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Editorial

Increased risk of herpes zoster in gynecological cancer patients receiving radiotherapy combined with chemotherapy: a need for paying attention to vaccines

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A prevalent viral disease, herpes zoster (HZ), is a threat to patients with cancer [1]. As the overall survival of patients with cancer increases in tandem with the newly developed treatments, HZ is expected to become more problematic. HZ is caused by the reactivation of latent varicella-zoster virus in the cranial-nerve or dorsal-root ganglia, leading to a painful vesicular rash along one or more dermatomes. HZ not only diminishes the quality of life but also causes several complications, such as meningitis/encephalitis, bacterial superinfection, and post-herpetic neuralgia (PHN), resulting in prolonged hospitalization in patients with cancer [1,2]. The risk of the occurrence of HZ increases when the level of T-cell immunity is reduced by advancing age or in case of organ or hematopoietic stem-cell transplantation [2]. Regardless of the treatment, a diagnosis of cancer was associated with about a 40% higher risk of HZ, especially high in the first year following diagnosis [3]. The risk of HZ increases because the cancer may share the underlying cause of immune system dysfunction. In addition, receiving chemotherapy (CT) for cancer can cause immune system dysfunction too.

In this issue of the *Journal of Gynecologic Oncology*, Lee et al. [4] examined the risk of HZ in patients with gynecological cancers from the National Health Insurance Research Database in Taiwan. The risk of HZ in cancer patients was higher than that in individuals without cancer (14.23 vs. 8.34 per 1,000 person-years, adjusted hazard ratio [aHR]=1.38, p=0.04). The patients receiving CT and radiotherapy (RT) had the highest cumulative incidence, with a 5-year actuarial incidence of 9.9%. Additionally, the authors presented an increased HZ risk in patients who received RT in the first year after diagnosis. Until recently, in patients with solid tumors, the higher risk of developing HZ appeared to be largely associated with receiving CT after the diagnosis was made, rather than with the cancer itself [3]. Few previous studies have separated the risk for HZ associated with the patient's cancer from the risk of HZ associated with the cancer treatment, represented by CT. In this context, this study had strength in detailed assessments of the association between the cancer treatment (CT and RT) and the risk of HZ.

Author Contributions

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However, it is difficult to say that RT had a direct effect on the systemic immune function because when stratified by CT, there was no significant increase in the risk of HZ in the RT group without CT (aHR [95% confidence interval], 1.40 [0.86–2.28]; p=0.17). Although a previous study showed that RT increased the incidence of HZ within the radiation field [5], we could not assess the association between the site of HZ and the RT-field in the study because the data were derived from a health insurance database, as the authors mentioned in the limitation. However, we could not exclude the possibility of RT increasing the risk of HZ by indirectly affecting the function of the immune system, considering that HZ is also related to various physical factors and even psychosocial stress [6]. In addition, there was no review of which cancer stage had the greatest influence on the immunity of cancer patients, as noted by the authors. Finally, since the study reviewed participants from 2000 to 2012, HZ vaccination (zoster vaccine live, ZVL [Zostavax; Merck and Co., Inc., Whitehouse station, NJ, USA] approved by the U.S. Food and Drug Administration (FDA) in 2005) before and after the diagnosis of cancer may have affected the occurrence of HZ, but the history of vaccination was not evaluated in the study.

Although there were some limitations, the results of the study were meaningful because RT and CT are the key elements in gynecological cancer treatment. Clinicians should be aware that HZ occurs frequently in patients with gynecological cancer undergoing CT and RT. These findings have important implications on not only the early diagnosis and treatment of HZ but also the prevention of HZ with vaccines. Two vaccines have been approved by the FDA: ZVL and recombinant zoster vaccine (RZV [Shingrix; GlaxoSmithKline, Brentford, UK]) [7]. Since ZVL is a live vaccine, it is difficult to administer it during RT or CT, and it has the disadvantage of its effectiveness against HZ decreasing over time [8]. To avoid adverse events and obtain sufficient immunity, ZVL vaccination may be needed as soon as possible after the diagnosis of cancer, before initiating immunosuppressive therapies. On the other hand, RZV, a 2-dose recombinant vaccine administered at 0 and 2–6 months, could be recommended for HZ prevention in patients with cancer, and is already commercially available in some countries such as the United States, Canada, and Australia. RZV has been shown to be more effective in preventing HZ and PHN, even in patients over the age of 70 years [7]. Moreover, revaccination with RZV in adults previously vaccinated with ZVL was found to be highly beneficial, since it was significantly effective in decreasing the incidence of HZ and PHN [9]. Although RZV can be administered during RT or CT and its efficacy is promising, data on RZV in immunocompromised patients are lacking [7]. Further research is urgently needed regarding the safety, efficacy, timing, and cost-benefit analysis of vaccinating cancer patients against HZ, considering cancer treatment options such as surgery, RT, and CT.

The study showed that RT combined with CT in patients with gynecological cancers was significantly associated with a higher incidence of HZ. Considering that HZ is a vaccine-preventable disease, clinicians who treat cancer patients should continue to pay attention to recent advances in not only early diagnosis and treatment but also the prevention of HZ.

REFERENCES

1. Kim ST, Park KH, Oh SC, Seo JH, Shin SW, Kim JS, et al. Varicella zoster virus infection during chemotherapy in solid cancer patients. Oncology 2012;82:126-30.
PUBMED | CROSSREF
2. Cohen JI. Clinical practice: herpes zoster. N Engl J Med 2013;369:255-63.
PUBMED | CROSSREF

3. Qian J, Heywood AE, Karki S, Banks E, Macartney K, Chantrill L, et al. Risk of herpes zoster prior to and following cancer diagnosis and treatment: a population-based prospective cohort study. J Infect Dis 2019;220:3-11.
PUBMED | CROSSREF
4. Lee PY, Lai JN, Chen SW, Lin YC, Chiu LT, Wei YT. Radiotherapy combined with chemotherapy increases the risk of herpes zoster in patients with gynecological cancers: a nationwide cohort study. J Gynecol Oncol 2021;32:e13.
PUBMED
5. Shimizuguchi T, Sekiya N, Hara K, Taguchi A, Nakajima Y, Miyake Y, et al. Radiation therapy and the risk of herpes zoster in patients with cancer. Cancer 2020;126:3552-9.
PUBMED | CROSSREF
6. Kawai K, Yawn BP. Risk factors for herpes zoster: a systematic review and meta-analysis. Mayo Clin Proc 2017;92:1806-21.
PUBMED | CROSSREF
7. Brotherton AL, Shah R. Recent updates to the advisory committee on immunization practices recommendations for pneumococcal and herpes zoster vaccination. R I Med J (2013) 2020;103:34-7.
PUBMED
8. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med 2005;352:2271-84.
PUBMED | CROSSREF
9. Grupping K, Campora L, Douha M, Heineman TC, Klein NP, Lal H, et al. Immunogenicity and safety of the HZ/su adjuvanted herpes zoster subunit vaccine in adults previously vaccinated with a live attenuated herpes zoster vaccine. J Infect Dis 2017;216:1343-51.
PUBMED | CROSSREF