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## Linezolid resistant *Staphylococcus haemolyticus*: First case report from India

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### ABSTRACT

Linezolid is being increasingly used in the treatment of infections with gram-positive organisms especially methicillin resistant Staphylococcal isolates. Though resistance to this antimicrobial is emerging but it is extremely rare. Here we document first case of linezolid resistant *Staphylococcus haemolyticus* (*S. haemolyticus*) from India. This organism was isolated from pus oozing from a postsurgical site in 61 year old male hailing from an adjoining state of Haryana.

## 1. Introduction

Linezolid is the first oxazolidinone antibiotic to be licensed for treatment of infections caused by gram-positive bacteria with potent activity against methicillin-resistant *Staphylococcus aureus* (*S. aureus*) (MRSA), glycopeptide-intermediate *S. aureus* (GISA) and vancomycin resistant enterococci (VRE)[1]. Linezolid acts by binding to the 50S subunit of the bacterial ribosome via interaction with the 23S rRNA hereby blocking an early step in protein synthesis[2]. The most frequent mutation, which is known to cause resistance to linezolid, is G2576T[3]. This mechanism of resistance has been documented in *S. aureus*[3]. Similar mechanism has been observed in *Staphylococcus epidermidis* (*S. epidermidis*)[4,5]. Recently cfr gene[6], which resides in a potentially mobile genetic element, has been shown to confer linezolid resistance to *S. aureus* and coagulase negative *Staphylococci*[7,8]. From India, reports of linezolid resistance have been documented in *Staphylococcus cohnii* (*S. cohnii*), *Staphylococcus kloosii* (*S. kloosii*) from Kashmir and *Staphylococcus hominis*,

*Staphylococcus lugdunensis* (*S. lugdunensis*) from Andhra Pradesh[9,10]. However, till date there is no report of resistance in *Staphylococcus haemolyticus* (*S. haemolyticus*) from India.

## 2. Case report

A 61 year old male patient had a history of fall one year back. He was admitted in a private hospital in Yamunanagar, Haryana. On examination he was found to have left sided fracture of the hip joint. The fracture was fixed with a plate but later on it was observed that there was non-union of the fracture and hence the plate was removed. There was oozing of pus from the surgical site. He was started on empirical treatment with linezolid and a combination of amoxicillin and clavulanic acid. There was no response to the treatment. Thereafter he presented to the Orthopaedics Outpatient Department of GMCH, Chandigarh with persistent drainage of pus from the same surgical site. The pus sample was sent to the Department of Microbiology for culture and antibiotic sensitivity testing. The pus sample showed growth of coagulase-negative *Staphylococcus* after overnight incubation. The isolate was characterized phenotypically as *S. haemolyticus* based on slide and tube coagulase tests, urease test, ornithine

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decarboxylase test, aerobic acid from mannose, novobiocin susceptibility and the test for acetoin production<sup>[11]</sup>. The species confirmation as *S. haemolyticus* was further done by using MicroScan Walkaway Automated system (NEW). Antimicrobial sensitivity testing was done by the Kirby–Bauer disc diffusion method in accordance with the CLSI guidelines<sup>[12]</sup>. The isolate showed sensitivity to teicoplanin and clindamycin but was resistant to penicillin, oxacillin, erythromycin, cotrimoxazole and linezolid. Minimum inhibitory concentration (MIC) was determined for linezolid, vancomycin, oxacillin, rifampin and teicoplanin by the E-test. The isolate was resistant to linezolid (MIC  $\geq 64 \mu\text{g/mL}$ ) so it was discontinued and the patient was started on a combination of clindamycin and rifampin. The patient responded well to the above treatment and the surgical site healed. For further management of the fracture the patient was still visiting orthopaedic clinic.

### 3. Discussion

Multidrug resistant coagulase–negative *Staphylococcus* species (CoNS) are becoming the common causes of mortality and morbidity mainly in hospital settings. Emergence of resistance of these organisms to an increasing number of antibiotics has become a real concern. For such infections, antimicrobials like linezolid and glycopeptides are the alternative therapeutic agents. But if resistance develops to these antimicrobials also then the clinicians will be left with no therapeutic options. Coagulase negative *Staphylococci* have been reported to be important pathogens in patients with implants in orthopaedic practice<sup>[13]</sup>.

Regarding the mechanism of resistance to linezolid, it is principally associated with distinct nucleotide substitutions in domain V of the 23S rRNA gene, arising in at least two copies of the rRNA operons, with a stepwise increase due to successive accumulation of single point mutations. Post-transcriptional methylation of A2503 in the 23S rRNA by the horizontally transferred *cfr* gene recently described in clinical isolates and derived from *Staphylococci* of animal origin has caused concern about the possible high transmission of linezolid resistance among clinical isolates<sup>[14]</sup>. Presently we do not have facilities to determine the exact mechanism of resistance.

The present case is the first case of a linezolid resistant *S. haemolyticus* from India in orthopaedic practice. The patient however responded to clindamycin and rifampin therapy after the removal of the plate.

Since these days there is an increasing trend of the use of linezolid for treating gram–positive organisms hence microbiologists should be cautious in reporting the antimicrobial sensitivity of the methicillin resistant isolates to the clinicians so as to prevent the injudicious use of this therapeutic agent.

### Conflict of interest statement

We declare that we have no conflict of interest.

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