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

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 prevalence 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>
<thead>
<tr>
<th>Autism Spectrum Disorder</th>
<th>Psychosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairment in non-verbal communication</td>
<td>Social withdrawal</td>
</tr>
<tr>
<td>Lack of social or emotional reciprocity</td>
<td>Affective flattening</td>
</tr>
<tr>
<td>Stereotyped use of language</td>
<td>Disorganized speech</td>
</tr>
<tr>
<td>Stereotyped motor mannerisms</td>
<td>Disorganized behaviors</td>
</tr>
<tr>
<td>General impairments in social communication</td>
<td>Negative symptoms</td>
</tr>
</tbody>
</table>

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, SLCA6A4, 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 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.
REFERENCES


2. Kumra S, Charles Schulz S. Editorial: research progress in early-onset schizophrenia. Schizophr Bull 2008; 34:15-17. [CrossRef]


6. Sebat J, Levy DL, McCarthy SE. Rare structural variants in schizophrenia: one disorder, multiple mutations; one mutation, multiple disorders. Trends Genet 2009; 25:528-535. [CrossRef]

7. Chubb JE, Bradshaw NJ, Soares DC, Porteous DJ, Millar JK. The DISC locus in psychiatric illness. Mol Psychiatry 2008; 13:36-64. [CrossRef]


