

MORNING REPORT

An Unexpected Doxylamine Nightmare

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A 63-year-old man with a past medical history of well controlled hypertension, prior transient ischemic attack, and rheumatic fever without heart disease was admitted to the hospital after his neighbor found him screaming and slumped over in the hallway of his apartment building. The neighbor noticed the patient's mental status was altered and he was in significant pain. Emergency Medical Services (EMS) was called and, upon initial examination, he was confused and only oriented to self. He was unable to provide any additional history regarding his presentation upon arrival to the hospital, but was noted to have intense bilateral shoulder pain. Physical examination revealed mildly elevated blood pressure, encephalopathy, a large left flank contusion, and intense tenderness to palpation to the bilateral shoulders without the ability for abduction. Laboratory labs revealed an elevated lactate to 5.8 mmol/L and leukocytosis of 25K WBCs. He underwent a CT of the head due to his encephalopathy, which was without abnormalities. X-rays demonstrated a right comminuted fracture about the humeral head including mildly displaced fracture of the greater tuberosity and a left comminuted displaced fracture of the left humeral head involving the lesser tuberosity. The shoulder dislocations were reduced in the ED. Orthopedics was consulted and determined the patient was not a surgical candidate. The patient was admitted to the medicine floor for further observation and workup.

By the following morning, the patient's encephalopathy had resolved



Right comminuted fracture about the humeral head including mildly displaced fracture of the greater tuberosity

and was thought to be consistent with a post-ictal state. Upon further questioning, the patient reported that he had been feeling well prior to his presentation. He remembered waking up in the middle of the night with excruciating bilateral shoulder pain and was unable to move his arms. He could not dial 911 due to the pain so he went into the hallway of his apartment building to seek help from his neighbors. The patient recalled screaming in the hallway until his neighbor found him, after which he lost consciousness; he did not recollect further events until evaluation in the ED. He denied prior history of seizures, family history of seizures, recent trauma, illicit drug use, or alcohol use. His medications prior to admission included amlodipine, rosuvastatin, lisinopril, and a baby aspirin. He was compliant with his medications and there had been no recent changes to his prescribed medications. The patient's only new medication was

doxylamine of which he took one tablet the previous night for insomnia. He has taken this medication one time previously and woke up the next day with severe muscle cramps.

Doxylamine (Unisom) is an over-the-counter, first-generation H1 antagonist, and commonly used for insomnia. In addition, doxylamine is frequently added to over-the-counter nighttime cold medications, including Nyquil (a combination of acetaminophen, dextromethorphan, and doxylamine). Common side effects of doxylamine include tachycardia, disorientation, vertigo, urinary retention, and diplopia. Doxylamine toxicity has been associated with seizures and rhabdomyolysis, but has been under-recognized. Clinical presentations of doxylamine toxicity vary, but should be considered in patients with new onset seizures and rhabdomyolysis given the potential for abuse. More concerning still is that previous studies suggest there is no correlation between the toxic effects of doxylamine and drug plasma levels, thus toxicity can occur even at recommended therapeutic doses. More often severe side effects occur in the setting of intentional overdose like medication abuse or suicide attempts making this patient's presentation atypical. Patients who have seizures associated with doxylamine can remain seizure-free in the future as long as they avoid taking doxylamine.

This patient's history is also significant for an atypical shoulder dislocation; posterior shoulder dislocations are rare and are responsible for less than 5 percent of

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all shoulder dislocations. Approximately 15 percent of posterior shoulder dislocations occur bilaterally. Posterior shoulder dislocations are typically caused by seizures, trauma, or electrocution. Seizures are the cause of 78 percent of reported bilateral posterior shoulder dislocations. Posterior shoulder dislocations rarely involve neurovascular compromise; however, the glenolabral and capsular injuries can lead to shoulder instability and increased risk for future dislocations. Diagnosing posterior shoulder dislocations can be difficult since frontal radiographs initially miss approximately half the dislocations. Sometimes, patients with late presentations complain of decreased range of motion in their shoulders and can mimic adhesive capsulitis. Bedside ultrasound may be used for diagnosis and CT imaging can assist with diagnosis or assessment of damage to the humeral head or glenoid.

Our patient also suffered greater and lesser humeral head tuberosity fractures (figures 1 and 2). Two part humeral fractures are typically associated with falling onto an outstretched hand, which is more common in elderly patients with osteoporosis. However, our patient had isolated tuberosity fractures, which are more frequently associated with dislocations or direct trauma to the shoulder. Non-displaced or minimally displaced fractures are usually treated conservatively with typically good outcomes. Displaced fractures can be treated surgically. Other injuries associated with posterior shoulder dislocation include humeral surgical neck fractures, labrum injuries, rotator cuff tears, and reverse Hill-Sachs lesions. The patient's fractures are consistent with his history of dislocated shoulders from his seizure.



Left comminuted displaced fracture of the left humeral head involving the lesser tuberosity

While the patient only took one tablet of doxylamine, his history suggests that he is sensitive to this medication. His severe muscle cramps associated with his first dose was indicative of either rhabdomyolysis or a possible seizure. The second time he took the medication, he had a combination of findings consistent with tonic-clonic seizures. He was not taking any other medications that have known interactions with doxylamine. The patient's history and presentation are most suggestive of a doxylamine-induced seizure that caused bilateral posterior shoulder dislocations and subsequent bilateral humeral tuberosity fractures. He was advised to avoid doxylamine in the future. The patient underwent a tertiary trauma examination that did not reveal any further injuries. Orthopedic surgery recommended conservative management and per occupational therapy's recommendation, the patient was discharged to his friend's home for a few weeks to recover. He worked with outpatient physical therapy and, within four weeks, had returned to work. He resumed his

normal activities, including cycling, within two months, and reported a full recovery from his injuries with no recurrence of seizures.

Take Home Points:

- Doxylamine toxicity is associated with seizures and rhabdomyolysis and can occur at any doxylamine plasma level;
- Posterior shoulder dislocations are rare (2-4% of shoulder dislocations); and
- 78% of bilateral shoulder dislocations are attributed to seizures.

References

1. Koppel C, Tenczer J, and Ibe K. Poisoning with over-the-counter doxylamine preparations: an evaluation of 109 cases. *Hum Toxicol.* 1987; 6(5):355-59.
2. Saupe N, White LM, Bleakney R, et al. Acute traumatic posterior shoulder dislocation: MR findings. *Radiology.* 2008 Jul; 248(1): 185-93.
3. Shaw J. Bilateral posterior fracture-dislocation of the shoulder and other trauma caused by convulsive seizures. *J Bone Joint Surg Am.* 1971 Oct; 53(7):1437-40.
4. Syed H, Som S, Khan K, et al. Doxylamine toxicity: seizure, rhabdomyolysis and false positive urine drug screen for methadone. *BMJ Case Rep.* 2009;2009. pii: bcr09.2008.0879. doi: 10.1136/bcr.09.2008.0879. Epub 2009 Mar 17.
5. Tellisi NK, Abusitta GR, and Fernandes RJ. Bilateral posterior fracture dislocation of the shoulders following seizure. *Saudi Med J.* 2004 Nov; 25(11): 1727-9.
6. Gor DM. The trough line sign. *Radiology.* 2002 Aug;224(2): 485-6.