A Question of Opioid Diversion or Compliance

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CASE DESCRIPTION

A 60-year-old female patient with a history of chronic pain and headache presented to the Pain Management Clinic for follow-up assessment of her prescribed medications, as well as to determine the patient's suitability for enrollment in the medical cannabis program. The patient's chronic pain and headache were secondary to traumatic brain injury sustained in a motor vehicle accident approximately 2 years before her appointment. The patient also was afflicted by chronic pain in her right arm due to nerve damage associated with surgery for de Quervain tendonitis. Following the motor vehicle accident, the patient had been evaluated at a multidisciplinary traumatic brain injury clinic and had been prescribed Tylenol #4 (acetaminophen 300 mg/codeine 60 mg) up to a maximum of 4 times daily for pain, and lorazepam (1 mg every 8 h as needed) for anxiety and insomnia.

To determine the patient's suitability for the medical cannabis program, the patient was required to submit a urine sample for drugs of abuse testing. Analysis of the sample was performed by a combination of immunoassay (amphetamines, barbiturates, benzodiazepines, benzoylecgonine, carboxy-tetrahydrocannabinol, and phencyclidine) and high-resolution accurate mass spectrometry (opioids). Following review of the patient's urine test results the clinician contacted the laboratory for assistance with the interpretation of the opioid results. A review of the immunoassay screens only demonstrated presumptive positive results for the amphetamine class; however, reflexive confirmatory testing via liquid chromatography–tandem mass spectrometry for amphetamines (amphetamine, methamphetamine, phentermine, methylenedioxyamphetamine, methylenedioxymethamphetamine, pseudoephedrine/ephedrine) was negative (Table 1).

The high-resolution accurate mass spectrometry results were more complex and demonstrated the presence of codeine, codeine-6-β-glucuronide, morphine, and morphine-6-β-glucuronide, which were consistent with the use of codeine (Table 1) (*1, 2*). However, the analysis also unexpectedly revealed the presence of hydrocodone, norhydrocodone, dihydrocodeine, and hydromorphone-3-β-glucuronide (Table 1).

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Table 1 Laboratory test results.

	February 2017	March 2017	
	Results	Results	Cutoff
Urine creatinine	28.7 mg/dL	251.2 mg/dL	≥20 mg/dL
Immunoassay screen results			
Amphetamines	Not detected	Presumptive positive	500 ng/mL
Barbiturates	Not detected	Not detected	200 ng/mL
Benzodiazepines	Not detected	Not detected	100 ng/mL
Cocaine (Benzoylecgonine)	Not detected	Not detected	150 ng/mL
Phencyclidine	Not detected	Not detected	25 ng/mL
Tetrahydrocannabinol	Not detected	Not detected	50 ng/mL
Targeted opioid screen results			
Codeine	Present	Present	25 ng/mL
Codeine-6-β-glucuronide	Present	Present	100 ng/mL
Morphine	Not detected	Present	25 ng/mL
Morphine-6-β-glucuronide	Present	Present	100 ng/mL
6-monoacetylmorphine	Not detected	Not detected	25 ng/mL
Hydrocodone	Present	Present	25 ng/mL
Norhydrocodone	Present	Present	25 ng/mL
Dihydrocodeine	Not detected	Present	25 ng/mL
Hydromorphone	Not detected	Not detected	25 ng/mL
Hydromorphone-3-β-glucuronide	Not detected	Present	100 ng/mL
Oxycodone	Not detected	Not detected	25 ng/mL
Noroxycodone	Not detected	Not detected	25 ng/mL
Oxymorphone	Not detected	Not detected	25 ng/mL
Oxymorphone-3-β-glucuronide	Not detected	Not detected	100 ng/mL
Noroxymorphone	Not detected	Not detected	25 ng/mL
Fentanyl	Not detected	Not detected	2 ng/mL
Norfentanyl	Not detected	Not detected	2 ng/mL
Meperidine	Not detected	Not detected	25 ng/mL
Normeperidine	Not detected	Not detected	25 ng/mL
Naloxone	Not detected	Not detected	25 ng/mL
Naloxone-3-β-glucuronide	Not detected	Not detected	100 ng/mL
Methadone	Not detected	Not detected	25 ng/mL
EDDP	Not detected	Not detected	25 ng/mL
Propoxyphene	Not detected	Not detected	25 ng/mL
Norpropoxyphene	Not detected	Not detected	25 ng/mL
Tramadol	Not detected	Not detected	25 ng/mL
O-desmethyltramadol	Not detected	Not detected	25 ng/mL
Tapentadol	Not detected	Not detected	25 ng/mL
N-desmethyltramadol	Not detected	Not detected	50 ng/mL
Tapentadol-β-glucuronide	Not detected	Not detected	100 ng/mL
Buprenorphine	Not detected	Not detected	5 ng/mL
Norbuprenorphine	Not detected	Not detected	5 ng/mL
Norbuprenorphine glucuronide	Not detected	Not detected	20 ng/mL

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QUESTIONS TO CONSIDER
• What are the metabolic pathways and products associated with the metabolism of codeine?
• Can manufacturing impurities of codeine play a role in of the interpretation of these test results?
• What additional testing would be helpful to discern between compliance with the prescribed codeine and undisclosed use of additional opioids?
• Are all the results of the initial testing consistent with the prescribed medications?

References

1. Snyder ML, Melanson SE. Drug addiction or false conviction? Clin Chem 2014;60: 1480 –3.

2. Reisfield GM, Chronister CW, Goldberger BA, Bertholf RL. Unexpected urine drug testing results in a hospice patient on high-dose morphine therapy. Clin Chem 2009; 55:1765– 8.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the February 2019 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol65/issue2 and follow the link to the Clinical Case Study and Commentaries.

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