Development of Neuroleptic Malignant Syndrome in a patient with Lewy body dementia after administration of Paliperidone

Sarah Schmitz, MD; Nino Kvantaliani, MD; Christina Martin, MD; Ho-Man Yeung, MD
Department of Medicine, Lewis Katz School of Medicine, Temple University, Philadelphia, PA

ABSTRACT

Neuroleptic malignant syndrome (NMS) is a potentially fatal diagnosis composed of hyperpyrexia, muscle rigidity, altered mental status, and autonomic instability. This syndrome has significant systemic manifestations including acute renal failure, rhabdomyolysis, hyperkalemia, and seizure. It is associated with the use of both typical and atypical antipsychotics. Due to the extensive neurodegenerative destruction of dopaminergic and acetylcholinergic pathways, patients with Lewy body dementia (LBD) are particularly sensitive to antidopaminergic and anticholinergic medications, making them more susceptible to extrapyramidal side effects and NMS. We present a case of a 72-year-old female with LBD who developed muscular rigidity, vital sign instability, and altered mental status after receiving one dose of paliperidone palmitate injection two weeks prior to admission. Initial blood work was unrevealing. Extensive work up including EEG, lumbar puncture with cerebrospinal fluid analysis, and brain MRI were unremarkable. She was treated with seven days of bromocriptine and a lorazepam taper with improvement in muscle rigidity. However, her mental status never improved, and she remained comatose. This case demonstrates the complexity and potential fatality of NMS. Clinicians should be aware of this complication of antipsychotic use in patients with LBD as these patients may be more susceptible to NMS.

CASE DESCRIPTION

A 72-year-old female with a past medical history of advanced dementia with Lewy bodies was brought to the ED by her granddaughter with acute change in mental status. Lewy body dementia was diagnosed several years prior and had been progressive with urinary incontinence, hallucinations and paranoia, and speech difficulty. Two weeks prior to admission, her primary doctor initiated paliperidone palmitate extended-release intramuscular injection of 156mg, as the patient had been off antipsychotic therapy for three months. On admission, the patient had a temperature of 101.8ºF, a heart rate of 110 bpm, a blood pressure of 172/87 mmHg, and an oxygen saturation of 97% on room air. On examination, the patient only responded to painful stimuli by grimacing. Pupils were equal but sluggishly reactive to light. Her head was deviated to the left and stiff when moved toward midline. She had muscular rigidity of her upper extremities and lower extremities bilaterally. Her patellar and brachial reflexes were brisk at 3+, and her toes were mute bilaterally. Work-up is shown in Table 1. She was transferred to the ICU and started on dantrolene, bromocriptine, and benzodiazepines for symptomatic management of suspected neuroleptic malignant syndrome. Unfortunately, her mental status never improved and her family decided to transition the patient to comfort care on hospital day 15.

TABLE 1: Patient Workup

Laboratory Data
Hemoglobin 14.3 g/dL
WBC 9.0 x 1000/mm^3
Sodium 139 mEq/L
Potassium 5.2 mEq/L
BUN 19 mg/dL
Creatinine 0.89 mg/dL
Glucose 193 mg/dL
LFTs wnl
Lactate 1.2 mmol/L
Ammonia wnl
TSH 0.970 mU/L
UDS negative
RPR nonreactive
Hepatitis C Ab non-reactive
HIV non-reactive
B12 wnl
Folate wnl

Culture Data
Blood cultures NGTD
CSF cultures NGTD
Urine culture > 100k E.faecalis
Sputum culture <10k S.aureus

Imaging Findings
Normal CT head
Normal MRI head
No seizure activity on EEG

CSF Fluid Analysis
Clear color
2 WBC/uL
Glucose 92 mg/dL
Protein 27 mg/dL
VDRL non-reactive
Cryptococcal Ag negative
AFB stain negative
NMDA receptor Ab negative

WBC - white blood cell; BUN - blood urea nitrogen, LFT - liver function test; TSH - thyroid-stimulating hormone; UDS - urine drug screen; RPR - rapid plasma reagin; NGTD - no growth to date; VDRL - venereal disease research laboratory; AFB - acid-fast bacillus; NMDA - N-methyl-D-aspartate; wnl - within normal limits

REFERENCES

1. Levine M, LoVecchio F. Antipsychotics. In: Tintinalli JE, Ma OJ, Yealy DM, Meckler GD, Stapczynski JS, Cline DM, et al., editors. Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 9e [Internet]. New York, NY: McGraw-Hill Education; 2020. Available from: http://accessmedicine.mhmedical.com/content.aspx?aid=1166599809
2. Keck Jr PE, Pope Jr HG, Cohen BM, McElroy SL, Nierenberg AA. Risk Factors for Neuroleptic Malignant Syndrome: A Case-Control Study. Arch Gen Psychiatry [Internet]. 1989 Oct 1;46(10):914–8. Available from: https://doi.org/10.1001/archpsyc.1989.01810100056011
3. Berman BD. Neuroleptic malignant syndrome: a review for neurohospitalists. The Neurohospitalist [Internet]. 2011 Jan;1(1):41–7. Available from: https://pubmed.ncbi.nlm.nih.gov/23983836
4. Petrie W, Kirshner HS. Neurocognitive Disorders. In: Ebert MH, Leckman JF, Petrakis IL, editors. Current Diagnosis & Treatment: Psychiatry, 3e [Internet]. New York, NY: McGraw-Hill Education; 2019. Available from: http://accessmedicine.mhmedical.com/content.aspx?aid=1158259019
5. Seeley WW, Tanner CM, Miller BL. Dementia with Lewy Bodies. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine, 20e [Internet]. New York, NY: McGraw-Hill Education; 2018. Available from: http://accessmedicine.mhmedical.com/content.aspx?aid=1155958612
6. Shalev A, Hermesh H, Munitz H. Mortality from neuroleptic malignant syndrome. Vol. 50, The Journal of Clinical Psychiatry. US: Physicians Postgraduate Press; 1989. p. 18–25.
7. Morris MT, Tarpada SP. Long-Acting Injectable Paliperidone Palmitate: A Review of Efficacy and Safety. Psychopharmacol Bull [Internet]. 2017 May 15;47(2):42–52. Available from: https://pubmed.ncbi.nlm.nih.gov/28626271
8. Kane JM, Correll CU, Delva N, Gopal S, Savitz A, Mathews M. Low Incidence of Neuroleptic Malignant Syndrome Associated With Paliperidone Palmitate Long-Acting Injectable: A Database Report and Case Study. J Clin Psychopharmacol [Internet]. 2019;39(2):180–2. Available from: https://pubmed.ncbi.nlm.nih.gov/30811377

DISCUSSION

Prior to making the diagnosis of NMS, other diagnoses including metabolic, toxicologic, infectious and endocrine disorders should be ruled out. Serotonin syndrome should also be on the differential, as it can present similarly. It is important to note, however, that Serotonin syndrome often has a more rapid onset of 2-24 hours, and presents with hyperreflexia, myoclonus, nausea, vomiting, diarrhea, and less intense muscle rigidity and fever.

The mainstay of treatment for NMS is discontinuation of the offending agent and supportive care. External cooling can be utilized to reduce the patient's temperature however antipyretics such as acetaminophen have not been shown to be beneficial.

Most deaths due to NMS are related to profound muscle rigidity resulting in complications including respiratory failure, rhabdomyolysis, renal failure, disseminated intravascular coagulation, and cardiovascular collapse. No treatment has been shown to be superior to supportive care, however, reported cases have described the use of dantrolene, bromocriptine, benzodiazepines, and amantadine. The mortality rate is around 10%, however, most patients completely recover in 2 to 14 days if NMS is recognized early and treated aggressively. If diagnosis and treatment are delayed, then those who survive may have residual catatonia or parkinsonism.

Paliperidone palmitate is a long-acting formulation of paliperidone, an active metabolite of risperidone. It is an antagonist of brain dopamine D_2 and serotonin 5-hydroxytryptamine receptors. Effects are usually seen about 8 days after injection and peak plasma level is reached about 13 days after injection. The half life ranges from 25-49 days. Intramuscular administration of a neuroleptic may result in higher peak levels and abrupt dopamine blockade.

CONCLUSION

The case described here is the first known case in the English literature of a patient with dementia with Lewy bodies that suffered from neuroleptic malignant syndrome after receiving an intramuscular injection of paliperidone palmitate. As the use of novel long-acting antipsychotics is still in its nascency, clinicians should be aware of this serious and potentially fatal complication of paliperidone palmitate use, especially in those with underlying dopamine sensitivity.