Emerging Toxidromes: A 25-Year-Old Woman with Syncope and ECG Changes

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CASE DESCRIPTION

A 25-year-old woman presented to the emergency department with a 1-day history of nausea, fatigue, exertional lightheadedness, and a syncopal event without witnessed seizure activity or urinary incontinence. The patient had a past medical history of fibromyalgia and nonepileptiform seizure disorder, and she was prescribed oxycodone for use as needed (although she reported as "not really taking") and ibuprofen for pain. She denied use of any other medications, illicit substances, or herbal supplements. Her family history was negative for cardiac problems or history of sudden death.

At presentation, her blood pressure was 75/42 mmHg; heart rate was 61 beats/min (intermittently dropping to the 30s); temperature was 36.3 °C (97.3 °F), respiration was 16 breaths/min; and oxygen saturation was 99% by pulse oximetry. Her physical examination was remarkable for ongoing near-syncopal events and an irregular cardiac rhythm with variable S1 and S2 without murmurs, rubs, or gallops. Initial electrocardiogram (ECG) showed bradycardia with a wide-complex rhythm and QTc prolongation to 554 ms (Fig. 1). Two prior ECGs within the past 2 years had shown normal sinus rhythm with normal intervals.

On admission, initial chemistries were within the reference range except for a serum creatinine concentration of 1.6 mg/dL (increased from a baseline of 0.9 mg/dL), and serum and urine toxicology tests were negative (Table 1). A complete blood count showed a normocytic anemia at the patient's baseline: hemoglobin was 10.8 g/dL (reference interval, 12.0 –15.0 g/dL) and mean corpuscular volume was 89.5 fL (reference interval, 80.0–100.0 fL). Thyroid function testing, electroencephalogram, and head computed tomography were unrevealing. A transthoracic echocardiogram was remarkable for abnormal septal motion consistent with a conduction abnormality. Continuous intravenous isoproterenol was initiated to induce tachycardia and shorten the QTc interval, and intravenous sodium bicarbonate was empirically started to counteract possible ingestion of sodium channel- blocking agents. The patient continued to deny substance ingestion, and subsequent serum and urine testing on days 2 and 3 of hospitalization was negative with the exception of fentanyl, which she received in the emergency department, and noroxycodone, a metabolite of her prescribed oxycodone (Table 1). She became more alert in appearance, but ECGs continued to show a wide ORS (up to 192 ms) and prolonged OTc intervals (up to 739 ms) with alternating left bundle branch block and right bundle branch block morphologies despite continuous isoproterenol and sodium bicarbonate infusions (Fig. 1).

QUESTIONS TO CONSIDER

- What is the differential diagnosis for a patient with a prolonged QT interval?
- What are the appropriate initial steps in evaluating patients with a suspected toxidrome?
- What is the clinical value of send-out toxicology testing?

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Day of		Patient Reference interval or		
admission	Test name	value	therapeutic range	Units
1	Salicylate, serum	<5	100-300	mg/L
1	Acetaminophen, serum	<5	10-30	mg/L
1	Ethanol, serum	<10	<10	mg/dL
1	Toxicology screen, urine (qualitative immunoassay)	None detected: amphetamine screen, barbiturate screen, benzodiazepine screen, cocaine metabolite screen, codeine/morphine, cannabinoid screen, methadone screen, phencyclidine screen		
2	Pain/rehab toxicology screen,	Positive: fentanyl, noroxycodone		
	urine (qualitative LC-MS/ MS)	Negative: 6-acetylmorphine, alpha- hydroxyalprazolam, alprazolam, amphetamine, benzoylecgonine, buprenorphine, carisoprodol, chlordiazepoxide, clonazepam, cocaine, codeine, cotinine, diazepam, dihydrocodeine, EDDP, flurazepam, hydrocodone, hydromorphone, lorazepam, MDA, MDEA, MDMA, meperidine, methadone, methamphetamine, methylphenidate, morphine, naloxone, nicotine, norbuprenorphine, nordiazepam, norfentanyl, oxazepam, oxycodone, oxymorphone, phentermine, tapentadol, temazepam, THC-COOH, tramadol ^a		
2	Phenytoin, total, serum	<0.8	10.0-20.0	mg/L
2	Tricyclics, total, serum	<150	150-300	ng/mL
2	Lamotrigine, serum	<0.5	4.0-18.0	µg/mL
2	Pregabalin, serum	0.1	None established	µg/mL
2	Carbamazepine, total, serum	<2.0	8.0-12.0	mg/L
2	Eslicarbazepine, serum	<0.4	None established	µg/mL
2	Buproprion, serum	<10.0	50.0-100.0	ng/mL
2	Hydroxybuproprion, serum	<10.0	600.0-2000.0	ng/mL
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Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the November 2019 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol65/issue11 and follow the link to the Clinical Case Study and Commentaries.

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