J Korean Med Sci. 2022 Jul 18;37(28):e232
https://doi.org/10.3346/jkms.2022.37.e232
eISSN 1598-6357·pISSN 1011-8934

JKMS

Editorial
Oncology & Hematology

Time to Care for Adrenal Insufficiency in Cancer Patients

Jung Hee Kim

Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

▸ See the article "Clinical Features and Risk Factors of Adrenal Insufficiency in Patients With Cancer Admitted to the Hospitalist-Managed Medical Unit" in volume 37, number 28, e222.

Received: Jul 8, 2022
Accepted: Jul 12, 2022
Published online: Jul 15, 2022

Address for Correspondence:
Jung Hee Kim, MD, PhD
Department of Internal Medicine, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea.
Email: jhee1@snu.ac.kr

ORCID iD
Jung Hee Kim
https://orcid.org/0000-0003-1932-0234

Disclosure
The author has no potential conflicts of interest to disclose.

Adrenal insufficiency (AI) was frequently seen in cancer patients, but the prevalence was not well known. In this study, Kwon et al.[1] reported a high prevalence of AI (35%) among cancer patients. The prevalence might be overestimated since they performed a rapid ACTH stimulation test only in cancer patients who presented suspected symptoms of AI. However, given that dynamic tests for AI were conducted in symptomatic patients such as anorexia, fatigue, and general weakness, it is helpful to give a clue that one-third of symptomatic patients might have AI.

In cancer patients, the cause of AI can be primary (adrenal), secondary (pituitary), or tertiary (hypothalamus). Unfortunately, Kwon et al.[1] did not differentiate subtypes of AI. Instead, the authors reported that corticosteroid and megestrol acetate use were risk factors for AI.[1] Exogenous use of corticosteroids caused tertiary AI, since chronic high-dose corticosteroids decreased the synthesis of proopiomelanocortin and secretion of ACTH. Han et al.[2] also revealed that at least three short courses of high-dose dexamethasone every two to four weeks as antiemetics led to AI within three to six months in 15% of cancer patients. However, in Kwon et al.'s study,[1] corticosteroid use of any duration, regardless of dosage, was a risk factor for AI, which needed to be reevaluated. Moreover, the proportion of high-dose corticosteroid users was only 36% in Kwon et al.'s study.[1] The other purpose of low or medium-dose users should be specified. The duration of corticosteroid use was calculated as the cumulative duration. Nevertheless, the effect of intermittent or daily use would be quite different. Moreover, the withdrawal period might affect the GI-AI. It would be more informative if the authors suggested the duration or dosage of drugs and the withdrawal period.

As another risk factor, Kwon et al.[1] identified the use of megestrol acetate, which has glucocorticoid activity via binding to the glucocorticoid receptor in the pituitary gland.[3] Thus, megestrol acetate causes secondary AI. Han et al.[2] also found that patients who also received megestrol acetate had a threefold higher risk of AI.

Notably, in Kwon et al.'s study, eosinophilia was a better indicator for AI rather than hyponatremia.[1] Therefore, this finding suggests that cancer patients with eosinophilia might have AI instead of drug hypersensitivity reaction or other diseases. However, relative lymphocytosis and hypercalcemia, which were also recognized as a manifestation of AI, needed to be evaluated.[4]

If there are simple tools for diagnosing AI in cancer patients, it would be helpful to circumvent the stimulation test for AI. Kwon et al.[1] suggested that morning fasting cortisol < 6.2 μg/dL showed a specificity of AI and < 12.85 μg/dL excluded AI with a probability of 98.9%. In other studies, early morning serum cortisol < 3.6 μg/dL was identified for diagnosing AI, which was lower than Kwon et al.'s study.[5] At this point, it remains unexplained, but it might reflect basal stress status in cancer patients.

Overall, Kwon et al.[1] showed that discriminatory features such as eosinophilia and significant risk factors such as the history of glucocorticoid or megestrol acetate increased the probability of AI in cancer patients with non-specific symptoms. In addition, they gave us useful tips that morning basal cortisol measurement might be enough to diagnose AI in some patients. Future studies should seek other discriminatory features and validate the pre-specified cutoff values of morning basal cortisol to diagnose AI.

REFERENCES

1. Kwon MK, Kim J, Ahn J, Woo CY, Kim H, Oh HS, et al. Clinical features and risk factors of adrenal insufficiency in patients with cancer admitted to the hospitalist-managed medical unit. *J Korean Med Sci* 2022;37(28):e222.
CROSSREF
2. Han HS, Park JC, Park SY, Lee KT, Bae SB, Kim HJ, et al. A prospective multicenter study evaluating secondary adrenal suppression after antiemetic dexamethasone therapy in cancer patients receiving chemotherapy: a Korean south west oncology group study. *Oncologist* 2015;20(12):1432-9.
PUBMED | CROSSREF
3. Mann M, Koller E, Murgo A, Malozowski S, Bacsanyi J, Leinung M. Glucocorticoidlike activity of megestrol. A summary of Food and Drug Administration experience and a review of the literature. *Arch Intern Med* 1997;157(15):1651-6.
PUBMED | CROSSREF
4. Hahner S, Ross RJ, Arlt W, Bancos I, Burger-Stritt S, Torpy DJ, et al. Adrenal insufficiency. *Nat Rev Dis Primers* 2021;7(1):19.
PUBMED | CROSSREF
5. Prete A, Bancos I. Glucocorticoid induced adrenal insufficiency. *BMJ* 2021;374(1380):n1380.
PUBMED | CROSSREF

https://doi.org/10.3346/jkms.2022.37.e232