

Neuroleptic Malignant Syndrome from Oxcarbazepine & Topiramate Withdrawal: A Case Report

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BACKGROUND

- Neuroleptic malignant syndrome is a dose-independent idiosyncratic reaction from dopamine modulating pharmacologic agents.
- Incidence rate between 0.02% to 3% from various regional studies.
- Mortality rates ranges from 7% to 15%.¹ Often associated with first gen. antipsychotic medications.
- We describe a unique NMS case that lack the use of antipsychotic and direct dopamine modulators.

CASE PRESENTATION

- 20yo male presented with altered mental status & poor oral feeding.
- PMHx: Autism spectrum disorder, disruptive mood dysregulation disorder, generalized anxiety disorder, spastic cerebral palsy, obesity.
- Psychotropic regimen: Oxcarbazepine 600mg BID for off-labeled DMDD, topiramate 200mg qHS for weight-loss and insomnia, lorazepam 1mg TID, and clonidine 0.2mg BID for anxiety.
- ED evaluation was limited due to patient being “mute”. Family states at baseline, he is talkative & confirmed medication compliance but had stopped in the past week due to poor oral feeding.
- In the ED, pt. was hemodynamically unstable → NS fluid resuscitation → admitted for failure to thrive & secondary acute kidney injury on preliminary lab work-up.
- On admission, pt. spiked a fever of 102.7F /w persistent tachycardia → activation of sepsis protocol & further lab workup (table 1).
- Simultaneously, C&L consulted for behavioral agitation. Pt noted to non-verbal /w bilateral upper extremities stiffness → recommended for IM/IV lorazepam & hold all psych meds amid suspicions for NMS.
- ID consultation → lumbar puncture → empiric ceftriaxone, acyclovir, vancomycin & dexamethasone. Despite fluids & NSAIDs, his fever was unwavering /w rising interval CPK → ICU upgrade.
- EEG r/o seizure activities. CT head, chest, & abd/pelvis showed no acute abnormality. CSF analysis r/o infectious meningoencephalitis & discontinued empiric coverage. Anesthesia consultation → unlikely malignant hyperthermia due to lack of exposure to inhaled anesthetics & neuromuscular paralytics.
- NMS criteria fulfilled as diagnosis of exclusion → C&L recommend for dantrolene 150mg TID x3 days & amantadine 100mg BID → clinical & interval lab improvements. Despite being on prophylactic SQ heparin, his recovery was complicated by worsening dyspnea & tachycardia → CTPA /w bilateral submassive PE (figure 1) → therapeutic LMWH.
- Repletion of dopamine agonist was tapered & LMWH was transition to oral apixaban. Pt was discharged w/o recurrence of NMS to date.

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Table 1. Significant Vitals & Work-Up

ED Vitals	BP 70/46	HR 148	RR 19	98F	98% RA
Admiss. Vitals	BP109/66	HR 136	RR 20	102.7F	98% RA
WBC 13,600/uL PMN 76.5%, Lymph 13.8%, Monocyte 8.5%, Eosinophil 0%, Basophil 1.2%			Platelet 200,000/uL, RBC 6.23x10 ⁹ /uL Hct 52.4%, Hgb 16.5 g/dL MCV 84.1fL, RDW 15.3%		
Gluc 156 mg/dL	BUN 30 mg/dL	Cr 2.0 mg/dL	Na ⁺ 148 mEq/L	K ⁺ 4.2 mEq/L	
Cl ⁻ 115 mEq/L	HCO ₃ ⁻² 18	Ca ⁺² 9.4	Mg ⁺² 2.2		
AlkPhos 89	ALT 146	AST 225	T. Bili 0.9	T. Protein 8.2	
Albumin 4.5	CPK Initial 15,428 U/L	CPK peaked 39,771			
Lactate 2.25	CRP 3.1	Procalcitonin 0.39			
Urine Tox: (+) benzos	U/A: Gluc 30mg/dL, protein >600mg/dL, (-) ketone, mod. blood, RBC 15/hpf, (-) nitrite, (-) leukocyte esterase, WBC 5/hpf, (-) bacteria				
EKG	Sinus tachycardia, HR 140s, corrected QT 379ms				

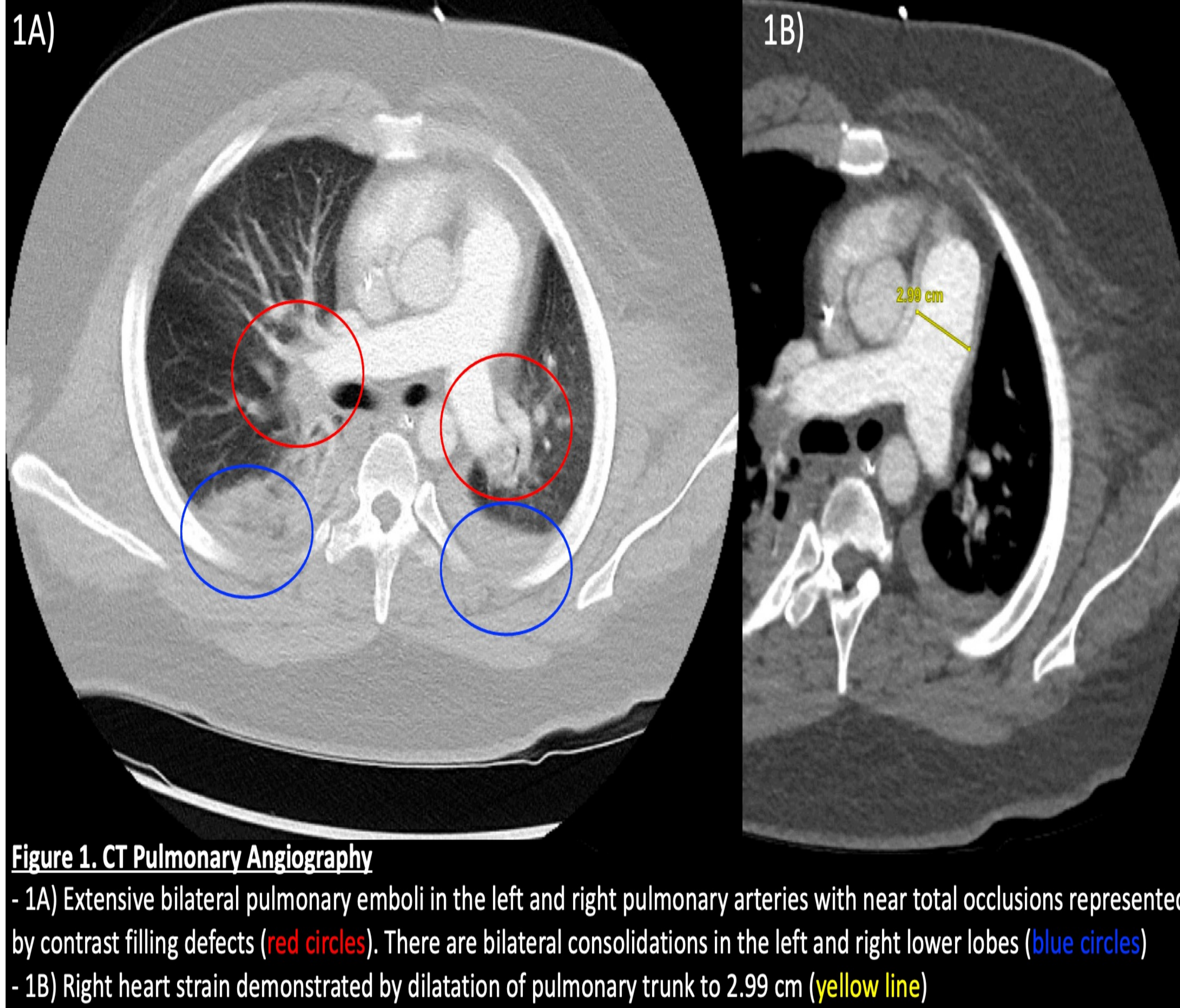
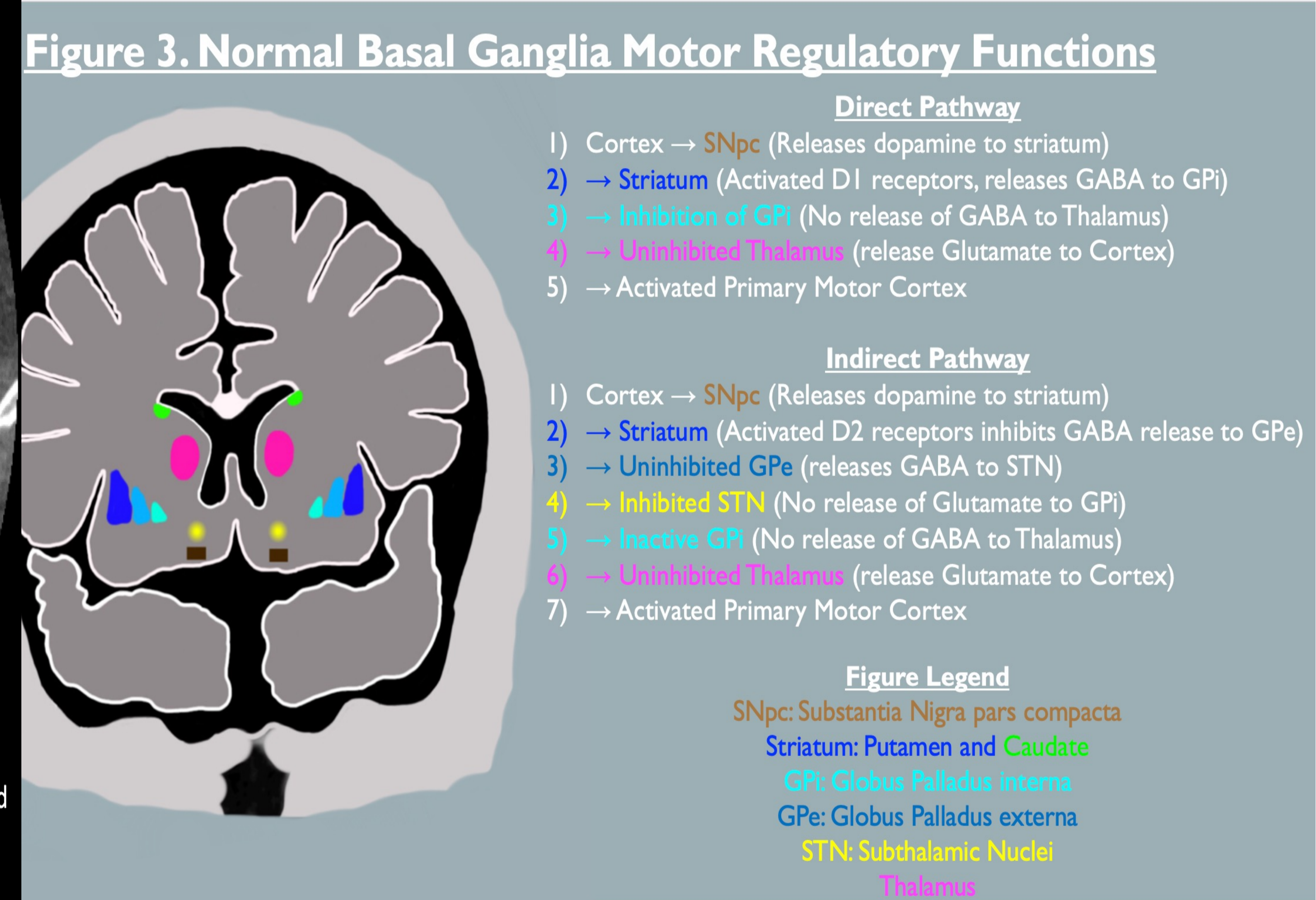
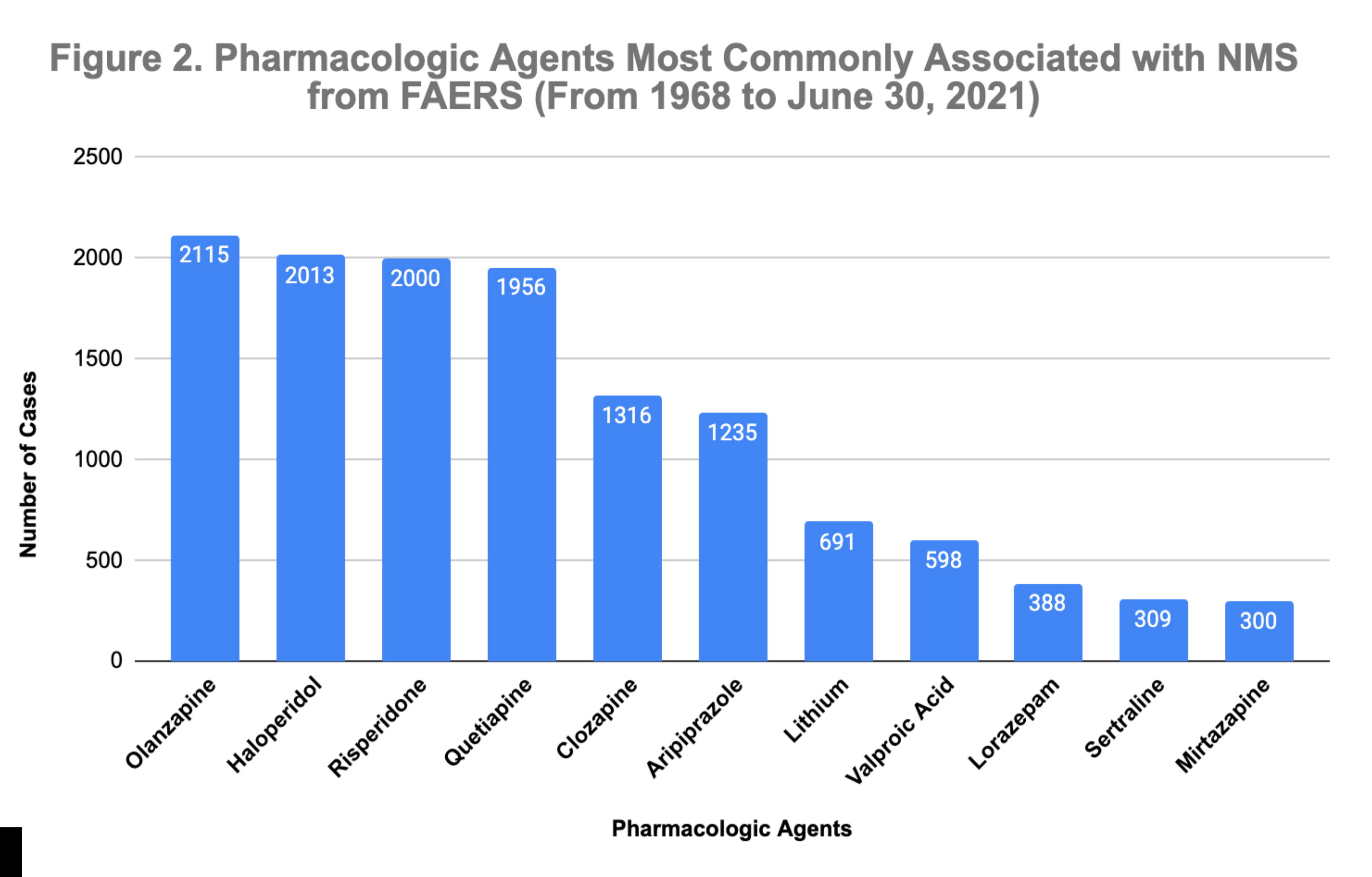


Figure 1. CT Pulmonary Angiography
 - 1A) Extensive bilateral pulmonary emboli in the left and right pulmonary arteries with near total occlusions represented by contrast filling defects (red circles). There are bilateral consolidations in the left and right lower lobes (blue circles)
 - 1B) Right heart strain demonstrated by dilatation of pulmonary trunk to 2.99 cm (yellow line)



DISCUSSION

- This case emphasizes the **need for having a high suspicion of NMS, even in the absence of antipsychotics**, and when it is masked by concurrent medical conditions.²
 - Figure 2 represents the identified causes of NMS reported by the FDA adverse event system from 1968-2021.
 - Figure 3 describes the basal ganglia regulatory function on motor movements. Disruption in dopamine for D1&D2 receptors → muscle rigidity.
 - Currently there are no literature recognizing oxcarbazepine & topiramate withdrawal as causation for NMS.
- However, these medications are well-recognized in promoting & indirectly increasing the release of dopamine within the CNS.³⁻⁵
- Physicians should be aware of possible triggers of NMS & preventatively warned pts. from abrupt antiepileptics discontinuation.
 - Additionally, it reiterates the need for early & aggressive treatment to prevent further morbidity and complications.

