

CASE REPORT

Two children exhibiting social withdrawal, school refusal, and underlying generalized anxiety disorder successfully treated using a selective serotonin reuptake inhibitor

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Abstract: Generalized anxiety disorder (GAD) sometimes exists in the background of social withdrawal and school refusal. Although clinical evidence suggests that selective serotonin reuptake inhibitors (SSRIs) are an effective treatment for GAD, they are not officially approved for GAD in Japan. In addition, it has been established that the use of SSRIs increases the risk for suicide and activation syndrome among young individuals. As such, there is currently little domestic clinical experience in prescribing SSRIs to young patients with GAD. The authors report two cases involving 10-year-old patients with GAD who were treated successfully with escitalopram and experienced subsequent improvement in social withdrawal and school refusal. One patient had autistic spectrum disorder and exhibited self-harm associated with anxiety symptoms, requiring careful use of SSRIs under hospitalization. The other patient was treated at an outpatient clinic without any side effects. In each case, improvement of anxiety symptoms with the use of SSRIs facilitated the introduction of psychoeducation and psychotherapy. It is important to accurately diagnose GAD, which may exist in the background of patients exhibiting social withdrawal and school refusal, and to treat the disorder appropriately. *J. Med. Invest.* 67:355-357, August, 2020

Keywords: *generalized anxiety disorder, social withdrawal, school refusal, selective serotonin reuptake inhibitor*

INTRODUCTION

In the field of child psychiatry, social withdrawal and school refusal are often caused by psycho-environmental factors such as problems at school or in the home. For such cases, it is necessary to appropriately manage these psycho-environmental factors. However, depressive episodes or anxiety disorders sometimes exist in the background of social withdrawal and school refusal, which require treatment. Depressive episodes and anxiety disorders of specific severity are usually treated with antidepressants such as selective serotonin reuptake inhibitors (SSRIs) (1); however, younger individuals are known to be at increased risk for suicide and activation syndrome induced by these agents (2). In particular, we should be cautious when prescribing SSRIs to children and adolescents in the early teenage years who have difficulty in verbalizing their subjective experiences, and those with intellectual or developmental disabilities who are prone to exhibit behavioral problems. However, there is a data that suicide risk has been increased as prescriptions of antidepressants have been refrained (3) after the United States Food and Drug Administration (FDA) warned about the increased suicidality risk associated with the use of antidepressants (4). The authors report two cases involving 10-year-old children with generalized anxiety disorder (GAD) treated with SSRIs, who experienced improvement in social withdrawal and school refusal. The parent's consent was obtained for the publication for each case.

CASE 1

A 10-year-old girl visited the authors' facility with complaints of anxiety, poor eating habits, and school refusal. She lived with her parents and a younger brother. Her father was being treated for depression and her younger brother was diagnosed with attention deficit hyperactivity disorder. A short stature of 2.2 SD was recognized. The patient exhibited normal physical and language development after birth; however, she was obsessed with specific belongings, had hyperacusis, exhibited one-sided conversation and poor communication skills since childhood. When she was 7 years of age, she began to worry about stomach pain and vomiting and did not regularly eat her school lunch. At 8 years of age, she became reluctant to attend school, and the amount of food intake further decreased, losing weight from 23 kg to 21 kg. She received inpatient treatment at a general hospital when she was 9 years of age, and her weight recovered to 27 kg. Even after being discharged from hospital, she felt highly anxious about various activities, such as going out, eating, and interacting with classmates. With increasing anxiety, self-harm was seen, peeling her fingertips, and chewing in the mouth. For this reason, she was referred to the authors' hospital.

Results of the Wechsler Intelligence Scale for Children- Fourth Edition (WISC-IV) revealed a borderline intelligence level (intellectual quotient [IQ], 78; Verbal Comprehension Index [VCI], 86; Perceptual Reasoning Index [PRI], 89; Working Memory index [WMI], 68; and Processing Speed Index [PSI], 81). She scored 13 points on the Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS), and was above the diagnostic threshold for autistic spectrum disorder (ASD). She experienced difficulty with understanding sentence meaning, metaphors and irony, and experienced persistent deficits in social communication and interpersonal interaction. She had also exhibited a repetitive mode of behavior, interest, and activity. In addition, she experienced excessive worry and anxiety about

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various daily events and activities, and was easily fatigued, with restlessness, stiffness, and nervousness. Based on the above, she was diagnosed with ASD and GAD. After unsuccessful outpatient treatment, she was admitted to the authors' department on January 30. She stayed in her room and complained about her meals and medical examinations. She harmed herself, chewing her mouth, and scratching her arms.

A structured daily schedule was set and behavioral therapy using tokens was initiated. Although she achieved a certain level of stability in the ward, she continued to worry and was unable to go out or attend school; consequently, pharmacotherapy was initiated. A small amount of aripiprazole (approximately 4 mg) had no effect. The authors explained to her parents that the SSRIs might be effective for GAD, although the drugs were not officially approved for GAD in Japan, and that the use of the drugs could increase the risk for suicide attempt and activation syndrome among young individuals. After obtaining parental consent for using SSRIs, escitalopram was used up to 10 mg. She began to go out and attend school for disabled children. However, she became emotionally unstable, and resumed self-harm, and she cried and abused her mother in the hospital room. The emotional response appeared to be due to environmental changes such as attending school. However, because there was also concern about activation syndrome from escitalopram, the dose of the drug was reduced to 2.5 mg. Anxiety then recurred, and she hesitated to attend school. After carefully increasing the dose of the drug to 10 mg again, she did not exhibit self-harm or emotional instability and was able to return to a local school after attending a school for disabled children. She was discharged in September of the same year and, after several visits to the authors' outpatient clinic, was referred to the previous physician. The clinical course of the case is shown in Fig.1.

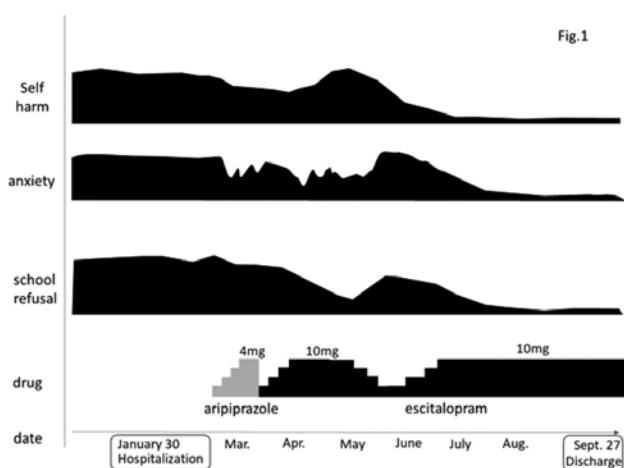


Figure 1. The clinical course of case 1

CASE 2

A 10-year-old girl visited the authors' hospital with various complaints and concerns. She lived with her parents and a younger brother. There was no family history of mental illness. The patient exhibited no particular problems through nursery school and kindergarten, and she enjoyed studying and playing with her friends at elementary school. However, when she left a good friend at class change one month previously, she could not adjust to the new class. Gradually, she became unable to sleep

because she recalled dreadful words such as "war", "illness", and/or "death". She was worried that her mother would not return from shopping, and frequently checked with her and asked for assurance. She frequently complained of physical symptoms, such as difficulties with swallowing and breathing, and discomfort in the chest and throat. Although she visited a nearby pediatrician, there were no abnormal findings. She became more ill and began to refuse to attend school. She visited the authors' hospital for the first time.

Although she was nervous, she understood well and conversed accordingly, exhibiting no problems with communication. Results of the WISC-IV revealed a normal intelligence level (IQ, 87; VCI, 88; PRI, 106; WMI 82; and PSI, 78). She was diagnosed with GAD, and was administered tandospirone at the outpatient clinic at a dose ranging from 15 to 30 mg. Despite some reduction in physical symptoms, she continued to worry and refused to attend school. When she saw news of disasters she could not go out. Although she liked pets, she was afraid to touch them due to fears of contracting an illness, which further contributed to withdrawal from life. Tandospirone was discontinued. The authors explained to her parents that the SSRIs might be effective for GAD, although the drugs were not officially approved for GAD in Japan, and that the use of the drugs could increase the risk for suicide attempt and activation syndrome among young individuals. After obtaining parental consent for using SSRIs, escitalopram was started at 2.5 mg and increased to 5 mg. Gradually, her symptoms decreased and virtually disappeared. Although refusal to attend school was prolonged, she was able to start short-term individual classes, and then was able to gradually return to normal school after 3 months of SSRI treatment. The clinical course of the case is shown in Fig.2.

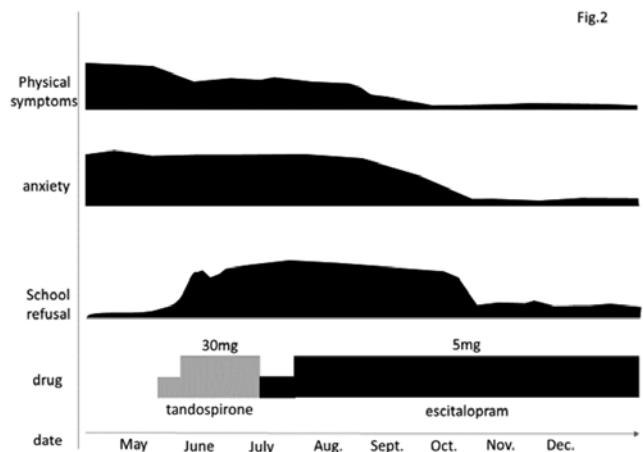


Figure 2. The clinical course of case 2

DISCUSSION

There is sufficient evidence supporting SSRIs as an effective treatment for GAD, as well as major depressive, panic, and social anxiety disorders(5). However, unlike other countries, no SSRIs have yet been formally approved for GAD in Japan; therefore, it is necessary to explain the off-label use when prescribing them. More importantly, the use of SSRIs and other antidepressants are known to be associated with higher risks for inducing suicide and activation syndrome in young individuals compared with adults(2). Therefore, it should be extremely cautious to use

SSRIs in children with GAD based on consideration of the risks as well as off-label prescription.

Nevertheless, GAD in childhood is, by no means, rare(6). The authors presented two cases involving children with social withdrawal and school refusal with underlying GAD. In each case, GAD was improved by carefully using escitalopram, and symptomatic improvement led to recovery from social withdrawal and school refusal. The first case had ASD and had self-harm ; as such, the SSRI was used in an inpatient setting. The emotional instability and re-emergence of self-harm that appeared when she became able to go out and attend school were believed to be due to a psychological reaction due to an environmental change but not due to activation syndrome. The second patient was treated on an outpatient basis at a low dose of the SSRI and experienced no specific side effects. In both cases, improvement in anxiety symptoms using an SSRI facilitated the introduction of psychoeducation and psychotherapy. These findings suggest that it is important to accurately diagnose GAD, which may be present in the background of patients with social withdrawal and school refusal, and to treat the disorder appropriately.

DECLARATION OF INTERESTS

None of the authors have any conflicts of interest.

REFERENCES

1. Driot D, Bismuth M, Maurel A, Soulie-Albouy J, Birebent J, Oustric S, Dupouy J : Management of First Depression or Generalized Anxiety Disorder in Adults in Primary Care : A Systematic Metareview. *Press Med* 46 : 1124-1138, 2017
2. Friedman RA, M.D., and Leon AC, Ph.D. : Expanding the Black Box - Depression, Antidepressants, and the Risk of Suicide. *N ENGL MED* 356 (23), 2343-2346, 2007
3. Gibbons RD, Hur K, Bhaumik DK, Mann JJ : The Relationship Between Antidepressant Prescription Rates and Rate of Early Adolescent Suicide. *AM J Psychiatry* 163 (11) : 1898-904, 2006
4. Stone M, Laughren T, Jones ML, Levenson M, Holland PC, Hughes A, Hammad TA, Temple R, Rochester G : Risk of Suicidality in Clinical Trials of Antidepressants in Adults: Analysis of Proprietary Data Submitted to US Food and Drug Administration. *BMJ(Clinical research ed.)*, 339, b2880, 2009
5. Bandelow B, Lichte T, Rudolf S, Wiltink J, Beutel ME : The Diagnosis of and Treatment Recommendations for Anxiety Disorders. *Dtsch Arztebl Int* 111 (27-28), 473-80, 2014
6. Gale CK, Millicham J : Generalised Anxiety Disorder in Children and Adolescents. *BMJ clinical evidence* 01 : 1002, 2016