A 16-Year-Old Girl With Altered Mental Status, Abducens Nerve Palsy, and Ataxia

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Case Report

A 16 year-old girl presented with altered mental status. The patient and her mother reported that she was in her normal state of health until the morning of admission, when she began to complain of dizziness and double vision. Her mother stated that she appeared “wobbly” when ambulating and noted that while sitting, she had slumped over in the chair at the hair salon earlier that day. She denied any loss of consciousness. She was taken to the local emergency department on the evening of admission, where she had several bouts of non-bloody, nonbilious emesis and became incoherent and somnolent. Her mother denied recent fevers, illness, or sick contacts. The patient had taken a few doses of ibuprofen during the previous week for menstrual cramps, but she denied any ingestion of other substances, including parental medications or illicit substances. There was no history of depression or other mental illness, and the patient was not taking any medications regularly.

Her pulse was 85, blood pressure 85/51 mm Hg, and temperature 36.6°C. She appeared somnolent but did rouse to voice and follow commands. She was oriented only to self. Speech was slurred. Pupils were 3 mm bilaterally, round and reactive to light. There was horizontal nystagmus. She was unable to abduct the right eye past midline. Grip strength was diminished in her right hand. The remainder of cranial nerve and strength testing was normal. She had prominent truncal ataxia. Deep tendon reflexes were 1+ and symmetric.

Laboratory studies were notable for an elevated venous lactate of 4.3 mmol/L and serum potassium of 2.8 mmol/L. Remainder of serum chemistries, complete blood count, thyroid-stimulating hormone, free T4, random cortisol, venous blood gas, urinalysis, urine pregnancy test, and basic metabolic panel were within normal limits. Urine toxicology, acetaminophen, salicylate, and ethanol levels were negative. Computed tomography of the head was normal. Cerebrospinal fluid (CSF) cell count, protein, and glucose were normal. An electrocardiogram showed normal sinus rhythm with normal axis and intervals.

Final Diagnosis

The final diagnosis was carbamazepine toxicity.

Hospital Course

Following admission, the patient was noted to be hypotensive, with a blood pressure of 85/51 mm Hg, which responded well to intermittent normal saline boluses. Magnetic resonance imaging/magnetic resonance angiogram of the head and neck were without abnormality. An electroencephalogram (EEG) showed no evidence of seizure activity. Multiple providers reviewed the history with the patient and family on numerous occasions in regard to the possibility of accidental or intentional ingestion; both the patient and her family adamantly denied ingestion of any medications found in the home or illicit or nonmedical substances.

Local poison control officials were contacted, who recommended obtaining a serum carbamazepine level given the patient’s altered mental status and prominent ataxia. This was added on to the patient’s admission laboratory studies and found to be >20.0 µg/mL (reference range 4-12 µg/mL).

When presented with the result of serum carbamazepine testing, the patient admitted to taking 4 tablets of her mother’s carbamazepine on the evening prior to admission, stating that she was “angry that she had to do homework on a Saturday.” She denied suicidal intent or ideation. Psychiatry was consulted and recommended outpatient follow-up.

Within 24 hours of admission, the patient’s physical exam began to return to baseline. Serum carbamazepine levels were followed and returned to within normal limits by hospital day 2. She was discharged home with her parents in her normal state of health.

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Discussion

Ataxia is a relatively common pediatric neurological complaint, with an estimated prevalence of 26 per 100,000. Although the majority of underlying processes are benign and generally self-limited, there are life-threatening illnesses that may present with ataxia. The differential for ataxia is quite broad (Table 1), though a 19-year case series found that approximately 80% of children presenting to the emergency department with acute ataxia and subsequently hospitalized were ultimately diagnosed with 1 of 3 conditions: acute cerebellar ataxia, toxic ingestion, or Guillain-Barré syndrome. Acute cerebellar ataxia, sometimes called “postinfectious acute cerebellar ataxia,” accounts for approximately 40% of acute cases of ataxia in the pediatric population, with an estimated incidence of 1 per 100,000 to 500,000, making it the most common cause of ataxia in children. Toxic ingestion is the second most common cause, accounting for approximately 30% of cases. Life-threatening causes of ataxia in children include mass lesions, intracranial hemorrhage, stroke, and infectious processes such as cerebellar abscesses and brainstem encephalitis. These conditions are fortunately uncommon but should be considered in the appropriate clinical context.

A detailed history is invaluable in determining the etiology of ataxia. For example, a history of an acute illness, such as an upper-respiratory infection, a few weeks prior to presentation suggests acute cerebellar ataxia as a potential cause. Recurrent or persistent headache with diplopia or vomiting indicates possible increased intracranial pressure and can be suggestive of a mass lesion. Timing of onset; concurrent symptoms such as fever, medication, and recent vaccination history; or a history of trauma can also help significantly narrow the differential.

The physical exam of the ataxic patient is also crucial. Vital signs should be carefully reviewed. Fever may suggest an infectious process such as encephalitis. The presence of Cushing’s Triad of bradycardia, hypertension, and widening pulse pressure is a sign of increased intracranial pressure and can be suggestive of a mass lesion. Timing of onset; concurrent symptoms such as fever, medication, and recent vaccination history; or a history of trauma can also help significantly narrow the differential.

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In the absence of altered consciousness, focal neurological signs, or marked asymmetry of ataxia, the yield of neuroimaging is low, though it is often obtained to rule out space-occupying lesions. If there are signs or symptoms of central nervous system (CNS) infection, such as meningitis or encephalitis, CSF should be obtained; otherwise CSF is rarely indicated for emergent
evaluation of the child with acute ataxia. Similarly, an EEG is rarely indicated, except in the setting of altered consciousness or fluctuating clinical signs, which may suggest seizure activity. Acute ataxia in the setting of developmental delay, similar prior episodes, or a positive family history may suggest genetic causes and/or inborn errors of metabolism.

Carbamazepine is a commonly prescribed medication with a relatively narrow therapeutic window; toxicity has been well described in adult and pediatric patients. According to the Annual Report of the American Association of Poison Control Centers' National Poison Data System for 2013, there were a total of 1961 reported toxic exposures to carbamazepine as isolated ingestions, 531 (27%) of which were in individuals aged 19 years or younger. Of these single-exposure events, 501 resulted in moderate to severe outcomes, with 1 event resulting in death. Toxic exposures to carbamazepine were mentioned in 3946 cases of adverse substance exposure overall. These rates appear to be consistent with prior years, suggesting that carbamazepine poisoning continues to be an entity with which clinicians should be familiar.

Carbamazepine toxicity has a number of associated signs and symptoms (Table 2). Toxicity is primarily manifested by neurological and cardiac effects, though it may present with a number of signs and symptoms, including evidence of cholinergic blockade, respiratory depression, altered mental status, ataxia, somnolence, paradoxical seizures, coma, and ventricular arrhythmias. Importantly for the pediatric clinician, it should be noted that children appear to be at risk for major toxicities at lower serum concentrations than are adults.

Neurological manifestations are believed to be a result of carbamazepine’s anticholinergic activity as well as antagonist effect on central adenosine receptors when at high serum concentrations. An exam typically reveals altered mental status, with CNS depression ranging from drowsiness to coma, which may be cyclical. Seizures may also occur, especially in the setting of underlying epilepsy, and are often self-limited. Cranial nerve abnormalities and ataxia have been well described, as in our case.

The cardiac effects seen in carbamazepine toxicity are believed to be a result of sodium channel blockade causing a proarrhythmic response. Tachycardia is most commonly seen, though QRS prolongation and other arrhythmias have also been reported. Hypotension, as in our patient, is also associated with toxicity, especially with higher serum concentrations.

Carbamazepine also has anticholinergic effects, thus manifestations of anticholinergic excess are seen with carbamazepine toxicity. Classic cholinergic blockade symptoms such as dry mucous membranes, flushed skin, hyperthermia, urinary retention, miosis, and altered mental status have been described.

### Conclusions

Ataxia is a relatively common pediatric neurological complaint with a broad differential diagnosis, though acute cerebellar ataxia, toxic ingestions, and Guillain-Barré Syndrome account for the large majority of cases. Carbamazepine toxicity may present with a number of nonspecific signs and symptoms, many of which are commonly seen in a variety of neurological disorders such as stroke, CNS infection, or malignant processes. As a consequence, a detailed and thorough history of the onset of symptoms, associated complaints, and the patient’s and household contacts’ home medications is warranted. Ingestions in general, and carbamazepine toxicity in particular, should be considered in patients with acute alteration in mental status with either ataxia or focal neurological complaints. Consulting Poison Control early in the course of illness, especially when a thorough evaluation has not yielded an explanation, can be of significant benefit. Our case likewise illustrates the importance of revisiting the history of present illness and physical exam as testing results return to additionally distinguish potential etiologies of the patient’s underlying illness.

In conclusion, the identification of carbamazepine toxicity requires a high index of suspicion in a patient who is either nonverbal or reluctant to provide a full history, as is often the case in the pediatric population, or in patients who are somnolent, deeply sedated, or comatose. Similarly, in pediatric patients presenting with a chief complaint of acute ataxia, a thorough history, physical exam, and time may be all that is needed to come to a final diagnosis.

### Author Contributions

KD acted as primary author of the manuscript, acquired and interpreted previously published data for reference and developed the initial draft of the article.
JRS contributed to the design and points of emphasis in the case report discussion, provided important revisions to the manuscript and approved the final manuscript version.

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