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Case Report

Vertical gaze palsy due to medication error

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ABSTRACT

We present a teenage boy with recent onset of seizures, who was erroneously treated with a large dose of an antiseizure medication as a result of drug mix-up. The ensuing drug toxicity caused vertical gaze palsy, an unusual manifestation related to overdose of the agent. Timely recognition of the error and discontinuation of the drug resulted in complete recovery to baseline.

1. Introduction

Acute decline in sensorium may be the presenting feature of a variety of underlying processes that affect the central nervous system. Drug-induced encephalopathy is an important consideration in this setting as it is a potentially reversible cause of encephalopathy. The lack of early recognition may result in continued exposure to the inciting agent and worsening clinical status. Well-described conglomeration of clinical signs often assists the clinician to suspect and manage toxidromes associated with many neurotropic agents [1]. However, less commonly known toxic effects of drugs may prevent early recognition of their overdose. Vertical gaze palsy is a classical feature described in association with lesions involving the tectum of the midbrain [2]. However, rarely this symptom may be associated with acute drug toxicity as seen in our patient.

2. Case report

A 16-year-old left-handed Caucasian boy with Duchenne Muscular Dystrophy and bipolar disorder was admitted to our institution for BiPAP initiation trial. About 2 months prior to admission, he had a new-onset unprovoked seizure described as right head and eye version with loss of consciousness. Computerized tomography (CT) of the head was normal and EEG was devoid of epileptiform abnormalities, hence an antiseizure drug (ASD) was not initiated. The day before admission, he had a second unprovoked seizure with similar semiology and was prescribed an ASD by his neurologist. While in the hospital, he was continued on all of his daily medications as reported by the family: Seroquel® (Quetiapine) 50 mg daily, Paxil®(Paroxetine) 20 mg daily and Lamictal® (Lamotrigine) 300 mg twice daily. On the 3rd day of hospitalization, he became progressively lethargic, sleeping for the majority of the day. A day later, he developed dysarthria and was noted to have abnormal eye movements, after which neurology was consulted.

On physical examination, he was awake and alert, although he was slow in responding to questions. He could follow simple commands and was oriented to time, place and person. Significant dysarthria was noted. Visual acuity was 20/20 and visual fields were intact on confrontation testing. Pupils were bilaterally equal and reactive to light. Horizontal saccades and pursuits were normal eye movements, however, there was reduced upward gaze in both eyes. He also had sustained nystagmus in all directions of gaze. Funduscopic examination was normal. There were no other abnormalities detected on a detailed cranial nerve evaluation. Particularly, there were no deficits on facial sensory and motor examination, and movements of the jaw, palate, uvula and tongue were symmetrical. Gag reflex was not tested. Muscle strength testing demonstrated power of 3/5 in the upper extremities and 2/5 in the lower extremities, which was comparable to baseline. Sensory examination was unremarkable. Deep tendon reflexes were hypoactive, and plantars were downgoing. There were no signs of meningeal irritation.

CT scan of the head was unremarkable. Given that Lamictal® was initiated at a very high dose (12.5 mg/kg/day) and was the only recent addition to his home medications, drug toxicity was suspected and Lamictal® was discontinued. His primary neurologist was contacted

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who clarified that the patient was prescribed Trileptal® (Oxcarbazepine 300 mg BID) and not Lamictal® as was erroneously stated by the family. The patient showed gradual improvement and eventually returned to baseline 3 days after discontinuation of Lamictal®. No cardiac rhythm abnormalities or skin changes developed over the course. Lamotrigine level drawn at the time of initial consultation showed significant elevation at 24 μg/ml (normal 3–14 μg/ml). Once the patient returned to his baseline neurological status, oxcarbazepine was initiated. The incident was reported to the institutional incident reporting system for further investigation.

3. Discussion

Rational management of epilepsy entails consideration of a variety of antiseizure drugs, with no single agent being effective in all patients. Carbamazepine, lamotrigine, levetiracetam, oxcarbazepine, topiramate and valproic acid are often considered preferred first line ASDs for focal epilepsy [3]. Oxcarbazepine (Trileptal®) is approved for treatment of focal epilepsy, while Lamotrigine (Lamictal®) is a broad spectrum ASD approved for use in both focal and generalized epilepsy [3,4]. Both oxcarbazepine and lamotrigine work by causing blockade of the voltage-dependent sodium channels thereby inhibiting the release of glutamate by stabilizing the presynaptic membrane [5]. Due to this pharmacokinetic redundancy, combined used of these agents may potentially lead to supraadditive toxic effects [6].

The most common adverse effects related to the use of lamotrigine include nausea, vomiting, ataxia, diplopia, dizziness and somnolence. Steven-Johnson syndrome and toxic epidermal necrolysis are some of the rare, but serious adverse effects with this medication mandating immediate drug withdrawal [7]. Lamotrigine use has been associated with diverse neurological manifestations including tics, obsessive–compulsive behavior, repetitive eye blinking, blepharospasm and oculogyric crisis [8]. Disorders of eye movements, including impairment of smooth pursuits and saccadic eye movements, have been reported with many ASDs including lamotrigine, carbamazepine and phenytoin, which are all inhibitors of the sodium channel. Although the exact pathophysiology of ocular dysmotility in these cases is unknown, it is hypothesized that inhibition of release of presynaptic excitatory amino acids could lead to an alteration of dopamine metabolism, resulting in abnormal eye movements.

Das et al. reported 2 patients with eye movement abnormalities associated with lamotrigine use, including abnormalities in smooth pursuit movements, oculomotor apraxia with upward saccade initiation failure, eyelid retraction and vertical gaze palsy [9]. In their report, eye movement abnormalities were seen with chronic lamotrigine use and at therapeutic doses of the drug. In contrast, our patient developed vertical gaze palsy in the setting of an acute overdose of lamotrigine. A large series describing nine patients with acute lamotrigine toxicity related to accidental or intentional overdose reported mental status changes (depression or agitation) as a consistent finding. However, vertical gaze palsy was not described in any of them [10]. Although our patient had a slow response time and increased sleepiness, overt mental status changes were not seen. As it is impossible to evaluate for vertical gaze palsy in a sedated or uncooperative patient, this abnormality may not have been hitherto evident in previous patients with lamotrigine toxicity.

Errors in drug dispensing are a global occurrence. They may cause serious patient harm and can be potentially fatal. There has been increasing literature on drug dispensing errors, resulting in the development of systems-based models with multiple checks to minimize potential error [11,12]. The process of medication history reconciliation is vital to prevent mixing up drugs with similar names. In our case, there was a discussion about lamotrigine (Lamictal®) as well as oxcarbazepine (Trileptal®) with the family prior to initiating treatment for epilepsy, leading to the confusion in parental reporting. While this mishap appears seemingly possible, there are no previous reports related to inadvertent use of Lamictal® for Trileptal®. As both of these drugs are used to treat seizures, no alarms were raised when the drug was ordered in the electronic system. Despite adopting rigorous processes to detect pharmacy errors at our institution, occurrences like these highlight the role of continued surveillance and the need for escalating measures to improve patient safety. Medication information obtained from the patient or parents may need to be verified with existing hospital records, healthcare plans or pharmacy networks. Other suggested measures include verification by a dedicated floor pharmacist, review of written prescriptions or a physical verification of the labels on the medication bottles. While some of these goals may be unrealistic, when medication errors occur, an early suspicion of the same is crucial. In addition, the role of a diligent reporting system to review and improve processes cannot be overemphasized.

4. Conclusions

Lamotrigine overdose may rarely result in vertical gaze palsy. There should be a low threshold to suspect medication toxicity and potential medication error when a patient has an unusual neurological symptom.

Conflict of interest

None of the authors have any potential conflicts of interest.

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References

[1] Mégarbane B. Toxidrome-based approach to common poisonings. Asia Pac J Med Toxicol 2014;3:2–12.
[2] Christoff N. A clinicopathologic study of vertical eye movements. Arch Neurol 1974; 31:1–8.
[3] Schmidt D, Schachter SC. Drug treatment of epilepsy in adults. BMJ 2014;348:g254.
[4] Lagae L. The need for broad spectrum and safe anti-epileptic drugs in childhood epilepsy. Acta Neurol Belg 2009;109:167–70.
[5] Aneja S, Sharma S. Newer anti-epileptic drugs. Indian Pediatr 2013;50:1033–40.
[6] Patsalos PN, Perucca E. Clinically important drug interactions in epilepsy: general features and interactions between antiepileptic drugs. Lancet Neurol 2003;2: 347–56.
[7] Choi H, Morrell MJ. Review of lamotrigine and its clinical applications in epilepsy. Expert Opin Pharmacother 2003;4:243–51.
[8] Veerapandiyan A, Gallentine WB, Winchester SA, Baker J, Kansagra SM, Mikati MA. Oculogyric crises secondary to lamotrigine overdosage. Epilepsia 2011;52:e4–6.
[9] Das KB, Harris C, Smyth DP, Cross JH. Unusual side effects of lamotrigine therapy. J Child Neurol 2003;18:479–80.
[10] Moore PW, Donovan JW, Burkhart KK, Haggerty D. A case series of patients with lamotrigine toxicity at one center from 2003 to 2012. Clin Toxicol (Phila) 2013;51: 545–9.
[11] James KL, Barlow D, McArtney R, Hiom S, Roberts D, Whittlesea C. Incidence, type and causes of dispensing errors: a review of the literature. Int J Pharm Pract 2009; 17:9–30.
[12] Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA 2001;285:2114–20.