

[Case Report]

Marked Improvement of Meige Syndrome in a Japanese Male Patient with Schizophrenia After Switching from Risperidone to Paliperidone: A Case Report

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Abstract : Meige syndrome is a relatively rare type of oral facial dystonia. The dominant symptoms involve involuntary eye blinking and chin thrusting. Some patients may experience excessive tongue protrusion, squinting, muddled speech, or uncontrollable contraction of the platysma muscle. A 44-year-old Japanese male was suffering from schizophrenia. The initial presentation of his psychosis consisted of auditory hallucinations, delusions of persecution, psychomotor excitement, loosening association, and restlessness. After being prescribed several antipsychotic drugs, risperidone was started and gradually increased to 4 mg/day. The above symptoms were relieved, particularly auditory hallucination and excitement were promptly improved. Persecutory delusion, however persisted, and deteriorated. At one year after the start of this risperidone regimen, he exhibited severe blepharospasm symptoms (increased rate of eye blinking, light sensitivity) and oromandibular symptoms (trismus, jaw pain, dysarthria). He was diagnosed with Meige syndrome. His antipsychotic drug was changed from risperidone to paliperidone. Two months after switching from risperidone to paliperidone, his eye blinking, light sensitivity, jaw pain, and trismus gradually improved, although the dysarthria persisted. Six months after starting paliperidone, his symptoms of Meige syndrome were completely remitted. He has been well without relapse at 12 mg/day of paliperidone. The case suggests that Meige syndrome is relieved by changing from risperidone to paliperidone. The precise mechanism of the relief remains, however, unknown.

Keywords : Meige syndrome, risperidone, paliperidone.

(Received February 16, 2016, accepted May 25, 2016)

Introduction

Meige syndrome is a form of idiopathic cranial dystonia characterized by oromandibular symptoms and symmetrical blepharospasm symptoms. It was first described in the French literature in 1910 by Henri Meige. The disease typically occurs in individuals between 30 and 70 years of age and is more common in women [1]. It affects facial expressions and can cause social and cosmetic disturbances, and the potential un-

controllable bilateral closure of the eyelids may cause visual impairment. Meige syndrome developing after long term first generation antipsychotics has been described [2, 3]. A literature search revealed only a few cases of Meige syndrome secondary to newer second generation antipsychotics [4–6]. It has been reported that risperidone treatment resulted in Meige syndrome [6–8]. Here we report the case of a Japanese male patient with schizophrenia and Meige syndrome whose Meige syndrome symptoms improved after a change

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of treatment agent from risperidone to paliperidone.

Case presentation

A 44-year-old Japanese male was suffering for 16 years from schizophrenia diagnosed by the Diagnostic and Statistical Manual of Mental Disorders -IV. His family history of neuropsychiatry disorders was negative. His development and past history of physical illness was not particular. The initial presentation of his psychosis consisted of auditory hallucinations, delusions of persecution, psychomotor excitement, loosening association, and restlessness. He was prescribed sulpiride (maximal dose: 1000 mg/day) and haloperidol (maximal dose: 6 mg/day), then changed to risperidone. He never had any extrapyramidal side effects. Risperidone was started and gradually increased to 4 mg/day. The above symptoms were relieved, particularly the auditory hallucinations and excitement gradually improved. Persecutory delusion persisted and deteriorated. At one year after the start of this risperidone regimen, he exhibited severe blepharospasm symptoms (increase rate of eye blinking, light sensitivity) and oromandibular symptoms (trismus, jaw pain, dysarthria), and he reported that he could not drive a car because of the blepharospasm. His magnetic resonance imaging (MRI) was not particular, with no infarctions or lacunar infarctions. He was referred to a neurologist, and diagnosed with Meige syndrome. His plasma levels at the trough of risperidone and 9-OH-risperidone, a major metabolite of risperidone, were 24.4 ng/ml and 20.9 ng/ml, respectively, when he was administered 4 mg/day of risperidone. His genotype of cytochrome P450 2D6 (cyp 2D6) was *10/*10, which is an intermediate metabolizer. At the appearance of the increase rate of eye blinking, light sensitivity, trismus, jaw pain, and dysarthria we changed his antipsychotic drug from risperidone to paliperidone, because these two drugs have similar pharmacological profiles. Paliperidone was started at 3 mg/day and increased to 6 mg/day. He was maintained with 12 mg/day of paliperidone at the plasma level of 9-OH-risperidone was 41.2 ng/ml. Two months after switching from risperidone to paliperidone, his eye blinking, light sensitivity, jaw pain, and trismus gradually improved, although the dysarthria persisted. Six months

after starting paliperidone, his symptoms of Meige syndrome were completely remitted. He has been well without relapse at 12 mg/day of paliperidone.

Discussion

The exact cause of Meige syndrome is not known, but a hypothesis speculating that dopaminergic and cholinergic imbalances underlie this syndrome is generally accepted [9]. The reason why our patient's Meige syndrome was relieved also remains unknown. It is not unlikely that the patient's plasma levels of risperidone and 9-OH-risperidone were responsible for the improvement of his symptoms. It is also not plausible that a correct amount of a dopamine and cholinergic imbalance was responsible for the improvement, as anticholinergic agents were not described in the present case. We reported that hyperactivities of the central dopaminergic and noradrenergic neurons are involved in the pathophysiology of Meige syndrome by measured monoamine metabolites [8]. We also reported that a case of schizophrenia with Meige syndrome induced by long-term aripiprazole was successfully treated with perospirone, tight binding to dopamine receptors (D2). Olanzapine, a loose binding to D2, also occurs Meige syndrome [10]. Taking these findings into account, complicated mechanisms might be involved in Meige syndrome.

Another explanation for the decrease in the fluctuation of D2 blockers might play an important role in the recovery from Meige syndrome. In our study of 54 Japanese schizophrenic patients with or without emerging extrapyramidal symptoms (EPS and non-EPS groups, respectively) who were treated with 4 mg/day risperidone, we compared the plasma levels of the active moiety (i.e., risperidone plus 9-hydroxy-risperidone) in the steady state. No differences were observed in the plasma levels of the active moiety at these two time points 4 and 8 weeks after risperidone administration in either group. However, the EPS patients showed a greater number of fluctuations/larger fluctuations in the plasma active moiety levels compared to the non-EPS group [11]. These results indicated that a stable plasma active moiety level may be important for preventing EPSs such as Meige syndrome during treatment with risperidone. Taking these

findings into account, the fluctuation of blood levels of risperidone and its active moiety may be related to the emergence of Meige syndrome. It remains unknown if the emergence of Meige syndrome is related to fluctuation of blood levels of risperidone and its active moiety, because we presented only one case report. Further study with accumulating cases is needed to confirm the hypothesis.

In conclusion, changing a patient's treatment from risperidone to paliperidone may help improve his Meige syndrome symptoms.

Consent

Written consent was obtained from the patient for publication of the manuscript.

Author's contributions

HH, AK, and KA analyzed the data and wrote the manuscript. RY was involved in all the processes of drafting the manuscript. All the authors have read and approved the final manuscript.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

1. Akiyama K (1999): Algorithms for neuroleptic-associated tardive movement disorders. *Psychiatry Clin Neurosci* 53(suppl): 23–29
2. Kurata K, Yuasa S, Kazukawa S, Kurachi M & Fukuda T (1989) : Meige's syndrome during long-term neuroleptic treatment. *Jpn J Psychiatry Neurol* 43:627–631
3. Bogdanov I & Sirota P (2003): Meige's syndrome associated with neuroleptic treatment and alcohol abuse. *Int J Psych Clin Pract* 7: 49–51
4. Mendhekar DN & War L (2009): Olanzapine induced acute Meige's syndrome. *J Neuropsychiatry Clin Neurosci* 21: 225
5. Ananth J, Burgoyne K & Aquino S (2000): Meige's syndrome associated with risperidone therapy. *Am J Psychiatry* 157: 149
6. Nishikawa T & Nishioka S (2002): A case of Meige dystonia induced by short-term quetiapine treatment. *Hum Psychopharmacol* 17: 197
7. Miyamoto S, Miyake N, Ogino S, Endo T & Yamaguchi N (2007): Successful treatment of Meige's syndrome induced by risperidone and fluvoxamine with olanzapine monotherapy in schizophrenia. *Psychiatry Clin Neurosci* 61: 702–703
8. Yoshimura R, Kakiyama S, Soya A, Ueda N, Shinkai K & Nakamura J (2001): Effect of clonazepam treatment on antipsychotic drug-induced Meige syndrome and changes in plasma levels of Gamma-aminobutyric acid, homovanillic acid, and 3-methoxy-4-hydroxyphenylglycol during treatment. *Psychiatry Clin Neurosci* 55: 543–546
9. Stahl SM, Yesavage JA & Berger PA (1982): Pharmacologic characteristics of Meige dystonia: differentiation from tardive dyskinesia. *J Clin Psychiatry* 43: 445–446
10. Umene-Nakano W, Yoshimura R, Hori H, Okamoto T & Nakamura J (2011): A case of schizophrenia with Meige syndrome induced by long-term aripiprazole successfully treated with perospirone. *Prog Neuropsychopharmacol Biol Psychiatry* 35: 273
11. Yoshimura R, Ueda N, Ikenouchi-Sugita A, Umene-Nakano W, Hori H, Kakiyama S & Nakamura J (2009): Fluctuating plasma levels of the active moiety of risperidone is related to occurrence of extrapyramidal symptoms. *Int J Psychiatry Clin Pract* 13: 21–24

リスペリドンからパリペリドンへの変更によりメージュ症候群が改善した統合失調症の1例

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要 旨：メージュ症候群は、顎口腔部や顔面のジストニアを特徴とする比較的稀なジストニアである。不随意に生じる瞬目や顎の突出も伴う。舌の突出、閉眼滑舌不良あるいは広頸筋の突っ張りなどの症状が認められる事もある。症例は44歳の日本人統合失調症の患者である。初発症状は、幻聴、迫害妄想、精神運動興奮、連合弛緩、落ち着きのなさであった。何種類かの抗精神病薬が試みられた後、リスペリドンによる治療が開始され緩徐に4 mg/日まで増量された。その結果上記の症状の改善が認められた。リスペリドン4 mg/日投与開始1年後から、顎口腔部の不随運動や眼瞼痙攣、光過敏症、開口障害、顎の痛み、構音障害などの症状が出現した。これらの症状からメージュ症候群と診断された。抗精神病薬がリスペリドンからパリペリドン 6 mg/日へと変更となった。その結果、瞬目、光過敏症、顎の痛み、開口障害は徐々に改善した。しかし、構音障害は持続した。パリペリドンに変更6ヶ月後にはこの患者のメージュ症候群の症状は完全に治癒した。患者は現在パリペリドン12 mg/日で精神症状の再燃もなく統合失調症の寛解状態を維持している。本症例はリスペリドンでメージュ症候群が生じた場合には、パリペリドンへの変更により改善する可能性を示唆している。しかし、その機序に関しては不明である。

キーワード：メージュ症候群、リスペリドン、パリペリドン。

JUOEH(産業医大誌) 38(3): 233 – 236 (2016)