Early-onset bipolar disorder is difficult for child psychiatrists in terms of both diagnosis and treatment. The proper diagnostic evaluation is negatively impacted by the atypical clinical manifestation and rapid cycling pattern of the disease, together with common comorbidity with attention-deficit hyperactivity disorder and anxiety disorder. In addition to poor insight, nonadherence to treatment, poor family coping skills, and insufficient child psychiatric inpatient units make clinicians unsuccessful in following up and treating such patients. Risperidone is a commonly used atypical antipsychotic; it has been approved for the treatment of manic and mixed episodes of bipolar disorder even in 10–17-year-old patients, and it is commonly used. It has a long-acting injectable formulation. Studies on its long-acting form in younger children are limited. In this case presentation, the diagnostic procedure in an 11-year-old child with bipolar disorder will be presented. Long-acting injectable risperidone use in the case of nonadherence to treatment and observed side effects will be discussed.

**Keywords:** Bipolar disorder, risperidone, antipsychotic drugs, blurry vision

**INTRODUCTION**

Bipolar disorder (BD) is a multidimensional illness characterized by fluctuating periods of depression and mania, cognitive dysfunction, abnormal circadian rhythms, and multiple comorbid psychiatric and general medical conditions. Early-onset BD is difficult to diagnose due to definition problems such as “narrow type–broad type,” the rapid cyclic pattern, and the unclear transition between manic and hypomanic episodes. Besides the diagnostic problems, poor insight, nonadherence to conventional treatment, irritability, characteristics of the disease itself, and insufficient documented data on child pharmacotherapy make the treatment more complicated (1). Risperidone is a commonly used second-generation antipsychotic agent (SGA) recently approved for the treatment of schizophrenia in adolescents aged 13–17 years and for the short-term treatment of manic or mixed episodes of bipolar I disorder in children and adolescents aged 10–17 years (2). Recent studies have suggested that depot formulations of SGA are considered for controlling mood episodes in BD patients who have relapsed due to medication nonadherence or who failed to respond to standard therapies (3,4). Fu et al. (5) reported case series with the usage of long-acting injectable risperidone in children with pediatric BD who showed treatment nonadherence.

Here we report the case of an 11-year-old girl with BD who presented with atypical symptoms before the onset of the disease. Furthermore she was nonadherent to standard oral treatments. She became euthymic after the administration of long-acting injectable risperidone doses. We aimed to discuss the clinical course and observed side effects. Her family provided consent on writing the report, and we disguised her identity.
CASE

The patient was an 11-year-old girl who had visited many clinics (e.g., general pediatrics, pediatric surgery) with several complaints such as boredom, shortness of breath, agitation, school refusal, dyspnea, stomach ache, and sleep disturbances. She was also negativist and was rude to her parents. No organic etiology was found by other disciplines. When she had school refusal, she was referred to our child psychiatry outpatient clinic.

She was brought in by her biological parents with complaints of fear of being alone, shortness of breath, and not wanting to go to school. She was negativist and hit her parents many times. Her medical history records showed that her prenatal and postnatal histories were unremarkable. She had normal mental and motor developmental milestones. She had no chronic physical disorder, trauma, or accident. Her school performance was unremarkable till this year. There was a positive history for obsessive-compulsive disorder for her father and hypothyroidism for her mother; otherwise, her family was healthy. Her mother was a housewife, and her father was a civil-servant with a primary school degree. She had two elder sisters.

At the first visit, she was diagnosed with separation anxiety disorder and comorbid oppositional defiant disorder: Fluoxetine (10 mg/day) for anxiety disorder and olanzapine (2.5 mg/day) for sedation and temper outbursts were suggested. After 3 weeks, she quarreled with her mother again and attempted suicide with her mother's thyroid hormone drugs. When she was admitted to our clinic, she was hopeless and tearful. She was diagnosed with major depressive disorder. Her fluoxetine dosage was increased to 20 mg/day.

At the end of the 6th week, she showed manic symptoms, such as impulsivity, irritability, mood elevation, decreased sleep time, and talkativeness. No psychotic symptoms were observed. Therefore, fluoxetine was stopped, and the olanzapine dosage was increased to 10 mg/day.

Her family brought her after 3 days because she refused to swallow the prescribed pills. She had poor insight. Solution forms of sodium valproate (400 mg/day) and risperidone (2 mg/day) were chosen as medications to drink with water. However, her family was unsuccessful in keeping her safely and properly giving her the medications. She would hit her parents and run away from home. During the follow-up, she had attempted to commit suicide 3 times and refused to take medications. After 7 weeks from the first visit to our clinic, as she was suicidal, she was suggested to be hospitalized. There was no child psychiatry inpatient clinic in our center. Her family gave permission to treat her in the adult psychiatry ward. She was followed up by a child psychiatrist in the inpatient clinic.

In the inpatient unit, her psychiatric assessment was as follows: her affect was lively, and her mood was elevated. No hallucinations were observed. She had grandiose delusions; she believed that she was immortal and the strongest child in the city. She threatened to bite the medical stuff if they tried to hold her. She was diagnosed with BD by a DSM-IV-based diagnostic tool, Schedule for Affective Disorders and Schizophrenia for School Age Children-Parental and Lifetime Version-Turkish Version assessment (6,7). The Young Mania Rating Scale (YMRS) was used at follow-up (8,9).

Her YMRS score was 40 at the first visit. Side effects were evaluated at every visit. During hospitalization, electroencephalography and cranial magnetic resonance imaging were conducted, and no abnormality was observed. Her IQ was measured. It was in the normal range with many attentional problems.

During the follow-up, she was negative to every approach; she had agitated many times in the ward. Her mood changed quickly in a day. An oral form of haloperidol was given, but she refused it. In the first 3 days, for acute sedation, intramuscular injections of haloperidol (20 mg/day) and biperiden (4 mg/day) were administered. Alprazolam (3 mg/day) was added on the third day. She developed dystonia; therefore, haloperidol injections were stopped. She suffered from insomnia; chlorpromazine (100 mg/day) for 2 days and clonazepam (4 mg/day bid) were tried. She had taken oral form risperidone before, so on the 4th day, olanzapine was started. Olanzapine (20 mg/day) and clonazepam (2 mg/day) were given two times a day. For mood stabilization, valproate (400 mg/day) was added on the 8th day.

Due to agitation and nonadherence to the oral forms of drugs, olanzapine (10 mg, two times a day) injections were started on the 10th day of hospitalization. Her mood was moderately high, and her YMRS score was 20. The ward was designed for both male and female adult patients. She started to imitate adult patients, for example, she started to smoke. Therefore, a quick discharge was planned. After 2 weeks, her final mental state examination was as follows: her affect was irritable, her mood was slightly high, and she had no thought problems or hallucinations. She could sleep enough. Her grandiosity level was lowered, and she did not think she was immortal. She was discharged with olanzapine (10 mg/day i.m.) and Na-valproate solution (400 mg/day).

Unfortunately, nonadherence was experienced again. Her family was incapable of administering drugs. She showed temper tantrums while going to the nurse's office for daily injections. Therefore, after obtaining her family's consent, long-lasting risperidone (25 mg) injection (i.m.) two times a month was given. Olanzapine and valproate were stopped. Oral risperidone (2 mg/day) was added in its depot form. However, she did not take oral form. At the end of 6 weeks, after three injections, she became euthymic, her YMRS score was 4, and she started going to school again.

Unfortunately, side effects were observed; there were weight gain (10 kg in a 2-months period) and blurred vision (no ophthalmological reason was found). Her eye complaints started after 7 weeks of risperidone medication. Therefore, the long-acting risperidone regime was stopped at the end of the 8th week of medication. After a week, her vision became normal. We provided psychoeducation. She was prescribed only valproate (400 mg/day), and she was cooperative and took her medications. However, she gained 1 kg after 2 months, and she was still euthymic by valproate maintenance.

DISCUSSION

The patient presented above exhibited different symptoms before the onset of pediatric BD. Lack of treatment adherence and adequate family cooperation, she failed to treat with conventional psychotropes. We used long-acting risperidone to maintain proper mood stability and compliance to oral treatment. Our patient's clinical presentation was similar to the first case of Fu et al (5). Their case was of an 11-year-old boy with major depressive disorder and school refusal, and when an antidepressive agent was administered, he developed a manic shift; he also showed daily mood changes that were similar to those in our patient.

The definite diagnosis of early-onset BD is difficult due to overlapping symptoms of other psychiatric disorders such as anxiety disorder; attention-deficit hyperactivity disorder; and conduct disorder (1,5). The episodic pattern of BD is mostly rapid cycling in children. Ultradian cycling (>365 cycles per year) was defined by Geller in 1998 (10). Considering this pattern, the treatment of pediatric-onset BD is more complicated than that of adult-onset BD. However, mood stabilization is more important in pediatric BD because earlier-onset BD is associated with a higher incidence of suicide attempts and violence (2).

In our case, we failed to observe mood stability with oral preparations. Therefore, injections were considered. First, olanzapine i.m. injection was administered. However, maintenance treatment with daily injections of olanzapine was inconvenient and frightening for a child. Finally, long-acting risperidone injection per 2 weeks was considered as the best choice for our patient.
Many studies on long-acting injectable risperidone have showed effectiveness. The FDA approved long-acting injectable risperidone as a monotherapy and adjunctive therapy to lithium or valproate for the maintenance of bipolar I disorder in 2009 (11). Long-acting risperidone may be advantageous over first-generation antipsychotics; it has less extrapyramidal adverse effects. Two important side effects were observed in our case. Weight gain is a commonly encountered side effect of all SGAs (12). Significant antihistaminic properties, 5HT2-C receptors, and muscarinic–acetylcholine receptors are responsible for weight gain (2). Our first therapeutic choice, olanzapine and then risperidone, had negative impacts on weight. Blurry vision is not a rare side effect of antipsychotics, although it is not commonly evaluated in children on risperidone treatment. Ozibilin and Adams (13) reported that the prevalence of blurred vision observed on risperidone treatment was 11.9%. This effect is temporary until the dosage decreases.

A definite pharmacological treatment is often required for BD, yet the modest effects of available treatments and frequent difficulties with tolerability and adherence present complex challenges. Long-acting injectable medications offer a therapeutic alternative to oral mood stabilizers and may help facilitate long-term treatment adherence (10). When mood stabilization is accomplished, maintenance treatment for 6 months–2 years is needed in BD. However, up to 50% of BD patients are nonadherent or partially adherent to antipsychotic treatment (14). For this reason, novel delivery systems that may improve adherence require careful consideration (15).

Our case shows that long-acting risperidone injection is useful for patients with BD who cannot receive oral preparations and who are nonadherent to treatment. Side effects must be closely monitored in a developing child.

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