False-Positive Tricyclic Antidepressant Drug Screen Results Leading to the Diagnosis of Carbamazepine Intoxication

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ABSTRACT. Ingestion of toxic substances is a common problem in pediatrics. When presented with the limited history of an unknown ingestion in a patient with altered mental status, a clinician depends on the physical examination and a toxic screen to determine the ingested substance(s). Some toxic screens yield false-positive or false-negative results that confound identification of ingested toxins. Three cases are presented in which carbamazepine ingestions were identified because of the false-positive tricyclic antidepressant serum toxic screen result in each case.

Carbamazepine ingestion is one of the most common pediatric overdoses. Side effects include altered mental status, tachycardia, mydriasis, seizures, coma, and death. Several other substances also cause false-positive tricyclic antidepressant toxic screen results, including certain antipsychotic medications, antihistamines, and the muscle relaxant cyclobenzaprine. Specific tests and drugs causing false-positive results are presented in table form. More modern methods, specifically gas chromatographic-mass spectrometric, are more reliable in distinguishing these drugs. Knowledge of which substances commonly cause false-positive results on a given toxic screen can still lead the clinician to the correct diagnosis. Pediatrics 2000;105(5). URL: http://www.pediatrics.org/cgi/content/full/105/5/e66; tricyclic, carbamazepine, ingestion, intoxication, drug screen.

ABBREVIATIONS. TCA, tricyclic antidepressant; BID, twice daily; PRN, as required; EEG, electroencephalograph; CBC, complete blood count.

Ingestion of toxic substances is a common problem in pediatrics.1 When presented with the limited history of an unknown ingestion in a patient with altered mental status, a clinician depends on the physical examination and a toxic screen to determine the ingested substance(s). Some toxic screens yield false-positive or false-negative results that confound identification of ingested toxins. However, knowledge of which substances commonly cause false-positive results on a given toxic screen can still lead the clinician to the correct diagnosis. Below are 3 cases of carbamazepine ingestions that were identi-
mg each evening), lorazepam (1 mg 3 times daily/.5 mg BID PRN), Metaculon (1 pack once daily), quetiapine (200 mg BID), fluoxetine (150 mg BID), trazodone (50 mg every night), and methylphenidate (10 mg every morning/every 1 pm).

Physical examination on transfer revealed vital signs of: temperature, 37.0°C; heart rate, 115; respiratory rate, 16; and blood pressure, 107/71. The patient was drowsy with dilated, reactive pupils from 6 pm to 2 mm bilaterally; no nystagmus on lateral gaze. Speech was slurred. She had dysmetria, with poor finger-to-nose. Gait was not tested at that time because of truncal ataxia when sitting.

Electrolytes and liver function test results were normal. A urine toxicity screen result was negative for drugs of abuse. Serum aspirin and acetaminophen levels were nondetectable, but serum TCA screen result was positive.

The patient was given activated charcoal (1g/kg) and sorbitol. Because of the positive TCA, an electrocardiograph was performed that showed only sinus tachycardia. A carbamazepine level was sent that revealed a serum concentration of 18.6 μg/mL at ~12 hours post ingestion. Activated charcoal and sorbitol were again administered. Repeat carbamazepine level at ~18 hours postingestion was 10.0 μg/mL. Her clinical condition rapidly improved with resolution of ataxia, and she was transferred back to the psychiatric facility.

Case 3

A 10-year-old female was transferred from a community hospital after a possible seizure. She had a past history of seizure disorder since 8 years of age and psychiatric admissions for behavior disturbances. The patient had been on multiple medications (carbamazepine, gabapentin, valproic acid, and phenytoin) but was currently taking only lorazepam (1.5 mg 3 times daily). The previously used medications were stored in the basement.

The patient had taken diphenhydramine briefly during the past week. Another family member was taking piroxicam.

The patient had been well until the day of admission when she had taken a nap and her grandmother heard banging in the room. The patient was lethargic, confused, complaining of double vision, and had an uncoordinated gait. Suspecting that a seizure had occurred, the grandmother brought the patient to a community hospital where CBC and electrolytes were normal, and she was transferred to our facility.

In the emergency department, vital signs were: temperature, 36.2°C; heart rate, 88; respiratory rate, 18; and blood pressure, 107/65. The patient was somnolent with a Glasgow coma scale score of 6 (withdrawing to pain and no eye opening or verbal response). Deep tendon reflexes were 1-2 without clonus. Gait was ataxic. Head computed tomography was negative. Serum toxicity result was negative for ethanol, acetaminophen, and aspirin but positive for TCA. Carbamazepine, quantitative TCA, and comprehensive toxic screen results were sent. The patient was given activated charcoal (50g) with magnesium citrate and admittance.

EEG showed diffuse seizure activity; lorazepam was restarted. Quantitative serum TCA was negative, but carbamazepine level returned elevated at 20.1 μg/mL. A second dose of activated charcoal was given. The patient’s mental status and gait normalized by hospital day 2; carbamazepine level was 6.7 μg/mL.

Examination of the patient’s carbamazepine bottle from home revealed that thirty-three 200-mg pills were missing. Carbamazepine level on hospital day 3 was 3.2 μg/mL; the patient was transferred to a psychiatric facility.

**DISCUSSION**

Carbamazepine ingestion is one of the most common pediatric overdoses. In a series by Kentucky Regional Poison Center, patients <17 years old accounted for 70% of carbamazepine ingestions. Carbamazepine ingestions are associated with the anticholinergic side effects seen in our patients, including changes in mental status, tachycardia, and mydriasis. Seizures can occur, most often in patients with a known seizure disorder; 1 study described seizures as an indicator of fatal outcome. Patients with coma may develop respiratory depression requiring mechanical ventilation. EEG changes were described in one 16-year-old patient, which consisted of occipital δ-activity and resolved on clearance of the carbamazepine. Cardiac effects include sinus tachycardia in most patients and a life-threatening syndrome of heart block or bradyarrhythmias, which has been described only in elderly patients.

Those patients with very high levels (>85 μg/mL) were found to have worse outcomes in a mixed age group, but death has been reported in a pediatric patient with a moderately high peak level of 54 mg/L. A Milwaukee group determined that pediatric patients with levels >28 μg/mL were at higher risk for dystonia, coma, and apnea. Similarly, a group in Oregon found levels >35 mg/L in pediatric patients were significantly associated with major toxicities—seizures, coma, and need for intubation.

The combination of the positive serum TCA screen result plus review of the history led to the identification of carbamazepine as the ingested substance in the above cases. Several substances are known to cause a false-positive serum TCA screen result. These substances all possess ringed structures, which simulate the tricyclic rings in some toxic screens. In addition to carbamazepine, a positive TCA result may be caused by antipsychotic medications, such as thioridazine, even in the therapeutic range. Antihistamine medications, specifically diphenhydramine and cyproheptadine, have been shown to interfere with TCA screen results. The commonly used muscle relaxant cyclobenzaprine can now be distinguished from TCAs by mass spectrometric meth-
ods but does cause false-positive TCA results on older immuno- and liquid chromatographic methods, which are still in use (Table 1).

Three cases are reported above in which pediatric patients presented after ingestion of unknown substance(s). In each case, a positive TCA screen result led to the diagnosis of carbamazepine ingestion. A positive TCA screen result in a pediatric patient with an unknown ingestion should lead the clinician to consider carbamazepine, thioridazine, cyclobenzaprine, and antihistamines as potentially ingested substances yielding a false-positive TCA screen result.

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