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Multiple therapies relieve long-term tardive dyskinesia in a patient with chronic schizophrenia: A case report.

Multiple therapies relieve tardive dyskinesia

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Abstract

BACKGROUND

Tardive dyskinesia (TD) is a serious and disabling movement disorder; it impairs social function and quality of life and increases the mortality rate. TD is usually induced by the use of antipsychotic drugs; however, the underlying mechanism remains unclear. Pharmacotherapy of TD includes cholinergic drugs, benzodiazepines, *Ginkgo biloba* extract, antioxidants, amantadine, propanolol, botulinum toxin, valbenazine, and deutetrabenazine, whereas the non-pharmacotherapy approach includes modified electroconvulsive therapy (MECT) and deep brain stimulation.

We successfully treated a chronic schizophrenia patient with comorbid long-term severe TD using deutetrabenazine, clozapine, and MECT. We here report this case and the treatment.

CASE SUMMARY

A 69-year-old woman who was diagnosed as having schizophrenia 16 years ago developed severe TD after 6-month prescription of risperidone oral solution. Her TD symptoms did not resolve despite various treatments, such as *Ginkgo biloba* extract, vitamin E, trihexyphenidyl, promethazine, benzodiazepines, and switching to

quetiapine and olanzapine. After admission, she was given deutetrabenazine 6 mg bid. Her buccal tremor was slightly resolved three days later; however, her tongue remained protruded and could not be retracted. Quetiapine was switched to clozapine on day 4, and the buccal tremor remarkably resolved, and the tongue could be retracted into the mouth day 6 onward. After three sessions of MECT, the buccal tremor resolved further. Since then, she has been able to take a semifluid diet, and her quality of life improved remarkably during the six months of follow-up.

CONCLUSION

TD is a serious condition which could be caused by antipsychotic medications; however, the best strategy against TD is prevention and monitoring during using antipsychotics. For patients with TD caused by antipsychotic medication use, multiple measures should be considered like switching to clozapine, adjunction with deutetrabenazine, or even MECT.

Key Words: tardive dyskinesia; antipsychotics; clozapine; deutetrabenazine; electroconvulsive therapy

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Core Tip: This report describes the treatment of tardive dyskinesia (TD) caused by risperidone in a schizophrenia patient. Her TD symptoms were relieved remarkably after multiple measures like switching to clozapine, adjunction with deutetrabenazine, and modified electroconvulsive therapy (MECT).

INTRODUCTION

Tardive dyskinesia (TD) is a serious and disabling movement disorder, which usually occurs after long-term use of antipsychotic drugs. TD is defined as the involuntary tic or dance-like movement (lasting for at least several weeks) of the tongue, lower jaw, as well as the extremities (1). It is evaluated with tools like Abnormal Involuntary Movement Scale (AIMS)(2). TD impairs social function and quality of life and increases the mortality rate(1, 3).

Common risk factors of TD include first-generation antipsychotics (FGAs), age, sex, and long-term exposure to dopamine receptor blocking agents (DRBA). In patients with schizophrenia, the prevalence of TD induced by antipsychotics is 20%–25%(4). Although FGAs are much more likely to induce TD than second-generation antipsychotics (SGAs), the incidence of TD has been increasing with a widespread use of SGAs, including their off-label use(5).

Although the mechanism underlying TD remains unclear(6), there are three pathophysiological hypotheses for TD, namely dopamine hypersensitivity, GABA deficiency, and oxidative stress. The treatments of TD include pharmacotherapy and non-pharmacotherapy(7). Pharmacotherapy includes the administration of cholinergic drugs, benzodiazepines, Ginkgo biloba extract (GBE), antioxidants, calcium channel blockers, amantadine, propanolol, and botulinum toxin, whereas non-pharmacotherapy includes modified electroconvulsive therapy (MECT) and deep brain stimulation (DBS)(8). However, only valbenazine and deutetrabenazine (Austedo) have been approved by the FDA for treating TD.

We successfully treated a chronic schizophrenia patient with comorbid long-term severe TD using deutetrabenazine, clozapine, and MECT. We here report this case and the treatment.

CASE PRESENTATION

Chief complaints

Uncontrollable, abnormal, and repetitive movements of the tongue and lower jaw for 16 years

History of present illness

A 69-year-old woman, who was diagnosed as having schizophrenia 16 years ago, was treated with risperidone oral solution for delusion and auditory hallucination. Six months later, her psychotic symptoms remitted, but she developed TD with abnormal involuntary movement in the mouth, tongue, and cheek. She was hospitalized twice since these symptoms appeared; however, her TD symptoms did not resolve despite various treatments, which included adjunction with GBE, vitamin E, trihexyphenidyl, promethazine, and benzodiazepines, as well as switching to quetiapine and olanzapine (Table 1). She has been on a liquid diet for many years because her teeth had to be removed due to severely worn tongue.

History of past illness

The patient was diagnosed as having schizophrenia 16 years ago. She was found to be hypertensive 2 years ago, which has been well controlled with valsartan 80 mg/d and amlodipine besylate 10 mg/d.

Personal and family history

The patient denied any other specific personal or family history of other diseases.

Physical examination

Her physical examination was not remarkable except for TD symptoms (Video 1). Mental examination showed clear consciousness, passive contact, poor thinking with delusion of reference, and depressive mood because of involuntary movements. Her insight was poor. She was not found to be experiencing hallucinations.

Laboratory examinations

After admission, many related examinations were conducted, but no abnormalities were found.

Imaging examinations

Her head CT scan was normal.

FINAL DIAGNOSIS

She was admitted with a diagnosis of schizophrenia, TD, and hypertension.

TREATMENT

After admission, she was given deutetrabenazine 6 mg bid. Her buccal tremor was slightly resolved three days later, but her tongue was still protruded and could not be retracted back. Quetiapine was switched to clozapine on day 4; consequently, the buccal tremor remarkably resolved, and the tongue could be retracted into the mouth day 6 onward (Video 2). She was encouraged to undergo and accepted additional MECT. After obtaining written informed consent, she was given three sessions of MECT, and the buccal tremor resolved further. On day 14, she was discharged with clozapine (25 mg bid) and deutetrabenazine (6 mg bid). (Table 1)

OUTCOME AND FOLLOW-UP

After discharge, she could take a semifluid diet with clozapine (25 mg bid) and deutetrabenazine (6 mg bid), and her quality of life improved remarkably during the six months of follow-up (Video 3, Table 1).

DISCUSSION

TD is mainly caused by FGAs and is managed with lowering the FGA dose or switching to SGAs, or it can be treated with deutetrabenazine and valbenazine. In this case, TD was induced by taking 4 mg risperidone daily for six months, and TD did not completely resolve after switching to other SGAs like quetiapine and olanzapine. This was a case of late-onset schizophrenia with possible hypersensitivity to risperidone. In this case, the underlying mechanism of TD could be that the plasma concentration of

risperidone was high because of reduced metabolic functions in older patients. It could also possibly be explained by reduced number of dopamine receptors, leading to increased sensitivity to SGAs(9, 10). This case suggests that SGA use is also associated with high risk for developing TD in patients with late-onset schizophrenia, which should be monitored with instruments like AIMS.

The patient responded poorly to medications like GBE, vitamin E, benzodiazepines, and promethazine. Her TD symptoms resolved partially with deutetrabenazine, a selective vesicular monoamine transporter 2 inhibitor (11), but resolved remarkably with clozapine. Clozapine is associated with a low risk of TD, which may be due to its low affinity to and rapid dissociation with dopamine D_2 receptors(12), suggesting that TD can be aggravated by long-term binding of dopamine D_2 receptors.

TD symptoms and mental symptoms of the patient resolved markedly after three sessions of MECT. Although MECT is not a first-line recommendation for treating TD (13), it poses no risk of precipitating, aggravating, or perpetuating TD and may be an important alternative choice for TD treatment.

CONCLUSION

In summary, TD is a serious condition caused by long-term use of antipsychotic medications. The underlying mechanism of TD is complex and remains unknown. The best treatment strategy for TD is prevention and monitoring during using antipsychotics. When it comes to treatment, multiple measures like switching to clozapine or combining it with deutetrabenazine or MECT could lead to a better prognosis than a single treatment.

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PRIMARY SOURCES

1	Lei Zhang, Wen-Juan Yu, Hui Zhu, Hua-Fang Li, Jie Qiao. "Successful treatment of hyperglycemia with liraglutide in a hospitalized 27-year-old patient with schizophrenia: A case report", World Journal of Clinical Cases, 2022 Crossref	21 words — 1%
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