

Black Hairy Tongue Associated with Olanzapine Treatment:

A Case Report

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Abstract

Olanzapine is an atypical antipsychotic drug approved for acute and long-term treatment of bipolar disorder. Although relatively safe as compared to other classical antipsychotic medications, there are a number of uncommon adverse effects of olanzapine such as oral cavity lesions. In addition to the relatively common side effect of dry mouth, several articles have reported an association between olanzapine treatment and the development of oral lesions such as aphthous stomatitis, pharyngitis, glossitis and oral ulceration. Although there are several cases in which the tongue was affected in conjunction with stomatitis or pharyngitis, we could not find a case report indicating a direct relationship between olanzapine use and a tongue lesion. We present here the case of a patient with bipolar disorder, who developed recurrent black hairy tongue on two different occasions following the addition of olanzapine to lithium treatment. In the present case, xerostomia (dry mouth), which is an adverse reaction of both olanzapine and lithium, may have played a role in the development of black hairy tongue. All agents with a possible side effect of xerostomia may predispose patients to black hairy tongue, especially when they are administered in combination. To preclude the development of this complication with such drugs, extra time and effort should be given to improving oral hygiene.

Key Words: Black hairy tongue, olanzapine, lithium, xerostomia, dry mouth, bipolar disorder, adverse effect.

Introduction

OLANZAPINE is an atypical antipsychotic drug approved for the acute and long-term treatment of bipolar disorder (1). It is considered an atypical antipsychotic because it alters affinities for serotonin and dopamine receptors. The most common adverse effects of olanzapine are somnolence, orthostatic hypotension, headache, constipation, weight gain, mild hyperglycemia, hypertriglyceridemia, extrapyramidal symptoms, dyspepsia and dry mouth (1, 2). Apart from these common side effects, there are a number of uncommon adverse effects of olanzapine, such as oral cavity lesions (3). Specifically, several authors have reported an association between olanzapine treatment and the development of such oral lesions as aphthous stomatitis, pharyngitis, glossitis and oral ulceration (3, 4).

Although several cases have been reported in which the tongue is affected in conjunction with stomatitis or pharyngitis (4), we could not find an article reporting a direct relationship between olanzapine use and a tongue lesion.

In this article, we present the case of a patient with a diagnosis of bipolar disorder, who developed recurrent black hairy tongue (BHT) on two different occasions following the addition of olanzapine to her treatment.

Case Report

A 25-year-old woman who presented with manic symptoms (i.e., euphoria, overtalkativeness, insomnia, grandiosity) to the emergency room, was admitted to our psychiatry inpatient clinic with a diagnosis of bipolar disorder I. Her psychiatric history revealed that the current admission was her fifth hospitalization since the beginning of her illness six years previously. Since her first episode, almost every year she had discontinued her treatment without consulting her physician. Each time, her nonadherence was eventually followed by the recurrence of manic symptoms and ended with hospitalization. During the first three hospitalizations, her symptoms were stabilized

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with a combined treatment of classical antipsychotic drugs (i.e., haloperidol, zuclopenthixol) and mood stabilizers (i.e., lithium, valproate). At the time of discharge in her first two hospitalizations, she was prescribed lithium (900 mg/day) as the mood stabilizer, and sodium valproate (1,000 mg/day) was added to the lithium therapy in the third one. In her last two hospitalizations (fourth and fifth), olanzapine (20 mg/day) was initiated as the antipsychotic drug concurrently with the mood stabilizers to decrease manic symptoms.

In the first month of her fourth hospitalization, while she was on the combined treatment of olanzapine (20 mg/day), lithium (900 mg/day), and sodium valproate (1,000 mg/day), she noticed discoloration at the back of her tongue. She also described alteration of taste and sensation of thickness in the dorsum of her tongue. She was not receiving any additional medications on a regular basis and was in good physical health except for the oral lesion. Her medical files did not reveal any history of diabetes mellitus or any other systemic illness. The blood levels of lithium and sodium valproate were within normal limits (0.7 mEq/L, 92.6 µg/mL, respectively). There was no significant laboratory finding, including HIV and thyroid hormone levels. Her family and hospital staff confirmed that she regularly brushed her teeth and practiced daily oral hygiene. She had been smoking 1–2 cigarettes per day for the last 2 years, but she described her smoking as irregular. No use of alcohol or any illicit drug was described.

After physical examination, the diagnosis of BHT was made by a consultant dermatologist. A possible association between olanzapine and BHT was suspected, as the patient had already been using other medications for longer periods without any complication. Upon recommendations of the dermatologist, olanzapine treatment was discontinued. The patient was also advised to brush her tongue with a soft toothbrush two times a day, and give more care to her oral hygiene. Twenty days after the cessation of the drug, BHT completely disappeared. After her discharge from hospital, the patient was in full remission for 10 months, while she was using lithium and sodium valproate combination therapy. During this period there were no drug-related complications, including tongue lesions.

Ten months later, she had discontinued her drug treatment again, which resulted in her fifth (current) hospitalization (twelve months after her fourth hospitalization). The combined treatment of olanzapine (20 mg/day) and lithium (1,200 mg/day) was again reinstated. As in her fourth hospitalization, she developed BHT after one month of therapy (Fig. 1). There were no signifi-



Fig. 1. Bilateral dark brown hairy appearance at midline of the posterior dorsal tongue.

cant changes in her medical status and smoking habit since her last hospitalization. The physical and neurological examinations were totally normal except for her tongue. The visual intraoral inspection revealed a localized bilateral dark brown hairy appearance at midline of the posterior dorsal tongue. The other parts of the tongue (tips and both sides) were not involved. The patient denied any pain or discomfort in the tongue. The consultant dermatologist confirmed the diagnosis and made recommendations similar to those made before. The consultant did not find it necessary to conduct further investigations, including culture or biopsy from the lesion. As the patient was displaying hypomanic symptoms while the BHT was recurring, we decided to continue olanzapine treatment at a lower dose (5 mg/day) instead of stopping it completely.

Despite continuation of the lower dose of olanzapine, and the lithium treatment (1,200 mg/day), the BHT completely disappeared over the next three weeks (Fig. 2). The patient was discharged in good condition from the hospital, without any tongue lesions. At her follow-up visit in the fourth month after her discharge, she was free of any tongue lesions while using lithium alone.

Discussion

Black hairy tongue, also known as *lingua villosa nigra*, is an abnormal coating of the tongue re-

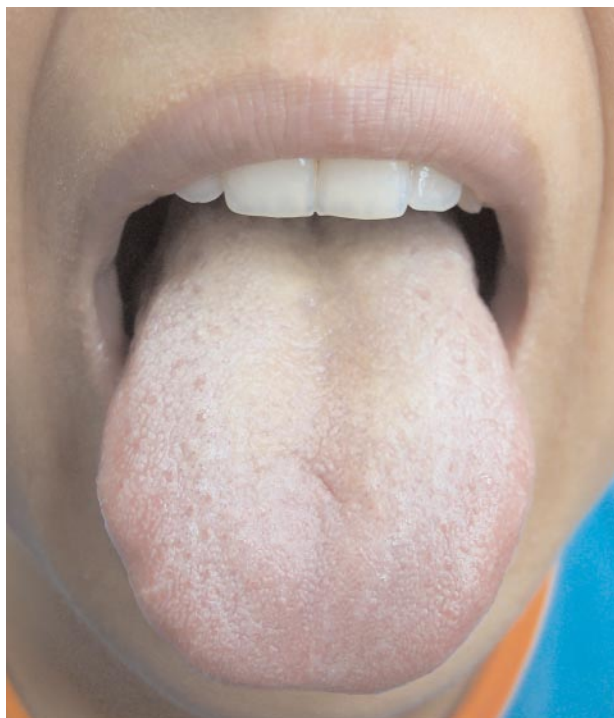


Fig. 2. The patient's tongue after lowering of olanzapine dose and empirical treatment.

sulting from elongation and lack of desquamation of the filiform lingual papillae (5–10). The hairy appearance is due to the elongation of keratinized filiform papillae, which may have different colors varying from white, yellow-brown to black depending upon the involved extrinsic factors (i.e., tobacco, coffee, tea or food) and intrinsic factors (i.e., chromogenic organisms in normal flora) (8, 10). Hairy tongue is diagnosed when filiform papillae are elongated more than 3 mm (7). This lesion is usually found on the dorsal tongue; it usually begins on the posterior tongue near the foramen cecum and then spreads laterally and anteriorly. The involvement of other parts of tongue is relatively rare (9).

The presentation of BHT is usually asymptomatic; however, in some cases like ours, symptoms such as alteration of taste, metallic taste, nausea or halitosis may be noted (5, 8). Occasionally, the papillae are so elongated that the patient may experience a tickling or gagging sensation in the soft palate during swallowing (5). In addition, overgrowth of candida albicans within elongated papillae may cause a variety of symptoms, such as glosopyrosis (burning tongue) (6).

The prevalence estimates of BHT vary widely, from 0.15–11.3% in the general population (7, 9). It has been observed with greater frequency in males, heavy smokers, intravenous drug users,

edentulous patients, those who heavily drink coffee and tea, the elderly disabled and HIV patients (6, 10–13). Several precipitating factors have been implicated in the development of BHT, such as the use of broad-spectrum antibiotics (e.g., tetracycline, amoxicillin), the use of oxidizing mouthwashes or antacids, toothpastes containing neomycin, general debilitation due to old age, poor oral hygiene, heavy smoking, and radiation therapy (3, 6). Some other psychotropic drugs (i.e., phenothiazines, tricyclic antidepressants, benzodiazepines, thiothixene, tranlycypromine, fluoxetine) are also reported to be associated with BHT (3, 13).

Information about the pathogenesis of black hairy tongue is limited. *Candida* and *Aspergillus* can frequently be demonstrated in the cultures taken from the sides of the lesion. Cytological smears stained with Gram stain or periodic-acid-Schiff (PAS) stain may reveal candidal organisms in these tongue lesions (6). However they are not believed to be the causative agents (5). According to some authors, the limitation of tongue movements due to painful oral situation or other illnesses may be responsible for the development of hairy tongue (5, 14). The lack of tongue movements prevents the normal desquamation of the keratinized surface layers of the filiform papillae through friction of the tongue with food, the palate and the upper anterior teeth (14). This mechanism could be an explanation for the increased prevalence of BHT among the elderly and patients with chronic illness.

In our case, the patient developed BHT following the co-administration of olanzapine with lithium and valproate for stabilizing her acute manic symptoms. Although smoking (less than 2–3 cigarette per day) may have been partially responsible, BHT was not present until the co-administration of olanzapine with other drugs. Furthermore, the patient had already been taking other drugs (lithium throughout her course of treatment and sodium valproate for 10 months after her fourth hospitalization). The re-introduction of olanzapine treatment at a daily dose of 20 mg resulted in development of BHT at about the same time as in her previous admission. The rechallenge of olanzapine and resultant recurrence of BHT in one month corroborated the possible association between olanzapine and BHT. The BHT was treated successfully by lowering the dose of olanzapine and improving oral hygiene. In this patient, the relationship between olanzapine and BHT was possibly a dose-dependent relationship, as the sustained administration of olanzapine in lower doses (5 mg/day) did not cause progression or endurance of the lesion.

Apparently the xerostomia (dry mouth), which is an adverse reaction to olanzapine and to lithium, may have played a role in the pathogenesis of BHT (15). Dry mouth is a common adverse effect of treatment with lithium salts (3, 15). Although the most obvious feature of this complaint is hyposalivation, other factors, such as the experience of thirst due to polyuria, may also play a role. On the other hand, olanzapine also causes dry mouth—at a relatively low incidence (16%)—by blocking both muscarinic cholinergic receptors and alpha 1-adrenoceptors (1, 15). In the literature, it is consistently reported that drug combinations can increase the side effects of medications, particularly xerostomia (15). It is likely that concomitant administration of these two xerostomia-inducing agents (olanzapine and lithium) caused a cumulative effect which resulted in the development of BHT.

BHT is a benign and self-limiting condition (5, 6). Empirical approaches such as brushing or scraping the tongue, improving oral hygiene, and elimination of any potential offending factors (tobacco, candies, strong mouthwashes, antibiotics, etc.) would be sufficient to remove the lesions. Brushing or scraping the tongue would remove elongated filiform papillae and retard the growth of additional ones. Rinsing the mouth with diluted hydrogen peroxide may also help bleach the color. In most instances, the tongue returns to its normal state subsequent to physical debridement and proper oral hygiene (13). Other alternatives involve lifestyle management, which includes drinking lots of water and eating raw fruit and vegetables such as celery, apples and carrots to provide roughage on the tongue. If the etiology of a patient's BHT appears to be primarily due to poor oral hygiene, a consultation with a dentist is strongly suggested (5).

Pharmacological interventions are rarely required in the treatment of BHT. In the presence of superimposed candidal infection with consequent glossopyrosis, topical antifungal medications such as clotrimazole or nystatin could be used (6). In some other cases, topical retinoids, oral retinoids such as isotretinoin, topical triamcinolone acetonide, gentian violet, salicylic acid, vitamin B complex, and 40% urea solution, have been reported to be successful in the treatment of BHT. Yogurt or other *Lactobacillus acidophilus* cultures may be of benefit (5, 8, 16). Clipping of the elongated papillae (using local anesthesia) or surgical excision of the papillae is rarely required and is

suggested only as a last resort. If the lesion persists, a consultation with a dentist would be appropriate, to rule out other clinically similar entities (6).

In conclusion, BHT may develop as an adverse reaction to olanzapine treatment, especially when combined with lithium. In the present case, the relationship between olanzapine and BHT was possibly a dose-dependent relationship, as the sustained administration of olanzapine in lower doses did not cause progression or permanency of the lesion. All agents with a possible side effect of xerostomia can be a source of BHT, especially when they are administered in combination. To preclude the development of this complication with such drugs, extra time and effort should be given to improving oral hygiene.

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