Thrombocytopenia Can be Avoided By Monitoring Linezolid Blood Levels – Enabling Long-Term Linezolid Use for the Successful Treatment of Refractory Pyogenic Spondylodiscitis

MedicalA male in his 50s (height 172 cm, weight 78 kg, S-cr 0.34 mg/dL) washistoryhospitalized with fever and a diagnosis of pyogenic spondylodiscitis.

Day 1 During incisional drainage, **Methicillin-resistant Staphylococcus** epidermidis (MRSE) was detected in the incision. Treatment with 600 mg of intravenous linezolid (LZD) two times per day started. (LZD MIC ≤ 1).

- Day 138 Patient was placed on a continuous rotation of MRSA antibiotics due to LZD-induced thrombocytopenia, but no improvement was observed. Patient switched to LZD with **reduced** dosage of 600 mg once per day.
- Day 148 LZD blood concentration was measured due to thrombocytopenic tendency and found an AUC<sub>24</sub> of 299.7 μg-h/mL, which was high despite the dosage reduction.

- Average AUC<sub>24</sub> for a healthy adult on twice daily 600 mg: 220  $\mu$ g-h/mL - When AUC<sub>24</sub>  $\ge$  280  $\mu$ g-h/mL, risk of thrombocytopenia is 50%

Pea F et al. J. Antimicrob. Chemother. 2012, 67: 2034-42.

- $\rightarrow$  Intravenous LZD dosage was **reduced** to 400 mg once daily.
- ightarrow Patient was then switched to oral medication at the same dosage.
- Day 184  $\rightarrow$  Oral LZD was **reduced** to 300mg.
- Day 188 An LZD blood concentration test showed AUC<sub>24</sub> was 127.2  $\mu$ g-h/mL, within effective range (AUC<sub>24</sub>/MIC  $\geq$  100), so the same dosage was continued.
- Day 203 The patient was transferred to another hospital with no thrombocytopenia with the same LZD dosage.

- When LZD is administered for 14 days or longer, thrombocytopenia risk increases.

- The LZD package insert states no dosage adjustments are required for patients with impaired renal function.

- However, some reports suggest dosages should be adjusted for patients with impaired renal function. Matsumoto K et al. Int. J. Antimicrob. Agents 2014, 44:242-7.

- <u>In this case study, LZD blood concentration was high despite normal renal function.</u> Dosage adjustment made it possible to avoid thrombocytopenia, continue long-term LZD administration, and provide successful treatment.

## **Beware of thrombocytopenia when administering LZD.** When long-term administration is necessary, it is possible to avoid thrombocytopenia with proactive therapeutic drug monitoring (TDM)



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A\*: VCM 1000 mg 2 times/day; B\*: VCM 1250 mg 2 times/day LZD: Linezolid, DAP: Daptomycin, VCM: Vancomycin, TZD: Tedizolid



AMR Alliance Japan requested this case report as a part of a project to compile examples of antimicrobial stewardship and cases with and without the use of antibiotics. For more information, please contact AMR Alliance Japan. Grand Cube, 3rd Floor, 1-9-2 Otemachi Financial City, Otemachi, Chiyoda-ku, Tokyo 100 0004 Tel: 03-4243-7156 Fax: 03-4243-7378 E-mail: info@hgpi.org