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Carbamazepine Induced Ataxia: A Case Report in Pediatrics

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ABSTRACT

Ataxia is a manifestation which is characterized by lack of coordination in the movement of different muscles in the body due to variety of diseased conditions. Carbamazepine is used as an antiepileptic and for pain disorders and a range of psychiatric diagnoses that shows ataxic symptoms in a dose-dependent manner. Toxic effects are due to the drug's anti-cholinergic activity, sodium channel blockade, CNS depression and myocardial depressant properties. Even at therapeutic doses, patient might show mild signs of toxicity and hence serum drug concentration needs to be monitored regularly. In case of mild to moderate toxicity, treatment is not required. This is a common yet rarely reported case report of carbamazepine induced ataxia in a pediatric patient of 6 years old male child who was presented with chief complaints of headache, stiffness of body, generalized weakness and nausea since one week. He had 2 episodes of vomiting at morning and stiffening of body which lasted for few seconds on the day of admission. He had history of ingestion of 3 tablets of carbamazepine of strength 100mg for headache. Supportive treatment was provided and was closely monitored by a multi-disciplinary team for clinical features of ataxia which was reversed after 3 days of hospital stay.

Introduction

Ataxia in simple term refers to the presence of abnormal and uncoordinated movements. It refers to a group of neurological disorders in which motor behavior appears uncoordinated. Patients with ataxia may show abnormality in activities requiring motor control like walking, speaking clearly, swallowing, writing, etc. Ataxia is caused due to abnormality in different parts of nervous system, either central nervous system (brain and spinal cord) or peripheral nervous system (roots and nerves that connect CNS to muscles, skin and the outside world).

Carbamazepine (CBZ) induced ataxia in children is a topic of interest as carbamazepine intoxication is becoming more common due to frequent prescription for seizure disorders, chronic pain and mood disorders and it is a challenging task to recognize ataxia in children.

According to the American Association of Poison Control Centre, there were 1880 documented cases of symptomatic carbamazepine toxicity in 2014, of which 37% were intentional overdose, 57% were an unintentional overdose and 4% were an adverse reaction [1,2]. In case of children, acute ataxia may be caused due to excessive drug ingestion, drug intoxication and post-infectious cerebellitis. Symptoms of toxicity are dose-dependent and hence monitoring drug concentration is a useful approach for diagnosis as well as treatment of carbamazepine induced ataxia.

Case Report

A 6 years old male child came to pediatric OPD with complaints of diffuse frontal headache, associated with nausea, not associated with blurring of vision since last one week. The patient had 2 episodes of vomiting in the morning that was non-projectile in nature, contained food and water.

The patient also complained of generalized body weakness and stiffness of body since last one week. Stiffening of body lasted for few seconds which was not associated with drooling of saliva and involuntary passage of urine.

There was no up rolling of eyes. Patient had history of ingestion of 3 tablets of carbamazepine of strength 100mg. The child was drowsy and had experienced 2 episodes of stiffening at the time of admission. The patient had similar complaint of headache 2 months back. There was no history of fever, abdominal pain, burning micturition, constipation, loose stools, cough and cold.

Vital signs upon arrival included a blood pressure of 120/80 mmHg, heart rate of 96 beats per minute, respiratory rate of 22 breaths per minute and temperature of 98.6°F.

Laboratory Investigations

Laboratory analysis was recommended and following results were recorded as mentioned in table 1. Complete blood picture examination was done that revealed low hemoglobin level. Liver function test revealed the parameters within normal range. Upon measuring the serum drug level, it was 15 mg/L which is a toxic concentration of CBZ.

Table 1: Complete Blood Picture

Hb	10.7 gm/dl
PCV	32.8%
WBC	5,600 cells/mm^3 Adequate, no abnormal forms or immature cells seen.
RBC	3.99 millions/mm^3 Predominantly normocytic and normochromic cells with mild hypochromia seen. No nRBC's seen.
PLATELETS	3,70,000-3,80,000 Adequately present.

Table 2: Liver Function Tests

Test	Value
Total bilirubin	0.3 mg/dl
Direct bilirubin	0.1 mg/dl
SGOT	15 IU/L
SGPT	25 IU/L
ALP	218 IU/L
Total proteins	7.6 gm/dl
Albumin	4.2 gm/dl
Serum potassium	3.9 meq/L

Treatment

Ataxia induced by carbamazepine was suspected and hence the drug was stopped and observed for the symptoms as treatment is generally not required in case of acute cerebellar ataxia.

In the 3 days of IPD, his treatment regimen consisted of Inj. Monocef to prevent the bacterial infections, Inj. Acyclovir to treat viral infections, Inj. Pantoprazole to provide relief from acidity related disorders, Inj. Ondansetron to treat nausea & vomiting, Zincovit as nutritional supplement and IV fluid Isolyte-P to maintain fluid and electrolytes balance in the body.

Table 3: Treatment Plan

Drug name	Dose	Dosage form & R.O.A.	Frequency
Monocef	75 mg/kg/day	Inj. / I.V.	BID
Acyclovir	5 mg/kg/day	Inj. / I.V.	BID
Pantop	20 mg	Inj. / I.V.	OD
Zincovit	5 ml	Syrup / PO	OD
Isolyte-P	100 ml	IV fluid / I.V.	8 drops / min
Ondem	4 mg	Inj. / I.V.	OD

Discussion

Carbamazepine is an anti-convulsant and analgesic drug that is a drug of choice for the management of focal epilepsy and is commonly used for various forms of headache. Up to 50% of patients taking carbamazepine present ataxic signs in a dose-dependent manner [3]. Table 4 shows the CBZ concentration and the associated clinical feature of toxicity.

Table 4: CBZ concentration

mg/L	micromol/L	Effect
5-12	20-50	Therapeutic range
10-20	40-85	Nystagmus, Sedation, Ataxia
20-40	85-170	Horizontal and vertical nystagmus, Coma
40	>170	Respiratory depression, Seizures, Cardiac arrythmia

The underlying mechanism involved in CBZ induced ataxia is the susceptibility of cerebellum to intoxication as cerebellum has the major function of maintaining balance and coordinating movement. Among all cerebellar cells, Purkinje neurons are especially susceptible to this form of injury. Cerebellar circuits are also a main target of drug exposure [4]. There are two significant pharmacological parameters to be considered in case of CBZ, first one is the potential for a delayed or prolonged absorption pattern from tissue stores to bloodstream as it has significant protein binding capacity of 70 – 80 % with large volume of distribution and second is the production of a toxic metabolite i.e. Carbamazepine-10,11-epoxide by oxidation via enzyme CYP 3A4 to major extent and CYP 2C8 to a lesser extent. As the absorption of CBZ from the gut is slow and changeable, it takes up to 72 hours for the drug to reach a peak level leading to marked elevation of serum concentration in case of large overdose which has been observed in this case [5].

Management in case of CBZ toxicity depends upon the concentration of drug and type of toxicity. In case of acute toxicity, as in the case of our report, treatment is generally not required and is mainly based on physiological clearance of the drug that ultimately leads to the improvement of ataxic symptom. However, other treatment approaches range from use of activated charcoal to extracorporeal therapy such as hemodialysis or plasmapheresis.

Conclusion

Various drugs like Phenytoin (PHT) and Carbamazepine (CBZ) causes cerebellar ataxia as a part of their side-effect profile which are generally associated with positive outcome and can save a patient's life if a prompt management strategy has been made. Healthcare professionals dealing with such case must go through detailed history, neurological examinations and proper diagnostic tests until the clinical diagnosis has been established.

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Conflict of Interest

Nil

Abbreviations

CNS: Central Nervous System

CBZ: Carbamazepine

OPD: Outpatient department

Hb: Haemoglobin

PCV: Packed Cell Volume

WBC: White Blood Cell

RBC: Red Blood Cell

SGOT: Serum Glutamic-Oxaloacetic Transaminase

SGPT: Serum Glutamic-Pyruvic Transaminase

ALP: Alkaline Phosphatase

IPD: Inpatient department

BID: Twice daily

OD: Once daily

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