Childhood Bipolar Disorder: A Clinical Vignette

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Bipolar disorder in children and adolescents can easily be misdiagnosed, as symptom patterns overlap with other mood disorders and attention-deficit/hyperactivity disorder and commonly differ from adult presentations. A detailed description of the child's behavioral history and previous treatment response is critical to accurate diagnosis. Although studies with children are limited, a number of psychopharmaceuticals have been shown to provide therapeutic benefit. Parent/caregiver and educational support are essential components of successful treatment. This article describes an 11-year-old patient with bipolar disorder and then summarizes related treatment issues and options.

(Prim Care Companion J Clin Psychiatry 2005;7:231–234)

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Bipolar disorder in children and adolescents, though perhaps more prevalent than generally acknowledged,[1] is difficult to recognize and treat for several reasons. It has a similar symptom pattern with the more widely recognized disorder of attention-deficit/hyperactivity disorder (ADHD),[2,3] can be comorbid with ADHD,[1] and may be associated with behavior patterns such as antisocial behavior and school failure that are different from what is typical in their adult counterparts (Table 1).[4]

Children with a family history of bipolar disorder are about twice as likely as others to develop the illness,[5] and a family history of early onset suggests an even greater risk.[6] Earlier age at onset of mood disorders in general has been associated with an increased likelihood of switching from childhood major depressive disorder to mania.[7]

As noted in DSM-IV, "Attention-Deficit/Hyperactivity Disorder and a Manic Episode are both characterized by excessive activity, impulsive behavior, poor judgment, and denial of problems."[2(p332)] ADHD is described, however, as being "chronic rather than episodic"[2(p337)] and more consistent in presentation over time.[2] While ADHD is said to have a generally earlier age at onset than bipolar disorder,[2] there is evidence to suggest that ADHD may lower the age at onset for comorbid bipolar disorder.[8,9] Given the variability and lack of specificity regarding symptom patterns for childhood bipolar disorder, it has been suggested that the core feature of bipolar disorder in this population is mood lability or "marked state fluctuations."[10] This article will present a case illustration of a child with bipolar disorder followed by a summary of related treatment issues and options.

CLINICAL PRESENTATION

Eleven-year-old Megan (not her real name) was first seen in our office almost 3 years ago for concerns raised by her stepmother regarding progressive behavioral problems. In the 4 to 5 years prior to that visit, multiple mental health evaluations and treatments had been undertaken; however, little clinical improvement had been noticed. At the time of her first visit to our office, Megan's only medication was methylphenidate for ADHD. Both Megan and her stepmother agreed that methylphenidate was helping somewhat with schoolwork, although compulsive behaviors (e.g., repeatedly sharpening pencils down to the eraser), extreme mood swings, and impulsive behavior seemed to be increasing.

At this visit, Megan's stepmother, an emergency medical technician, stated that she was not aware of Megan's experiencing hallucinations of any kind, although she did note that Megan frequently seemed to have difficulty engaging in meaningful conversation. Despite having what appeared to be above-average intelligence, Megan had problems with concentration that continued to hinder her ability to complete homework assignments.

Megan was born by cesarean section at approximately 36 weeks' gestation with a birth weight of 6 lb 2 oz. Although her mother had adequate prenatal care, it is possible that Megan was exposed to alcohol, marijuana, narcotics, and/or benzodiazepines in utero. Little family history is available, but it is known that both Megan's mother and maternal grandmother had been diagnosed with bipolar disorder. Prior to and after Megan's birth, her mother had been on and off treatment with multiple medications and struggled with substance abuse, severe depression, and suicidal ideation.

Table 1. Common Developmental Presentations of Childhood and Adolescent Bipolar Disorder[a]

Early childhood—disorder is rarely diagnosed at this time
Middle childhood—the beginning symptoms as described for adolescents start to appear
Adolescence—during manic episodes, adolescents may wear flamboyant clothing, distribute gifts or money, and drive recklessly. They display inflated self-esteem, a decreased need for sleep, pressure to keep talking, flights of ideas, distractibility, unrestrained buying sprees, sexual indiscretion, school truancy and failure, antisocial behavior, and illicit drug experimentation
Special information
Substance abuse is commonly associated with bipolar disorder
Stimulant abuse and certain symptoms of attention-deficit/hyperactivity disorder may mimic a manic episode
Manic episodes in children and adolescents can include psychotic features and may be associated with school truancy, antisocial behavior, school failure, or illicit drug experimentation. Long-standing behavior problems often precede the first manic episode
One or more manic episodes frequently occur with 1 or more major depressive episodes. The symptoms are not better accounted for by other severe mental disorders (eg, schizoaffective, schizophrenogenic, delusional, or psychotic disorders). The symptoms cause mild impairment in functioning in usual social activities and relationships with others

[a]Reprinted with permission from the American Academy of Pediatrics.[4]

For the first 5 years of her life, Megan lived with both of her biological parents, who were experiencing a strained relationship. Her mother's refusal during this time to take medication coupled with a labile personality led to inappropriate behaviors, many of them perhaps witnessed and subsequently mimicked by Megan.

As early as 18 months of age, Megan was noted by her pediatrician to be "difficult to discipline." She was being raised primarily at that time by her paternal grandparents, who described her behavior as "hyper" and noted an erratic sleep pattern. By the time Megan was 3 years old, the diagnosis of oppositional defiant disorder had been applied, although no medications were prescribed and the patient was not referred for psychiatric evaluation.

As a 4-year-old, Megan experienced problems with asthma and recurrent sinus infections and frequently complained of being cold and tired. Night terrors, a regular occurrence by the age of 5, and difficulty making friends with other children her age were attributed to adjustment concerns related to her parents' pending divorce proceedings. Following her parents' divorce in 1999, Megan's father became the sole custodial parent. While her paternal grandparents continued to play a role in caring for her, they were ill-prepared to deal with Megan's active behavioral pattern.

Megan was first diagnosed as having ADHD at the age of 7 when she was in the second grade. Methylphenidate was initiated and seemed to be quite helpful, although the dose frequently needed to be increased in order to maintain its effectiveness. Obsessive-compulsive disorder (OCD) symptoms also became more apparent during this time (e.g., broken branches remaining in a tree produced a significant and unreasonable distraction). Although her father and new stepmother were concerned that Megan's behaviors represented something more than just ADHD, they attributed associated developmental delays to family and environmental stressors.

Following Megan's first visit to our office at the age of 9, a psychiatry consultation was requested, which resulted in a medication change from short-acting methylphenidate to a longer-acting formulation and a diagnosis of bipolar disorder with comorbid ADHD and OCD. An initial trial of oxcarbazepine produced no noticeable benefit. Subsequent use of risperidone in combination with ongoing use of long-acting methylphenidate was quite effective in decreasing mood lability, improving attention span, and enhancing Megan's ability to initiate and maintain appropriate peer relationships. An increase in prolactin levels after just 4 months, however, resulted in discontinuation of risperidone and a decision to limit Megan's medication to long-acting methylphenidate for the summer between the fifth and sixth grades.

Efforts to deal constructively with Megan's behavior at home during this time period demanded a significant investment of time, energy, and financial resources. Megan's older stepsisters provided daily after-school care in order to maintain the structure needed for her to complete her homework. Megan's father chose to delay a promotion with his company in order to avoid relocating to a new community, and her stepmother took frequent time away from work without pay using the Family and Medical Leave Act in order to meet regularly with Megan's teachers and accompany her on medical visits.

When Megan started sixth grade in the fall at the age of 11, her psychiatrist added aripiprazole to her ongoing use of long-acting methylphenidate. Aripiprazole seemed helpful in modifying mood swings but resulted in a somewhat depressed state. Efforts to manage the depression by adding sertraline resulted in rapid and significant development of hypomania. Following sertraline discontinuation, Megan's hypomania resolved somewhat, yet her mood remained "high energy." Initiation of valproic acid, in addition to ongoing use of aripiprazole and long-acting methylphenidate, seems to be helping to resolve this residual hypomania while also improving overall mood stability. The goal at this point is to consider possible future discontinuation of aripiprazole if ongoing use of valproic acid can be safely and effectively regulated.

DISCUSSION

Early recognition, intervention, and treatment are important for providing the stability necessary for bipolar children to experience normal developmental milestones, develop healthy peer relationships, and have a positive self-image. Important treatment goals should encourage (1) elimination of acute symptoms, (2) relapse prevention,

(3) reduction of long-term morbidity, and (4) achievement of age-appropriate growth and development.[11]

As suggested in the introduction, establishing an accurate diagnosis in children with bipolar disorder can be difficult. Related psychiatric disorders to be considered include schizophrenia, agitated depression, posttraumatic stress disorder, borderline personality disorder, and childhood disruptive behavioral disorders such as ADHD. Mood disorders due to a medical condition, such as medication side effects, and substance abuse must also be considered. Primary care providers with ongoing, longitudinal patient relationships have the distinct advantage of being able to observe both the rate and appropriateness of developmental changes over time. Parents who suspect that their child may have an illness of this type can assist their child's physician in the diagnostic process by keeping a log or diary of their child's behavior. This record should include information regarding mood states and lability, behavioral patterns, behavioral concerns, and sleep schedule. Regular contact with the primary care physician, even after psychiatric referral, can be very helpful in providing ongoing support, identifying possible drug interactions, and addressing ongoing developmental issues.

Using DSM-IV guidelines for diagnosing bipolar disorder in children is difficult, as there are no separate criteria for children. Obtaining an accurate longitudinal history of symptoms, life events, and previous treatment responses can be very helpful in limiting the initial list of differential diagnoses. Recognition that bipolar disorder may present differently in children than in adults is also important. Mania may present as irritability and belligerence rather than euphoria, while mood swings may cycle so rapidly as to mask distinct phases of the illness or allow for extended periods of "normalcy" between them.

According to the American Academy of Child and Adolescent Psychiatry, "A multimodal treatment plan, combining medications with psychotherapeutic interventions, is needed to address the symptomatology and confounding psychosocial factors present in children and adolescents with bipolar disorder."[11(p162S)] As alcohol and drug abuse is common in this population, concurrent substance abuse treatment may also be necessary.

Psychopharmacologic treatment of children has, unfortunately, become the topic of much debate. Few controlled studies have examined the use of psychiatric medications in children, and pharmaceutical companies have recently been accused of concealing information suggesting potentially harmful side effects. While use of psychotropic medication in children should always be approached cautiously, failure to treat may result in illness progression and related psychosocial (e.g., school failure) and physical (e.g., accidents due to acting-out behavior) risks.

Although there are few proven methods for the pharmacologic treatment of childhood bipolar disorder, recent small studies have suggested that, as in adults, mood stabilizers such as lithium, valproic acid, and carbamazepine are the medications of choice.[12] Although few studies have been done in children and adolescents, recently approved anticonvulsants such as lamotrigine are also viable options.

The *Journal of the American Academy of Child and Adolescent Psychiatry*[13] recently published a proposed 6-stage algorithmic approach to treatment of pediatric bipolar disorder with and without psychosis. Stage 1 begins with monotherapy with a mood stabilizer or an atypical antipsychotic. If the child has a partial response, stage 1A therapy augments treatment with a second medication. If no response is noted, initial medication(s) are discontinued, and medication from a different class is begun as stage 2 therapy. Stage 2 and stage 3 progress similarly to stage 1, with augmentation therapy added only when initial treatment response is noted. Stage 4A utilizes combination therapy first-line, and stage 4B adds a second mood stabilizer to combination therapy with a mood stabilizer and second-generation antipsychotic. Stage 5 is monotherapy with medications that have few or no data in children, such as oxcarbazepine, ziprasidone, and aripiprazole. Stage 6, reserved for nonresponders to all prior therapies, is electroconvulsive therapy for adolescents only, or clozapine for both children and adolescents. At each stage of treatment, comorbid diagnoses such as ADHD must be taken into account when measuring treatment response. However, it is never appropriate to treat comorbid diagnoses before achieving stable moods, as many medications used in the treatment of these diagnoses can destabilize moods.

Mood stabilizers function to decrease number and severity of mood swings, key therapeutic criteria in pediatric bipolar disorder, in which rapid cycling is nearly pathognomonic. Choice of initial medication should be based on a risk-benefit discussion among clinician, patient, and parents to ascertain which drug is most appropriate. Difficulties in lithium use include a narrow therapeutic range and lengthy side effect profile including fine tremor, nausea, weight gain, excessive thirst, and memory loss. Serious complications of lithium therapy include renal disease related to toxicity, thyroid dysfunction, and teratogenic cardiac effects in the first trimester of pregnancy. Valproic acid has a wider therapeutic window and fewer side effects, although liver functions should be checked periodically. Valproic acid also has a black-box warning due to the risk of life-threatening pancreatitis that is not dependent on dose or length of use. Neural tube defects in pregnancy have been associated with valproic acid; therefore, prevention of pregnancy in this high-risk population is essential. Multiple studies have noted that polycystic ovary syndrome seems to be more prevalent in young women taking valproic acid, so close monitoring of weight and menstrual regularity is important. Common side effects of carbamazepine include mild gastrointestinal disturbances

and central nervous system effects such as ataxia, dizziness, and blurry vision. Carbamazepine activates the cytochrome P450 (CYP) metabolism in the liver and interferes with other medications that utilize the CYP metabolic system, such as selective serotonin reuptake inhibitors, valproic acid, and multiple antibiotics. A dangerous combination, carbamazepine and lithium used concomitantly at therapeutic serum drug levels can increase the risk of neurotoxicity. Agranulocytosis is a severe side effect of carbamazepine that is sudden in onset and difficult to monitor.[14]

The newer anticonvulsant medications such as lamotrigine and oxcarbazepine are often easier to use in this population because blood monitoring is unnecessary. It is important to note, however, that many of the anticonvulsant medications, especially lamotrigine, can induce Stevens-Johnson syndrome, a potentially life-threatening skin condition, and must be titrated slowly to decrease this risk. The risk of Stevens-Johnson syndrome is 1 in 1200 adult patients, but has been found to be as frequent as 1 in 100 pediatric patients.[13]

As previously mentioned, second-generation antipsychotic medications, whether as monotherapy or in combination therapy, play a significant role in treatment of childhood bipolar disorder. Although less toxic than their first-generation cousins, the second-generation antipsychotics such as risperidone, olanzapine, and quetiapine are not free of side effects. The most common side effect is weight gain, which has been much more significant in adult trials with olanzapine than with risperidone or quetiapine. The American Diabetes Association protocol recommends screening for lipid and glucose disorders and weight monitoring for all individuals placed on treatment with a second-generation antipsychotic therapy.[15] Although less prevalent than with first-generation antipsychotics, extrapyramidal effects such as tardive dyskinesia, akathisia, and dystonia may occur. Hyperprolactinemia, most commonly found with risperidone use, is easily detected and resolves when the medication is discontinued. Ziprasidone, although not commonly used in children, has been shown to cause a clinically significant corrected QT interval prolongation, and a screening electrocardiogram prior to initiation of therapy is essential.

Clinicians must emphasize to patients and parents that each stage in pharmacologic therapy entails incremental increases in dose to effective or maximum suggested doses and can take from 2 to 4 months depending on the drug. As was seen with Megan, these trials can be very difficult for the patient and family to endure, and adequate support systems are paramount to successful therapy in this population.

While medications can be very effective in helping to control symptoms and stabilize mood patterns, counseling is frequently needed to address self-defeating behavioral patterns, stressful family interactions, and delayed developmental issues. Parents need to educate themselves regarding symptoms and behavior patterns to look for. Reading about[16] or interacting with other parents experiencing similar challenges, either online or in person, can also be very helpful. Peer support may help parents learn to more effectively deal with their child's behavior by reducing stress and providing structure in the home, support their efforts to prioritize concerns and "choose their battles," identify and encourage their child's unique abilities, and advocate for appropriate accommodations at school.

Drug names: aripiprazole (Abilify), carbamazepine (Carbatrol, Equetro, and others), clozapine (Clozaril, FazaClo, and others), lamotrigine (Lamictal), lithium (Lithobid, Eskalith, and others), methylphenidate (Ritalin, Concerta, and others), olanzapine (Zyprexa), oxcarbazepine (Trileptal), quetiapine (Seroquel), risperidone (Risperdal), sertraline (Zoloft), valproic acid (Depakene and others), ziprasidone (Geodon).

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