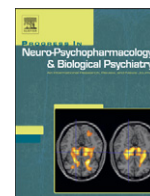




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Letter to the Editor (Case report)

Quetiapine-induced rabbit syndrome in a patient with bipolar disorder

1. Background

Rabbit syndrome (RS) is characterized by rapid, fine, rhythmic movements of the perioral muscles along with a chewing-like actions at a frequency of approximately 5 Hz (Villeneuve, 1972). RS usually begins a few days after antipsychotic medication treatment, but the onset of RS can be observed after a long-term exposure of neuroleptic agents (Schwartz and Hocherman, 2004; Dell'Osso et al., 2007). Second-generation antipsychotics (SGA)-induced RS has been reported in eleven cases to date; however, none of them is induced by quetiapine (Dell'Osso et al., 2007). Here, we reported the first case with quetiapine-induced RS, whose movement symptoms responded well to olanzapine substitution.

2. Case report

Ms. A, a 56-year old married Taiwanese woman, has been diagnosed with bipolar I disorder for eighteen years. She had had stable mental status followed at our outpatient department under treatment with lithium 1200 mg/day and sulpiride 200 mg/day for more than four years. However, she discontinued all the psychotropic medication due to poor insight, and then she was admitted to our psychiatric ward because of a severe psychotic manic relapse, with symptoms of labile mood, outside wandering, decreased sleep need, buying spree, impulsivity, disturbing behaviors, and delusion of grandiosity. During hospitalization, 900 mg/day of lithium and 100 mg/day of quetiapine was gradually titrated in five days. After 2-week treatment (with quetiapine and lithium), Ms. A began suffering from RS, including symptoms of involuntary rhythmic movements of her mouth, but not her tongue, and vertical fine, and rapid movements with a popping sound. Her score of the subcategory of "lips and perioral area" in the Abnormal Involuntary Movement Scale (AIMS) (Guy, 1976) was three points. Moreover, akathisia, restlessness, and pacing behaviors were also noted. The results from the blood biochemistry test, including complete cell count, serum electrolytes, liver and renal function, CPK, thyroid function tests, lithium level, and EEG were all in normal ranges. Quetiapine was therefore tapered gradually, and cardirolol 20 mg/day was given. Akathisia improved, but there was no improvement in RS despite a reduction of quetiapine. In order to optimize the treatment for her psychotic manic episode and RS, we decided to shift from quetiapine to olanzapine 5 mg/day initially, and up-titration to 10 mg/day two days later. After 3 weeks of olanzapine treatment, Ms. A remitted not only from psychotic manic symptoms, but also RS. Her score of subcategory of "lips and perioral area" in the AIMS (Guy, 1976) dropped from three to zero. Six months after combination treatment with olanzapine 10 mg/day and lithium 900 mg/day, Ms. A remained in full remission from her manic symptoms and extrapyramidal symptoms.

3. Discussion

Rabbit syndrome, first described in 1972, is a rare antipsychotic-induced extrapyramidal side effects (Villeneuve, 1972). RS is similar to the mild oral form of tardive dyskinesia (TD) except there is no tongue symptoms in RS (Levin and Heresco-Levy, 1999). RS has been extensively reported to be associated with the treatment with first-generation antipsychotics (Schwartz and Hocherman, 2004). Only eleven cases of SGA-induced RS have been reported in the literature, among them, nine being linked to risperidone, one to clozapine, one to olanzapine and the other to aripiprazole (Dell'Osso et al., 2007). To our knowledge, our case reported here is the first patient with RS induced by quetiapine.

Quetiapine has a low striatal D2 receptor-binding profile, with the rapid release from D2 receptors making it less likely to cause extrapyramidal side effects (EPS) or TD (Seeman and Tallerico, 1999). Even though EPS syndromes or TD are less commonly reported with quetiapine use comparing with other atypical antipsychotics, there are nine cases reported of TD secondary to quetiapine (Ghelber and Belmaker, 1999; Ghaemi and Ko, 2001; Sharma, 2003). The mechanism of quetiapine-induced RS is unclear. Nishiyama et al. (1993) postulated that the underlying mechanism of RS, similar to TD, is a state of cholinergic hypofunction due to dopaminergic hypersensitivity in the basal ganglion. Therefore, the syndrome has been linked with other antipsychotic-induced extrapyramidal side effect, such as TD, akathisia, or drug induced Parkinsonism, which are the result of D2 receptor blockade in basal ganglion (Deshmukh et al., 1990).

Our case had several risk factors of RS, including old age, being female (Dell'Osso et al., 2007), and a diagnosis of mood disorder (Eren et al., 2004), which may accelerate the onset of RS.

An olanzapine-treated patient has been reported to develop RS (Sabolek and Bayerle, 2005). Hence, the improvement of RS during olanzapine treatment could not rule out the possibility that RS ameliorated spontaneously over time after discontinuing quetiapine. In conclusion, this observation from this case suggests that there is a possible risk of RS with quetiapine therapy, especially in high-risk patients. Clinician should be aware that RS is a potentially disfiguring but easily treated phenomenon. Olanzapine may be a useful strategy both for dealing with rabbit syndrome and treating psychotic and mood symptoms.

References

- Dell'Osso MC, Fagiolini A, Ducci F, Masalehdan A, Ciapparelli A, Frank E. New antipsychotics and the rabbit syndrome. *Clin Pract Epidemiol Ment Health* 2007;3: 6.
- Deshmukh DK, Joshi VS, Agarwal MR. Rabbit syndrome: a rare complication of long-term neuroleptic medication. *Br J Psychiatr* 1990;157:293.
- Eren I, Ozcankaya R, Altinyazar V. Risperidone-induced rabbit syndrome in mood disorder. *Eur Psychiatr* 2004;19:452–3.
- Ghaemi SN, Ko JY. Quetiapine-related tardive dyskinesia. *Am J Psychiatr* 2001;158:1737.
- Ghelber D, Belmaker RH. Tardive dyskinesia with quetiapine. *Am J Psychiatr* 1999;156: 796–7.

- Guy W, editor. Washington (DC): US Department of Health, Education and Welfare; 1976. p. 534–7.
- Levin T, Heresco-Levy U. Risperidone-induced rabbit syndrome: an unusual movement disorder caused by an atypical antipsychotics. *Eur Neuropsychopharmacol* 1999;9 (1–2):137–9.
- Nishiyama K, Masuda N, Kurisaki H. A case of rabbit syndrome—its unique pharmacological features. *Rinsho Shinkeigaku* 1993;33:663–5.
- Sabolek M, Bayerle M. Rabbit syndrome due to olanzapine. *Psychiatr Prax* 2005;32: 202–4.
- Schwartz M, Hocherman S. Antipsychotic-induced rabbit syndrome: epidemiology, management and pathophysiology. *CNS Drugs* 2004;18(4):213–20.
- Seeman P, Tallerico T. Rapid release of antipsychotic drugs from dopamine D2 receptors: an explanation for low receptor occupancy and early clinical relapse upon withdrawal of clozapine or quetiapine. *Am J Psychiatr* 1999;156:876–84.
- Sharma V. Treatment-emergent tardive dyskinesia with quetiapine in mood disorders. *J Clin Psychopharmacol* 2003;23:415–7.
- Villeneuve A. The rabbit syndrome. A peculiar extrapyramidal reaction. *Can Psychiatr Assoc J* 1972;17:69.

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