Codeine Withdrawal Presenting as Acute Delirium in an Older Adult

Gerontology & Geriatric Medicine
Volume 10: 1–2

DOI: 10.1177/23337214241284909
journals.sagepub.com/home/ggm
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Manuscript received: April 2, 2024; **final revision received:** June 26, 2024; **accepted:** August 29, 2024.

To the Editor,

Delirium and seizures are common in alcohol or benzodiazepine withdrawal, but rare in opioid withdrawal (Raj et al., 2017) and not previously reported with codeine.

An independent 89-year-old man presented after his son found him utterly confused. He had CAD and stenting 20 years prior, BPH and painful lumbar disc herniation treated with codeine tablets 20 mg four-five times daily over the last 3 months. There was no history of alcohol consumption nor other medications as he was opposed to drugs and vaccinations.

On admission he was confused, not recognizing his son or the doctors, disoriented and speaking irrelevantly, unable to relate or cooperate, and in marked psychomotor agitation. Sinus tachycardia, sweating and dilated pupils were noted. Other vital signs were normal and examination was otherwise unremarkable. Chest X-ray, blood count, CRP, blood gases, endocrine panel, and serum biochemistry were normal, other than unchanged CKD (creatinine 1.3 mg/dL, eGFR 48 mL/min). Blood/urine screen were negative for alcohol, benzodiazepines, and opiates. Head CT revealed mild brain atrophy, unchanged from previous imaging.

He was sedated with intravenous haloperidol and intramuscular diazepam for acute delirium. When intravenous fentanyl 25 µg was started, delirium dramatically resolved within 2 hr. He was discharged home on fentanyl 12.5 µg/hr patch due to the severity of his chronic pain. Asked about his intake of codeine, he revealed that he ran out of his stock of codeine tablets 2 days before admission, and was unable to go out and get a new supply owing to low back pain.

Our patient's acute delirium was associated with codeine withdrawal, an unusual occurrence (Raj et al., 2017). Codeine binds to opioid receptors in the CNS, inhibiting pain pathways and suppressing cough. Adverse reactions include the potential of opioid dependence. When such patients stop using opioids abruptly, they manifest a well-known withdrawal syndrome of autonomic hypereactivity with mydriasis, tachycardia, hypertension, sweating, muscle cramps/pain, piloerection, diarrhea, nausea, yawning, and lacrimation/rhinorrhea. However, *delirium* was reported only in a handful of patients, mostly with heroin use disorder, some developing seizures, and none involving codeine withdrawal (Aggarwal et al., 2011; Raj et al., 2017).

Delirium is frequent in elderly patients, often associated with several concurrent underlying conditions especially acute infection, metabolic derangements, and polypharmacy/drug-toxicity, frequently on the background of underlying dementia and hospitalization (Schattner, 2023). Our patient had none of those, though advanced age, CKD, and significant pain are acknowledged delirium risk factors (Inouye et al., 2014). The history supported codeine withdrawal, and replacement with fentanyl quickly resolved his entire symptomatology. Applying the adverse-drug-reaction probability scale (Naranjo scale) adapted to drug withdrawal, yields a total score of 6 points, supporting a "probable" association (Naranjo et al., 1981; 0 points: doubtful; 1–4: possible; 5–8: probable; >9: definite).

With the current opioid epidemic (Planalp and Stewart, 2023) and efforts to treat addicted patients, emergency physicians and geriatricians are likely to encounter increasing numbers of the "opioid withdrawal syndrome." Thus, even its unusual manifestations may be encountered and need to be better recognized, including delirium reported above. Moreover, elderly and older adult patients receiving codeine or other opioids long-term, should be advised against abruptly stopping the drug, even when the doses involved are not very high.

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Author Contributions

Both authors treated the patient and researched and wrote the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Patient Consent

Signed.

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