Olanzapine Treatment for Tics in an Adult Woman with Severe Tourette Syndrome

Wen-Juh Hwang

Abstract-

Purpose: Olanzapine had been reported to be effective in the control of tics in a few adult female patients who had a short follow-up period. The author reports the successful outcome of long-term olanzapine treatment in an adult woman with severe Tourette syndrome.

Case Report: A 33-year-old woman who had severe motor and vocal tics (Modified Rush Videotape Rating Scale: 17/20) showed an excellent response to olanzapine 10 mg/day within 2 months. Her tic symptoms were well controlled with gradual reduction of her dose of olanzapine to 2.5 mg/day during the following 8 years. She was symptom-free without medications in the past 2 years. In addition, she had a normal menstrual cycle and became pregnant during the period of olanzapine treatment.

Conclusion: Olanzapine may be the drug of first choice for treating severe Tourette syndrome in pubescent female adolescents and young women who wish to have children.

Key Words: adult woman, olanzapine, Tourette syndrome

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INTRODUCTION

Tourette syndrome (TS) is a neuropsychiatric disorder characterized by fluctuating multiple motor tics and one or more vocal tics over a period of more than 1 year. It is often associated with attention-deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and other behavioral disorders.

The most frequently used drugs for tics are antipsychotics (e.g., haloperidol and pimozide) and clonidine. Typical antipsychotics are effective for tics[1]; however, they are associated with many side effects, including drowsiness, fatigue, acute dystonic reaction, neuroleptic malignant syndrome, akathisia, parkinsonism, tardive dyskinesia or dystonia, intellectual impairment, weight gain, dry mouth, orthostatic hypotension, secondary amenorrhea, and possible prolongation of the QT-interval on electrocardiograms[2]. In contrast to haloperidol and pimozide, which potently block dopamine D2 receptors, the atypical antipsychotics (e.g., risperidone, olanzapine, clozapine, quetiapine), to varying degrees, block both dopamine and serotonin receptors and have less frequent extrapyramidal side effects[2,3].

Olanzapine had been reported to be effective in the

From the Department of Neurology, National Cheng Kung University College of Medicine and Hospital, Tainan, Taiwan.
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Correspondence to: Wen-Juh Hwang, MD. Department of Neurology, National Cheng Kung University College of Medicine and Hospital, No. 138, Sheng-Li Road, Tainan 704, Taiwan.
E-mail: wjhwang@mail.ncku.edu.tw

control of tics in 3 case reports[4-6], one case series[7], 3 open-label trials[8-10], one single-blind study[11], and one double-blind study[12]. These studies enrolled a small number of patients and had a short follow-up period (4-9 weeks), except for the double-blind study, which had a 1-year follow-up. Because TS occurs predominantly in males, there were only 9 female patients (3 children and adolescents, 6 adults) reported in these studies. The management of female patients at reproductive age may need special attention, because of the effect of antipsychotics on their prolactin level and, therefore, fertility. The author reports the successful outcome of long-term (10 years) olanzapine treatment in a 33-year-old woman with severe TS.

CASE REPORT

This 33-year-old woman developed a vocal tic at 7 years old. She visited our hospital when she was 23 years old. She did not have ADHD, OCD, or other behavioral or psychiatric disorders.

The patient began to involuntarily utter the sound "e" when she was 7. She was diagnosed with some kind of lung disease and was treated with herbal medicine, but in vain. The involuntary utterance occurred about 20 times per minute and waxed and waned for the following 13 years. At the age of 20, the abnormal "e" sound was replaced by very loud snorting. Also, she started to notice excessive blinking, teeth gnashing, shoulder shrugging, arm shaking, fist clenching, leg jerks, sudden violent contraction of the abdominal wall (abdominal tensing), hiccupping, and jerky movement of the trunk like that of a startle response. The frequency and severity of these motor and vocal tics waxed and waned over the next 3 years, without complete remission. Because the tics had a significant negative impact on her activities of daily living, social relationships, and ability to work, she was referred to our Movement Disorders Clinic at the age of 23 and was admitted for further evaluation and treatment in August 2001.

Her medical history was unremarkable. There was no family history of TS or other neurological disorders. Her blood pressure was 110/80 mmHg and body weight was 49.5 kg. Her higher cortical function and cranial nerves were normal. The motor system showed normal muscle bulk, muscle tone, and muscle power. The deep tendon reflexes were normal and symmetric. The sensory system, coordination, and autonomic system were all normal. There were no other involuntary movements except for the tics. Her hemogram, biochemistry, and thyroid function tests were all normal. An electrocardiogram showed a normal sinus rhythm. The wakeful EEG study showed normal cortical function and no epileptiform discharges. Brain magnetic resonance imaging without contrast medium revealed normal findings. The [99mTc]TRODAT-1 and [123I]IBZM single photon emission computed tomographic studies for the dopamine transporter and D2 receptor binding potentials showed normal results. The Modified Rush Videotape Rating Scale[13] was 17 (its maximum score of 20 is for the most severe conditions).

She was treated with risperidone (1 mg/day), clozapine (50 mg/day), pergolide (0.1 mg/day), clonazepam (1.5 mg/day), and quetiapine (12.5 mg/day) in sequence between August 2001 and July 2002. These drugs produced either mild improvement or no effect, and caused intolerable drowsiness, which prevented further dosage titration. In addition, she had an elevated prolactin level and secondary amenorrhea after taking risperidone. She began treatment with olanzapine in August 2002. The initial dose was 5 mg/day at bedtime. She experienced mild drowsiness and no improvement of her tic symptoms. The dose of olanzapine was increased to 10 mg/day at bedtime one month later, and after 2 months, both her motor and vocal tic symptoms significantly improved without increased drowsiness. Because of this improvement, she reduced the dose of olanzapine to 5 mg/day and her symptoms recurred in the following 2 weeks. She then took 10 mg/day of olanzapine again, and once more her tic symptoms improved in a few days. She was maintained on 10 mg/day of olanzapine between January 2003 and January 2004. Because her tics were under control and she was concerned about gaining weight, she reduced her dose of olanzapine to 5 mg/day in February 2004. Because her tics had not returned after this dose reduction, she further tapered her

dose of olanzapine to 2.5 mg/day between February 2005 and April 2009. She had no vocal tics and rare minor motor tics during those 50 months. From May 2009 until May 2011, she was symptom-free without medications. Her activities of daily living, ability to work, and social relationships were all normal.

The side effects of olanzapine treatment included mild drowsiness at the beginning and a weight gain of 4 kg in 2 months, 10 kg in 1.5 years, and 16.5 kg in 2 years (maximum body weight 66 kg). She had a weight loss of 14 kg in 6 months after tapering the dosage of olanzapine. She weighed 52 kg in May 2004 and weighs 57.5 kg now. She had no extrapyramidal symptoms, memory impairment, dry mouth, orthostatic hypotension, or secondary amenorrhea during the treatment period with olanzapine. She had a normal menstrual cycle during olanzapine treatment and became pregnant in January 2003 and May 2006. Her serum glucose, cholesterol, liver function, and kidney function were checked every 6 months and showed normal results between January 2003 and January 2005, when she took a higher dose of olanzapine. There was no prolongation of the QT-interval on her electrocardiogram during the same period. She has a good long-term tolerability profile for olanzapine.

DISCUSSION

The beneficial effects of olanzapine on both motor and vocal tics are shown in this report and in previous studies[4-8,10-12]. One study[9] reported a positive effect on motor tics, but without any significant improvement in vocal tics. The effects of olanzapine on TS-associated comorbidities are controversial. Two studies[4,8] reported improvements in ADHD, aggression, and OCD. The effect on aggression is unclear in one report[11], because the parents and the teachers had different ratings on the aggression scores. One study[9] reported no effect on comorbidity. Most of the previous studies did not deal with the effects of olanzapine on comorbidities[5-7,10,12]. The therapeutic effects of olanzapine on TS-associated comorbidities need further study.

The dosage of olanzapine for treating tics ranged from 2.5 mg/day to 20 mg/day, with a mean of about 10-15 mg/day[4-12]. Drowsiness and weight gain are the most common side effects[4-12], with a maximum increase of 1.2 kg/week in 2 studies[8,11]. The effects of olanzapine on the menstrual cycle and prolactin level were not discussed in the short-term (6-9 weeks) studies on fertile female patients with TS[6,9,10]. The natural history of TS is typically characterized by the onset of symptoms in childhood, a prepubertal exacerbation, postpubertal attenuation, and stabilization of symptoms in adulthood[14,15]. Because there is a tendency for symptoms to decrease after a plateau, and in order to reduce or avoid undesirable side effects, medication doses should, if possible, be reduced after the tics are under control. Weight gain is a concern for prolonged olanzapine use, and it usually leads to discontinuation of the drug. Using the lowest effective dose and diet control may improve compliance with long-term olanzapine treatment.

This patient showed an excellent treatment outcome with olanzapine (10 mg/day) and also experienced the most common side effects of drowsiness and weight gain. During the treatment and follow-up period over the past 10 years, she did not have extrapyramidal side effects, hyperglycemia, hypercholesterolemia, prolongation of the QT-interval on electrocardiograms, or secondary amenorrhea. Olanzapine has structural and pharmacological properties resembling those of the atypical antipsychotic clozapine[3]. It has a relatively greater antagonistic activity for serotonin-2A and -2C receptors, and dopamine D4 receptors. There have been no reports of granulocytopenia (which occurs with clozapine) or any other hematological side effects caused by olanzapine[3]. It is also associated with an improved tolerability profile and significantly fewer extrapyramidal side effects and hyperprolactinemia than the typical antipsychotic haloperidol[3]. In summary, olanzapine can effectively control tics and improve the patient's quality of life and ability to work. It also has a lower potential to cause hyperprolactinemia and infertility. Olanzapine may be the drug of first choice for treating severe TS in pubescent female adolescents and young women who wish to have children.

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