EMERGENCE OF LINEZOLID RESISTANCE IN COAGULASE-NEGATIVE STAPHYLOCOCCUS ISOLATED FROM A POST-SURGICAL CASE OF CORONARY ARTERY BYPASS AT A TERTIARY CARE CARDIAC SETUP IN PAKISTAN

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ABSTRACT

Linezolid is first choice in the treatment of methicillin resistant Staphylococci. Resistance to this antibiotic is quite rare. We report the first case of linezolid resistant coagulase negative Staphylococcus from a tertiary care cardiac setup in Pakistan. The strain was isolated from pus swab of a 62 year old female from post-coronary bypass grafting sites.

Keywords: Coagulase negative *Staphylococcus*, Linezolid resistance.

INTRODUCTION

Linezolid is the first licensed antibiotic to be used for gram positive bacteria having adequate efficacy for the methicillin resistant *Staphylococcal* species[1]. Oxazolidinones block the initiation complex formation, by binding to the 50S ribosomal subunit, resulting in a bacteriostatic action[2]. Staphylococcus causes various infections of skin and soft tissues, of surgical sites, endocarditis and hospital acquired infections[3]. The organism develops resistance by mutating and DNA transfer resulting in difficulties in treating infections that contribute to increased morbidity and mortality. The increasing use of broad spectrum antibiotics is resulting in emergence of resistance in coagulase negative *staphylococci* (CoNS) as well[4]. Apart from linezolid resistance in *Staphylococcus aureus*, its resistance has been documented in various species of CoNS such as *Staphylococcus cohnii*, *Staphylococcus kloosii*, *Staphylococcus hominis* and *Staphylococcus lugdunensis*[5]. A study that was conducted in Pakistan in the department of Microbiology, University of Health Sciences, Lahore to determine the in-vitro activity of linezolid against clinical isolates of methicillin resistant *Staphylococci* showed that linezolid was effective against all the strains of methicillin resistant *Staphylococcus aureus* (MRSA) and methicillin resistant coagulase-negative Staphylococci (MRCoNS) in the range of 1.0–4.0 mg/L and 0.5-4.0 mg/L MICs, respectively[6]. Here we report a post-surgical case from the largest tertiary care cardiac setup in Pakistan in which an MRCoNS Staphylococcus haemolyticus showed resistance to linezolid. This further emphasizes on the fact that if linezolid becomes ineffective we shall be left with very limited options for MRSA and MRCoNS.

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CASE REPORT

A 62 years old hypertensive and diabetic female patient was admitted in Armed Forces Institute of Cardiology, Pakistan for coronary artery bypass grafting (CABG) surgery for triple vessel coronary artery disease (TVCAD). She underwent CABG on 10th July, 2017 and was put empirically on the antibiotics amikacin and cefazolin parenterally. After four days, her intravenous antibiotics were stopped and she was put on oral linezolid. About ten days later, graft sites showed bleeding and soakage, her right leg wound was stitched and debridement was done for the left leg wound. Patient was then put on injections linezolid and piperacillin-tazobactam. Serial pus swab samples yielded multi-drug resistant strains of *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.

Secondary suturing of her left leg wound was done. On 7th July, culture yielded growth of CoNS that was characterized phenotypically as Staphylococcus haemolyticus, based on coagulase and DNAse tests and biochemical reactions. The species was confirmed to be Staphylococcus haemolyticus at Armed Forces Institute of Pathology, by VITEK-2® Walkaway automated culture system. The isolate showed susceptibility to teicoplanin, vancomycin and tigecycline mainly. The isolate was resistant to linezolid (MIC≥8 g/mL) so it was stopped and the patient was started on a combination of clindamycin and rifampicin according to susceptibility report. The patient responded well to the above treatment and her surgical site healed.

DISCUSSION

Bacteria as we know seem to develop resistance against the antibiotics rapidly. Recent studies have shown increasing resistance in strains of MRSA and MRCoNS that contributes to morbidity and mortality in the hospital. Linezolid and glycopeptides are the main choice of treatment for such patients. However since cases have been reported around the world that have documented the emerging resistance to linezolid, physicians shall have limited options in future[8]. In a country like Pakistan with limited resources this is an even bigger issue. The recent prevalence of multidrug resistant Staphylococcus species in Lahore, Quetta, and Rawalpindi was 83%, 86% and 75%, respectively[6,7]. Studies around the world have shown variable results regarding resistance to linezolid such as the one conducted in Cleveland in which 10.4% MRSA strains were resistant to it. These included strains isolated from patients of cystic fibrosis who had history of prolonged antibiotic therapy[8]. Although a study carried out in Karachi, Pakistan showed 100% susceptibility of MRSA isolates to linezolid[9].

Cases have been reported in which strains developed linezolid resistance after taking a course of linezolid for MRSA treatment. Similar situation occurred in our patient in whom the culture of pus swab had revealed an MRSA strain that was susceptible to linezolid initially. However after about 10 days linezolid resistant strain of *Staphylococcus haemolyticus* was isolated from her wound pus swab. This strengthens the view point that prolonged admissions and antibiotic therapy leads to the development of multi-drug resistant strains of bacteria.

The linezolid resistance has become a serious concern worldwide and is based on multi-resistance gene cfr[10]. This gene is located near plasmids in different strains of MRSA. The location of gene near the plasmids helps to spread the resistance against linezolid. We were not able to do sequence analysis of the isolate due to non-availability of the technique readily. However, this case should alert us to follow the infection control guidelines stringently.

CONFLICT OF INTEREST

This study has no conflict of interest to be declare by any author.

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