

Case Study

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Anticholinergic Delirium Secondary to Over-the-Counter Medication Abuse

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Abstract

This case study examines a patient who presented to the emergency room with an unknown delirium that subsequently was discovered to be anticholinergic in nature. Diagnosis was difficult because the anticholinergic medications were predominantly taken as over-the-counter medicines and the patient initially presented the problem as gastrointestinal rather than psychiatric. This case demonstrates the extreme difficulty in making a diagnosis of anticholinergic toxicity in patients without a straightforward presentation.

Case Patient

In February 2001, a 34-year-old patient presented to the emergency room (ER) at the Indiana Regional Medical Center with complaints of gastrointestinal (GI) upset and nausea. She was given prochlorperazine (Compazine) intramuscularly (IM) and diphenhydramine (Benadryl) intravenously (IV). She was told to follow up later in the day at her doctor's office. During that visit she was given additional dosage of oral diphenhydramine and diazepam (Valium) for the nausea. Later that evening she presented back at the ER with tightening of her jaw and rigidity and was given benzotropine (Cogentin) 2 mg IM to combat a possible extrapyramidal side effect from the prochlorperazine, and lorazepam (Ativan) 1.5 mg for her agitation. She was also given famotidine (Pepcid) 20 mg IV for her GI upset. When she continued to have difficulty turning her head or swallowing and had jaw-clenching tremors that were generalized in nature, an additional 2 mg of benzotropine was tendered.

Her review of symptoms was negative for any cardiac pulmonary or genital urinary symptoms. She had no neurologic events prior to this episode. Her past medical history was positive for a hysterectomy with bilateral salpingo-oophorectomies and periods of gastroesophageal reflux. She had been on lansoprazole (Prevacid) 30 mg/day previously and Estradiol (Estrace) injections monthly. She had received prochlorperazine on several occasions previously in her medical history and these produced some tightening of the jaw but never required any visits to the emergency room.

At the time of her presentation the patient was separated but not divorced.

Case Study

Her family history was not contributory. Once the patient's dystonic reaction was controlled with two doses of benzotropine she showed evidence of extreme agitation. Her gait was broad based. Her deep tendon reflexes were +3 and equal for biceps, triceps, brachioradialis, patellar, and achilles.

In addition to the acute dystonia, she had one episode of oculogyric crisis. She had difficulty with finger-to-nose testing and heel-to-shin testing. Rapid alternating movements were similarly poor. Funduscopic examination was benign. Her pupils were 6.5 mm and reactive to 4 mm. Her extraocular muscles movements were within normal limits in all six cardinal fields of gaze. There was a pronator drift. Her head was turned to the left secondary to the rigidity in the sternocleidomastoid and there was some tremor. She had difficulty swallowing. Her thyroid was not enlarged. Her mouth was moist. Her neck was supple. Her sclera was not anicteric. Her lymph nodes were not palpable. Cardiovascular examination revealed a pulse of 100 beats per minute (BPM) without evidence of murmur, rub, or gallop. Her lungs were clear to percussion and auscultation. The abdomen was soft and nontender. Her extremities showed no edema.

Treatment

The patient was admitted to the hospital from the ER and at that time had a right-handed tremor. After receiving lorazepam she was drowsy but arousable. She became unsteady approximately 4 hours after her admission and then had a small emesis. Shortly after the emesis she became markedly more tremulous and was given an additional 1 mg of lorazepam, this time via IV. By midnight she was confused but oriented. She was talking to herself and continued to be confused throughout the night. From midnight until 6AM the next morning the patient was picking at things she was seeing in the air. She was tremulous and confused. She would get in and out of bed without any idea of her direction and was completely disoriented and psychotic.

At 6AM that morning the patient showed obvious signs of delirium with bilateral external tremors and an inability to respond to questioning. She was attempting to get out of bed to pull out her IV. She had a complete blood count with differential, which was normal and

a normal sedimentation rate. Her reflexes were now hyperactive and equal at -4/4 for biceps, triceps, brachioradialis, patellar, and achilles. Her Babinskis were down. Her pupils continued to be large at 6 mm and reactive to 4.5 mm. She had a temperature of 101° with a pulse ranging from 95–100 BPM and a blood pressure of 120/80. The diagnosis of organic delirium was made at that time.

At approximately 8AM she showed evidence of a return of her acute dystonia with her head turning to the left and was given an additional 2 mg of benzotropine. Forty-five minutes later she was again oriented only to person. Her speech was slurred. She was restless, inattentive, hyperactive, and unsteady on her feet. She became increasingly more agitated and by 9AM had been given an additional 2 mg of lorazepam. This did not in any way control her.

The possibility that she had received an excessive dose of lorazepam was then considered. As a result, flumazenil (Romazicon) was given at 2/10 of a mL IV, an additional 3/10 1 minute later, and an additional 5/10 2 minutes after that. The patient continued to be agitated. Her gait continued to be unsteady and she was extremely psychotic. Olanzapine (Zyprexa) 5 mg was given at that point and the patient was sent for an emergency electroencephalogram (EEG), computed tomography, and lumbar puncture, as she was now expressing paranoid ideation, having visual, tactile, and auditory hallucinations, and appeared to be acutely psychotic. Her lumbar puncture was negative. Her computed tomography, with and without contrast, was normal. Her EEG showed an enormous amount of β activity.

Because the patient was so agitated, midazolam (Versed) was used to control her agitation in 1-mg IV pushes. From 12:08PM to 1:06PM she received midazolam 6 mg. Since the EEG was done after the midazolam was given, there was an enormous amount of β artifact noted.

Diagnosis

Since there was no other etiology for the patient's delirium, the possibility existed that she was suffering from an anticholinergic delirium due to her elevated temperature, her large pupils, and her extreme delirious behavior. As a result, she was given physostigmine (Antilirium) 1 mg IV every 2 minutes until a total of 2 mg was given. Three

minutes after the second IV instillation the patient was fully awake, no longer confused, and completely oriented. There was no dissociation. There were no tremors. She was coherent, conversed well, and was appropriate. Her pupils were now 3 mm instead of 6 mm. Her extraocular eye movements continued to be normal. She had some mild GI upset secondary to the physostigmine but was otherwise well.

Her family visited her at 2:10PM and she did well until 4PM, at which point she became delirious again with thickened speech, tremors, and psychosis. She was given another 2 mg of physostigmine at that time and she had a brief episode of atrial fibrillation with a controlled ventricular rate. At that point it was decided that she had received as much physostigmine as was stable.

For the next 72 hours the patient's tremors and disorientation waxed and waned. At this point it was decided that the only safe way to treat her was with midazolam 1 mg at a time separated by 5 minutes with a maximum of 3 mg in any 2-hour period. The Pittsburgh Poison Center suggested terminating further use of physostigmine and initiation of benzodiazepines to control her. When the patient was calm from the midazolam, a lorazepam drip at 2 mg/hour was started at 4AM and continued for the next 4 days.

Thirty-six hours later the patient was able to verbalize what had caused the toxicity. She reported that since the breakup with her boyfriend she had been unable to sleep and was taking huge amounts of Tylenol PM—a combination of acetaminophen and diphenhydramine. She was taking 8–12 tablets every day for 10–15 days prior to the time she presented to the emergency room—a total in excess of 100 tablets over 7–10 days. Although her liver enzymes were within normal limits, it was thought that the patient was unable to tolerate the anticholinergic load of the diphenhydramine.

The patient ultimately was transferred to Transitional Care—an intermediate unit—and was discharged from the hospital on February 8, 2001, after being hospitalized for 1 week. Two subsequent follow-up examinations showed the patient to be completely normal. She had normal mental status, normal neurologic examination, and no sequelae whatsoever from her delirium.

Discussion

This is an extremely unusual presentation of a patient with an unknown anticholinergic delirium, in which medical treatment added to and ultimately peaked her anticholinergic delirium. The primary problem occurred as a result of the patient taking very large amounts of over-the-counter diphenhydramine. This produced GI upset, which was treated with prochlorperazine, which then produced the acute dystonic reaction. Once the dystonia was treated aggressively with diphenhydramine and benztropine, the patient's anticholinergic

load was unacceptable and she was pushed into a delirium that in many ways was iatrogenic. She was acutely delirious for a period of 3 days and seriously ill for a period of 5 days.

It is very important to consider the possibility that over-the-counter drugs may produce delirium with anticholinergic agents. Were it not for the patient's large pupils and low-grade temperature, diagnosis may have been impossible and treatment might have been delayed endangering the patient's life.

It is our feeling that this case expertly demonstrates the danger of over-the-

counter medications, and more significantly, the danger of anticholinergic medications. The addictive cholinergic effects of the diphenhydramine with its concurrent anticholinergic properties, the benztropine used to treat the extrapyramidal symptoms precipitated by prochlorperazine, and the famotidine used to treat the patient's gastrointestinal symptoms, all contributed greatly to this patient's delirium. ●●●

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