

## Case Report

# Black tongue caused by linezolid in children: One case report and literature review

Chunyu Zhang<sup>a</sup>, Hongxia Shen<sup>b</sup>, Jing Zhang<sup>a</sup>, Lujie Xu<sup>b</sup>, Meixing Yan<sup>b</sup>, Chang Liu<sup>b,\*</sup>

<sup>a</sup> Department of Pharmacy, Dongming People's Hospital, Dongming, Shandong Province 274500, China

<sup>b</sup> Department of Pharmacy, Qingdao Women and Children's Hospital, Qingdao, Shandong 266000, China

## ARTICLE INFO

## Keywords:

Black tongue

Linezolid

Children

Medicine

Antibacterial drug

Adverse reaction

## ABSTRACT

Linezolid is commonly used to treat multidrug-resistant Gram-positive bacterial infections. Among children, the most common adverse reactions associated with linezolid administration encompass diarrhoea, vomiting, headache and thrombocytopenia. It is noted that tongue discoloration can occur with linezolid in the medication package insert. In this article, we present a case of a child with black tongue as a rare adverse reaction to linezolid and review of relevant literature.

## Introduction

Linezolid, listed in the United States in April 2000, is the world's first synthetic oxazolidinone antibiotic.[1] The mechanism of action involves the binding of the compound with the 50S subunit of the bacterial ribosome, thereby impeding the interaction between mRNA and ribosomes. This interference hinders the formation of the 70S initiation complex, ultimately leading to the inhibition of bacterial protein synthesis. A common use of this antibiotic is to treat infections caused by drug-resistant bacteria (such as methicillin-resistant *Staphylococcus aureus* (MRSA)).[2] In December 2002, it was approved by the US FDA for pediatric patients with hospital-acquired pneumonia, community-acquired pneumonia, skin and soft tissue infection, and vancomycin-resistant *Enterococcus* infection.[3] Linezolid exhibits a distinctive pharmacological target and mode of action, making it less susceptible to cross resistance to other antibacterial drugs in vitro. Fast absorption and almost 100 % bioavailability make it ideal for oral administration.[4] Moreover, it demonstrates favorable distribution in body fluids and tissues, thus experiencing a growing utilization in various clinical applications. The common adverse reactions of linezolid in children include fever, diarrhoea, vomiting, rash, headache, etc. Laboratory tests showed thrombocytopenia, leukopenia, anaemia, abnormal liver function, elevated blood urea nitrogen, etc.[5] In this case, the adverse reaction of black tongue occurred subsequent to the administration of linezolid. This article discussed the case and summarized the relevant literature to provide a reference for safe medication

use in pediatric patients.

## Case report

A 3-year-old girl, 16 kg, had a fever for 2 days at the beginning of the disease, with a maximum temperature 39°C. There was a lymph node (approximately 5 × 5 cm in size) with tenderness under the right jaw. After taking cefdinir orally for 2 days (the specific usage and dosage are unknown), the body temperature dropped to normal, but the lymph node did not shrink. Four days later, CRP showed an increase (32.45 mg/L), and diagnosed with lymphadenitis and tonsillitis. Following the administration of cefotaxime 1.5 g intravenously every day for five days, the lymph node decreased in size from 5 × 5 cm to 3 × 3 cm, and the pain was diminished. One week later, the right sub-mandibular mass of the child increased again, approximately 5 × 5 cm, and the pain increased. The child was hospitalized with severe suppurative lymphadenitis and parotitis and was empirically given piperacillin-tazobactam 0.8 g every 8 h. After 11 days of treatment, the neck mass was significantly reduced to approximately 1 × 2 cm, and routine blood tests and CRP test results were within normal limits. The patient was discharged the next day with the following drug regimen: linezolid tablets 160 milligrams every 8 h for 7 days, 1 g every 8 h. of bifidobacterium triple viable tablets for 15 days. She developed black tongue after taking 7 days of linezolid (Fig. 1). The parents called the pharmacist to inquire whether it was a drug-related adverse reaction. The pharmacist instructed the patient to stop taking the medication for

\* Corresponding author.

E-mail address: [lch1001@yeah.net](mailto:lch1001@yeah.net) (C. Liu).

<https://doi.org/10.1016/j.idcr.2025.e02181>

Received 5 November 2023; Received in revised form 18 December 2024; Accepted 4 February 2025

Available online 5 February 2025

2214-2509/© 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

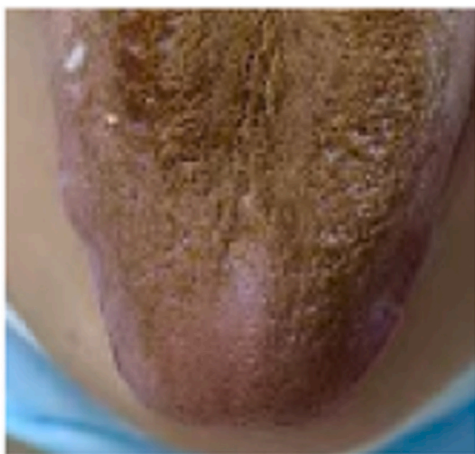


Fig. 1. Black tongue.

observation. After stopping the medication for 7 days, the black symptoms on the tongue subsided and returned to normal (Fig. 2).

The child developed a black tongue 7 days after taking linezolid tablets, and the tongue's colour returned to normal one week after stopping the drug. The child had no primary diseases of the tongue or mouth in the past, and it is not considered to be closely related to the disease. During hospitalization, the patient did not consume foods such as coffee, strong tea, or colored beverages that could cause staining of the tongue coating. This made tongue staining secondary to exogenous substances unlikely. Before taking linezolid, the child also used piperacillin-tazobactam and bifidobacterium triple viable tablets. No adverse reactions to the black tongue in bifidobacterium triple viable tablets have been reported, suggesting a low likelihood of correlation until the disappearance of the black tongue color. One week after the withdrawal of piperacillin tazobactam, the child developed a black tongue, which has little relevance from the perspective of time correlation, and no adverse reaction to a black tongue was found in the instruction manual. Although there was a case reported in the literature that piperacillin-tazobactam caused black tongue in children, a 17-year-old girl with central neurocytoma developed black tongue 12 days later due to postoperative infection with piperacillin-tazobactam for intravenous use.[6] Symptoms disappeared 8 days after discontinuation of piperacillin tazobactam. However, according to the Adverse Drug Reaction Probability Scale of Naranjo et al. the adverse reaction score of linezolid was 6 points, and the correlation evaluation is very likely. The instructions for linezolid formulations indicate that tongue discoloration or tongue disease has occurred in clinical and postmarketing

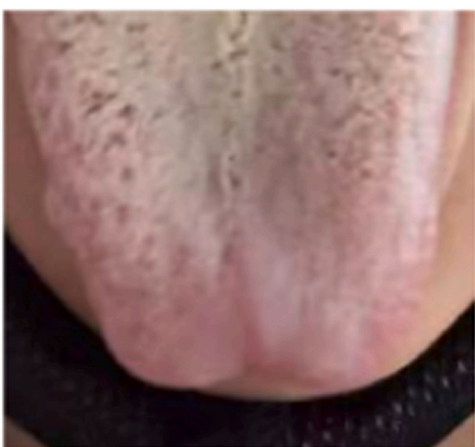


Fig. 2. Black tongue returned to normal.

studies, but the incidence is relatively low. The black tongue symptoms of the child disappeared 7 days after discontinuation of linezolid, which was consistent with the relevant reports in the literature.[7] We speculated that linezolid may be the cause of the blackening of the patient's tongue.

## Discussion

Black tongue is discoloration of densest area of the central filamentous papilla in front of the herringbone groove on the back of the tongue, which can be black, brown, or yellow without any other obvious signs.[8] In addition to the appearance of blackening on the surface of the tongue, the black-haired tongue also exhibits abnormal hypertrophy and elongation of the filamentous papilla on the tongue surface, characterized by brown or black combined with hair-like changes on the tongue surface, which should be distinguished. Based on existing literature, the presence of black tongue is frequently associated with various factors, including but not limited to smoking, excessive intake of coffee and black tea, inadequate oral hygiene, dry mouth, and potential drug therapy implications.[9] The blackening of the tongue surface caused by some antibiotics may be due to changes in the normal oral microbiota, resulting in changes in the inherent oral environment, providing a breeding environment for porphyrin-producing bacteria or yeast, ultimately leading to blackening of the tongue surface. In addition, mold infection can also cause black changes in the tongue. The mechanism may be that the mold acts on the necrotic tissue on the tongue mucosa to produce sulfur dioxide, which combines with haemoglobin to form iron (III) sulfide and deposits on the tongue surface.[7] The likelihood of children's tongues turning black is relatively low due to external factors such as smoking, excessive consumption of coffee and black tea. If the occurrence is attributed to oral medication, it could potentially be linked to direct contact between the medication and the tongue. If it is caused by parenteral administration, it may be associated with the high affinity between the medication and the tissue of the tongue. Further investigation is warranted to gain a comprehensive understanding of the precise mechanisms involved.

The incidence of adverse reactions in children using linezolid is 20.1 %. The main adverse reactions include thrombocytopenia, transient elevation of liver enzymes, leukopenia, anaemia, renal function impairment, rash, pruritus and other skin reactions, which are reversible. The median time of adverse reactions is 7.5 days (4–18 days). Seventy-two percent of children experience adverse reactions on the 10th day of treatment.[10] On the 7th day following the administration of linezolid, the child developed a black tongue. Due to the child's location outside of the hospital, pertinent test indicators were not assessed, and no additional adverse reactions were observed. There were currently five case reports in the literature on rare adverse drug reactions of linezolid in children with black tongue, as detailed in Table 1.

Based on literature and analysis of this patient, the age range of children with adverse reactions to black tongue is from 3 years and 1 month old to 15 years old, with a male-to-female ratio of 3:4. Except for one case where the specific dosage is unknown, all other children with black tongue have used the recommended standard dose of 10 mg/kg every 8 h or 600 mg every 12 h in the instruction manual. The administration methods include intravenous drip and oral administration, and the time for black tongue appearance varies from 5 to 21 days. The clinical manifestations are black and dark brown on the tongue's surface and dark brown colour changes. In this case, the drug was stopped immediately after the onset of black tongue, and the time for the tongue symptoms to return to normal was relatively short (7 days). And the remaining 6 cases ( Table 1 ) continued to use linezolid for sufficient treatment courses. The recovery time after discontinuing the drug was relatively long, basically 7–30 days, and even more than 30 days, they were only in the process of recovery and had not yet achieved complete restoration to their original state. The average course of medication is 17 days (7–25 days), and the longer the course, the longer it takes to

**Table 1**

Summary of reported adverse drug reactions in children with black tongue caused by Linezolid.

Author	Diagnosis	Age	Sex	Administration method	Dosage	Course of treatment	Appearance time of black tongue	Clinical manifestations	Conversion time
Xie Guoqiang [7]	Severe pneumonia	4 years and 2 months	Female	intravenous	10 mg/kg every 8 h	10 d	5th day	Black changes appear on the surface of the tongue	Resuming normal after 7 days of discontinuation
Wang Li [11]	Sepsis; Gram-positive bacteria septicemia	15 years	Male	intravenous	600 mg every 12 h	25 d	16th day	The surface of the tongue is discoloured, showing a dark brown colour	12 days after discontinuation of medication; Not fully recovered
MaJS [12]	Bloodstream infections, arthritis	8 years	Female	per os	10 mg/kg every 8 h	21 d	14th day	The tongue turns dark brown	14 days after discontinuation of medication
Petropoulou T [13]	Severe pneumonia	5 years	Male	intravenous	10 mg/kg every 8 h	21 d	third <sup>th</sup> week	The tongue turns brown	Gradually recover after 1 month of discontinuation
	Left orbital cellulitis	14 years	Female	intravenous	10 mg/kg every 8 h	21 d	third <sup>th</sup> week	The tongue turns brown	Gradually recover after 1 month of discontinuation
RaoAG [14]	Arthritis	7 years	Male			14 d	7th day	Tongue turns black	Symptoms disappear after 14 days

recover to normal after the occurrence of black tongue. In cases of black tongue caused by linezolid, there were no deaths, and all cases could be relieved and recovered through drug discontinuation, symptomatic treatment, and other measures.

## Conclusion

The positive efficacy of linezolid in the treatment of infections caused by drug-resistant gram-positive bacteria, such as MRSA, has been observed. Although linezolid-induced black tongue in children is a reversible adverse reaction with a good prognosis, its pathogenesis has not been fully clarified, and the occurrence of black tongue causes panic in children and parents. The adverse reaction of tongue blackening usually occurs within 1–3 weeks after medication. Whenever an adverse reaction to black tongue is observed in children using linezolid, clinicians should explain this to the family and decide whether to discontinue the drug after weighing the advantages and disadvantages according to the severity of the infection.

## Ethics approval

Not Applicable.

## Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by yanpeng Wang, hongxia Shen and lujie Xu. The first draft of the manuscript was written by chunyu Zhang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## Informed consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal.

## Funding

No funding was received for this specific study.

## CRedit authorship contribution statement

**Shen Hongxia:** Writing – review & editing. **chunyu zhang:** Writing – original draft. **Liu Chang:** Supervision. **Yan Meixing:** Validation, Supervision. **Xu Lujie:** Investigation. **Zhang Jing:** Formal analysis.

## Declaration of Competing Interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work. There is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled “Black tongue caused by linezolid in children: one case report and literature review”.

## Data Availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

## References

- [1] Ager S, Gould K. Clinical update on linezolid in the treatment of Gram-positive bacterial infections. *Infect Drug Resist* 2012;5:87–102.
- [2] Wilson DN, Schlunzen F, Harms JM, et al. The oxazolidinone antibiotics perturb the ribosomal peptidyl-transferase center and effect tRNA positioning. *Proc Natl Acad Sci* 2008;105(36):13339–44.
- [3] Pharmacia & Upjohn. Zyvox (linezolid) package insert. Kalamazoo, MI; December 2002.
- [4] Fu Wang, Yingyuan Zhang. *Practical Anti Infection Therapy* [M]. 3rd Edition. Beijing: People's Health Publishing House; 2020. p. 379–80.
- [5] Instructions for Linezolid glucose injection (Pfizer AS) Approved on September 12, 2006.
- [6] Ren J, Zheng Y, Du H, Wang S, Liu L, Duan W, et al. Antibiotic-induced black hairy tongue: two case reports and a review of the literature. *J Int Med Res* 2020 Oct;48(10). 300060520961279.
- [7] Xie Guoqiang, Li Jianan, He Xuefang, Ren Guangli. Analysis of adverse drug reactions in a case of black tongue in children caused by linezolid. *Pharm Care Res* 2021 Aug;318–20.
- [8] Arab JP, Vargas JI, Morales C, Arrese M. Black hairy tongue during interferon therapy for hepatitis C. *Ann Hepatol* 2015;14(3):414–5 (May–Jun).
- [9] Rakesh TR, Rajnish R, Jitender N, Raj K. Linezolid induced black hairy tongue an uncommon phenomenon: a case report with update of review of literature. *Am J Med Sci Med* 2016;4(4):71–6.
- [10] Bayram N, Düzgöl M, Kara A, Özdemir FM, Devrim I. Linezolid-related adverse effects in clinical practice in children. *Arch Argent Pedia* 2017 Oct 1;115(5):470–5.
- [11] Wang Li, Ma Peizhi. Black tongue induced by linezolid: report of two cases. *Chin J Drug Abuse Prev Treat* 2020;26(3):161–2.

- [12] Ma JS. Teeth and tongue discoloration during linezolid therapy. *Pedia Infect Dis J* 2009 Apr;28(4):345–6.
- [13] Petropoulou T, Lagona E, Syriopoulou V, Michos A. Teeth and tongue discoloration after linezolid treatment in children. *Pedia Infect Dis J* 2013 Nov;32(11):1284–5.
- [14] Rao AG, Aparna K, Reddy VS, Farheen SS, Hakkani R, Parimala D, et al. Linezolid-induced black pigmentation of tongue and perioral region. *Indian J Paediatr Dermatol* 2019;20(2):189–90.