

Atypical Symptoms Before the First Episode in Bipolar Children and Adolescents

Bipolar Bozukluğu Olan Çocuk ve Ergenlerde İlk Ataktan Önce Atipik Belirtiler

Ayşegül Yolga TAHİROĞLU, Gonca Gül ÇELİK, Ayşe AVCI

Çukurova Üniversitesi Tıp Fakültesi, Çocuk ve Ergen Ruh Sağlığı ve Hastalıkları Anabilim Dalı, Adana, Turkey

ABSTRACT

In this study, atypical symptomatology and difficulties concerning the differential diagnosis of bipolar disorder (BPD) in children and adolescents before the first episode are discussed through 4 cases aged 5, 13, 14 and 16 years. Although all cases were treated and followed for months/years with diagnoses such as conduct disorder, attention deficit hyperactivity disorder, borderline disorder, dissociation, and psychosis, their diagnoses were considered as BPD after months or years. Misdiagnosis and/or delayed diagnosis of BPD are common among children and adolescents. Use of stimulant or antidepressant agents provoked manic symptoms, while antipsychotics (risperidone and aripiprazole) and mood stabilizers (valproic acid and lithium) were useful as combined and/or mono therapy for these cases. BPD should be considered in the differential diagnosis in child and adolescent cases with atypical symptomatology and treatment resistance. (*Archives of Neuropsychiatry 2009; 46: 34-6*)

Key words: Bipolar disorder, differential diagnosis, child, adolescent

ÖZET

Bu çalışmada 5, 13, 14 ve 16 yaşlarında 4 olgu sunumu aracılığı ile çocuk ve ergenlerde bipolar bozukluğun (BPB) ilk atağından önceki tipik olmayan belirti dağılımı ve ayırıcı tanı güçlükleri tartışılmıştır. Tüm olgular başlangıçta davranım bozukluğu, dikkat eksikliği hiperaktivite bozukluğu, sınırdaki bozukluk, disosiyatif bozukluk, psikoz gibi farklı tanımlarla aylar/yıllar boyunca izlenmiş olmalarına rağmen, daha sonra tanıları BPB olarak değiştirilmiştir. Çocuk ve ergenlerde BPB'nin yanlış ve/veya geç tanısı sık rastlanan bir durumdur. Olgularımızda stimulan ya da antidepresanların kullanımı manik belirtilerde artışla sonuçlanmış; antipsikotiklerin (risperidon, aripiprazol) ve duygudurum düzenleyicilerin (valproik asit ve lityum) tek tek ya da birlikte kullanılmaları ise fayda sağlamıştır. Ruh sağlığı uzmanları tipik olmayan ve tedaviye dirençli belirtileri olan çocuk ve ergenlerin ayırıcı tanısında BPB'yi göz önünde bulundurmalarıdır. (*Nöropsikiyatri Arşivi 2009; 46: 34-6*)

Anahtar kelimeler: Bipolar bozukluk, ayırıcı tanı, çocuk, ergen

Introduction

According to studies in large community samples, pediatric BPD prevalence was found to be 0.1 - 2% (1). Additionally, 50 - 60% of bipolar adults recalled the initial onset of mania or depression at 19 years or younger (2,3) and one-third of subjects with BPD had early onset (4). Pediatric bipolar disorder (BPD) is characterized by the early age of onset of mood disturbance; long duration; fluctuating course; high familial loading for mood and other psychiatric disorders; high rates of co-morbid psychiatric disorders particularly attention deficit/ hyperactivity disorder (ADHD), disruptive behavior, anxiety disorders, and psychosis; and prevailing mixed/ rapid cycling episodes (2,5,6). Early recognition and treatment of BPD

in children and adolescents is important to ameliorate ongoing symptoms and to reduce or prevent serious psychosocial morbidity (6,7,8). In 74% of individuals with BPD, psychopathology is recognizable before age 3, usually as mood and sleep disturbances, hyperactivity, aggression, and anxiety but pediatric BPD is often mis- or undiagnosed (9).

Comorbid psychiatric disorders are common in BPD. However, it is not well known whether individuals with bipolar disorder are at risk for future psychiatric disorders or whether individuals with other psychiatric disorders are at risk for bipolar disorder. In this study, atypical symptomatology before the first episode and diagnostic difficulties of BPD among children and adolescents are discussed through the description of 4 cases.

Address for Correspondence/Yazışma Adresi: Dr. Ayşegül Yolga Tahiroğlu, Çukurova Üniversitesi Tıp Fakültesi, Çocuk ve Ergen Ruh Sağlığı ve Hastalıkları Anabilim Dalı, Adana, Turkey E-mail: ayolga@gmail.com **Received/Geliş tarihi:** 22.11.2008 **Accepted/Kabul tarihi:** 07.02.2009

© Nöropsikiyatri Arşivi Dergisi, Galenos Yayıncılık tarafından basılmıştır. Her hakkı saklıdır. / © *Archives of Neuropsychiatry*, Published by Galenos Publishing. All rights reserved.

Case Reports

Case 1: A 5 year old girl with symptoms of hyperactivity, impulsivity, acting outs, oppositional behavior, aggression to other children and her mother. Methylphenidate 10 mg/day was started with a diagnosis of (ADHD) in another psychiatry clinic through 8 months. After initiation of this treatment, her hyperactivity improved slightly, while other symptoms were aggravated, with prominent mood lability and irritability. Her mother had reported that her symptoms were episodic with a duration of one or two days, these episodes were more frequent and severe through the 8 months of methylphenidate treatment. This treatment was stopped for 4 months, and her symptoms moderated to the level of pretreatment with methylphenidate. Diagnostic reevaluation of the case put BPD in the differential diagnoses because of mood lability, severe irritability as a cardinal symptom, lacking efficacy of methylphenidate, and increased frequency of episodes with stimulant treatment, Valproic acid 20 mg/kg/day was started. Her symptoms markedly improved after the second month of this treatment; and this might also support the BPD diagnosis.

Case 2: A 13 year old girl presented with audio-visual hallucinations, disorganized behaviors, insomnia, bizarre outfit and secondary diurnal enuresis. Risperidone 2 mg/day was given with a diagnosis of atypical psychosis. This treatment was maintained through 18 months with a moderate improvement but full remission was not seen. Because of side effects, including galactorrhea and extrapyramidal symptoms (EPS), this treatment was changed to aripiprazole 10 mg/day. Her symptoms improved dramatically in the first few months of medical treatment. She stopped taking her drugs herself at the end of 6 months of this treatment, then insomnia, grandiosity, seductive behaviors, increased sexual behavior and irritability symptoms emerged. Therefore her first clinical presentation was evaluated in detail. Her mother reported mood lability with depressive and euphoric states more than once in a day, so BPD was considered in the differential diagnosis because of the labile mood, beneficial effects of antipsychotic and manic excitation just after stopping antipsychotic drugs. Aripiprazole resulted in successful mood regulation and she is now in remission for two years.

Case 3: A 16 year old girl. had audio-visual and tactile hallucinations, conversion attacks such as syncope and fugue, bizarre anxiety attacks including self-mutilation and amnesia. Risperidone 1 mg/day was started with a diagnosis of dissociative disorder. This treatment helped symptom reduction. However, one year later she had one mixed (insomnia, depressive mood, suicide ideas, impulsivity, seductive behaviors, increased sexual behaviors and irritability) and one manic episode (grandiosity, impulsivity, excessive talkativeness, seductive behaviors, increased sexual behaviors and irritability) while she was still using the drug. BPD was considered as the differential diagnosis because of the observed typical mixed and manic excitations despite regular antipsychotic using. Valproic acid 20 mg/kg/day was added to the regimen after which her symptoms were significantly improved for two years.

Case 4: A 14 year old girl had symptoms of agitation, impulsivity, acting outs, important conflicts with other family members, seductive behaviors and self-mutilation. Risperidone 1 mg/day and valproic acid 20/mg/kg/day were given with a diagnosis of conduct disorder (CD) and/or borderline personality disorder. Moderate improvement of symptoms was observed as from the second month of this treatment. A manic episode including grandiosity, insomnia, excessive talkativeness, seductive behaviors, increased sexual behaviors, excessive spending and severe irritability was observed a year later while she was under this treatment. Her diagnosis was considered as BPD due to the observed typical manic excitation despite regular antipsychotic using. Her symptoms improved with a combination of risperidone 2 mg/day and lithium 900 mg/day so the diagnosis of BPD was supported.

Discussion

It is thought that one-third of subjects with BPD had an early onset characterized with an onset before 18 years old (10). Early onset BPD is associated with; female gender, more lifetime psychotic symptoms, greater overall co-morbidity, and a greater length of time from first episode to treatment (4). Similarly, all cases in this study were female, although the symptoms of all cases were atypical in the first presentation and follow-up.

Psychotic symptoms are more common among children and adolescents with BPD than in adults, and dysphoria is more likely than euphoric or depressive moods. Asymptomatic intervals rarely exist, whereas rapid cycling is frequent (11). Similarly, case 2 and 3 had psychotic symptoms such as hallucinations and disorganized behaviors. When psychotic symptoms are seen, clinicians may diagnose the condition as "psychosis" because of their daily routine practices. However, psychotic symptoms can be present in many conditions apart from psychosis in children and adolescents. It was reported that none of the subjects reporting atypical psychotic symptoms went on to develop a classic psychotic illness by the second year follow-up (12), and 24% had bipolar disorder, 41% had major depression, 21% had sub-syndromic depression, and 14% had schizophrenia spectrum disorders (13).

Children with BPD and comorbid ADHD have higher initial rates of other comorbidities, more symptoms of ADHD, worse scores on checklists, and a greater family history of mood disorder (14). This comorbidity is common but diagnostic errors are also frequent in these cases. Children who presumably have ADHD often have an unrecognized affective illness. There is a widely accepted view that modified criteria of BPD should be used for children because of atypical symptomatology and course of BPD through childhood so many children and adolescents with BPD are misdiagnosed as ADHD because of the similar diagnostic criteria for both diagnoses (15). The clinical future of childhood BPD is unlike the adult cases, and reconsideration of diagnostic criteria is an important need. Stimulants may be useful for some symptoms especially inattention and hyperactivity in the children with ADHD-BPD comorbidity (16,17). It is well documented than antidepressants have a greater risk of manic switch (18,19). Stimulants seem

safer than antidepressants but it should be kept in mind that manic symptoms may be aggravated by stimulants, also (20,17). This was illustrated in case 1 where irritability and aggression symptoms were aggravated by methylphenidate despite limited beneficial effects.

Irritability as a symptom of mania is an important finding when manic symptoms in pediatric bipolar disorder present episodically (21). Irritability in ADHD, oppositional defiant disorder (ODD) and childhood BPD must be differentiated. There are certain features helping the clinician in making this distinction; irritability in BPD includes more severe insomnia, agitation, distractibility, racing thoughts, flight ideas, pressured speech, intrusiveness, temper tantrums triggered by negative emotional stimuli and frustration (21). All cases in this study had irritability and two of four cases were also diagnosed as destructive behavior disorders at first. Consistent with the literature, their behavioral and emotional problems were more severe than expected for children with ADHD, ODD or CD (21,22).

Mood stabilizers such as lithium, divalproex and carbamazepine are suggested for treatment of children and adolescents with BPD which are known to have acute anti-manic effects and provide relapse prevention (11,16,23,24). In addition, atypical antipsychotics have recently gained more importance in the treatment of manic states in children and adolescents, (11,13,23,24,25). However, more information is needed about the long-term treatment of mania, treatment of bipolar depression, and treatment of co-morbid psychiatric conditions. Mono therapy or combination therapy of atypical antipsychotic and mood stabilizers were both useful and well tolerated in the treatment of all cases in this study.

In summary, BPD in children and adolescents can commonly be mis- and/or undiagnosed. Clinicians should consider BPD in child and adolescent cases who have atypical symptomatology, and treatment resistance.

References

- Johnson JG, Cohen P, Brook JS. Associations between bipolar disorder and other psychiatric disorders during adolescence and early adulthood: a community-based longitudinal investigation. *Am J Psychiatry* 2000; 157: 1679-81.
- Lish JD, Dime-Meenan S, Whybrow PC et al. The National Depressive and Manic-Depressive Association (DMDA) survey of bipolar members. *J Affect Disord* 1994; 31: 281-94.
- Perlis RH, Miyahara S, Marangell LB et al. STEP-BD Investigators. Long-term implications of early onset in bipolar disorder: data from the first 1000 participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Biol Psychiatry* 2004; 55: 875-81.
- Suominen K, Mantere O, Valtonen H et al. Early age at onset of bipolar disorder is associated with more severe clinical features but delayed treatment seeking. *Bipolar Disord* 2007; 9: 698-705.
- Axelson D, Birmaher B, Strober M et al. Phenomenology of Children and Adolescents With Bipolar Spectrum disorders. *Arch Gen Psychiatry* 2006; 63: 1139-48.
- Birmaher B, Axelson D, Strober M et al. Clinical Course of Children and Adolescents With Bipolar Spectrum Disorders. *Arch Gen Psychiatry* 2006; 63: 175-83.
- Biederman J, Faraone SV, Wozniak J et al. Further evidence of unique developmental phenotypic correlates of pediatric bipolar disorder: findings from a large sample of clinically referred preadolescent children assessed over the last 7 years. *J Affect Disord* 2004; 82: 45-58.
- Kowatch RA, Fristad MA, Birmaher B et al. Child Psychiatric Workgroup Members. Treatment guidelines for children and adolescents with bipolar disorder: Child Psychiatric Workgroup on Bipolar Disorder. *J Am Acad Child Adolesc Psychiatry* 2005; 44: 213-35.
- Faedda GL, Baldessarini RJ, Glovinsky IP et al. Pediatric bipolar disorder: phenomenology and course of illness. *Bipolar Disord* 2004; 6: 305-13.
- Frazier JA, Hodge SM, Breeze JL et al. Diagnostic and Sex Effects on Limbic Volumes in Early-Onset Bipolar Disorder and Schizophrenia. *Schizophr Bull* 2008; 34: 37-46.
- Aichhorn W, Stuppach C, Kralovec K et al. Child and adolescent bipolar disorder. *Neuropsychiatr* 2007; 21: 84-92.
- Hlatala SA, McClellan J. Phenomenology and diagnostic stability of youths with atypical psychotic symptoms. *J Child Adolesc Psychopharmacol* 2005; 15: 497-509.
- Ulloa RE, Birmaher B, Axelson D et al. Psychosis in a pediatric mood and anxiety disorders clinic: phenomenology and correlates. *J Am Acad Child Adolesc Psychiatry* 2000; 39: 337-45.
- Biederman J, Faraone SV, Mick E et al. Attention-deficit hyperactivity disorder and juvenile mania: an overlooked comorbidity? *J Am Acad Child Adolesc Psychiatry* 1996; 35: 997-1008.
- Dilsaver SC, Henderson-Fuller S, Akiskal HS. Occult mood disorders in 104 consecutively presenting children referred for the treatment of attention-deficit/hyperactivity disorder in a community mental health clinic. *J Clin Psychiatry* 2003; 64: 1170-6.
- Kowatch RA, DelBello MP. Pharmacotherapy of children and adolescents with bipolar disorder. *Psychiatr Clin North Am* 2005; 28: 385-97.
- Pagano ME, Demeter CA, Faber JE et al. Initiation of stimulant and antidepressant medication and clinical presentation in juvenile bipolar I disorder. *Bipolar Disord* 2008; 10: 334-41.
- Leverich GS, Altshuler LL, Frye MA et al. Risk of switch in mood polarity to hypomania or mania in patients with bipolar depression during acute and continuation trials of venlafaxine, sertraline, and bupropion as adjuncts to mood stabilizers. *Am J Psychiatry* 2006; 163: 232-9.
- Truman CJ, Goldberg JF, Ghaemi SN et al. Self-reported history of manic/hypomanic switch associated with antidepressant use: data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *J Clin Psychiatry* 2007; 68: 1472-9.
- Wingo AP, Ghaemi SN. Frequency of stimulant treatment and of stimulant-associated mania/hypomania in bipolar disorder patients. *Psychopharmacol Bull* 2008; 41: 37-47.
- Rich BA, Schmajuk M, Fox NA et al. Different Psychophysiological and Behavioral Responses Elicited by Frustration in Pediatric Bipolar Disorder and Severe Mood Dysregulation. *Am J Psychiatry* 2007; 164: 309-17.
- Leibenluft E, Charney DS, Towbin KE et al. Defining Clinical Phenotypes of Juvenile Mania. *Am J Psychiatry* 2003; 160: 430-7.
- MacMillan CM, Withney JE, Korndörfer SR et al. Comparative clinical responses to risperidone and divalproex in patients with pediatric bipolar disorder. *J Psychiatr Pract* 2008; 14: 160-9.
- Pavuluri MN, Henry DB, Carbray JA et al. Open-label prospective trial of risperidone in combination with lithium or divalproex sodium in pediatric mania. *J Affect Disord* 2004; 82: 103-11.
- Chang KD. The use of atypical antipsychotics in pediatric bipolar disorder. *J Clin Psychiatry* 2008; 69: 4-8.