July 2020 Critical Care Case of the Month: Not the Pearl You Were Looking For...

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History of Present Illness

A 75-year-old man presented with unsteady gait, difficulty concentrating and abdominal pain with loose stools. One day prior to admission, he experienced waxing and waning nausea, cramping abdominal pain, one episode of emesis and loose stools. He described acute gait disorder related to difficulty with balance. Due to concern for dehydration, he drank 10-12 cans of carbonated water without further emesis. He also experienced vague and alternating sensations of feeling “hot” in half of his body and “cold” in the other half of his body. Forty-eight hours prior to presentation, he had just returned from a five-day trip to New Orleans.

PMH, SH, and FH

The patient has hypertension and hyperlipidemia that is well-controlled. Regular medicines include losartan, diltiazem, HCTZ and simvastatin. He is a professor of medicine. He had distant tobacco use with a 10 pk-yr history. He denies recreational drug use. He endorsed drinking one glass of wine per day during his recent trip. He had eaten oysters and redfin fish during his trip.

Physical Examination

- Afebrile, HR=38, RR=12, BP=134/72, O2 sat=95% on RA
- In general, patient was slightly argumentative and in obvious distress due to abdominal pain. HEENT - nonicteric, pupils reactive, moist oral mucosa
- Neck - No elevated JVP, LAD or thyromegaly
- CV - Bradycardic, regular, no murmur
- Pulmonary - Clear to auscultation all lung fields
- Abdomen - Soft with diffuse tenderness to palpation, bowel sounds present, no HSM or mass
- Lower extremities - Cool to the touch without cyanosis, intact and symmetric distal pulses
- Neuro – Cranial nerves intact, no focal motor or sensory deficits, oriented but with difficulty concentrating on thoughts, poor short-term recall, no obvious visual or auditory hallucinations.

Laboratory
Initial laboratory testing was notable for hyponatremia of 126, otherwise a metabolic panel, complete blood count, troponin, urinalysis, urine drug screen and thyroid stimulating hormone were unremarkable. EKG showed sinus bradycardia without ischemic changes. An abdominal flat plate (KUB) showed a nonspecific bowel gas pattern without evidence of obstruction. Chest x-ray was negative for acute cardiopulmonary abnormality.

He was given 1 liter of normal saline with improvement of sodium to 131, but his pulse remained low at 36. He also developed worsening nausea and mentation, was incoherent at times, and began telling staff that “I’m going to die.”

For the initial presentation of nausea, vomiting, bradycardia, hyponatremia, mental status changes, what is your ***leading diagnosis***?

1. Acute porphyria
2. Excessive water intake
3. Neurotoxic shellfish poisoning
4. Recreational drug use
5. Small cell lung cancer

Correct!
3. Neurotoxic shellfish poisoning

Although all of these diagnoses are possible, neurotoxic shellfish poisoning is the most likely given recent trip to New Orleans. Neurotoxic shellfish poisoning (NSP) is associated with "red tides" along the southeastern coast of the US, Gulf of Mexico and the Caribbean. Marine dinoflagellates (*Karenia brevis*) produce neurotoxins and hemolytic toxins collectively called brevetoxins. Eating contaminated shellfish is the most common form of NSP with immediate symptoms up to 24 hours post ingestion. Symptoms usually resolve within 24 hours but can last up to 72 hours (1). Presenting symptoms include nausea, vomiting, diarrhea, abdominal pain as well as facial and extremity paresthesias, vertigo, incoordination and convulsions. Another common symptom is temperature reversal, when patients experience alternating hot and cold sensations between the torso and lower extremities. For physicians in non-endemic areas, such as the Southwest, patients presenting with the odd constellation of sudden-onset gastrointestinal and neurological symptoms and temperature reversal should prompt close questioning of recent travel and dietary intake. The patient recovered with supportive care. Neurotoxic shellfish poisoning from brevetoxin was the presumed diagnosis due to the patient's constellation of symptoms, recent travel, and dietary history.

Acute porphyria is also possible given the highly variable presentation of this disease often presenting with acute abdominal pain in acute attacks accompanied by nausea, vomiting, sensory and motor neuropathies. The autonomic nervous system is commonly affected with patients presenting with hypertension, tachycardia, diaphoresis and tremor which this patient did not have.

This patient's hyponatremia is likely explained by his excessive water intake but this does not explain the other symptoms. Metastatic small cell lung cancer with SIADH might explain these symptoms but is not likely given such acute onset in a previously healthy man. Recreational drug use could also explain these symptoms but is less likely than other diagnoses.

What is the ***most likely cause*** of his bradycardia in the ICU?

1. Aortic valve endocarditis with ring abscess
2. Cholinergic medications
3. Cushing's reflex due to increased intracranial pressure
4. Excess diltiazem
5. Neurotoxic shellfish poisoning

Correct!
5. Neurotoxic shellfish poisoning

Less common symptoms of neurotoxic shellfish poisoning include bradycardia, mydriasis, motor weakness and decreased reflexes. Brevetoxin can also be inhaled from sea spray causing rhinorrhea and bronchoconstriction. It can kill fish, invertebrates, seabirds and marine mammals such as manatees (1). Brevetoxins and their metabolites are lipid soluble and easily cross the blood brain barrier. Brevetoxins are tasteless and not diminished or removed by cleaning, cooking or freezing. The other answers above can cause bradycardia but are less likely given this patient's clinical presentation.

How do you ***diagnose*** neurotoxic shellfish poisoning?

1. ELISA
2. Gram stain of white call buffy coat
3. Liquid chromatography / mass spectrometry
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

The diagnosis is based upon clinical presentation and a thorough history of a patient's recent dietary intake and environmental exposures. Symptoms typically resolve within 2 to 3 days of exposure. Treatment focuses on supportive care, with fluid replacement and close monitoring of a patient's respiratory status.

Structure-based immunoassay (i.e., ELISA) and liquid chromatography-mass spectrometry methods can identify brevetoxin metabolites in urine and meal remnants (2,3). While detection of metabolites in urine may be useful in endemic areas, there are inadequate studies to determine whether these assays are sensitive or specific and the laboratory tests may not be readily available to every medical center. In addition, monitoring for *K. brevis* blooms and the prompt closure of affected harvest areas have been very effective in preventing NSP outbreaks (4).

What is the predicted ***mortality*** rate of neurotoxin shellfish poisoning?

1. Rare to none
2. 15%
3. 25%
4. 60%
5. 75%

Correct!
1. Rare to none

Mortality is extremely low with neurotoxin shellfish poisoning. Older case reports suggest possible death from neurotoxin shellfish poisoning but the exact cause of death was not known. One review from 2008 states there have been no documents deaths from NSP although patients can have serious critical illnesses related to respiratory failure (5).

Which of the other marine toxin related illnesses ***can be lethal***?

1. Diarrhetic, amnestic, or paralytic shellfish poisoning
2. Ciguatera fish poisoning
3. Pufferfish poisoning
4. 1 and 3
5. All of the above

Correct!
5. All of the above

Diarrhetic shellfish poisoning occurs after eating mussels, scallops, clams and is caused by okadaic acid. Symptoms include nausea, vomiting, abdominal pain, and diarrhea. This illness occurs worldwide and carries a low risk for mortality with supportive treatment alone.

Amnestic shellfish poisoning results from ingestion of domoic acid and has been reported in Canada and the US. Initial symptoms are vomiting and abdominal cramps. Short-term memory loss with severe antegrade memory deficits have been reported (6). Seizures, coma and death have been reported with 4 deaths in a 107-person outbreak after consumption of contaminated mussels in Canada.

Paralytic shellfish poisoning from saxitoxins presents with acute onset paresthesias and in severe cases, respiratory paralysis. In an outbreak in Alaska in 1973 and 1992, 29 (25%) of 117 ill persons required emergency transport to a hospital, 4 (3%) required intubation and one died (6). Case fatality rate in untreated patients is 12% but with supportive care, most patients survive (7). Paralytic shellfish poisoning is typically seen in the New England states, Alaska, California and Washington.

Ciguatera fish poisoning typically presents in the Caribbean, South Pacific, and the US Virgin Islands. It is the result of ingestion of tropical reef fish such as barracuda, grouper, snapper or eel. Ciguatoxin or ciguatoxin-like toxin is tasteless and not destroyed by cooking. Common symptoms are nausea, vomiting, abdominal pain followed by circumoral and extremity paresthesias, pain and weakness in the lower extremities. Temperature reversal also occurs with this poisoning; "ice cream tastes hot, hot coffee seems cold" (6). Respiratory arrest and coma can occur within 24 hours.

Pufferfish poisoning, typically seen in Japan, is caused by tetrodotoxin found in globefish, a delicacy. Tetrodotoxin is not removed by washing or cooking and is one of the deadliest natural toxins known. Saxitoxin, the cause of paralytic shellfish poisoning, can also be in pufferfish and can cause generalized paralysis with respiratory failure. The patient remains conscious while paralyzed. Neostigmine or edrophonium may partially reverse the paralysis.

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