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Selected Topics: Toxicology

POSTOPERATIVE ANTICHOLINERGIC POISONING: CONCEALED COMPLICATIONS OF A COMMONLY USED MEDICATION

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☐ **Abstract—Background: Scopolamine is a potent anticholinergic compound used commonly for the prevention of postoperative nausea and vomiting. Scopolamine can cause atypical anticholinergic syndromes due to its prominent central antimuscarinic effects. Case Report: A 47-year-old female presented to the emergency department (ED) 20 h after hospital discharge for a right-knee meniscectomy, with altered mental status (AMS) and dystonic extremity movements that began 12 h after her procedure. Her vital signs were normal and physical examination revealed mydriasis, visual hallucinations, hyperreflexia, and dystonic movements. Laboratory data, lumbar puncture, and computed tomography were unrevealing. The sustained AMS prompted a re-evaluation that revealed urinary overflow with 500 mL of retained urine discovered on ultrasound and a scopolamine patch hidden behind her ear. Her mental status improved shortly after patch removal and physostigmine, with complete resolution after 24 h with discharge diagnosis of scopolamine-induced anticholinergic toxicity. Why Should an Emergency Physician Be Aware of This?: Although therapeutically dosed scopolamine transdermal patches rarely cause complications, incomplete toxidromes can be insidiously common in polypharmacy settings. Providers should thoroughly evaluate the skin of intoxicated patients for additional adherent medications that may result in a delay in ED diagnosis and curative therapies. Our case, as well as rare case reports of therapeutic scopolamine-induced anticholinergic toxicity, demonstrates that peripheral anticholinergic effects, such as tachycardia, dry mucous membranes, and hyperpyrexia are often not present, and incremental doses of physostigmine may be required to reverse scopolamine's long duration of action. This further complicates identification of the anticholinergic toxidrome and diagnosis. Published by Elsevier Inc.**

☐ **Keywords—scopolamine; anticholinergic syndrome; physostigmine; reversal; emergency department; pharmacology; toxicology**

INTRODUCTION

Anticholinergic syndrome is a common and essential diagnosis, accounting for nearly 15,000 toxic exposure cases in 2014 (1). Emergency physicians should be able to identity and manage classical physical and neurologic findings of anticholinergic toxicity, such as fever, altered mental status, tachycardia, flushing, and dry oral membranes.

Scopolamine hydrobromide is an anticholinergic medication commonly used for the prevention of motion sickness and postoperative nausea and vomiting (PONV) (2). Scopolamine is most often administered in the form of a small, circular transdermal patch, which is placed behind the ear. Even at therapeutic doses, patients on scopolamine are at risk for anticholinergic toxicity, especially when used concurrently with home medications or remedies with anticholinergic effects.

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CASE REPORT

A 47-year-old female was brought to the ED, 20 h after hospital discharge, by her husband for altered mental status, slurred and nonsensical speech, and disorganized extremity movements that began 12 hours after an elective partial meniscectomy. The patient had an unremarkable postoperative recovery throughout the day at home until late evening, when she was noted to be talking "nonsense," producing incoherent speech, and was unable to support herself and completely flaccid when supported. Review of system was limited due to her altered mental status. Her medical history included depression, alcohol abuse with relapses, and motion sickness. Her surgical history included hand, wrist, and knee surgeries. Current medications included quetiapine 50 mg three times daily, gabapentin 800 mg three times daily, bupropion SR 150 mg twice daily, trazodone 200 mg at bedtime, and hydroxyzine 100 mg three times daily. Her husband denied any recent illicit drug use or alcohol ingestion (last drink was 4 weeks ago) and she has never had any suicidal attempts or drug overdose.

On arrival to the ED, the patient's vital signs were blood pressure 121/90 mm Hg, pulse rate 67 beats/min, respiratory rate 20 breaths/min, temperature 37.4°C (99.4°F), and SaO_2 94% on room air. Initial physical examination revealed a woman at her stated age, appearing to be drowsy and responding to internal stimuli and occasionally trying to reach for objects in mid-air. Her head and neck was notable for 5-mm pupils with sluggish reaction to light and moist mucous membranes. Heart and lung sounds were normal and abdominal examination was significant for a palpable bladder. Her extremities were slightly cool to the touch without rashes or erythema. On neurologic examination, she spontaneously opened her eyes, talked nonsensically, but was intermittently able to follow some commands. She flailed her extremities in disorganized, choreoathetotic movements with 3 + patellar and brachial deep tendon reflex, without clonus or joint rigidity; she had downward-going Babinski's sign.

Laboratory results were significant for thyroid-stimulating hormone 5.907 uIU/mL (reference range, 0.35–5.5 uIU/mL), free T4 0.95 ng/dL (reference range, 0.8–1.8 ng/dL). The urine toxicology screen was negative and the serum ethanol, acetaminophen, and salicylate levels were undetectable. Her ammonia, carboxyhemoglobin, ceruloplasmin, vitamin B12, creatinine phosphokinase, and serum osmolality and venous blood gas levels were normal. Electrocardiogram (ECG) showed normal sinus rhythm without QRS or QTc abnormality. Imaging revealed a normal chest x-ray study and normal computed tomography (CT) angiogram of brain and neck. A lumbar puncture was performed and revealed normal cerebrospinal fluid.

Her overall examination and presentation with altered mental status, mydriasis, hyperreflexia, and dystonia, in the absence of tachycardia, hypertension, fever, or flushing were concerning, but not completely consistent with alcohol withdrawal or sympathomimetic and anticholinergic toxidromes. On repeat examination after her initial workup, the providers noted the patient to have dry mucous membranes, urinary overflow incontinence with a post-void residual exceeding 800 mL, and a small circular medication patch was found behind her left ear, which was subsequently identified through review of the operative report as scopolamine; the patch had been placed preoperatively to the 2-h procedure. The patch was removed and she received two doses of physostigmine 0.5 mg given intravenously over 10 min while on telemetry with immediate but transient improvement of her mental status.

The patient was diagnosed with scopolamine-induced central anticholinergic syndrome compounded by her home doses of hydroxyzine, trazodone, and quetiapine. She was admitted to the intensive care unit for further monitoring and management of her altered mental status. She was discharged to home on day 6 after her hospitalization, delayed by a spontaneously self-resolving episode of QTc prolongation from 509 ms to 424 ms, orthostatic and nocturnal hypotension—likely potentiated by α-1 antagonistic properties of quetiapine and trazodone—that responded to intravenous fluids, as well as urinary retention that resolved after 48 h of Foley placement.

DISCUSSION

More than 600 unique pharmacologic and herbal compounds can cause anticholinergic effects through their ability to competitively inhibit the binding of acetylcholine to muscarinic acetylcholine receptors (3). Common prescription medication categories with high anticholinergic properties include antihistamines (i.e., diphenhydramine), tricyclic antidepressants ([TCAs] i.e., amitriptyline), sleep aids (i.e., doxylamine), antiemetics (scopolamine), and cardiac dysrhythmogenic medications (i.e., atropine). Plants such as jimson weed (*Datura stramonium*) and nightshade (*Atropa belladonna*) also contain significant concentrations of belladonna alkaloids, which contain both atropine and scopolamine and can cause severe anticholinergic toxicity (4).

Anticholinergic toxidromes are reflective of the location of the muscarinic receptors. Peripheral muscarinic receptors can be found in smooth muscles (intestinal,