effect

of aripiprazole – the reduction of the level of dopamine in the nucleus accumbens and the increase in its level in the prefrontal cortex [22].

Summary

Using aripiprazole in monotherapy at a dose of 15 mg/d divided into two doses per day in a patient with Asperger's syndrome, with regular episodes of fantasizing and body rocking lasting for many hours, resulted in a marked improvement of his mental state, which has made it possible for the patient to function properly on a daily basis and enabled his further development. This is yet another known case of a patient who has been successfully treated using aripiprazole. Perhaps further similar descriptions and research on a wider scale will confirm the effectiveness of this medication in persons diagnosed with the autism spectrum or autism itself, and shed more light on the etiology of these disorders and their relationship with schizophrenia at the biological level, which could also support the neurodevelopmental theory of autism spectrum disorder. It is possible that the use of this medication will reduce the use of psychoactive substances by the presented patient.

References

1. Gałęcki P, Szulc A. *Psychiatria*. Wrocław: Edra Urban & Partner; 2018.
2. Puzyński S, Wciórka J. *Klasyfikacja zaburzeń psychicznych i zaburzeń zachowania ICD-10. Opisy kliniczne i wskazówki diagnostyczne*. Warszawa: Uniwersyteckie Wydawnictwo Medyczne „Vesalius”, Instytut Psychiatrii i Neurologii; 2000.
3. Gałęcki P, Pilecki M, Rymaszewska J, Szulc A, Sidorowicz S, Wciórka J, eds. *Kryteria diagnostyczne zaburzeń psychicznych (5th ed.). DSM-5*. Wrocław: Edra Urban & Partner; 2018.
4. <https://icd.who.int/en/> (retrieved: 1.09.2023).
5. Sochocky N, Milin R. *Second generation antipsychotics in Asperger's disorder and high functioning autism: A systematic review of the literature and effectiveness of meta-analysis*. *Curr. Clin. Pharmacol.* 2013; 8(4): 370–379.
6. Rausch J, Sirota E, Londino D, Johnson M, Carr B, Bhatia R. *Open-label risperidone for Asperger's disorder: Negative symptom spectrum response*. *J. Clin. Psychiatry* 2005; 66(12): 1592–1597.
7. Jahromi L, Kasari C, McCracken J, Lee L, Aman M, McDougle C. *Positive effects of methylphenidate on social communication and self-regulation in children with pervasive developmental disorders and hyperactivity*. *J. Autism Dev. Disord.* 2009; 39(3): 395–404.
8. Domes G, Kumbier E, Heinrichs M, Herpertz S. *Oxytocin promotes facial emotion recognition and amygdala reactivity in adults with Asperger syndrome*. *Neuropsychopharmacol.* 2014; 39(3): 698–706.
9. Jarema M. *Standardy leczenia farmakologicznego niektórych zaburzeń psychicznych*. Gdańsk: Via Medica; 2015.
10. Brakoulias V, Stockings E. *A systematic review of the use of risperidone, paliperidone and aripiprazole as augmenting agents for obsessive-compulsive disorder*. *Expert Opin. Pharmacother.* 2019; 20(1): 47–53.

11. Amerio A, Odone A, Ghaemi S. *Aripiprazole augmentation in treating comorbid bipolar disorder and obsessive-compulsive disorder: A systematic review*. J. Affect. Disord. 2019; 249: 15–19.
12. Maneeton N, Maneeton B, Putthisri S, Suttajit S, Likhitsathian S, Srisurapanont M. *Aripiprazole in acute treatment of children and adolescents with autism spectrum disorder: A systematic review and meta-analysis*. Neuropsychiatr. Dis. Treat. 2018; 14: 3063–3072.
13. Khouzam H, El-Gabalawi F, Pirwani N, Priest F. *Asperger's disorder: A review of its diagnosis and treatment*. Compr. Psychiatry 2004; 45(3): 184–191.
14. Foster B, King B. *Asperger syndrome: To be or not to be?* Curr. Opin. Pediatr. 2003; 15(5): 491–494.
15. Sasayama D, Sugiyama N, Imai J, Hayashida A, Harada Y, Amano N. *High-dose paroxetine treatment for an adolescent with obsessive-compulsive disorder comorbid with Asperger's disorder*. Psychiatry Clin. Neurosci. 2009; 63(2): 251.
16. Myers S, Johnson C; American Academy of Pediatrics Council on Children With Disabilities. *Management of children with autism spectrum disorders*. Pediatrics 2007; 120(5): 1162–1182.
17. Dratcu L, McKay G, Singaravelu V, Krishnamurthy V. *Aripiprazole treatment of Asperger's syndrome in the acute psychiatric setting: Case report*. Neuropsychiatr. Dis. Treat. 2007; 3(1): 173–176.
18. Staller JA. *Aripiprazole in an adult with Asperger disorder*. Ann. Pharmacother. 2003; 37(11): 1628–1631.
19. Celik G, Tahiroglu A, Firat S, Avci A. *Aripiprazole improved obsessive compulsive symptoms in Asperger's disorder*. Clin. Psychopharmacol. Neurosci. 2011; 9(3): 134–136.
20. McAlonan G, Daly E, Kumari V, Critchley H, Amelvoort van T, Suckling J et al. *Brain anatomy and sensorimotor gating in Asperger's syndrome*. Brain 2002; 125(Pt 7): 1594–1606.
21. Stahl S. *Stahl's essential psychopharmacology neuroscientific basis and practical application*, 4th ed. Cambridge: Cambridge University Press; 2013.
22. Anton R, Schacht J, Veronin K, Randall P. *Aripiprazole suppression of drinking in a clinical laboratory paradigm: Influence of impulsivity and self-control*. Alcohol. Clin. Exp. Res. 2017; 41(7): 1370–1380.

Address: Maciej Dul
Dr. Joseph Babinski Specialist Hospital in Cracow
e-mail: maciej.dul@interia.pl