

CASE REPORT

Black hairy tongue after alprazolam intake

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Key Clinical Message

A 31-year-old female with a diagnosis of bipolar disorder developed black hairy tongue after alprazolam therapy. Her symptom resolved 10 days after the cessation of alprazolam.

Abstract

Alprazolam is a widely used antidepressant and antianxiety drug. Mild to moderate side effect of alprazolam was commonly seen, including lethargy, dizziness, headache, dry mouth, nausea, fatigue, constipation, and blurred vision. In this case, we reported a patient developed black hairy tongue after alprazolam intake, and her symptom resolved after 10-day discontinuation of alprazolam. This rare adverse event should be of concern to clinicians. This is the first paper to report an alprazolam-induced BHT. This rare side effect of alprazolam should be concern of clinicians; we hope our report will promote the understand of BHT and acknowledge clinicians of this rare side effect of alprazolam.

KEYWORDS

adverse drug reaction, adverse effect, alprazolam, black hairy tongue

1 | INTRODUCTION

As a common antidepressant and antianxiety drug, alprazolam has been widely used and proven to have a definite therapeutic effect. Occasional mild to moderate side effects associated with alprazolam include lethargy, dizziness, headache, dry mouth, nausea, fatigue, constipation, and blurred vision.¹ The likelihood of experiencing side effects is strongly related to the duration and dosage of alprazolam use. Long-term using of alprazolam may lead to tolerance, addiction, and withdrawal reactions upon sudden discontinuation; therefore, long-term using should be avoided.¹ Swelling of the tongue has been reported as a side effect of alprazolam,² but other forms of tongue abnormalities have not been reported. In this case report, we present a case of black hairy tongue (BHT) following

alprazolam intake. By reporting this rarely observed side effect, we aim to emphasize the safety of alprazolam in clinical use. Understanding the link between alprazolam and BHT can significantly impact patient care, prompting cautious prescription practices and timely intervention to prevent unnecessary distress and complications for patients with bipolar disorder.

2 | CASE PRESENTATION

A 31-year-old female with a chief complaint of alternating distress and excitement for over a year was admitted to our hospital. The patient had previously been diagnosed with bipolar disorder and was in the depressive phase at the time of admission. Prior to admission, she had been

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intermittently taking quetiapine for long-term treatment. Her past medical history was unremarkable. She had been smoking eight cigarettes per day for 2 years without quitting, but she did not consume alcohol or any addictive drugs. The patient had stable vital signs, and no abnormalities were found upon physical examination. By utilizing routine biochemical, endocrine, and immunological markers, it helps to rule out organic diseases in the patient. Laboratory tests, including complete blood count, metabolic panel, coagulation function, immunity, adrenocorticotropic (ACTH), β -HCG, inflammatory index, and autoimmune antibody spectrum, were mostly within the normal range. Abdominal, urinary, and thyroid gland ultrasonic examinations revealed no abnormalities. A chest CT scan showed a suspicious infection lesion. Lithium carbonate 250 mg twice a day and quetiapine 300 mg once before bed were prescribed for initial treatment. Several days after hospitalization, the patient complained of insomnia, and alprazolam 0.8 mg once before bed was added. After 1 week of alprazolam using, the patient complained of a black tongue. Intraoral examination revealed darkening and a hair-like appearance of the dorsal tongue (Figure 1A). Suspecting a side effect related to alprazolam, we discontinued alprazolam while keeping other medications unchanged. The color of the dorsal tongue gradually returned to normal 10 days after cessation of alprazolam, as shown in Figure 1B,C.

3 | DISCUSSION

In this case, we report a patient diagnosed with bipolar disorder who developed BHT after taking alprazolam. The color of her tongue returned to normal after discontinuing alprazolam while other medications remained unchanged, indicating a strong relationship between BHT and alprazolam.

Black hairy tongue is a benign condition characterized by brown-to-black pigmentation and a furry appearance.^{3,4}

Elongated filiform lingual papillae play an important role in this process, as they can become stained by endogenous or exogenous pigment, resulting in a darkened appearance of the dorsal tongue.^{4,5} The elongation of filiform lingual papillae can be caused by decreased desquamation and/or increased production of keratin.^{3,6} Risk factors for BHT include smoking or chewing tobacco, using e-cigarettes, poor oral hygiene, oxidizing mouthwashes, excessive consumption of coffee or black tea, trigeminal neuralgia, radiation therapy, chemotherapy, and the use of a broad spectrum of medications.^{4,6-9} The elongated filiform lingual papillae provide an environment for organisms to colonize. The use of broad-spectrum antibiotics may facilitate this process by disrupting the oral cavity's microecology and promoting fungal overgrowth.¹⁰ The development of BHT is also associated with changes in saliva quantity and pH, as evidenced by reports of Vitamin C-induced BHT.¹¹

Both the elongation and discoloration of filiform lingual papillae are necessary for the diagnosis of BHT. However, discoloration of the dorsal tongue can occur in specific conditions and should not be considered as BHT. Certain foods and drugs rich in pigments (such as sour plum, black sesame paste, mulberry, iron agents, compound glycyrrhiza tablets, and bismuth agents) may directly stain the tips of non-elongated filiform lingual papillae, which should be classified as pseudo-BHT. Some systemic diseases, such as Addison's disease, Peutz-Jeghers syndrome, and Laugier-Hunziker syndrome, can also cause oral cavity pigmentation, but they usually affect multiple sites and not exclusively the dorsal tongue.⁴ Smoker's melanosis is another possible cause of black tongue, characterized by accumulated melanin due to noxious chemicals in cigarettes or protective melanin production by melanocytes.^{4,9}

Furthermore, we reviewed case reports of BHT or black tongue caused by medications published in the past 10 years with available full texts (Table 1). A total of 14 cases from 11 reports were included. Most BHT cases (10/14, 78.6%) were associated with antibiotic agents, with linezolid being the most frequently implicated drug (8/14,



FIGURE 1 (A) 1 week after intaking alprazolam; (B) 5 days after cessation of alprazolam; (C) 10 days after cessation of alprazolam.

TABLE 1 Literature review of medication-induced black hairy tongue/black tongue in the past 10 years.

Author	Patient	Year	Journal	Causative drug
Shangguan et al. ⁵	3	2022	<i>Infect Drug Resist</i>	Linezolid
Kato et al. ¹²	1	2022	<i>Am J Case Rep</i>	Moxifloxacin
Niiyama et al. ¹³	1	2021	<i>Braz J Infect Dis</i>	Metronidazole
Ren et al. ⁸	2	2021	<i>J Int Med Res</i>	Piperacillin-tazobactam+linezolid
Lee et al. ¹⁴	1	2021	<i>Sci Prog</i>	Linezolid
Zhao et al. ¹⁵	1	2020	<i>J Clin Pharm Ther</i>	Imipenem cilastatin
Owczarek et al. ¹¹	1	2020	<i>Am J Case Rep</i>	Ascorbic acid
Braggio et al. ¹⁶	1	2018	<i>Acta Biomed</i>	Linezolid
Akcaboy et al. ¹⁷	1	2017	<i>Pediatr Dermatol</i>	Ranitidine
Jhaj et al. ¹⁰	1	2016	<i>Indian J Pharmacol</i>	Olanzapine+fluoxetine
Balaji et al. ¹⁸	1	2014	<i>Indian J Pharmacol</i>	Linezolid

57.1%). Only one case was found to be associated with antipsychotic drugs.¹⁰ Other medications, such as ascorbic acid and ranitidine, can also cause BHT in extremely rare conditions. But the underlying pathophysiology behind the association between antipsychotic agents and BHT are still unknown.

During hospitalization, most cases of BHT were associated with antibiotic agents. The dysbiosis in the oral cavity that leads to the growth of chromogenic pathogens is one of the hypothesized mechanisms of antibiotic-induced BHT.⁵ The human oral cavity is inhabited by approximately 700 bacterial species, contributing to the diversity of oral microbiota. Prevailing bacteria in the oral cavity include Veillonella, Actinomyces, Streptococcus, and Neisseria, most of which are susceptible to broad-spectrum antibiotics.¹⁹ Antibiotic agents can significantly affect the balance and diversity of oral microbiota by eliminating sensitive strains. Decreased microbiota diversity increases the likelihood of colonization and growth of foreign pathogens among the filiform lingual papillae that can survive the antibiotics. Interestingly, in the report by Shangguan et al.,⁵ the causative pathogens were Gram-negative bacteria that are not sensitive to linezolid, partially supporting this hypothesis.

Among various antipsychotic agents, chlorpromazine, clonazepam, lithium, maprotiline, olanzapine, paroxetine, and thiothixene have been previously reported to cause BHT.^{3,10} The pathophysiological basis of this effect is not well understood, but a widely accepted hypothesis is that antipsychotic agents can cause xerostomia, leading to the development of BHT.⁴ In our case, the patient received a combined therapy of alprazolam, lithium, and seroquel, among which lithium-induced BHT has been previously documented.²⁰ However, when we discontinued alprazolam while maintaining the lithium therapy, the patient's tongue returned to normal, suggesting that lithium may not be the causative drug in this case. Alprazolam, widely used as an anti-anxiety and antidepressant drug, commonly exhibits side effects such as lethargy, dizziness, headache,

xerostomia, nausea, fatigue, constipation, and blurred vision,¹ with xerostomia potentially being associated with BHT in this case. To our knowledge, this is the first case report of BHT induced by alprazolam. Although this side effect has not been previously reported, it should be taken into account, especially in patients with mental illnesses who may be prone to pessimism due to the emergence of new symptoms. While BHT related to antipsychotic agents has been rarely reported in recent years, physicians should be aware of this rare side effect, which may have a greater impact on psychotic patients compared to others.

Black hairy tongue is a benign, self-limited, and commonly asymptomatic condition with a good prognosis and therefore does not require specific treatment. However, it may cause aesthetic concerns.³ Management of predisposing factors and withdrawal of the causative agent(s) are the primary measures to resolve the symptoms. Maintaining oral hygiene may also aid in the recovery of BHT. Oral antibiotic therapy should be considered when BHT shows no signs of improvement despite optimal management of potential predisposing factors. The limitation of this study lies in the small number of observed cases. Currently, the incidence of BHT is relatively low, further research and observation of more cases to enhance our understanding of this condition.

4 | CONCLUSION

Black hairy tongue is a benign, self-limited, asymptomatic disease, predominantly caused by antibiotic agents. We reported the first case of BHT caused by alprazolam. This rare adverse event should be of concern to clinicians. Discontinuing or adjusting the suspected drug is crucial in managing BHT to prevent its progression and promote symptom resolution. Further research in this area is warranted to better understand the prevalence, underlying mechanisms, and optimal management strategies for BHT.

AUTHOR CONTRIBUTIONS

Long Jiang: Conceptualization; investigation; resources; writing – original draft; writing – review and editing. **Kun Li:** Conceptualization; data curation; resources; writing – original draft; writing – review and editing. **Lu Tan:** Conceptualization; data curation; writing – original draft; writing – review and editing. **Xiangdong Tang:** Conceptualization; investigation; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declared that they have no conflicts of interest to this work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

ETHICS STATEMENT

Ethical approval was obtained from Ethics Committee of West China Hospital.

CONSENT STATEMENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not involved.

CLINICAL TRIAL REGISTRATION

Not involved.

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