

Rare side effects of linezolid treatment on the tongue

Linezolid tedavisine bağlı dilde nadir görülen yan etkiler

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ABSTRACT

Linezolid is a widely utilized antibiotic due to its efficacy against difficult-to-treat Gram-positive bacterial infections, including methicillin-resistant *Staphylococcus aureus* (MRSA) and glycopeptide-resistant enterococci. However, rare but reversible adverse effects such as black discoloration and fissured appearance of the tongue have been reported during linezolid therapy. In this study, we present four cases exhibiting black tongue discoloration and fissured tongue associated with linezolid use. These oral manifestations resolved shortly after discontinuation of linezolid and implementation of appropriate oral hygiene measures. Given the limited number of case reports in the literature, these findings underscore the importance of increasing clinician awareness regarding potential adverse effects of linezolid and facilitating early recognition of similar clinical presentations. In conclusion, identification and proper management of structural and pigmentary changes in the tongue during linezolid treatment are crucial for ensuring patient safety.

Keywords: Linezolid, Side effect, Tongue discoloration, Fissured tongue

ÖZ

Linezolid, metisiline dirençli *Staphylococcus aureus* (MRSA) ve glikopeptid dirençli enterokoklar gibi tedavisi güç Gram-pozitif bakteriyel enfeksiyonlarda etkinliği nedeniyle klinikte yaygın olarak kullanılan bir antibiyotiktir. Ancak, linezolid tedavisi sırasında dilde siyah renk değişikliği ve fissürlü dil gibi nadir ancak geri dönüşümlü advers etkiler bildirilmektedir. Bu çalışmada, linezolid tedavisi gören dört hastada gelişen dilde siyah renk değişikliği ve fissürlü dil olguları sunulmuş, bu yan etkilerin tedavinin kesilmesi ve uygun ağız hijyenine yönelik önlemlerle kısa sürede gerilediği gözlemlenmiştir. Literatürde sınırlı sayıda vaka raporu ile bildirilen bu durumlar, klinisyenlerin linezolidin potansiyel yan etkileri konusunda farkındalığını artırmak ve benzer klinik bulguların erken tanınmasını sağlamak amacıyla önem taşımaktadır. Sonuç olarak, linezolid kullanımı sırasında dilde ortaya çıkan renk ve yapı değişikliklerinin tanımlanması ve uygun yönetimi, hastaların tedavi güvenliği açısından kritik bir husustur.

Anahtar Kelimeler: Linezolid, Yan etki, Dilde renk değişimi, Fissürlü dil

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INTRODUCTION

Linezolid is a clinically valuable antibiotic primarily used against challenging Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA) and glycopeptide-resistant enterococci. Despite its bacteriostatic mechanism, linezolid demonstrates significant therapeutic efficacy. Commonly reported adverse effects encompass gastrointestinal symptoms such as diarrhea, as well as headache, nausea, anemia, and taste disturbances. Less frequent but clinically relevant side effects include hematologic abnormalities (e.g., leukopenia, neutropenia, thrombocytopenia) and visual disturbances (1). Rarely, black discoloration of the tongue and the condition known as black hairy tongue (BHT) have been documented (2). In this report, we present a series of four patients who developed black discoloration of the tongue accompanied by oral and lingual ulcerations following linezolid therapy. All patients provided written informed consent, and they were followed up at Atatürk University Research Hospital between 2024 and 2025.

CASES

Case 1

A 59-year-old male with no prior chronic conditions or regular medication use was admitted due to soft tissue infection of the left leg following trauma from a traffic accident. Empirical intravenous ceftriaxone (2 g twice daily) was initiated. Due to worsening purulent discharge, therapy was switched to linezolid (600 mg IV twice daily) targeting MRSA. Clinical and laboratory improvement was noted with decreased purulence and reduced inflammatory markers. On day 7 of linezolid treatment, the patient developed a scrotal-like tongue (Figure 1) appearance and perioral ulcers, prompting discontinuation of linezolid. All treatments received by the patient, including non-antibiotic therapies, were evaluated, and it was determined that the patient was not receiving any other therapy that could affect linezolid metabolism. He had no history of smoking or alcohol use; however, his oral hygiene was poor. Supportive oral care including gentle tongue brushing three times daily and post-meal mouth rinses were advised. The lesions and discoloration resolved within two weeks, and the patient was discharged.



Figure 1. Scrotal tongue appearance and accompanying perioral ulcers developing during linezolid treatment

Case 2

A 41-year-old female with a history of spondylodiscitis was admitted for persistent symptoms despite prior treatment. No surgical interventions had been performed, and imaging revealed no abscess, spinal cord compression, or neurological deficits. Empirical treatment with ceftriaxone (2 g IV twice daily) and linezolid (600 mg IV twice daily) were started. Blood cultures yielded no significant growth. Inflammatory markers improved; however, on day 25 of therapy, black discoloration of the tongue (Figure 2) was observed. It was observed that the patient had not used any medication that could affect linezolid metabolism for several months including during her hospitalization. Additionally, it was learned that the patient, whose oral hygiene was suboptimal, consumed 5–6 cups of tea per day but did not use tobacco or alcohol. Linezolid was discontinued. Following oral hygiene measures including tongue brushing, discoloration improved within one week. Ceftriaxone and vancomycin therapy were continued for six weeks. The patient was discharged in stable condition.



Figure 2. Black hairy tongue-like discoloration developing during prolonged linezolid treatment

Case 3

A 65-year-old female with no known comorbidities was hospitalized for septic arthritis. Initial treatment with vancomycin was discontinued due to intolerance, and linezolid (600 mg IV twice daily) was initiated. No evidence of bacteremia, endocarditis, or secondary infectious foci was found. On day 14, fissured tongue (Figure 3) developed. The patient was not receiving any medication other than linezolid. The patient, whose oral hygiene was suboptimal, had no history of smoking or alcohol use but reported a habitual consumption of two cups of coffee per day. Given clinical and laboratory improvement, linezolid was stopped. The patient was advised to perform gentle tongue brushing and postprandial rinsing. Resolution of tongue fissuring was observed within a week, and the patient was discharged with amoxicillin-clavulanate (875 mg twice daily orally) and oral care instructions.



Figure 3. Fissured tongue observed on day 14 of linezolid therapy

Case 4

A 37-year-old female without previous chronic illness presented with presumptive *Mycobacterium tuberculosis* meningitis. Standard quadruple anti-tuberculosis therapy (isoniazid, rifampicin, ethambutol, pyrazinamide) was initiated. Due to persistent neurological symptoms and while awaiting resistance testing, linezolid (600 mg IV twice daily) was added. The patient, who was not receiving any medication known to interact with linezolid, had a history of smoking half a pack of cigarettes per day and exhibited poor oral hygiene. On day 28, black tongue discoloration (Figure 4) was noted, leading to discontinuation of linezolid. With supportive oral hygiene, discoloration resolved within one week. Resistance tests confirmed susceptibility to the initial regimen. The patient was discharged on day 45 with continuation of quadruple therapy and scheduled outpatient follow-up.



Figure 4. Black tongue discoloration developing during prolonged linezolid use, resolving after drug discontinuation

DISCUSSION

In this case series, one patient exhibited fissured tongue, while three developed black discoloration of the tongue following linezolid administration. Although rare, linezolid-associated tongue discoloration has been previously reported. A retrospective analysis spanning 12 years identified similar adverse events, with median onset around two weeks and

resolution within approximately one week after drug cessation (3). Other studies corroborate these findings, noting reversibility within two weeks post-treatment (4). Multiple case reports also describe this uncommon side effect (5, 6).

Black hairy tongue and discoloration can result from a variety of antibiotics, including tetracyclines, penicillins, clarithromycin, cephalosporins, and sulfonamides, as well as drugs such as corticosteroids, fluoxetine, lansoprazole, methyldopa, and nortriptyline. Non-pharmacological causes include tobacco use, bismuth ingestion, and cocaine. The precise pathogenesis remains unclear but is believed to involve alterations of oral microbiota leading to microbial overgrowth (7). Behavioral contributors such as smoking, excessive intake of coffee and tea, alcohol consumption, and poor oral hygiene increase susceptibility. Immunocompromised states (HIV, malignancies, recent radiotherapy) and factors impairing tongue cleaning (edentulism, soft diets) further predispose to BHT. Xerostomia and overuse of oxidizing mouthwashes are additional risk factors (8). Literature suggests that discontinuing the causative agent and improving oral hygiene facilitate resolution (9).

Fissured tongue is a common, generally benign condition characterized by multiple grooves on the dorsal tongue surface, affecting 20–30% of the population. It's more prevalent with age and associated with conditions such as geographic tongue, psoriasis, Down syndrome, Melkersson-Rosenthal syndrome, and pernicious anemia. The condition is usually asymptomatic and management focuses on oral hygiene to reduce microbial load and odor (10).

In our patients, fissured tongue appeared as early as day 7 and resolved within two weeks after stopping linezolid and improving oral hygiene. Discoloration typically emerged between days 14 and 28 of treatment, consistent with but slightly longer than reported onset times. This supports the possibility of this adverse effect during prolonged therapy. The reversibility upon cessation and oral care reinforces a drug-related etiology. Awareness of these manifestations during linezolid therapy is important for early recognition and management.

CONCLUSION

Black tongue discoloration and fissured tongue are infrequent but reversible adverse effects associated with linezolid therapy. Our case series demonstrates that these manifestations resolve promptly with drug discontinuation and appropriate oral hygiene measures. Recognizing these rare changes is crucial for clinicians to ensure timely diagnosis and management during linezolid treatment.

Ethical Approval

This study was conducted in accordance with ethical principles. Written informed consent was obtained from all patients prior to inclusion, and additional approval from an ethics committee was not required due to the nature of the case series.

Informed Patient Consent

All patients provided written informed consent for the publication of their clinical data and related images

Conflict of Interest

The authors report no conflicts of interest related to this work.

Financial Disclosure

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Authors' Contributions

Conceptualization, H.A., R.T.Ç., Z.Ö., F.K.C., Y.E., A.A., K.Ö.; Data collection and processing, H.A., R.T.Ç., Z.Ö., F.K.C., Y.E., A.A., K.Ö.; Data analysis and interpretation, H.A., R.T.Ç., Z.Ö., F.K.C., Y.E., A.A., K.Ö.; Literature review, H.A., R.T.Ç., Y.E., A.A.; Writing, R.T.Ç., H.A.; Review and editing, H.A., Z.Ö., F.K.C., A.A., K.Ö.; Supervision, H.A.

Data Sharing Statement

The data supporting the findings of this study are fully available within the article.

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