Chapter 51
Serotonin Syndrome

Bryan Corbett and Kimberly D. Nordstrom

Introduction

Serotonin syndrome (SS) is the result of excess serotonergic activity in the CNS. It can occur with therapeutic use of multiple serotonergic medications or from supratherapeutic dosing of a single serotonergic medication. Classic manifestations include altered mental status, autonomic hyperactivity, and clonus. Like Neuroleptic Malignant Syndrome (NMS), SS exists on a continuum and not all above mentioned manifestations need be present for a diagnosis. Onset is typically rapid occurring over the course of minutes up to about 24 h.

B. Corbett, M.D.
Division of Medical Toxicology, Department of Emergency Medicine, University of California Health Sciences, San Diego, CA, USA

K.D. Nordstrom, M.D., J.D (✉)
Colorado Department of Human Services, Office of Behavioral Health, Denver, CO, USA

American Association for Emergency Psychiatry, Parker, CO 80134, USA
e-mail: Nordstrom_kimberly@yahoo.com

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Symptoms

- Agitation
- Disorientation
- Restlessness
- Delirium

Signs

- Clonus (typically more pronounced in the lower extremities)
- Hyperreflexia
- Muscular hyperactivity
- Diarrhea
- Akathisia
- Rigidity
- Hypertension
- Tachycardia
- Diaphoresis
- Hyperthermia
- Mydriasis
- Seizures

Life-Threatening Symptoms/Signs

Serotonin Syndrome is a medical emergency and should be treated as such. Life-threatening manifestations include rhabdomyolysis with resultant renal failure. Hyperthermia can lead to multi-organ system failure, cardiopulmonary collapse, and death. Episodes of disseminated intravascular coagulation have also been reported.

Differential

- Antimuscarinic poisoning
- Dystonic reaction

Encephalitis
Excited catatonia
Heat-stroke
Malignant hyperthermia
Meningitis
Nonconvulsive status epilepticus
Pheochromocytoma
Porphyria
Rabies
Serotonin syndrome
Strychnine poisoning
Sympathomimetic intoxication, cocaine, methamphetamine, PCP
Tetanus
Thyroid storm
Baclofen Withdrawal

Testing

- Diagnosis is based on history, clinical findings, and exclusion of other diagnoses.
- The Hunter Criteria (see below) are a set of decision rules used to diagnose SS. They are internally validated and found to have good agreement with the diagnosis by a clinical toxicologist.
- Basic labs including a BMP, CBC, and UA
- A CPK should be checked to assess for muscle breakdown
- A liver panel, ammonia, TSH, CT head, LP, CXR, Vitamin B12 and Thiamine levels, HIV, RPR, and VDRL should be considered in the clinical context

Treatment

- Largely supportive, stabilize ABCs.
- IV fluid resuscitation
- Liberal use of benzodiazepines is a mainstay of treatment
- Aggressive cooling measures

- Patients with resistant hyperthermia can be intubated and paralyzed to prevent heat production from muscles
- Discontinuation of all serotonergic medications
- Cyproheptadine, an early anti-histamine with anti-serotonergic activity, can also be used. It is only available as an oral preparation complicating administration in critically ill patients. No evidenced based dosing recommendations exist. A starting dose of 8 mg repeated as necessary is reasonable based on case reports.

Tool

Tool 1: Hunter Criteria

If any of the following, may diagnose SS:
Spontaneous clonus
Inducible clonus + agitation OR diaphoresis
Ocular clonus + agitation OR diaphoresis
Tremor + hyperreflexia
Hypertonia + temp above 38 + ocular clonus OR inducible clonus

Sensitivity 84%, specificity 97%

- How to induce clonus: Clonus refers to a persistent reflex contraction of a muscle after an initial stimulus. Clonus can often be best appreciated with regard to the Achilles reflex. To check for clonus, forcefully dorsiflex the foot at the ankle and maintain slight dorsal pressure on the foot.

Tool 2

Neuroleptic Malignant Syndrome Vs. Serotonin Syndrome

Differentiating Factors	Neuroleptic Malignant Syndrome	Serotonin Syndrome
Medication Type	Dopamine antagonists, withdrawal of dopamine agonists	Serotonin Agonist
Predictability	Idiosyncratic	Drug-drug interaction or overdose
Onset	Insidious	Rapid
Recovery	Prolonged	Generally rapid (excluding medications with long half life)
Neuromuscular findings	Lead-pipe rigidity	Clonus

References

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