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Case Report

Emergence of resistance to linezolid in methicillin resistant *Staphylococcus haemolyticus* reported from the sub Himalayan region of India

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ABSTRACT

The spread of resistance among coagulase negative *Staphylococci* against major drugs is alarming as it limits the treatment options for serious infections. Resistance to linezolid in these organisms is emerging and further compounded by being observed in multidrug resistant strains. It is the only antibiotic available as an oral formulation for resistant *Staphylococcal* infections and due to the presence of a novel structure and unique mechanism of action, it does not display cross resistance with other classes of antimicrobial agents. However, the widespread use of Linezolid has gradually turned the impending fear of emergence of resistance against this novel drug into a reality. Herein we report a case of sepsis due to methicillin resistant *Staphylococcus haemolyticus* in a 16-year-old male child found resistant to linezolid, rarely reported from Sub Himalayan region of Indian sub-continent.

Keywords: Methicillin resistant *Staphylococcus haemolyticus,* Linezolid resistance

INTRODUCTION

Linezolid is a synthetic antimicrobial agent of the oxazolidinone class active against multidrug resistant gram-positive bacteria, including methicillin-resistant, vancomycin-intermediate, and vancomycin-resistant strains of *Staphylococci*. Minimum inhibitory concentrations (MIC) of the antibiotic for strains of *Staphylococcus aureus* and coagulase-negative *Staphylococci* (CONS) is ≤4µg/ml.[1] Though it has bacteriostatic effect in vitro, it behaves as a bactericidal antibiotic because it inhibits the production of toxins by *Staphylococci*. It also has a post antibiotic effect lasting one to four hours for most bacteria and the bacterial growth is temporarily suppressed even after the drug is discontinued.[1] The most frequent point mutation, which is known to cause resistance to linezolid, is G2576T and has been documented in *S. aureus* and *Staphylococcus epidermidis*.[2-4] Data on linezolid resistance from Asian countries are scarce with most of them having not reported on resistance in *Staphylococci*. We hereby present a case depicting resistance to the drug in methicillin resistant *Staphylococcus haemolyticus* from Sub Himalayan region of India.

CASE REPORT

A 16-year-old male child presenting with fever, cough and loss of appetite was admitted in Department of Paediatrics at a tertiary care hospital in Shimla. On examination the fever was documented 103^0 F with heart rate of 96/min and respiratory rate of 22/minute. His WBC count was 6.34 thou/µl with 75% neutrophils. C reactive protein levels (CRP) were highly raised (105.2

mg/lt). He developed a shock like state and was shifted to the pediatric intensive care unit. Empiric treatment of intravenous ceftriaxone 2g BD and amikacin 750mg OD was started and considering the provisional diagnosis of septicaemia and pulmonary tuberculosis blood culture/sensitivity and gastric aspirate for detection of tubercle bacilli through cartridge based nucleic acid amplification tests (CBNAAT) were requested and samples were sent to the Department of Microbiology. The Gene Xpert (CBNAAT) detected presence of *Mycobacterium tuberculosis* sensitive to rifampicin and blood culture revealed growth of non-haemolytic grey colored colonies.

On Gram staining, gram positive cocci in clusters were seen, catalase test was positive and conventional tests for clumping factor, tube coagulase and mannitol fermentation were negative. Susceptibility testing was performed by Kirby Bauer disc diffusion method following the CLSI guidelines.[5] The isolate was found resistant to linezolid. The growth extending up to the edge of the linezolid disc could be easily visualized and further on Gram staining the smear made from the growth around the disc showed gram positive cocci in clusters. It was also resistant to ampicillin, cotrimoxazole, cefoxitin, erythromycin, clindamycin and gentamicin (Figure 1).

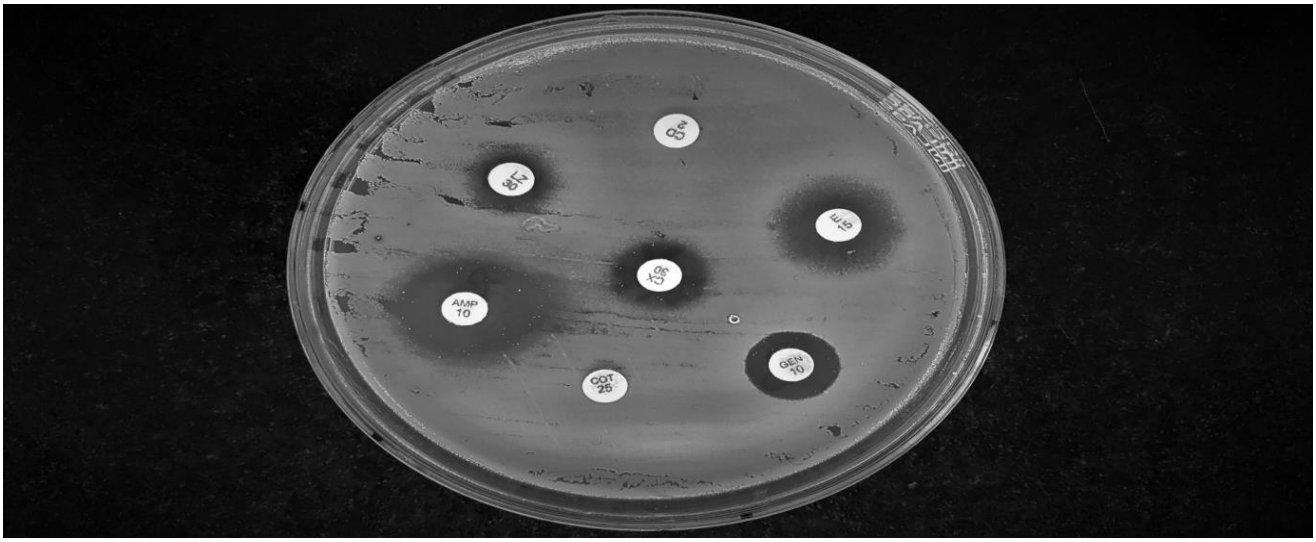

Figure 1: The antibiotic susceptibility pattern of coagulase negative *Staphylococcus* for ampicillin (AMP 10), cotrimoxazole (COT 25), cefoxitin (CX 30), erythromycin (E 15), clindamycin (CD 2) and gentamicin (GEN 10).

The further identification to species level and MIC values were evaluated by using BD Phoenix™ automated identification and susceptibility testing system. The system revealed the isolate to be *Staphylococcus haemolyticus* (Confidence Value 97%) and the MIC for linezolid as >4µg/ml. It was found sensitive to vanomycin (MIC≤ 1µg/ml), daptomycin (MIC ≤0.5), tetracycline (MIC1) and teicoplanin (MIC4) and resistant to penicillin, oxacillin, cefoxitin, cotrimoxazole, erythromycin, clindamycin and gentamicin. The isolate was reported as methicillin resistant *Staphylococcus* (MRS). The empirical treatment was stopped and intravenous vancomycin was started. The child responded and became afebrile. The antitubercular therapy was also started, but due to co-morbid conditions he could not recover and expired 10 days after admission.

DISCUSSION

Various Indian authors have previously reported resistance for linezolid in coagulase negative *Staphylococci*.[6,7] *S. haemolyticus* is the second most frequently isolated coagulase negative *Staphylococcus* from blood stream infections and is often multidrug resistant.[8] In recent times case reports mentioning linezolid resistance in the species both in blood and pus samples have also been published from India.[9,10] Most of the linezolid resistance reported in *Staphylococci* has emerged after prolonged exposure to linezolid. However, some linezolid resistant isolates have been isolated from patients with no prior linezolid exposure.[11,12]

In this patient there was no history of prior intake of the drug and still the isolate was not sensitive. Such a case has not been reported previously from our institute.

The MIC >4µg/ml cannot be ignored, and measures should be taken to prevent the emergence of resistant strains in Sub-Himalayan region of India, especially in multidrug-resistant (MRS) isolates which cause life threatening infections. Linezolid is a clinically valuable option as a form of therapy. Antibiotic susceptibility testing for all *Staphylococcus* isolates before using linezolid is recommended.[13]

CONCLUSION

Linezolid usage for empiric therapy in hospital acquired *Staphylococcus* infection should be avoided. It is a reserve antibiotic that should be used judiciously so that it will remain effective as a drug of last resort against potentially intractable *Staphylococcal* infections.

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