

Early Myelosuppression Secondary to Linezolid Use in the Context of Hematologic Malignancy

Case Report

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Abstract: Cytopenia is a common adverse effect following anti-cancer therapy. Among the various cell line reductions, neutropenia is most strongly associated with an increased risk of infection. Severe infections may further suppress hematopoietic function and thereby prolong cytopenic periods. Here, we present a case of relapsed and refractory leukemia with profound cytopenia and infectious complications following intensified chemotherapy. This case highlights the concept of an early and pronounced myelosuppressive effect in patients with impaired bone marrow function secondary to anti-neoplastic therapy. Clinicians should be particularly vigilant in recognizing the vulnerability of such patients to enable earlier detection and intervention.

Keywords: Cytopenia • myelosuppression • linezolid • hematologic malignancy

1. Introduction

Cytopenia is a common treatment-related complication in the daily practice of hematology and oncology. The etiology of cytopenia in cancer patients is diverse, with drug-induced cytopenia being the predominant cause.^[1] Chemotherapeutic agents account for the majority of drug-induced cytopenia. In addition, antimicrobials play a significant role in the development of acquired cytopenia.^[2] Managing the combined effects of chemotherapy and antimicrobial-induced cytopenia is challenging. Here, we report a case of refractory and relapsed (R/R) acute lymphoblastic leukemia (ALL) in a patient who experienced prolonged cytopenia after intensified chemotherapy and the administration of antimicrobials.

2. Case Presentation

A 21-year-old female was initially diagnosed with precursor B-cell ALL at the age of 3.5 years. Molecular analysis revealed a ZNF384-related fusion transcript, and her chromosomal karyotype was complex. Conventional chemotherapy utilizing a high-risk regimen

was administered, and she remained disease-free for 8 years before experiencing her first bone marrow relapse.

Complete remission (CR) 2 status was achieved after salvage chemotherapy followed by a matched unrelated donor allogeneic hematopoietic cell transplantation. CR2 was maintained for 7 years, but at age 18, she experienced repeated bone marrow relapses approximately every 6 months. The R/R condition was managed with multidisciplinary, intensified therapy, including an intensive hyper-CVAD regimen, donor lymphocyte infusion, blinatumomab immunotherapy, carfilzomib-based chemotherapy, and a myeloid-based intensified chemo-regimen.

At the time of her current hospitalization, she was undergoing treatment for her 6th bone marrow relapse with a myeloid-based chemotherapy regimen (Ida-FLAG protocol). Circulating blasts disappeared following the regimen, but she developed significant neutropenia by post-chemotherapy day 4. Empirical antimicrobial therapy was escalated from cefazolin and amikacin to meropenem, teicoplanin, and micafungin due to febrile neutropenia. A continuous infusion of granulocyte colony-stimulating factor (G-CSF) at a dose of 6 mcg/kg/day was initiated to promote neutrophil recovery.

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On post-chemotherapy day 20, she developed a catheter-related bloodstream infection (CRBSI), with *Stenotrophomonas maltophilia* identified in the microbial analysis. Antimicrobial therapy was adjusted to intravenous ciprofloxacin based on susceptibility testing. On post-chemotherapy day 30, her white blood cell (WBC) count rose from $0.1 \times 10^9/L$ to $0.3 \times 10^9/L$, but the patient unexpectedly developed septic shock, complicated by altered consciousness, and was transferred to the intensive care unit for further management and monitoring.

For the management of the breakthrough infection, after consultation with the infectious disease specialist, her antimicrobials were adjusted to meropenem, linezolid (LNZ), and voriconazole. Three days later, her WBC count decreased following the initiation of LNZ. Laboratory tests revealed elevated serum procalcitonin and lactate levels, indicating the progression of septic shock. Despite the use of inotropic agents, the shock remained refractory. Profound hypotension led to respiratory failure, heart failure, and renal dysfunction. The G-CSF infusion was increased to 12 mcg/kg/day, but the response was limited. Given the poor prognosis due to R/R ALL complicated by multi-organ failure, palliative care was initiated after obtaining informed consent. The patient succumbed to the illness on post-chemotherapy day 39.

3. Discussion

Cytopenia is a common challenge in hematology and oncology, particularly with chemotherapy, which often leads to significant hematologic impairment. Prolonged neutropenia and CRBSI necessitated the use of broad-spectrum antimicrobials. Several antimicrobials, including trimethoprim, LNZ, and ganciclovir, have been associated with myelosuppression.^[1, 3, 4] Antibiotic-associated neutropenia has been identified in various clinical scenarios. The reported incidence ranges from 5% to 30% depending on the study population and the use of different antibiotics.^[1, 2] Risk factors for developing antibiotic-associated neutropenia include the type of antibiotics, duration of use, concomitant medications, and pre-existing bone marrow dysfunction.

Among these, the association between LNZ use and neutropenia is well established. However, most of the data and experience have been derived from healthy populations. The pathophysiology and risk factors of neutropenia secondary to various antibiotics, particularly LNZ, in hematology and oncology populations remain poorly understood.

In our case, the second episode of neutropenia likely resulted from the administration of LNZ. Documented myelosuppression typically occurs 2 weeks after initiating LNZ therapy.^[4] While this observation is well established in the general population, the timeline may differ in cancer patients, whose bone marrow function is already compromised due to various chemotherapy treatments. In this patient, a bone marrow examination revealed hypocellular marrow, consistent with impaired marrow function from prior treatments. As a result, the onset of myelosuppression after LNZ use may be more rapid. In this case, the WBC count declined 3 days after starting LNZ, despite escalating G-CSF support. The sustained myelosuppression contributed to the development of sepsis, which ultimately led to shock and multi-organ failure, resulting in the patient's death.

While we cannot definitively prove that LNZ was the sole cause of the second episode of neutropenia, it is highly plausible that the sustained cytopenia was exacerbated by the addition of this antimicrobial. Research on LNZ-induced myelosuppression in cancer populations is limited, with only a few studies available.^[5, 6] Nonetheless, from a heuristic point of view, our single-institution experience highlights the potential for early myelosuppression secondary to LNZ use in heavily treated cancer patients.

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Conflicts of Interest

The authors declare no competing interests.

References

- [1] Curtis BR. Non-chemotherapy drug-induced neutropenia: key points to manage the challenges. *Hematology Am Soc Hematol Educ Program* 2017;2017:187-93.
- [2] Han H, Yan H, King KY. Broad-Spectrum Antibiotics Deplete Bone Marrow Regulatory T Cells. *Cells* 2021;10.

- [3] Selby PR, Shakib S, Peake SL, et al. A Systematic Review of the Clinical Pharmacokinetics, Pharmacodynamics and Toxicodynamics of Ganciclovir/Valganciclovir in Allogeneic Haematopoietic Stem Cell Transplant Patients. *Clin Pharmacokinet* 2021;60:727-39.
- [4] Vinh DC, Rubinstein E. Linezolid: a review of safety and tolerability. *J Infect* 2009;59 Suppl 1:S59-74.
- [5] Nedved AN, DeFrates SR, Hladnik LM, Stockerl-Goldstein KE. Effect of Linezolid on Hematologic Recovery in Newly Diagnosed Acute Myeloid Leukemia Patients Following Induction Chemotherapy. *Pharmacotherapy* 2016;36:1087-94.
- [6] Zhou D, Shi T, Zhao S, et al. Linezolid is safe on platelet count for AML patients during myelosuppression after consolidation chemotherapy. *J Clin Pharm Ther* 2020;45:755-8.