



Case Series

Black Hairy Tongue: A Rare Adverse Event in Patients Receiving BPALM Regimen for MDR-TB: A Case Series

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ABSTRACT

Black hairy tongue (BHT) is a rare, benign, and self-limiting disorder characterized by black or brown discoloration of the dorsal surface of tongue due to elongation of filiform papillae. Linezolid, an important component of the BPALM regimen for multidrug-resistant tuberculosis (MDR-TB), has been rarely associated with BHT. We report many cases of linezolid-associated BHT in patients receiving BPALM regimen for MDR-TB. The patients developed painless brown discoloration of the tongue without systemic symptoms. Clinical findings and Naranjo causality assessment suggested a probable association with linezolid. The lesion resolved completely following completion of therapy and maintenance of oral hygiene. These cases highlight the importance of recognizing BHT as a rare adverse drug reaction associated with linezolid-containing MDR-TB regimens to avoid unnecessary investigations and treatment interruption.

Keywords: Black hairy tongue, BPALM regimen, MDR-TB.

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) remains a major global health challenge requiring prolonged treatment with second-line anti-tubercular drugs.[1] The recently recommended BPALM regimen, comprising bedaquiline, pretomanid, linezolid, and moxifloxacin, has improved treatment outcomes in MDR-TB patients.[3] Among these drugs, linezolid is an important oxazolidinone antibiotic with potent antimycobacterial activity; however, its prolonged use is associated with several adverse drug reactions.[1,4]

Black hairy tongue (BHT), also known as *lingua villosa nigra*, is a rare, benign, and self-limiting condition characterized by elongation and hypertrophy of filiform papillae causing black or brown discoloration of the dorsal tongue.[2] The condition is thought to result from defective desquamation and accumulation of keratin, microorganisms, and debris.[4] Poor oral hygiene, smoking, alcohol intake, xerostomia, and certain antibiotics are recognized predisposing factors.[2,5] Linezolid-associated BHT is uncommon, with an estimated incidence of approximately 0.2%.[2] Although generally asymptomatic and reversible, its unusual appearance may cause significant anxiety and unnecessary treatment interruption. [1,4] Therefore, awareness of this rare adverse effect is important in patients receiving linezolid-containing regimens such as BPALM. Here, we report rare cases of black hairy tongue developing in a patient receiving BPALM regimen for MDR-TB.

CASE SERIES

This case series comprised of seven patients (three females and four males) aged between 18 and 45 years who developed black hairy tongue while receiving the BPALM regimen for drug-resistant tuberculosis. The onset of tongue discoloration showed considerable variability, occurring as early as the 3rd day of treatment in one patient, on the 5th day in another, on the 10th day in two patients, on the 13th day in one patient, and within the 2nd month of therapy in two patients. The discoloration ranged from brownish to black and was asymptomatic in all cases, with no associated pain, ulceration, dysphagia, or impairment of oral intake.

The clinical course was variable. Partial resolution was observed after 10 days, 1 month, and 2 months in different patients, while one patient experienced recurrence of black discoloration during the 3rd month following partial improvement. In four patients, the lesion persisted in a partially resolved state throughout the remainder of treatment. Nevertheless, all patients completed therapy without dose modification, treatment interruption, or discontinuation of the BPalm regimen.

Complete spontaneous resolution of the tongue discoloration was observed in all seven patients. Resolution occurred during ongoing treatment in two patients, one within 10 days of onset and another by the 2nd month of therapy. In the remaining five patients, complete resolution was noted after treatment completion, occurring within 1 week to 10 days in three patients and shortly after completion of therapy in the other two. The consistent spontaneous recovery and absence of serious sequelae across all cases highlight the benign, reversible, and self-limiting nature of black hairy tongue associated with linezolid-containing BPalm therapy.

Development of Black Hairy Tongue	Resolution of Black Hairy Tongue
<p style="text-align: center;">A.</p> 	
<p style="text-align: center;">B</p> 	
<p style="text-align: center;">C</p> 	
<p style="text-align: center;">D</p> 	
<p style="text-align: center;">E</p> 	

Table 1. Clinical Characteristics of Patients Developing Black Hairy Tongue During BPalm Therapy

Case	Age (Years)	Sex	Regimen	Onset of Tongue Discoloration	Clinical Course	Complete Resolution
1	32	Female	BPalm	3rd day	Partial resolution after 1 month; persisted throughout treatment	Within 1 week after treatment completion
2	36	Female	BPalm	10th day	Partial resolution by 2nd month; recurrence during 3rd month; persisted thereafter	10 days after treatment completion
3	27	Female	BPalm	5th day	Partial resolution by 10th day	By 2nd month during ongoing treatment
4	31	Male	BPalm	10th day	Gradual spontaneous improvement	Within 10 days during ongoing treatment
5	31	Male	BPalm	2nd month	Persisted in partially resolved state throughout treatment	Within 1 week after treatment completion
6	18	Male	BPalm	13th day	Persisted in partially resolved state throughout treatment	After treatment completion
7	45	Male	BPalm	Within 2 months	Persistent brownish discoloration during treatment	After treatment completion

Table 2. Naranjo Adverse Drug Reaction Probability Scale

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	+2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
Total Score				

Interpretation: A total Naranjo score of 5 indicates a Probable Adverse Drug Reaction (ADR).

DISCUSSION

Black hairy tongue (BHT), or *lingua villosa nigra*, is a rare, benign, and reversible condition characterized by elongation and hypertrophy of the filiform papillae with accumulation of keratin, resulting in brown, black, or yellow discoloration of the dorsal surface of the tongue. Although several predisposing factors have been implicated, including smoking, poor oral hygiene, xerostomia, and antibiotic exposure, linezolid has emerged as a recognized but uncommon cause of drug-induced BHT.

In the present case series, seven patients receiving the BPalm regimen for drug-resistant tuberculosis developed tongue discoloration consistent with BHT. The temporal association between initiation of therapy and onset of the lesion strongly suggests a drug-related adverse event. The onset varied considerably, ranging from as early as the 3rd day of treatment to as late as the 2nd month, indicating that BHT may occur at any stage during linezolid-containing therapy. Such variability has also been reported in previous literature, where the time to onset ranged from a few days to several weeks after drug exposure.

A notable finding in this series was the heterogeneity in the clinical course of the lesion. While two patients experienced complete spontaneous resolution during ongoing treatment, the remaining five exhibited persistence of discoloration

throughout therapy, albeit often in a partially resolved state. One patient demonstrated recurrence of black discoloration after initial improvement, highlighting the fluctuating nature of the condition. Despite these differences, all cases ultimately resolved completely either during treatment or shortly after completion of therapy, reinforcing the self-limiting character of the adverse event.

The exact mechanism underlying linezolid-induced BHT remains incompletely understood. Proposed mechanisms include disruption of the normal oral microbiota, impaired desquamation of the filiform papillae, and accumulation of chromogenic microorganisms, keratin, food debris, or pigments on the tongue surface. The prolonged duration of linezolid administration in the BPalm regimen may contribute to the development and persistence of these changes. The complete resolution observed following continuation or completion of therapy further supports a reversible drug-induced process rather than an underlying pathological oral condition.

Importantly, none of the patients in this series experienced pain, ulceration, dysphagia, impairment of oral intake, or other clinically significant oral complications. No patient required dose reduction, temporary interruption, or discontinuation of the BPalm regimen. Recognition of the benign nature of BHT is therefore crucial, particularly in the management of drug-resistant tuberculosis, where treatment adherence is essential for successful outcomes. Misinterpretation of this unusual adverse effect may result in unnecessary investigations, patient anxiety, or avoidable modification of an effective anti-tubercular regimen.

The consistent temporal relationship, absence of alternative explanations, spontaneous recovery, and previously documented association between linezolid and BHT support a probable causal relationship. Using the Naranjo Adverse Drug Reaction Probability Scale, the reaction would be classified as a probable adverse drug reaction. To our knowledge, reports describing multiple cases of BHT occurring during BPalm therapy remain limited, making this series a valuable contribution to the growing body of evidence regarding the safety profile of linezolid-containing regimens.

CONCLUSION

Black hairy tongue is an uncommon but benign adverse event associated with linezolid-containing regimens used in the treatment of drug-resistant tuberculosis. In this series, tongue discoloration appeared at varying intervals after treatment initiation, remained asymptomatic, and resolved spontaneously either during therapy or shortly after treatment completion without requiring specific intervention.

Early recognition of this reversible condition is essential to prevent unnecessary diagnostic procedures, treatment modification, or discontinuation of effective anti-tubercular therapy. Patient reassurance, maintenance of good oral hygiene, and careful clinical monitoring are usually sufficient for management. Increasing awareness of linezolid-associated black hairy tongue among tuberculosis care providers may improve treatment adherence and reduce anxiety related to this unusual but harmless adverse effect.

Conflict of Interest

Nil

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Nil

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