

## Editorial

### Infections in lymphoma patients

Chinadol Wanitpongpun

Hematology unit, Department of Internal Medicine, Faculty of Medicine, Srinagarind Hospital, Khon Kaen University

Infections are commonly observed in lymphoma patients due to both the disease itself and the effects of its treatment. The proposed mechanisms primarily include lymphoma-associated immune dysregulation and therapy-related immune suppression. Infections may be bacterial, fungal, viral, opportunistic, or tuberculous, and they significantly increase morbidity by causing treatment delays, reducing treatment tolerance, increasing hospitalization rates, and contributing to higher mortality.<sup>1-3</sup>

There are five key preventive strategies to reduce the risk and severity of infections:

1. Low-bacterial diet, along with strict hand and oral hygiene<sup>4</sup>
2. Supporting immune recovery through adequate nutritional support<sup>5</sup>
3. Vaccinations, such as influenza and COVID-19 vaccines<sup>6,7</sup>
4. Shortening the duration of neutropenia and increasing the white blood cell nadir by using G-CSF, especially in treatment protocols with a > 20% risk of febrile neutropenia, such as the R-CHOP regimen<sup>8-12</sup>
5. Routine use of antibiotic prophylaxis for *Pneumocystis jirovecii* pneumonia (PJP) using trimethoprim-sulfamethoxazole (Bactrim)<sup>13,14</sup> and for herpes zoster using acyclovir<sup>15,16</sup>

For other, more specific infections, the recommendations are as follows:

- Bacterial infections are common in lymphoma patients. However, routine antibacterial prophylaxis is not recommended due to the emergence of multi-drug-resistant (MDR) organisms in Thailand.<sup>17</sup>

- Fungal infections are frequently seen in febrile neutropenic patients. However, the duration of neutropenia is typically short and managed with G-CSF; therefore, routine antifungal prophylaxis is not routinely recommended.<sup>18,19</sup>

- Viral reactivation of hepatitis B virus (HBV), Epstein-Barr virus (EBV), and cytomegalovirus (CMV) can occur during lymphoma treatment and requires early and effective management:

- HBV reactivation requires antiviral agents such as entecavir or tenofovir.<sup>20-24</sup>
- EBV reactivation can be treated with rituximab, which targets B-cell lymphocytes, the primary reservoirs of the virus.<sup>25,26</sup>
- CMV reactivation requires immediate antiviral therapy, with ganciclovir commonly used to prevent CMV disease.<sup>27-29</sup>

- Tuberculosis (TB) remains endemic in Thailand. It can sometimes mimic lymphoma, leading to misdiagnosis or delayed treatment. Moreover, TB reactivation can occur during lymphoma therapy. Coexistence of TB and lymphoma should be carefully considered. Standard anti-TB regimens are preferred, but drug interactions with lymphoma treatments must be managed. For example, rifampicin is a potent cytochrome P450 (CYP) inducer that can reduce the effectiveness of corticosteroids.<sup>30-33</sup>

Although these preventive strategies can reduce the risk of infection, breakthrough infections may still occur. Therefore, close monitoring, early detection, and prompt treatment are essential to ensure survival and successful lymphoma management.

## References

1. Lantz B, Adolfsson J, Lagerlöf B, Reizenstein P. Causes of death in leukemia and lymphoma with modern treatment. *Acta Haematol.* 1980;63:61-7.
2. Bishop JF, Schimpff SC, Diggs CH, Wiernik PH. Infections during intensive chemotherapy for non-Hodgkin's lymphoma. *Ann Intern Med.* 1981;95:549-55.
3. Morrison VA. Infections in patients with leukemia and lymphoma. *Cancer Treat Res.* 2014;161:319-49.
4. Sonbol MB, Jain T, Firwana B, Hilal T, Deleon T, Murad A, et al. Neutropenic diets to prevent cancer infections: updated systematic review and meta-analysis. *BMJ Support Palliat Care.* 2019;9:425-33.
5. Ligibel JA, Bohlke K, May AM, Clinton SK, Demark-Wahnefried W, Gilchrist SC, et al. Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline. *J Clin Oncol.* 2022;40:2491-507.
6. Kamboj M, Bohlke K, Baptiste DM, Dunleavy K, Fueger A, Jones L, et al. Vaccination of Adults With Cancer: ASCO Guideline. *J Clin Oncol.* 2024;42:1699-721.
7. Pail O, Lin MJ, Anagnostou T, Brown BD, Brody JD. Cancer vaccines and the future of immunotherapy. *Lancet.* 2025;406:189-202.
8. Kansara R, Kumar R, Seftel M. Is primary prophylaxis with granulocyte colony stimulating factor (G-CSF) indicated in the treatment of lymphoma? *Transfus Apher Sci.* 2013;49:51-5.
9. Kim M, Ahn Y, Ahn HJ, Ha SH, Oh HS, Song JS, et al. Impact of primary prophylaxis by pegfilgrastim in diffuse large B-cell lymphoma treated with R-CHOP. *Ann Hematol.* 2023;102:3167-75.
10. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2015;33:3199-212.
11. Straus D, Collins G, Walewski J, Zinzani PL, Grigg A, Sureda A, et al. Primary prophylaxis with G-CSF may improve outcomes in patients with newly diagnosed stage III/IV Hodgkin lymphoma treated with brentuximab vedotin plus chemotherapy. *Leuk Lymphoma.* 2020;61:2931-8.
12. Pettengell R, Schwenkglenks M, Bacon P, Lawrinson S, Duehrsen U. Pegfilgrastim primary prophylaxis in patients with non-Hodgkin lymphoma: results from an integrated analysis. *Hematol Oncol.* 2011;29:177-84.
13. Liu C, Zhang X, Zhu Y, Wei J, Ye X, Yang C, et al. Trimethoprim-sulfamethoxazole prevents interstitial pneumonitis in B-cell lymphoma patients receiving chemotherapy: a propensity score matching analysis. *Ann Hematol.* 2023;102:2387-95.
14. Jiang X, Mei X, Feng D, Wang X. Prophylaxis and Treatment of *Pneumocystis jiroveci* Pneumonia in Lymphoma Patients Subjected to Rituximab-Contained Therapy: A Systemic Review and Meta-Analysis. *PLoS One.* 2015;10:e0122171.
15. Abbasov E, Metzner B, Müller TH, Casper J, Kimmich C, Petershofen EK, et al. Herpes zoster prophylaxis with low-dose acyclovir in patients with malignant lymphoma and multiple myeloma treated with autologous stem cell transplantation. *Eur J Haematol.* 2022;109:298-304.
16. Henze L, Buhl C, Sandherr M, Cornely OA, Heinz WJ, Khodamoradi Y, et al. Management of herpesvirus reactivations in patients with solid tumours and hematologic malignancies: update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO) on herpes simplex virus type 1, herpes simplex virus type 2, and varicella zoster virus. *Ann Hematol.* 2022;101:491-511.
17. Gafter-Gvili A, Fraser A, Paul M, Vidal L, Lawrie TA, van de Wetering MD, et al. Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy. *Cochrane Database Syst Rev.* 2012;1:CD004386.
18. Pagano L, Maschmeyer G, Lamoth F, Blennow O, Xhaard A, Spadea M, et al. Primary antifungal prophylaxis in hematological malignancies. Updated clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL). *Leukemia.* 2025;39:1547-57.
19. Cornely OA, Sprute R, Bassetti M, Chen SCA, Groll AH, Kurzai O, et al. Global guideline for the diagnosis and management of candidiasis: an initiative of the ECMM in cooperation with ISHAM and ASM. *Lancet Infect Dis.* 2025;25:e280-93.
20. Huang HH, Hsiao FY, Chen HM, Wang CY, Ko BS. Antiviral prophylaxis for hepatitis B carriers improves the prognosis of diffuse large B-cell lymphoma in Taiwan - a population-based study. *Br J Haematol.* 2021;192:110-8.
21. Cao X, Wang Y, Li P, Huang W, Lu X, Lu H. HBV Reactivation During the Treatment of Non-Hodgkin Lymphoma and Management Strategies. *Front Oncol.* 2021;11:685706.
22. Pei SN, Chen CH. Risk and prophylaxis strategy of hepatitis B virus reactivation in patients with lymphoma undergoing chemotherapy with or without rituximab. *Leuk Lymphoma.* 2015;56:1611-8.
23. Buensalido JAL, Chandrasekar PH. Prophylaxis against hepatitis B reactivation among patients with lymphoma receiving rituximab. *Expert Rev Anti Infect Ther.* 2014;12:151-4.
24. Tan CJ, Kumar R, Koomanan N, Loo WS, Farid M, Tao M, et al. Clinical and economic evaluation of a surveillance protocol to manage hepatitis B virus (HBV) reactivation among lymphoma patients with resolved HBV infection receiving rituximab. *Pharmacotherapy.* 2021;41:332-41.
25. Ford M, Orlando E, Amengual JE. EBV Reactivation and Lymphomagenesis: More Questions than Answers. *Curr Hematol Malig Rep.* 2023;18:226-33.
26. Pociupany M, Snoeck R, Dierickx D, Andrei G. Treatment of Epstein-Barr Virus infection in immunocompromised patients. *Biochem Pharmacol.* 2024;225:116270.

27. Massoud R, Assi R, Fares E, Haffar B, Charafeddine M, Kreidieh N, et al. Cytomegalovirus reactivation in lymphoma and myeloma patients undergoing autologous peripheral blood stem cell transplantation. *J Clin Virol.* 2017;95:36-41.
28. Hatayama Y, Watanabe K, Ichikawa H, Kawamura K, Fukuda T, Motokura T. Differential Reactivation of Cytomegalovirus and Epstein-Barr Virus in Patients with B Cell Lymphoma. *Viral Immunol.* 2023;36:520-5.
29. Ding Y, Ru Y, Song T, Guo L, Zhang X, Zhu J, et al. Epstein-Barr virus and cytomegalovirus reactivation after allogeneic hematopoietic cell transplantation in patients with non-Hodgkin lymphoma: the prevalence and impacts on outcomes : EBV and CMV reactivation post allo-HCT in NHL. *Ann Hematol.* 2021;100:2773-85.
30. Banerjee A, Bhuller K, Sudhir R, Bajaj A. Diagnostic dilemma of Hodgkin's lymphoma versus tuberculosis: a case report and review of the literature. *J Med Case Rep.* 2021;15:351.
31. Mahajan A, Bakhshi S, Singh M, Seth R, Verma N, Jain S, et al. Empirical Antitubercular Treatment for Lymphadenopathy: Are We Missing Lymphoma? *Indian J Pediatr.* 2023;90:761-5.
32. Obando P, Verón DA, Castellanos M, Fernández KS. Simultaneous occurrence of Hodgkin lymphoma and tuberculosis in children and adolescents. *Pediatr Blood Cancer.* 2020;67:e28405.
33. Hu JN, Yu MQ, Hua LJ, Bao C, Liu Q, Liu C, et al. Tuberculosis combined with Burkitt lymphoma in a kidney transplant recipient: A case report and literature review. *Medicine (Baltimore).* 2023;102:e33671.

