Neuropsychiatric and Endocrine Adverse Effects Associated with Polypharmacy in a Young Female with Relapsing–Remitting Multiple Sclerosis: A Case Report

V. S. Venkateswara Rao[1], A. Narasimha Rao[1], V. S. Ramya Tripura Sundari[2]

[1] Department of Commerce and Management Studies, Andhra University, Visakhapatnam, Andhra Pradesh, India

[2] Vatrix Health Care Data India Pvt. Ltd., Kondapur, Hyderabad, Telangana, India

Corresponding Author: V. S. Venkateswara Rao

ABSTRACT

Relapsing–remitting multiple sclerosis (RRMS) often requires multidrug therapy, increasing susceptibility to adverse drug reactions (ADRs). This case report describes a 21-year-old female with RRMS who developed significant neuropsychiatric and endocrine complications during combined therapy with gabapentin, nortriptyline, dimethyl fumarate, and prednisolone. Within 20 days, the patient exhibited transient loss of consciousness, vivid dreams, rapid weight gain (50 kg to 73 kg), Cushingoid features, menstrual irregularities, hyperphagia, and behavioral disturbances. Clinical improvement followed dose modification and structured pharmacist-led monitoring. This report emphasizes the importance of individualized therapy, early ADR detection, and multidisciplinary management in RRMS.

Keywords: *Multiple sclerosis, adverse drug reaction, corticosteroids, polypharmacy, pharmacovigilance, gabapentin, nortriptyline*

INTRODUCTION

Relapsing–remitting multiple sclerosis (RRMS) is a chronic immune-mediated demyelinating disorder characterized by episodic neurological dysfunction and progressive disability (O'Connor *et al*., 2008). Disease management typically involves disease-modifying therapies such as dimethyl fumarate along with symptomatic agents for neuropathic pain, including gabapentin and nortriptyline (Gold *et al*., 2012; Moore *et al.*, 2015). Corticosteroids remain essential for managing acute relapses but are associated with significant systemic adverse effects (Liu *et al*., 2013).

Polypharmacy increases the risk of cumulative toxicity, particularly affecting the central nervous and endocrine systems. Neuropsychiatric disturbances and steroid-induced metabolic abnormalities are of particular concern in young patients (Soldin & Mattison, 2009). This case highlights clinically significant adverse outcomes arising from such therapeutic combinations.

CASE PRESENTATION

A 21-year-old unmarried female diagnosed with RRMS presented with neuropathic pain involving lower limbs, a common manifestation in MS patients (O'Connor *et al*., 2008).

MEDICATION REGIMEN

Gabapentin 100 mg twice daily

Nortriptyline hydrochloride 10–25 mg daily

Dimethyl fumarate 120 mg twice daily (Gold et al., 2012)

Prednisolone 50 mg once daily (Liu *et al*., 2013)

Table 1: Summary of Drug Therapy and Associated Adverse Effects.

Drug	**Dose**	**Indication**	**Observed ADRs**
Gabapentin	100 mg BD	Neuropathic pain	Drowsiness, unconsciousness (Moore *et al*., 2015)
Nortriptyline	10-25 mg OD	Neuropathic pain	Vivid dreams, sedation (Wilson & Argyropoulos, 2005)
Prednisolone	50 mg OD	Inflammation control	Weight gain, moon face, irritability, menstrual delay. (Liu *et al*., 2013)
Dimethyl fumarate	120 mg BD	RRMS	Possible systemic contribution (Gold *et al*., 2012)

CLINICAL MANIFESTATIONS

After 20 days of therapy, the patient developed the following adverse effects, consistent with known pharmacological profiles of the drugs used (Moore *et al.*, 2015; Liu *et al.*, 2013):

NEUROPSYCHIATRIC EFFECTS

- Brief episodes of unconsciousness
- Disturbing vivid dreams
- Daytime sedation
- Endocrine and Metabolic Changes
- Rapid weight gain (50 kg to 73 kg)
- Moon facies
- Increased appetite
- Emotional instability and irritability
- Menstrual Disturbance
- Cycle prolonged from 28 days to approximately 38–40 days, likely due to corticosteroid-induced hormonal imbalance (Liu *et al*., 2013)

INVESTIGATIONS

- Blood glucose: Mild elevation
- Serum electrolytes: Within normal limits
- MRI findings: No new demyelinating lesions

CAUSALITY ASSESSMENT

Causality was assessed using standard pharmacovigilance criteria:

- Gabapentin–nortriptyline combination: Probable association with neuropsychiatric effects
- Prednisolone: Definite association with metabolic and endocrine changes
- Dimethyl fumarate: Possible contributory role

Table 2: ADR Causality Assessment (Naranjo Scale Interpretation)

Adverse Effect	**Suspected Drug**	**Causality**
Unconsciousness	Gabapentin+ Nortriptyline	Probable
Vivid dreams	Nortriptyline	Probable
Weight gain	Prednisolone	Definite
Moon face	Prednisolone	Definite
Menstrual irregularity	Prednisolone	Definite
Irritability	Prednisolone	Probable

MANAGEMENT OF DRUG THERAPY

- Gradual tapering of prednisolone
- Adjustment of nortriptyline dosage
- Continuation of dimethyl fumarate under supervision
- Implementation of pharmacist-led monitoring and patient counseling

OUTCOME

- Within 2–4 weeks of intervention:
- Neuropsychiatric symptoms reduced significantly
- Appetite and mood stabilized
- Weight gain progression slowed
- Menstrual cycle showed partial normalization

DISCUSSION

This case demonstrates the risks associated with multi-drug therapy in RRMS. Gabapentin and nortriptyline may collectively enhance central nervous system depression, leading to altered consciousness and abnormal dream patterns (Moore *et al*., 2015; Wilson & Argyropoulos, 2005). Corticosteroids are known to induce metabolic disturbances, including weight gain, fat redistribution, and hormonal imbalance due to hypothalamic–pituitary–adrenal axis suppression (Liu *et al*., 2013).

The observed menstrual irregularities and behavioral symptoms further support corticosteroid-related endocrine disruption. Although dimethyl fumarate is generally well tolerated, its use in combination with other agents may contribute to overall physiological stress (Gold *et al*., 2012).

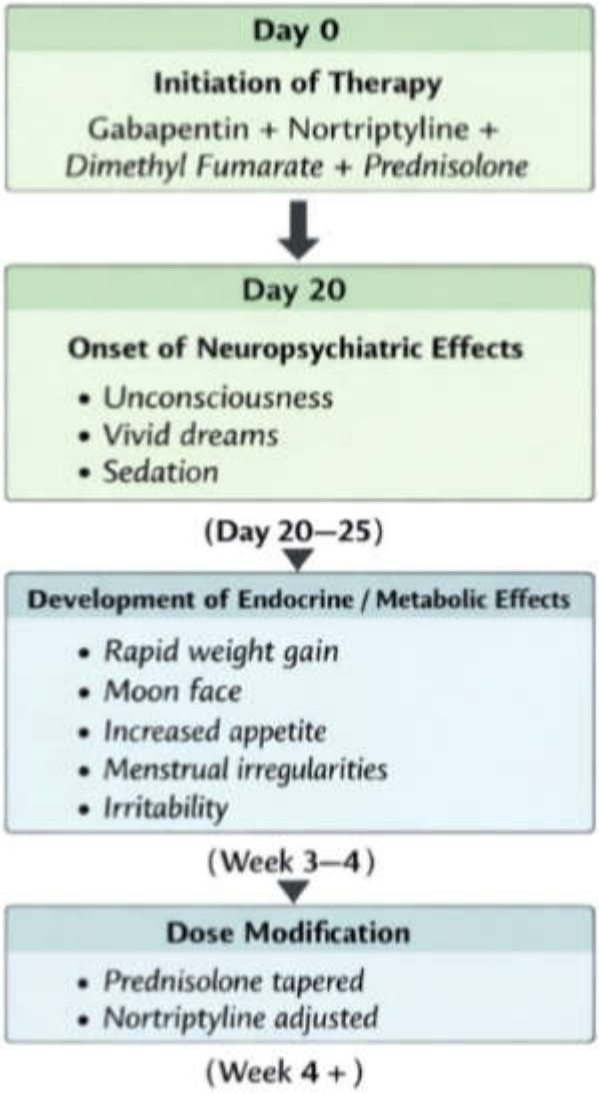

Figure 1: Timeline of Drug Therapy and Adverse Effects

DESCRIPTION:

Day 0: Initiation of therapy

Day 20: Onset of neuropsychiatric symptoms

Day 20–25: Development of metabolic/endocrine effects

Week 3–4: Dose modification

Week 4+: Symptom resolution

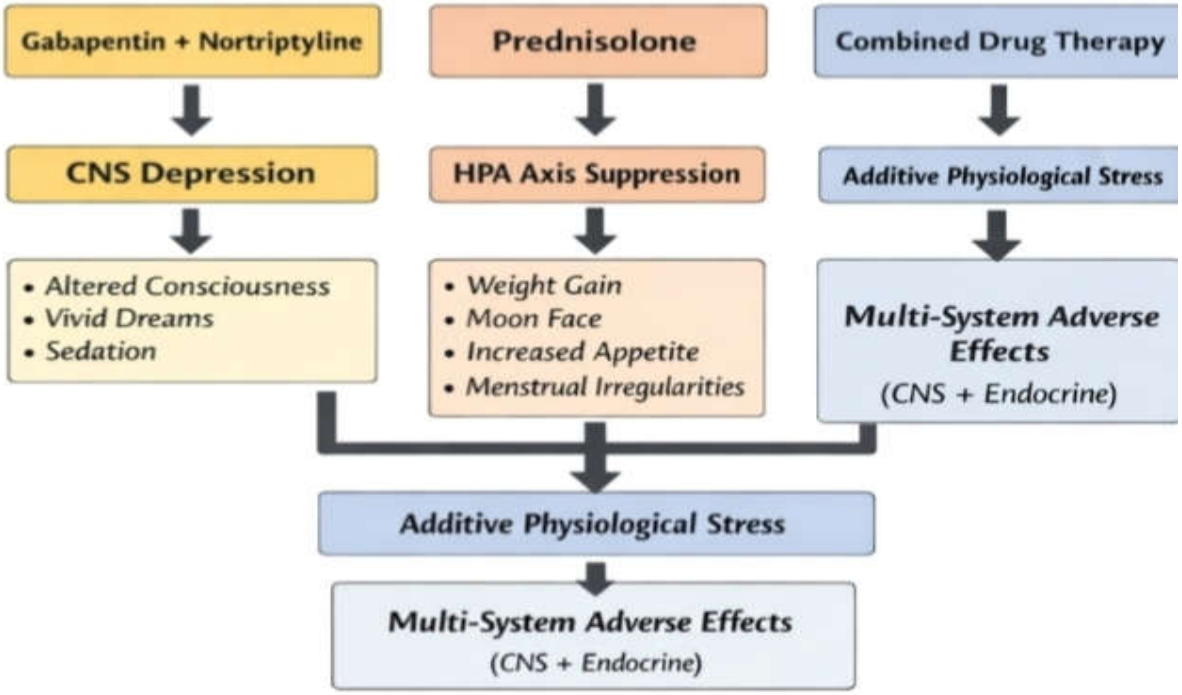

Figure 2: Mechanism of Drug-Induced Adverse Effects

DESCRIPTION

Gabapentin + Nortriptyline → CNS depression → altered consciousness and vivid dreams

Prednisolone → HPA axis suppression → metabolic and endocrine disturbances

Combined therapy → additive physiological stress leading to multi-system adverse effects

PHARMACIST-LED INTERVENTION AND MONITORING

- Clinical pharmacists play a critical role in optimizing therapy through:
- Comprehensive medication review and risk identification
- Early detection and reporting of ADRs
- Monitoring clinical parameters such as weight, glucose levels, and menstrual patterns
- Patient education regarding potential side effects
- Coordination with healthcare professionals for individualized care

Table 3: Pharmacist Monitoring Checklist

Parameter	Frequency	Purpose
Body weight	Weekly	Detect rapid gain
Blood glucose	Biweekly	Monitor steroid-induced hyperglycemia
Menstrual cycle	Monthly	Identify hormonal imbalance
CNS symptoms	Weekly	Detect sedation, dreams
Drug adherence	Every visit	Ensure compliance

CONCLUSION

Polypharmacy in RRMS may lead to clinically significant neuropsychiatric and endocrine adverse effects even at standard therapeutic doses. Evidence from this case aligns with previously reported pharmacological profiles of gabapentin, nortriptyline, and corticosteroids (Moore *et al*., 2015; Liu *et al*., 2013). Early recognition, dose adjustment, and structured pharmacist-led monitoring are essential to minimize complications and improve patient outcomes.

ETHICAL STATEMENTS

Ethical Approval: Not required for single case report as per institutional guidelines.

Patient Consent: Informed consent was obtained from the patient for publication of this case report.

Data Availability: Data supporting this study are available from the corresponding author upon reasonable request.

Author Contributions (CRediT)

Writing – original draft: All authors

Writing – review & editing: All authors

Conflict of Interest: None declared

Funding: No external funding received

ACKNOWLEDGMENT

The authors acknowledge clinical support and patient cooperation.

REFERENCES

Gold, R., Kappos, L., Arnold, D. L., Bar-Or, A., Giovannoni, G., Selmaj, K., et al. (2012). Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. New England Journal of Medicine, 367(12), 1098–1107. https://doi.org/10.1056/NEJMoa1114287

Liu, D., Ahmet, A., Ward, L., Krishnamoorthy, P., Mandelcorn, E. D., Leigh, R., et al. (2013). A practical guide to the monitoring and management of corticosteroid side effects. Allergy, Asthma & Clinical Immunology, 9(1), 30. https://doi.org/10.1186/1710-1492-9-30

Moore, R. A., Wiffen, P. J., Derry, S., & McQuay, H. J. (2015). Gabapentin for chronic neuropathic pain. Cochrane Database of Systematic Reviews.

O'Connor, A. B., Schwid, S. R., Herrmann, D. N., Markman, J. D., & Dworkin, R. H. (2008). Pain associated with multiple sclerosis: Systematic review and proposed classification. Pain, 137(1), 96–111.

Soldin, O. P., & Mattison, D. R. (2009). Sex differences in pharmacokinetics and pharmacodynamics. Clinical Pharmacokinetics, 48(3), 143–157.

Wilson, S., & Argyropoulos, S. (2005). Antidepressants and sleep: A qualitative review. Drugs, 65(7), 927–947.