POISON PEARLS

Toxicology Topics for the Healthcare Team of a Poisoned Patient

Neuroleptic Malignant Syndrome

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Background and Pathophysiology

Neuroleptic malignant syndrome (NMS) is a rare but potentially life-threatening disorder associated with exposure to dopamine receptor antagonists or the abrupt withdrawal of dopaminergic agents. Dopamine antagonists primarily include typical and atypical antipsychotics, such as haloperidol, whereas dopamine agonists are used in the management of conditions such as Parkinsons disease and restless leg syndrome and include agents such as ropinirole. NMS is classified as a severe extrapyramidal syndrome characterized by dysregulation of motor and autonomic function. Although the precise pathophysiology remains incompletely understood, the syndrome is believed to result from acute central dopamine hypoactivity, particularly within the hypothalamic and nigrostriatal pathways (**Berman, 2011**).

Clinical Presentation

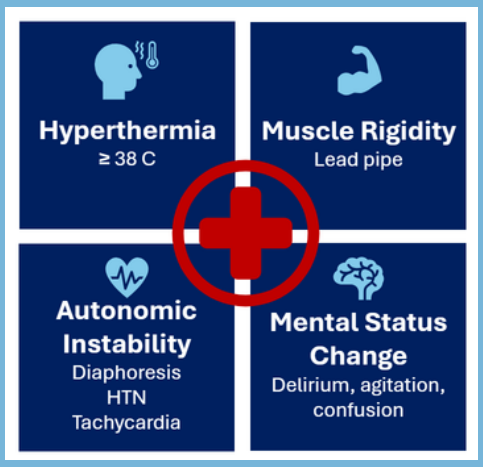
Neuroleptic malignant syndrome classically presents with a tetrad of clinical features: altered mental status, hyperthermia, severe muscle rigidity, and autonomic instability. Symptom progression typically occurs over 24–72 hours, although full clinical manifestation may evolve over several days to weeks. NMS does not appear to be a dose-dependent reaction; it is not observed more frequently with overdose. Altered mental status may range from inattentiveness and lethargy to confusion, agitation, catatonia, or delirium. Hyperthermia is defined as a core temperature ≥38°C (100.4°F). The associated muscle rigidity is characteristically described as “lead-pipe” rigidity, reflecting uniform, sustained resistance to passive movement. Autonomic dysfunction may manifest as tachycardia, hypertension, diaphoresis, pallor, urinary incontinence, and cardiac dysrhythmias (**Bruccoleri and Burns, 2017**). Common and frequently misdiagnosed conditions in the differential diagnosis of NMS include acute dystonia and serotonin syndrome, which occur far more commonly and may present with overlapping clinical features. Given the diagnostic complexity and potential severity of these presentations, consultation with a regional poison control center can provide valuable real-time guidance for diagnosis and management.

Treatment

The treatment for NMS may include:

- Discontinuing the offending agent
- Supportive care
- Benzodiazepines
- Bromocriptine (less commonly used)

Supportive care is first line, which includes proper ventilation, oxygenation, and cooling measures. Cooling measures can be non-invasive (cold packs, ice bath) or invasive (cold IV fluids, lavages, and foley catheter irrigation). Benzodiazepines are GABA receptor modulators that help relax muscles in NMS. Bromocriptine, a dopamine agonist, may be used, but has fallen out of favor due to lacking evidence in NMS and oral formulation which may take hours to be absorbed (**Bruccoleri and Burns, 2017**).



Key Points:

- NMS is a life-threatening condition associated with the use of dopamine antagonists and/or rapid withdrawal of dopamine agonists
- The mechanism of NMS involves dopamine hypoactivity
- The hallmark of NMS is the tetrad of symptoms:
  - Mental status change
  - Hyperthermia
  - Muscle rigidity
  - Autonomic instability
- First line treatment for NMS is supportive care and cooling measures
- Benzodiazepines may be used to relax muscles

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