International Journal of Infectious Diseases 17 (2013) e466–e467

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Severe sepsis caused by a linezolid-resistant *Enterococcus faecium* in a 10-year-old girl after multiple trauma

M. Mutschler [a,*], S. Trojan [b], J.M. Defosse [b], A. Helmers [c], C. Probst [a], B. Bouillon [a], F. Wappler [b], S.G. Sakka [b]

[a] *Department of Trauma and Orthopedic Surgery, University Witten/Herdecke, Cologne-Merheim Medical Center (CMMC), Ostmerheimerstr. 200, D-51109 Cologne, Germany*
[b] *Department of Anesthesiology and Intensive Care Medicine, University Witten/Herdecke, Cologne-Merheim Medical Center (CMMC), Cologne, Germany*
[c] *MVZ synlab Leverkusen GmbH, Leverkusen, Germany*

ARTICLE INFO

Article history:
Received 18 September 2012
Received in revised form 8 January 2013
Accepted 9 January 2013

Corresponding Editor: Eskild Petersen, Skejby, Denmark

Keywords:
Sepsis
Enterococcus faecium
Linezolid resistance
Child
Trauma

SUMMARY

While infections caused by *Enterococcus faecium* resistant to vancomycin (VRE) are increasing, linezolid-resistant strains are still rare. We present the case of a 10-year-old girl with severe sepsis caused by a linezolid-resistant *E. faecium* (Van-B VRE) after multiple trauma and right-sided hemipelvectomy. The off-label use of a targeted antimicrobial therapy with daptomycin (350 mg/day; approximately 8 mg/kg) for 17 days resulted in rapid normalization of infection parameters and improved clinical status. No side effects were observed and the patient was successfully discharged from the intensive care unit.

1. Introduction

Over the last decade, the application of vancomycin and other broad-spectrum antibiotics have led to an increase in infections with vancomycin-resistant strains of *Enterococcus faecium* (VRE).[1] These strains are commonly treated with linezolid. Despite its widespread usage, linezolid-resistant strains of *E. faecium* are still rare and have been identified mainly in patients who have undergone long courses of linezolid therapy before.[1,2]

2. Case report

We present the case of a 10-year-old girl who suffered from a rollover trauma by a truck, resulting in an unstable pelvic fracture with a severe decollement of the right trunk. While undergoing treatment in a district hospital, the patient received clindamycin and piperacillin/tazobactam (for *Pseudomonas aeruginosa* in tracheal secretion). The girl was transferred to our institution for further surgical treatment. After admission, the patient underwent a right-sided hemipelvectomy and negative pressure wound therapy. Despite continued antibiotic therapy with piperacillin/tazobactam and clindamycin, the patient became septic. A wound biopsy and blood cultures revealed Gram-positive cocci, therefore therapy was changed to linezolid and meropenem. However, even with this broad antibiotic medication, no clinical improvement was observed. Further differentiation revealed a vancomycin-resistant, but teicoplanin-sensitive strain of *E. faecium* (Van-B VRE). Additionally, a linezolid resistance was detected. The minimal inhibitory concentration (MIC) breakpoint for linezolid was >4 mg/l, both at our institutional site as well as at the reference laboratory (Robert Koch Institute, Wernigerode, Germany). The antimicrobial therapy was switched to daptomycin (350 mg/day; approximately 8 mg/kg), which was continued for 17 days. Due to this targeted therapy, infection parameters normalized and her clinical status improved rapidly. After secondary wound closure, we were able to transfer the patient to a rehabilitation center.

3. Discussion

Linezolid, as an oxazolidinone, is bacteriostatic by inhibiting protein synthesis.[3] As it is approved by the US Food and Drug Administration, linezolid is commonly used to treat VRE infections worldwide.[1] Linezolid resistance remains uncommon, but outbreaks and dissemination of linezolid-resistant strains have been reported.[2] The LEADER surveillance program, including a total of 61 medical centers in the USA, recovered a total of 934 *Enterococcus* species isolates; most were identified as *Enterococcus faecalis* (564;

* Corresponding author. Tel.: +49 211 89073769; fax: +49 211 89073085.
E-mail address: manuelmutschler@web.de (M. Mutschler).

1201-9712/$36.00 – see front matter
http://dx.doi.org/10.1016/j.ijid.2013.01.009

60.4%) and *E. faecium* (328; 35.1%).[4] Of these, 12 strains (two *E. faecalis* and 10 *E. faecium*) had a MIC for linezolid of ≥4 mg/l, resulting in an overall linezolid resistance rate of 0.75%. However, over the past 7 years, no significant increase in linezolid resistance has been observed.[4] The most common mechanism of resistance is mediated by G2576T mutations encoding the 23S rRNA. As *E. faecium* has six copies of the RNA genes, it is assumed that the level of resistance might be associated with the number of mutated alleles.[1] Linezolid resistance is thought to occur after prolonged treatment or inappropriate dosing. In contrast, our case shows that linezolid resistance might also occur in children and in patients who have never received this antibiotic drug before, as reported recently.[1,2] It remains unclear whether the linezolid-resistant strain was acquired from another patient or if the mutation occurred independently. Following the implementation of routine screening for VRE in our intensive care unit, we did not identify other patients with colonization or infections with linezolid-resistant strains.

Daptomycin is not approved for the treatment of VRE infections and especially not in children.[1] In our pediatric patient, the off-label use of daptomycin was initiated with interdisciplinary consent and parental approval, resulting in a rapid control of infection without the observation of any side effects. However, an acquired resistance to daptomycin as well as the underlying mechanism have been described recently.[5] This may limit the future antibiotic therapy of multiple resistant enterococci. Therefore, the use of linezolid and daptomycin should be considered carefully.

Conflict of interest: There are no competing interests associated with this article.

References

1. Arias CA, Murray BE. The rise of the Enterococcus: beyond vancomycin resistance. *Nat Rev Microbiol* 2012;**10**:266–78.
2. Ntokou E, Stathopoulos C, Kristo I, Dimitroulia E, Labrou M, Vasdeki A, et al. Intensive care unit dissemination of multiple clones of linezolid-resistant *Enterococcus faecalis* and *Enterococcus faecium*. *J Antimicrob Chemother* 2012;**67**: 1819–23.
3. Wilson DN, Schluenzen F, Harms JM, Starosta AL, Connell SR, Fucini P. The oxazolidinone antibiotics perturb the ribosomal peptidyl-transferase center and effect tRNA positioning. *Proc Natl Acad Sci U S A* 2008;**105**:13339–44.
4. Flamm RK, Farrell DJ, Mendes RE, Ross JE, Sader HS, Jones RN. LEADER surveillance program results for 2010: an activity and spectrum analysis of linezolid using 6801 clinical isolates from the United States (61 medical centers). *Diagn Microbiol Infect Dis* 2012;**74**:54–61.
5. Arias CA, Panesso D, McGrath DM, Qin X, Mojica MF, Miller C. Genetic basis for in vivo daptomycin resistance in enterococci. *N Engl J Med* 2011;**365**:892–900.