EM CASE OF THE WEEK.

BROWARD HEALTH MEDICAL CENTER
DEPARTMENT OF EMERGENCY MEDICINE

BROWARD HEALTH
Care Warriors

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Neuroleptic Malignant Syndrome

A 27-year-old male with a past medical history of schizophrenia presents to the ED with altered mental status and fever that began 1 day ago. His vitals are found to be temperature of 102 F, heart rate of 133, respiratory rate of 22, and blood pressure of 144/85. Patient can identify his name but does not know where he is or the date. What are the expected findings on physical exam?

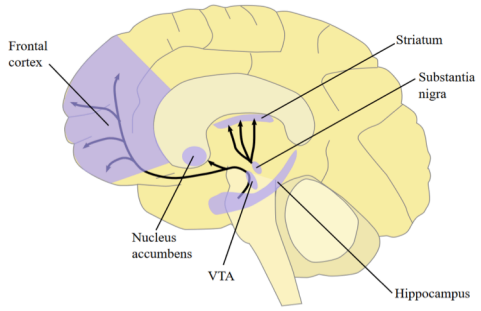
A. Rigidity that resists passive movement, hyperreflexia, mydriasis of the pupils, profuse diaphoresis, and increased bowel sounds

B. Rigidity that resists passive movement, normal reflexes, normal-sized pupils, profuse diaphoresis, and decreased bowel sounds

C. Rigidity that resists passive movement, hyporeflexia, normal-sized pupils, profuse diaphoresis, and increased/decreased bowel sounds

D. Normal muscle tone, normal reflexes, mydriasis of the pupils, dry skin and mucous membranes, and decreased bowel sounds

Mesocorticolimbic and nigrostriatal dopamine pathways



(Image via http://psychiatricdrugs.com/neurology/dopamine/)

Neuroleptic Malignant Syndrome is a medical emergency that occurs with use of neuroleptic medications, which blocks dopamine receptors. Although rare, diagnosis of this condition is crucial given the high mortality rate.

EM Case of the Week is a weekly "pop quiz" for ED staff.

The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.

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The correct answer is C. Rigidity that resists passive movement, hyporeflexia, normal-sized pupils, profuse diaphoresis and increased / decreased bowel sounds. Answer A. is seen with serotonin syndrome, while answer B. is seen with malignant hyperthermia. Answer D. is seen with an anticholinergic toxidrome.

Discussion

Neuroleptic malignant syndrome is a life threatening condition that results when taking an antipsychotic medication, also known as neuroleptics. When the syndrome was first identified in the 1960s, mortality was as high as 76 percent. Although better treatment modalities have improved the odds of survival since, there is still a 10-20 percent mortality rate.

The incidence neuroleptic malignant syndrome ranges from 0.2 to 3 percent for all patients taking antipsychotics. The syndrome affects all ages, sexes, and races equally. However, populations more likely to use first generation high-potency antipsychotics, such as haloperidol, will exhibit higher levels of this syndrome.

Every type of neuroleptic agent has been found to produce the syndrome. This includes typical and atypical antipsychotics, as well as antiemetic drugs like metoclopramide and promethazine. Symptoms most commonly occur during the first two weeks of starting or increasing medication. However, the syndrome can occur at any point, whether after the first dose or years of treatment.

The cause of neuroleptic malignant syndrome is unknown, although the mechanism is thought to involve dopamine blocking as that is how neuroleptic drugs work. One theory states that central dopamine receptor blockade in hypothalamus results in hyperthermia and autonomic dysregulation. The same blockade in the nigrostriatal dopamine pathways causes rigidity and tremor, similar to the dyskinesias seen in Parkinson's disease.

ALTERED MENTAL STATUS + ELEVATED TEMPERATURE
IN ADDITION TO SEPSIS, CONSIDER THE FOLLOWING
(CULPRIT IS OFTEN POLYPHARMACY)

	EXPOSURE	MUSCLE TONE	MUCOSA & SKIN	PUPILS	BOWEL SOUNDS	REFLEXES
NEUROLEPTIC MALIGNANT SYNDROME	ANTIPSYCHOTICS	RIGID	WET	NORMAL	↔	BRADYREFLEXIA
SEROTONIN SYNDROME	SEROTONERGICS (antidepressants, fentanyl, linezolid, sumatriptan, ondansetron)	RIGID	WET	↑	↑	↑
ANTICHOLINERGIC TOXIDROME	ANTICHOLINERGICS	NORMAL	DRY	↑	↓	NORMAL
MALIGNANT HYPERTHERMIA	INHLALED ANESTHETICS SUCCINYLCHOLINE	RIGID	WET	NORMAL	↓	↓

Boyer, 2005
(Image via http://foamcast.org/2015/05/04/episode-28- neuroleptic-malignant-syndrome-serotonin-syndrome-malignant-hyperthermia/)

Diagnosis

Diagnosis is clinical and should be considered when at least 2 of the 4 symptoms are present. These symptoms develop over 1-3 days and are present in 97-100% of patients. Symptoms typically appearing in order of:

1. Altered mental status
2. Muscular rigidity – "lead-pipe rigidity" or steady resistance through all ranges of movement.
3. Hyperthermia
4. Autonomic instability – tachycardia, high blood pressure, and tachypnea

Other findings include diaphoresis, tremor and urinary incontinence.

This syndrome is also characterized by elevated creatine kinase, which becomes elevated in proportion to the degree of muscle rigidity. Other less specific findings findings include leukocytosis, mild elevations of liver transaminases, electrolyte abnormalities, elevated creatinine secondary to the elevated creatine kinase, and low serum iron.

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Differential Diagnosis

Since the diagnosis is made clinically, there are a number of similar that need to be considered.

- Serotonin Syndrome
- Malignant Hyperthermia
- Malignant Catatonia
- Acute Intoxication of Recreational Drugs
- Sepsis
- Anticholinergic Toxidrome
- Meningitis/Encephalitis
- Dopamine Agonist Withdrawal

The symptoms of serotonin syndrome are very similar to neuroleptic malignant syndrome, making a correct diagnosis for either syndrome particularly difficult. However, patients with serotonin syndrome exhibit agitation, hyperreflexia, and clonus, while patients with neuroleptic malignant syndrome exhibit rigidity.

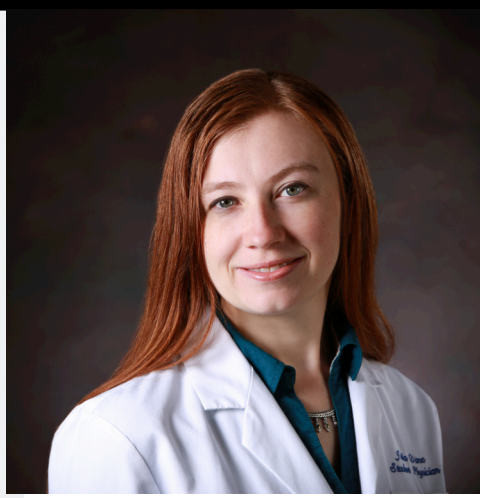
Treatment

Medical treatment for this syndrome is based on case reports as data from clinical trials is extremely limited. The most important step is to immediately stop all neuroleptic and psychotropic medications. After that, medication and other therapies are used to provide supportive care until symptoms resolve, usually within 2 weeks.

To reduce muscle rigidity, dantrolene and lorazepam can be given in less severe cases. In more severe cases bromocriptine or amantadine should be added. Supportive care is key, and involves maintaining cardiorespiratory stability and euvolemic status. Creatine kinase levels and kidney function should be monitored for potential acute kidney injury. Temperature can be lowered with cooling blankets, or if more aggressive treatment is required, ice water gastric lavage and ice packs in the axilla can be used. Clonidine is recommended to lower blood pressure. Severe case of this syndrome need admit to the ICU for constant monitoring of vitals. Most patients who survive the initial symptoms can be expected to make a full recovery.

Take Home Points

- Diagnosis of this syndrome is crucial as there is a 10-20% mortality rate even with treatment. Only patients who are taking neuroleptic drugs develop this syndrome.
- The typical order of appearance of symptoms is altered mental status, muscular rigidity, hyperthermia, and lastly, autonomic dysregulation. The syndrome develops over 1-3 days and takes about 2 weeks to resolve.
- The differential diagnosis needs to be broad, given the diagnosis is clinical and the similarity between this condition and several others.
- Treatment for this syndrome involves providing supportive care as well as medications such as dantrolene and benzodiazepines. If symptoms are severe, bromocriptine or amantadine can be added.



ABOUT THE AUTHOR

This month's case was written by Julia Danz. Julia is a 4th year medical student from KPNSU-COM. She did her emergency medicine rotation at BHMC in February and March of 2018. Julia plans on pursuing a career in Psychiatry after graduation.

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