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Challenges with linezolid therapy and reversible pancytopenia

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Linezolid is currently holding an important place in the antimicrobial armamentarium; however, not enough attention has focused on its hematotoxicity and its pathogenesis. We report here a case of reversible pancytopenia that appeared after 1 month of linezolid therapy.

A 60-year-old female had undergone back surgery and developed an abscess on the left paraspinal region, adjacent to vertebral fixation. The patient developed recurrent methicillin-resistant staphylococcus bacteremia (MRSA). She received linezolid 600 mg orally twice daily. Four weeks later, her hemoglobin (Hb) level decreased from 10.7 to 6.9 g/dl (mean corpuscular volume 86.5 fl). Her reticulocyte count dropped from 2.5 to 0.00/ μ l. Her WBC count dropped from 7.8 to 2.9 cells/ μ l. The platelet count dropped from 253,000 to 61,000/ μ l. Vitamin B12 levels and folate levels were normal. Serum iron level was reduced to 143 μ g/dl. Total iron binding capacity was 124 mg/dl and transferrin level was reduced to 99 mg/dl. Our patient required transfusion with two units of blood. She was treated with linezolid and esomeprazole. Linezolid was the drug suspected of inducing the patient's pancytopenia. Esomeprazole was not known to be associated with myelosuppression. In our patient a marked increase in WBC, Hb, and platelet count occurred immediately after linezolid was stopped. Within the next 2 weeks, the pancytopenia completely disappeared and the blood parameters were normal. This potentiates the theory that linezolid induced a reversible pancytopenia. Our case depicts a triad of linezolid use, hematotoxicity, and recovery [1, 2, 3].

Linezolid is currently holding an important place in the antimicrobial armamentarium; hence, greater attention should focus on its hematotoxicity and its pathogenesis. Many key questions regarding relationship between structure, mechanism of action, and toxicity remain unanswered. Many reports have compared linezolid with chloramphenicol toxicity [2]. It seems that in both the hematotoxicity is dosage-time dependant. There are some similarities in structure as well as function. Both share a nitro group, assumed to play a role in chloramphenicol myelosuppression. In addition, both act to inhibit protein synthesis at the ribosomal level. There is well-established evidence that reversible bone marrow suppression from chloramphenicol toxicity occurs from mitochondrial injury [4, 5]. The chloramphenicol concept for myelosuppression proved to be an excellent framework to study new potential myelotoxins. Whether this same concept will act for linezolid itself is a question that remains to be answered.

It is apparent that hematotoxicity remains the utmost challenge encountered with linezolid therapy [2, 3]. As with our case, the choice of antimicrobial therapy remains limited for most patients liable to recurrent chronic, multidrug-resistant gram-positive infections. Given that linezolid remains the drug of choice, we need to reintroduce and rechallenge smaller doses of linezolid in patients prone to repeated multidrug-resistant gram-positive infections in the face of its reversible myelosuppression.

References

1. Moellering RC (2003) Linezolid: the first oxazolidinone antimicrobial. *Ann Intern Med* 138:135–142
2. Green SL, Maddox JC, Huttenbach ED (2001) Linezolid and reversible myelosuppression. *JAMA* 285:1291
3. Attassi K, Hershtberger E, Alam R, Zervos MJ (2002) Thrombocytopenia associated with linezolid therapy. *Clin Infect Dis* 35:347–348
4. Yunis AA (1989) Chloramphenicol toxicity: 25 years of research. *Am J Med* 87 [Suppl 3N]:44N–48N
5. Jimenez JJ, Arimura GK, Abou-Khalil WH, Isildar M, Yunis AA (1987) Chloramphenicol-induced bone marrow injury: possible role of bacterial metabolites of chloramphenicol. *Blood* 70:1180–1185

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