Cisplatin-Etoposide–Induced Hyperammonemic Encephalopathy in a Lung Cancer Patient

Tanvi Mittal, MBBS; Arundhathi Krishna Komathodi, MBBS; and Nishanth Jalaja Haridas, MD

Delirium is a neurocognitive disorder predominantly affecting attention.[1] Cancer patients are particularly vulnerable to altered mental states and delirium due to various factors, some of which include structural brain lesions, preexisting dementia in the elderly population, hyponatremia, systemic infections, drugs, and malnutrition.[2]

Several chemotherapeutic agents are implicated in delirium (eg, etoposide, cisplatin, and vincristine).[3,4] These drugs can cause enhanced protein catabolism, gastrointestinal bleeding, enzyme alterations affecting urea synthesis, and sepsis. All these processes can increase ammonia production leading to confused behavior.[4] In this report, we present a case of cisplatin-etoposide–induced hyperammonemic encephalopathy in a patient with lung carcinoma.

Case Report

A 68-year-old male chronic smoker was diagnosed with carcinoma of the lung, with metastasis to cervical lymph nodes. Following diagnosis, he was initiated on a etoposide-cisplatin–based chemotherapy regimen. The initial 2 cycles were devoid of significant adverse events. During the third cycle of chemotherapy, on day 3, the patient exhibited altered behavior characterized by agitation, aimless pacing, irrelevant speech, and disorientation concerning time, place, and personal identity. He also suffered from disrupted sleep patterns and demonstrated marked irritability throughout this period. It was noted that he had no prior history of delirium or psychiatric illness. Apart from elevated serum ammonia levels (171 µg/dL), his blood investigations were mostly within normal limits. The ammonia levels later fell within normal limits (29 µg/dL) as the delirium resolved with symptomatic management. Contrast-enhanced computed tomography of the brain was conducted, revealing no signs of metastasis. He was discharged with no significant impairment in behavior. However, he continued to experience sleep disturbances at home after discharge.

Two weeks later, the patient was readmitted for his fourth cycle of chemotherapy. On the first day of the cycle, he experienced symptoms similar to the first episode, prompting the withholding of further chemotherapy doses. Serum ammonia levels were repeated and found to be 99 µg/dL, confirming hyperammonemic encephalopathy. Treatment included initiating quetiapine at a dose of 25 mg along with general strategies to reduce ammonia formation in the gut.

Discussion

Delirium is a common complication in patients with carcinoma.[5] Patients with carcinoma often require chemotherapeutic agents that contribute to delirium.[3,4] In the current case, the patient developed confused behavior due to hyperammonemic encephalopathy following the administration of etoposide and cisplatin.

Ammonia is a neurotoxin, and elevated levels can lead to delirium.[6] Elevated ammonia levels result in increased glutamate, which impairs *N*-methyl-D-aspartate receptor signal transmission. This is one of the mechanisms responsible for the cognitive dysfunction and delirium in hyperammonemia.[7] Nonhepatic hyperammonemia can be associated with 30%–50% mortality rates.[8]

This case highlights the importance of considering hyperammonemia in cancer patients presenting with delirium, especially in the context of chemotherapy. Early recognition and appropriate management are crucial for improving patient outcomes. Further research into the mechanisms of chemotherapy-induced hyperammonemia and delirium is suggested.

Article Information

Published Online: November 12, 2024. https://doi.org/10.4088/PCC.24cr03778

Prim Care Companion CNS Disord 2024;26(6):24cr03778

Submitted: May 25, 2024; accepted August 7, 2024.

To Cite: Mittal T, Komathodi AK, Haridas NJ. Cisplatin-etoposide–induced hyperammonemic encephalopathy in a lung cancer patient. *Prim Care Companion CNS Disord.* 2024;26(6):24cr03778.

Author Affiliations: Department of Psychiatry, Government Medical College, Kozhikode, Kerala, India (Mittal, Haridas); Government Medical College, Kozhikode, Kerala, India (Komathodi).

Corresponding Author: Tanvi Mittal, MBBS, Department of Psychiatry, Government Medical College, Kozhikode, Kerala 673008, India (tmpsymd@gmail.com).

Relevant Financial Relationships: None.

Funding/Support: None.

Patient Consent: Consent was received from the patient to publish the case report, and information has been de-identified to protect patient anonymity.

ORCID: Tanvi Mittal: https://orcid.org/0009-0009-4608-6413; Arundhathi Krishna Komathodi: https://orcid.org/0009-0005-4892-7360; Nishanth Jalaja Haridas: https://orcid.org/0000-0002-2517-2031

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association; 2013.
2. Tuma R, DeAngelis LM. Altered mental status in patients with cancer. *Arch Neurol*. 2000;57(12):1727–1731.
3. Verkerk K, Otten HM, Huitema ADR. Idiopathic hyperammonemic encephalopathy secondary to gemcitabine-cisplatin treatment. *Cancer Chemother Pharmacol*. 2022;90(5):417–419.
4. Kalra A, Norvell JP. Cause for confusion: noncirrhotic hyperammonemic encephalopathy. *Clin Liver Dis (Hoboken)*. 2020;15(6):223–227.
5. Bruera E, Bush SH, Willey J, et al. Impact of delirium and recall on the level of distress in patients with advanced cancer and their family caregivers. *Cancer*. 2009;115(9):2004–2012.
6. Yadav U, Sah PK, Mahadevamma LM. Non-cirrhotic hyperammonemia: a risk factor for altered mental status. *Ind J Pharm Pr*. 2021;14(1):62–64.
7. Ali R, Nagalli S. *Hyperammonemia*. StatPearls Publishing; 2023.
8. Balcerac A, Bihan K, Lebrun-Vignes B, et al. Drug-associated hyperammonaemia: a bayesian analysis of the WHO pharmacovigilance database. *Ann Intensive Care*. 2022;12(1):55.