



Baclofen withdrawal induced Neuroleptic Malignant-like Syndrome

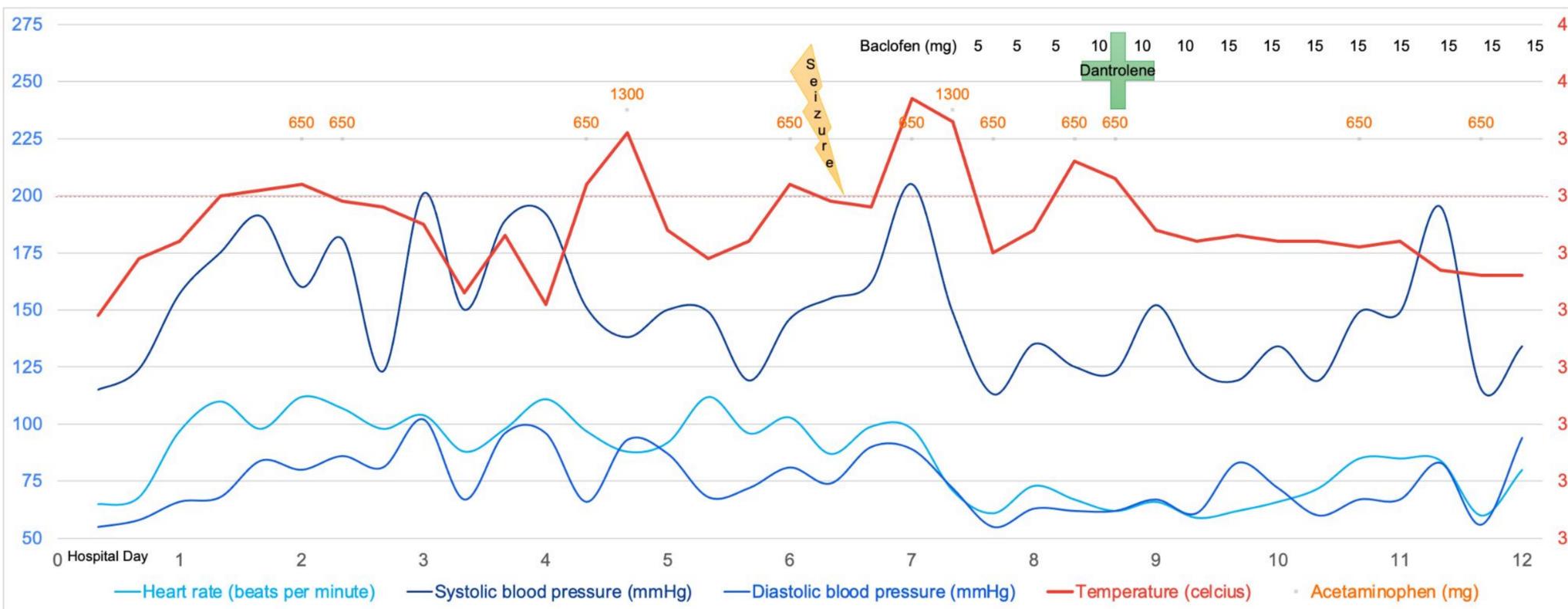
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Introduction

Neuroleptic malignant syndrome (NMS) is characterized by severe muscle rigidity, hyperthermia, autonomic dysregulation, and altered mental status in response to dopamine receptor blockade or withdrawal of dopaminergic agents. While it is typically noted after the initiation or increased dosing of antipsychotic agents, the phenomenon has been reported in association with antiemetics, tricyclic antidepressants, and lithium. Baclofen is an agonist to γ -Aminobutyric acid type B (GABA_B) receptors. Baclofen inhibits processes in the brain and spinal cord that cause muscle contraction, relieving spasticity and rigidity. Oral baclofen penetrates the blood brain barrier poorly and can be delivered intrathecally to increase bioavailability. Abrupt withdrawal of high dose baclofen can cause rebound excitation leading to autonomic dysregulation, muscle spasticity and seizures. We present a case of NMS-like syndrome due to withdrawal from oral baclofen.

Clinical Case

A 70 year old male with multiple sclerosis, ambulatory dysfunction, diabetes, hypertension, and obstructive uropathy with chronic urethral catheter presented with altered mental status. His CT showed bilateral hydronephrosis due to a dislodged catheter which was repositioned by urology. He was febrile, hypertensive, and altered; however infectious workup was negative and antibiotics were discontinued. Despite holding all sedating home medications, his mental status continued to decline. On day 6 of admission, he had a cardiac arrest requiring less than 2 minutes of CPR, thought to be provoked by a febrile seizure. MRI showed increased signal along the margins of lateral ventricles with a small-mod size focus at the level of head of the caudate nucleus and EEG showed diffuse slowing. Repeat infectious and thromboembolic workup was negative. Due to concern for withdrawal, Baclofen was restarted via nasogastric tube at 5 mg TID and increased by 5 mg daily. He continued to have fevers refractory to acetaminophen along with worsening muscle rigidity. Dantrolene 2.5 mg/kg was administered leading to resolution of symptoms and return to baseline status.



- Centrally acting home medications:
- Amantadine 200 mg QD - briefly reduced to 100 mg QD with concern for drug induced fever
 - Baclofen 40 mg TID - held on admission, discharged on 15 mg TID → maximum recommended dose 80 mg/ 24 hr
 - Dantrolene 50 mg HS - held on admission, restarted on day 7
 - Lamotrigine 50 mg qAM + 100 mg qPM
 - Oxycodone 10 mg q6h prn - held on admission

Laboratory Studies							
Hospital Day	4	5	6	8	9	10	11
AST	10	15	37	36	49	36	22
ALT	11	13	38	48	56	57	46
CK				223			83
Procalcitonin			0.47	0.57			

Discussion

To our knowledge, this is one of the first reports of NMS-like syndrome in a patient with abrupt oral baclofen withdrawal. Baclofen withdrawal is correlated with high rates of morbidity and mortality, with NMS-like syndrome being a rare complication. Additionally, it is associated with further provoked spasticity, fever, and autonomic dysfunction. The recommended treatment of baclofen withdrawal-induced NMS-like syndrome is reinitiation of baclofen and vigilant hemodynamic monitoring. At times, adjuvant therapy with IV medications such as benzodiazepines, propofol, dantrolene, or dexmedetomidine may be required. There are no studies comparing effectiveness of various treatment options. Frequent vital sign monitoring, avoidance of dehydration, and management of symptoms are the staples of treatment. Due to the complexity of patients that require high doses of baclofen, it is important to weigh risks and benefits of abrupt cessation of chronic baclofen.

Conclusion

Baclofen should not be held for patients on chronic baclofen unless toxicity is suspected. If oral baclofen is held, they should be closely monitored for withdrawal symptoms. Symptoms should be treated promptly to avoid life threatening complications.

References

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