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Case Report / Olgu Sunumu

Co-Occurrence of Autism Spectrum Disorder and Very Early Onset Schizophrenia: a Case Report

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ABSTRACT

Co-occurrence of autism spectrum disorder and very early onset schizophrenia: a case report

Very early onset schizophrenia (VEOS) is a chronic and debilitating psychiatric disorder and has received too little attention in the medical literature. Previous studies have suggested that VEOS had a tendency of a worse prognosis and outcome than adult onset schizophrenia. Autism spectrum disorder (ASD) is a life-long impairing heterogeneous disorder, characterized by severe and pervasive impairments in multiple areas of psychological development. Co-occurrence of ASD and VEOS is reported very rarely in the literature. This paper reports on a case diagnosed as ASD with a VEOS comorbidity. With this case report, it is aimed to review the differential diagnosis, common and different clinical features, neuroimaging findings and genetic and environmental etiologies of these two psychopathologies in the light of the literature.

Keywords: Autism spectrum disorder, child, obsessive compulsive disorder, very early onset schizophrenia

ÖZET

Otizm yelpazesi bozukluğu ve çok erken başlangıçlı şizofreni birlikteliği: Bir olgu sunumu

Çok erken başlangıçlı şizofreni (ÇEBŞ), kronik seyreden ve bireyi zayıf düşüren bir psikiyatrik bozukluk olup, literatürde yeterince ilgi görememiştir. Önceki çalışmalar ÇEBŞ'nin gidiş ve sonucunun erişkin başlangıçlı şizofreniden daha kötü yönde eğilim gösterdiğini ileri sürmüştür. Otizm yelpazesi bozukluğu (OYB), psikolojik gelişimin birçok alanında ciddi ve yaygın bozulmalarla karakterize yaşam boyu süren heterojen bir bozukluktur. Literatürde OYB ve ÇEBŞ komorbiditesi oldukça nadir olarak görülmektedir. Bu yazıda ÇEBŞ komorbiditesi olan bir OYB tanılı çocuk sunulmuştur. Bu vaka ile literatür ışığında, OYB ve ÇEBŞ'nin; ayırıcı tanısının yapılması, ortak ve farklı klinik özelliklerinin, beyin görüntüleme çalışmaları sonuçlarının ve genetik, çevresel etmenlerinin gözden geçirilmesi amaçlanmıştır.

Anahtar kelimeler: Otizm yelpazesi bozukluğu, çocuk, obsesif kompulsif bozukluk, çok erken başlangıçlı şizofreni

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INTRODUCTION

Very early onset schizophrenia (VEOS) is a rare neurodevelopmental disorder with severe clinical course and poor prognosis characterized with the onset of psychotic symptoms before the age of 13 causing significant cognitive and social dysfunction (1). VEOS is thought to represent a subgroup of individuals with genetic loading (2). The prevalance of VEOS is less than 1 in 10.000 children (3). It is noteworthy that in the past VEOS cases have been diagnosed as Autism spectrum disorder (ASD) due to similar clinical features, comorbidity or, misdiagnosis (4). Table 1 shows overlapping symptoms in ASD and psychotic disorders.

Table 1: Autism Spectrum Disorder and overlapping symptoms in psychotic disorders.

Autism Spectrum Disorder	Psychosis
Impairment in non-verbal communication	Social withdrawal
Lack of social or emotional reciprocity	Affective flattening
Stereotyped use of language	Disorganized speech
Stereotyped motor mannerisms	Disorganized behaviors
General impairments in social communication	Negative symptoms

Adapted from the study of Cochran et al. (5).

Despite the similar clinical features of VEOS and ASD, differential diagnosis can be made in terms of both the age of onset and the clinical presentation. In order to make schizophrenia diagnosis additionally in children with ASD, DSM-5 requires the presence of distinct hallucinations and delusions sustaining at least 1 month. Concurrent diagnosis of ASD and schizophrenia is not frequent in the literature and limited to case reports.

Studies suggest that similar regions of the chromosomes may have been affected in ASD and schizophrenia (6). Copy number variation (CNV) at 22q11.2 and 16p11.2 have been suggested to pose risks for both ASD and schizophrenia (6). In addition to chromosome regions, some candidate genes have also been affected in both diseases eg., DISC1, CNTNAP2 (7). On the other hand, EN2, reelin, 5-HTT, SLC6A4, AVPR1A genes have been associated with ASD whereas; NRG1, neuregulin, DTNBP1, dysbindin, DAOA, D-serine, DARPP-32, GRM3 and RGS4 genes with schizophrenia spectrum disorders (SSD) and have not been associated with ASD (8).

In a meta-analysis, advanced paternal age and several obstetric complications such as, antepartum bleeding, gestational diabetes mellitus, maternal drug use, low birth weight, congenital malformations and asphyxia, have been reported as common risk factors for schizophrenia and ASD (9).

Brain imaging studies have shown that gray matter volume in the limbic-striato-thalamic region decreased in both disorders (10). It has been shown that the putamen and left anterior insular zone volumes were smaller in the ASD than in the SSD whereas, the cortical surface area in the ASD was larger in contrast to the SSD (10). In addition, increased cerebral ventricular volumes, decreased white matter and total brain volume is a feature of SSD but not present in the ASD (11).

In this article, a case diagnosed with atypical autism at the age of 3 and acquired obsessive-compulsive and psychotic symptoms later on, will be presented.

After receiving the necessary approvals from the family, the patient was admitted to hospital.

CASE

F.D. a 12-year-old, male, sixth grade student has been followed up at an external center with the diagnosis of "atypical autism" and "obsessive compulsive disorder (OCD)". Patient has been referred to Ankara University Faculty of Medicine, Child and Adolescent Psychiatry Clinic by his family with the complaints of shutting down communication with parents, hearing voices, and thus closing the ears with hands, being disturbed by the gaze of people, seeing images that no one else sees, insomnia, anger outbursts, and aggressive behavior, intense obsessions and compulsions that started about 6 months before. F.D. stated that the voices he heard, programmed him, and told him to be afraid of parents and kill them. The symptom of avoiding eye contact has been interpreted as due to the fear of thought insertion or thought broadcasting. Other preliminary diagnoses have been considered and treatments have been applied accordingly at an external medical center, since the psychotic symptoms could not be controlled by outpatient follow-up and treatment and due to the risk of homicide and suicide patient was referred to our clinic and admitted for inpatient treatment.

His medical history lacked any maternal obstetric complications but revealed symptoms such as, delayed speech, lack of peer-related interaction and communication, lack of imaginary play, insistence on sameness, restricted interest, obsessive behaviors, avoiding interaction with the environment and unwillingness to communicate. Hearing tests, neurological testing (electroencephalography [EEG], cranial magnetic resonance imaging [MR]), genetic and metabolic assays have been performed previously and evaluated as "normal"; he was diagnosed with atypical autism at 3 years of age, and at about age of 6 he has had the OCD diagnosis due to cleaning obsessions, such as frequent hand washing and bathing; psychotic symptoms have been around for about 6 months, and increased in the last 3 months with family persecution. It has been identified that the patient has been treated with various

antipsychotic treatments (4mg/day risperidone, 10mg/day haloperidol, 600mg/day quetiapine, 200mg/day zuclopenthixol) for 6 months. It is inferred from the medical history that these antipsychotic treatments have been switched by gradual dose reduction and there is no cause to think of rebound psychosis. There is no history of substance use or non-antipsychotic drug use that may be related to the psychotic findings of the patient. Neither the patient nor the family members described any significant stressor prior to the onset of psychotic symptoms.

It was determined that before the psychotic symptoms started, F.D. had limited relationship with his peers but was able to establish easier relationship with elders and to initiate spontaneous conversation with them; he was specially trained based on the diagnoses of "Borderline Intellectual Functioning and Atypical Autism", and his success at the school was below the class average.

His family history revealed that that his uncle had been diagnosed with schizophrenia, onset of symptoms was similar to those of F.D., and he had been on medical treatment for many years.

In the psychiatric examination: the patient was conscious, although he was occasionally co-operative and oriented, the cooperation and orientation were disturbed while the psychiatric symptoms were active. His attention was distracted and his intelligence was considered roughly as dull. It was determined that his perception was impaired and he had auditory-visual hallucinations. In the process of thinking, perseverations, thoughts of being harmed, thought insertion or thought broadcasting were determined. His affect was blunted and was evaluated as angry, anxious or fearful at times during examination. In the interview, it was observed that, psychomotor activity was already increased but, the subject was prone to outburst, especially during periods of anger. He did not communicate with his parents, persistently asked to grandmother "Is it okay?" and repeated the question until he got the answer "Yes, okay". No pathology was detected in the laboratory examinations (hematological, biochemical and endocrinological examinations) performed before the hospitalization.

The patient had the diagnosis of schizophrenia according to the DSM-5 diagnostic criteria, and 5 mg olanzapine treatment was started, gradually increasing the dose up to 10mg; then, psychotic symptoms showed a significant remission. Olanzapine treatment did not cause any adverse effects including metabolic adverse effects such as weight gain, during the 3 months follow-up period as well. Meanwhile the patient has partially attained functioning he had before the onset of psychotic symptoms; and as the psychotic symptoms regressed, behavioral techniques, individual and family therapies have been added, along with the medical treatment of the patient. In follow-up of symptom severity and response to treatment, the clinical functioning level of the patient and the regression of severity of symptoms were taken into consideration, and no scale was used.

It has been observed that the autistic symptoms such as lack of social-emotional responses, not seeking for relief when distressed, difficulty in spontaneous talking and maintaining a talk, avoiding eye contact, stereotyped and echolalic use of language, insisting on music listening continued but decreased after the psychotic episode.

DISCUSSION

Organic disorders, mood disorders, posttraumatic stress disorder, schizophreniform and schizo-obsessive disorder were considered in the differential diagnosis of a case with positive familial burden but, no neurological, metabolic, hormonal and genetic disorder or history of a birth complication. The fact that previous tests, performed at the external medical centers to exclude organic etiology, appeared normal (MR, EEG, metabolic examinations), the absence of any previous trauma history, the absence of depressive or manic symptoms, and the presence of psychotic symptoms for 6 months drew us away from other diagnoses. In our case, although he had no insight at the beginning, he gained insight into his obsessions

with the treatment thus drawing away from schizo-obsessive disorder as well.

Although it is not a diagnostic subtype and there is no consensus on its definition, schizo-obsessive term is frequently addressed in the literature (12). In a meta-analysis published in 2009, the incidence of obsessive-compulsive symptoms in schizophrenia patients was reported to range 10-64% and OCD frequency varied between 0.0-31.7% (13). It has been suggested that obsessive-compulsive symptoms are associated with earlier onset of schizophrenia, longer hospitalizations, lower levels of age-related functioning, lower rates of employment and marriage, and increased dependence on others (14). Another study reported that the age at onset of obsessive-compulsive symptoms was markedly earlier than the onset of psychotic symptoms and that the first psychotic symptoms started earlier in the schizo-obsessive group (15).

Hallucinations, formal thought disorders, and disorganized behaviors may be difficult to detect in children with developmental disabilities and in young age groups, additionally since there is insufficient knowledge of how the psychotic symptoms will be presented, it is still controversial that whether the children could be diagnosed with schizophrenia prior to the age of six (16).

It is seen that the patient has received a diagnosis of ASD in the early developmental period, with symptoms of delayed speech, inadequacy in peer relations, significant impairment in social interaction and communication, lack of imaginary play, lack of separation anxiety, insistence on sameness, restricted interest and obsessive behavior; then he was followed-up by individual and family therapies and special education support without any medical treatment until adolescence. However, with the adolescence, obsessive symptoms were exacerbated as psychotic symptoms were added to the clinical presentation, the patient's clinic and functioning rapidly deteriorated along with resistance to various antipsychotic treatments.

While no studies comparing the efficacy of olanzapine and other antipsychotics in children with schizophrenia have been reported in the literature, adult studies have concluded that atypical antipsychotics are superior to classical antipsychotics in terms of efficacy and adverse effects (17,18). However, based on the clinical observation and the information obtained from the patient and his family, it is difficult to explain why the response to treatment with atypical antipsychotics such as, risperidone and quetiapine was poor compared to olanzapine treatment in our patient. There is a need for studies with children, using comparative quantitative scales. The study comparing olanzapine and risperidone in adult schizophrenic patients in the literature has not found any difference in terms of adverse effects and efficacy (19). In our patient, previous medical treatments may not have been used sufficient period of time to allow the symptoms to disappear. Apart from the medical treatment of our patient, it is considered that hospitalization and individual and family therapies contributed to the effectiveness of the treatment.

This patient was considered to be diagnosed with ASD in early childhood and later on OCD and schizophrenia diagnoses have been added on however; the lack of significant mental retardation, the patient's being in the high-functioning ASD range, the onset of schizophrenia symptoms being rapid and in very early childhood, symptoms being severe and disorganized, the uncle's having been diagnosed with schizophrenia suggest the idea that: symptoms of high functioning ASD observed in the early childhood might have been the prodromal symptoms of schizophrenia and since they have common clinical features, psychopathology has evolved along with the developmental phase of the child. A sufficient number of prospective follow-up cases are needed in order to make a definite interpretation as to whether it is a comorbidity added on during the clinical course or early autistic symptoms are prodromal symptoms of schizophrenia.

In this report we examined our case from a developmental point of view, common symptoms of ASD and schizophrenia, common and different genetic, environmental factors, brain imaging findings and differential diagnosis are addressed in the light of the literature. It is inferred that studies on etiopathogenesis, diagnosis and treatment of these disorders, which still have many unknown aspects, should continue.

Contribution Categories	Name of Author
Follow up of the case	D.K., P.U., A.S.A.
Literature review	D.K., P.U., A.S.A.
Manuscript writing	D.K., P.U.
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