Diagnostic problems of childhood-onset bipolar disorder comorbid with attention-deficit hyperactivity disorder: three-year follow-up study of six cases

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Abstract

The aim of this follow-up study was to investigate whether severe non-episodic irritability without elevated or expansive mood exhibited by children under 9 years old with attention-deficit-hyperactivity disorder (ADHD) is the first prodromal symptom of childhood-onset bipolar disorder (BP). From among 32 children aged under 9 years old who were referred to our outpatient department for assessment and treatment of ADHD in 2008, 6 children exhibiting severe temper tantrums and anger outbursts were the participants in this study. All participants were followed every few months for 3 years after the initial assessment. At each follow-up visit to our hospital, we administered the Kiddie Schedule for Affective Disorders-Present (K-SADS) modules for ADHD, mania, and depression in an interview with the child and/or parent and/or teacher to assess their symptoms. Among the 6 participants, 2 experienced an episode of hypomania during the follow-up period, and 3 were symptom-free during the follow-up period once their irritability had subsided. One participant repeatedly experienced severe non-episodic irritability and was symptom-free for no more than 2 months at any one time during the follow-up period. Our findings suggest that children with ADHD under the age of 9 years may have a developmental presentation of BP when exhibiting severe non-episodic irritability, and environmental factors surrounding a child should be also considered when deciding the treatment.

Key words: bipolar disorder, childhood, ADHD, severe mood dysregulation, irritability, environmental factors

Introduction

Adult criteria have been used to diagnose bipolar disorder in children since the publication of DSM-III in 1980. Since the late 1990s in the United States, clinicians and researchers have been focusing increased attention on the diagnostic classification of children with bipolar disorder (BP) type II and bipolar disorder not otherwise specified (BP-NOS). Children who exhibit severe non-episodic irritability without elevated or expansive mood also fall into the BP-NOS category; however, when children with attention-deficit hyperactivity disorder (ADHD), especially children under 9 years old, exhibit such irritability, it is difficult to assess whether this symptom is indicative of the onset of bipolar disorder. Also, since medications prescribed for the treatment of ADHD are relatively contraindicated in BP, it is clearly important to diagnose these children accurately.

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children under 9 years old with ADHD is the first prodromal symptom of childhood-onset BP.

Method

Participants

From among 32 children aged under 9 years old who were referred to our outpatient department for assessment and treatment of ADHD in 2008, 6 children exhibiting severe temper tantrums and anger outbursts were the participants in this study. They and their parents took part in a semi-structured interview using the Kiddie Schedule for Affective Disorders-Present and Lifetime Version (KSADS-PL) at the first visit. All children were diagnosed with BP-NOS as well as ADHD and other psychiatric disorders according to the Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV-TR) criteria. In addition, the following assessments were made to assess intelligence and to exclude PDD or neurologic disorders: the ADHD Rating Scale-IV (Home and School Version), Wechsler Intelligence Scale for Children-Third Edition (WISC-III), Childhood Autism Rating Scale-Tokyo Version (CARS-TV), Pervasive Developmental Disorders Assessment System (PDDAS), and electroencephalography. The characteristics of the 6 participants are shown in Table 1. Parents provided written informed consent for their children to participate after receiving a full explanation of the study procedure.

Follow-up assessment

All participants were followed every few months for 3 years after the initial assessment. At each follow-up visit to our hospital, we administered the K-SADS modules for ADHD, mania, and depression in an interview with the child and/or parent and/or teacher to assess their symptoms.

Results

Frequency of follow-up assessment

Participants were followed every 2.8 months on average (SD=3.5) and all 6 participants completed follow-up assessments over the 3-year period.

Clinical course

Conversion from severe non-episodic irritability to hypomanic episode

Among the 6 participants, 2 (Cases 2 and 6) experienced an episode of hypomania during the

Table 1 Participant characteristics

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first visit (years)</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
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<tr>
<td>Family history</td>
<td>M-Grandfather: MDD</td>
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<td>None</td>
<td>None</td>
<td>None</td>
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<tr>
<td>Past history</td>
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<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>WISC-III</td>
<td>FIQ 88</td>
<td>99</td>
<td>85</td>
<td>88</td>
<td>91</td>
</tr>
<tr>
<td></td>
<td>VIQ 86</td>
<td>105</td>
<td>84</td>
<td>91</td>
<td>96</td>
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<tr>
<td></td>
<td>PIQ 93</td>
<td>92</td>
<td>90</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>ADHD Comorbidity at the visit</td>
<td>Combined type BP-NOS, GAD, Nighturnal enuresis</td>
<td>Combined type BP-NOS, ODD</td>
<td>Combined type BP-NOS, GAD, Nighturnal enuresis</td>
<td>Combined type BP-NOS, ODD</td>
<td>Combined type BP-NOS, ODD</td>
</tr>
<tr>
<td>Comorbidity at end of 3-year follow-up</td>
<td>SMD, GAD, Nighturnal enuresis</td>
<td>BP-NOS</td>
<td>None</td>
<td>Nighturnal enuresis</td>
<td>None</td>
</tr>
</tbody>
</table>

Note: ADHD=attention-deficit/hyperactivity disorder; BP= bipolar disorder; BP-NOS=bipolar disorder not otherwise specified; GAD=generalized anxiety disorder; MDD=major depressive disorder; M-Grandfather=maternal grandfather; ODD=oppositional defiant disorder; SMD=severe mood dysregulation; VSD=ventricular septal defect; WISC-III=Wechsler Intelligence Scale for Children-Third Edition; FIQ=full-scale IQ; VIQ=verbal IQ; PIQ=performance IQ
follow-up period.

Case 2 exhibited various problematic behaviors caused by irritability in his first year at primary school. When he went on to the second grade, an experienced teacher took care of him and his irritability subsided over time. Thereafter, he experienced two episodes of hypomania during the entire follow-up period. He showed symptoms of hypersexuality during the second hypomanic episode.

Case 6 lived with her mother, who had been diagnosed with BP at another hospital. Her mother seemed extremely agitated at the first visit and we therefore provided counseling to the mother during the follow-up period. The child stopped feeling irritable as her mother showed improved mental calmness. Later, she experienced an episode of hypomania at the age of 9 and an episode of depression with non-suicidal physical self-damaging acts at the age of 10.

In both cases, risperidone or aripiprazole was used only when they exhibited severe irritability and the effect of these medications was mild. Lithium was used after hypomanic episodes.

Subsiding or persist of severe non-episodic irritability

Among the 6 participants, irritability subsided in 3 cases (Cases 3, 4, and 5) and persisted in one case (Case 1) during the follow-up period.

Case 3 had experienced psychological abuse, including neglect or rejection, from her father. Her parents divorced 7 months after her first visit and she started living with her mother. About 2 months later her irritability subsided.

Case 4 lived with his mother and her parents. At his first visit, he expressed loneliness because his mother was busy at work and was late coming home. His mother changed her job 6 months after the first visit. About 2 months later his irritability subsided. He was diagnosed with nocturnal enuresis concomitant with ADHD during the follow-up period.

In Case 5, her only and younger sister injured herself frequently because of inattention, which meant that her mother spent a great deal of time taking care of her younger sister. Her younger sister also visited our outpatient department 5 months after her sister’s first visit. Her younger sister was diagnosed with ADHD and started on ADHD medication. After around 2 months, alongside the improvement in her younger sister’s ADHD symptoms, her irritability subsided.

None of the 3 children experienced (hypo-) manic or mixed episodes during the follow-up period once their irritability had subsided. Risperidone or aripiprazole was used only when they exhibited severe irritability, and produced a mild effect. Extended-release methylphenidate was prescribed for ADHD symptoms in Case 3 after her irritability had subsided. Atomoxetine was prescribed for Case 4 because he could not take medication in capsule form. Case 5 discontinued extended-release methylphenidate because of loss of appetite and apathy and then was free from medication.

The one participant (Case 1) who repeatedly experienced severe non-episodic irritability and was symptom-free for no more than 2 months at any one time was also diagnosed as having generalized anxiety disorder and nocturnal enuresis during the follow-up period. He had undergone surgical treatment for a congenital ventricular septal defect in early childhood and had been examined periodically thereafter. Risperidone or valproic acid was given for irritability but with only a mild effect.

Consideration

According to the American Academy of Child and Adolescent Psychiatry guidelines for BP, severe non-episodic irritability may warrant a diagnosis of BP-NOS; however, controversy exists as to whether irritable children without distinct manic episodes have a developmental presentation of BP.

In 2003, Leibenluft et al. created a new category of BP called severe mood dysregulation (SMD) for the purpose of studying children presenting with severe non-episodic irritability. Using this category, Stringaris et al. showed that 83 of 84 children with SMD including 69 children with concomitant ADHD, with an average age of 12 years, did not experience a (hypo-)manic or mixed episode during a 2-year follow-up study. Brotman et al. also showed that 2.7% of children with SMD had a parent with bipolar disorder, compared to 33.3% of the parents of children who meet the full DSM-IV diagnostic criteria for hypomanic or manic. In the present study, all 6 participants met the criteria for SMD except the criterion of age 7-17 years. However, unlike in these studies, 2 of our participants experienced a hypomanic episode during a 3-year follow-up period and one of them had a parent with bipolar disorder.
Although it is difficult to compare these figures because of differences in the number of subjects across these studies, our findings suggest that children with ADHD under the age of 9 years may have a developmental presentation of BP when exhibiting severe non-episodic irritability and having a parent with bipolar disorder.

Another interesting finding of the present study was that the course of severe non-episodic irritability in our 6 cases seemed to be greatly influenced by the environmental factors surrounding them rather than the effect of pharmacological treatment. Severe non-episodic irritability subsided in 5 cases following an improvement in their environment: 2 participants experienced an episode of hypomania, while the remaining 3 participants did not exhibit a (hypo-)manic or mixed episode and did not relapse to severe non-episodic irritability. Moreover, the one participant for whom a detrimental environmental factor could not be improved continued to exhibit severe non-episodic irritability. These findings indicate that it is possible for a child with both ADHD and BP aged under 9 years old to fall into the category of SMD due to the presence of a detrimental environmental factor. Therefore, environmental factors surrounding a child should be considered when deciding the treatment strategy in cases of ADHD, aged under 9 years old, and exhibiting severe non-episode irritability.

More case reports are needed to clarify the nature of severe non-episodic irritability.

References