Case #134

NAME Educational Activities Committee

Case provided by:

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1. A 64-year-old man with a past medical history significant for HIV (on antiretroviral medication), depression, and possible ischemic cardiac injury was reported to have agitation, confusion, tremors, and diaphoresis prior to becoming unresponsive. He was pronounced deceased at home. An empty bottle of prescription medication was noted at the scene. Autopsy was significant for the above finding in the small bowel in addition to 400 mL of similar pink-tan granular material in the stomach.

Which of the following is the most likely mechanism of death?

- ◯ Myocardial infarction
- ◯ Serotonin syndrome
- ◯ Acute hepatic failure
- ◯ Neuroleptic malignant syndrome

Answer...

Answer: **B - Serotonin Syndrome**

(CORRECT ANSWER – 65.42 % of responses)

- The scene findings (empty prescription bottle near the decedent) and abundant pill material observed in the stomach and small bowel is suspicious for overdose. In the setting of this decedent's history of depression and suspicion of overdose, the symptoms reported prior to becoming unresponsive (altered mental status, tremors, and diaphoresis) are concerning for serotonin syndrome.
- Serotonin syndrome (or serotonin toxicity) results from an excess of serotonin activity in the central nervous system through increased serotonin synthesis and/or excretion, decreased serotonin breakdown, and/or alteration of uptake/clearance of serotonin in synaptic clefts resulting in a clinical triad of:
    - Mental status changes (agitation, confusion, delirium)
    - Autonomic hyperactivity (hyperthermia, hypertension, mydriasis, diaphoresis)
    - Neuromuscular excitability (tremor, hyperreflexia, clonus)
- While mild-moderate cases of serotonin syndrome can be managed with supportive care and/or medication, severe cases can result in death due to severe autonomic and metabolic derangements.

Answer: **B - Serotonin Syndrome** (cont'd)

- While antidepressants (mainly selective serotonin [and norepinephrine] reuptake inhibitors [SSRI/SNRI]) are most often implicated in serotonin syndrome, there are many substances (including supplements and therapeutic-level, over-the-counter medications*) that can precipitate it, especially when combined

  - Increased serotonin formation: Tryptophan*, oxitriptan*
  - Increased serotonin release: MDMA (3,4-methylenedioxymethamphetamine), cocaine, amphetamines (and derivatives)
  - Impaired serotonin reuptake: SSRIs (citalopram, fluoxetine), SNRIs (duloxetine, venlafaxine), MDMA, cocaine, tricyclic antidepressants (TCAs – amitriptyline), St. John's wort*, dextromethorphan*
  - Impaired serotonin metabolism: Monoamine oxidase inhibitors (MAOis), linezolid, phenelzine
  - Direct serotonin receptor agonism: Buspirone, triptans (sumatriptan), fentanyl, LSD (lysergic acid diethylamide)
  - Increased serotonin receptor sensitivity: Lithium

- In this case, the prescription bottle at the scene was for extended-release venlafaxine, consistent with the material found in the stomach and small bowel (beaded capsule)
- Postmortem toxicology was positive for Venlafaxine (110,000 ng/mL) and O-Desmethylvenlafaxine (16,000 ng/mL) - a major metabolite of venlafaxine

Other responses…

A. Myocardial infarction (3.97% of responses)

- While this decedent had a clinical history of a potential cardiac event, the decedent's reported symptoms (tremor and confusion) were less consistent with the prodrome of a myocardial infarct.
- While a drug overdose can precipitate a cardiac arrhythmia, the context of the overdose and other prodromal symptoms are more consistent with a toxic overdose than an independent cardiac event.

C. Acute hepatic failure (14.02% of responses)

- This decedent has a history of HIV and was taking antiretroviral medications (both of which can increase the risk for liver injury). Additionally, acute hepatic failure can result in altered mental status and asterixis. However, tremors and diaphoresis would be a less common presentation, and other symptoms of hepatic failure (fatigue, nausea, right upper quadrant pain, and jaundice) are not present.

D. Neuroleptic malignant syndrome (NMS) - (16.59% of responses)

- NMS is thought to be due to drug reaction to the dopamine receptor blockade, resulting in a reduction of dopaminergic signaling in the hypothalamus and basal ganglia leading to the classic symptoms of thermoregulatory disruption, skeletal muscle rigidity, increased sympathetic activity, and bradykinesia/bradyreflexia.

- While NMS and serotonin syndrome share similar symptoms (delirium, high fever), this individual did not have the more classic NMS symptoms of bradykinesia/bradyreflexia, and muscle rigidity.

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