Phencyclidine: A Rare Cause of Saccadic Intrusions

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Abstract

Saccadic intrusions such as opsoclonus and ocular flutter are often due to a paraneoplastic or a parainfectious condition. Toxins/drugs may rarely cause them. Herein, we report a rare case of ocular flutter/opsoclonus due to phencyclidine (PCP) toxicity. Our patient is a 21-year-old male who presented with a 3-day history of headache, generalized ill health, and aggressive behavior. He was admitted with reduced level of consciousness following generalized seizures. He had features of sympathetic overactivity with ocular flutter and opsoclonus. Urine toxicology was positive for PCP. Despite supportive care, he succumbed to complications of rhabdomyolysis. Several drugs including cocaine, phenytoin, lithium, and amitriptyline are known to cause ocular flutter/opsoclonus rarely. It is poorly described with PCP. This case highlights PCP as a rare cause of toxin-induced saccadic intrusions and attempts to postulate its pathogenesis.

Moreover, our report is the first case of PCP intoxication in Sri Lanka and one of the few documented reports in the South Asian region. Therefore, it represents a significant worrisome alarm about the spread of this substance in this region.

Keywords: Ocular flutter, opsoclonus, phencyclidine toxicity, saccadic intrusions

Introduction

Saccadic intrusions are involuntary conjugate saccades (fast eye movements) that interrupt fixation.[1] They often reflect dysfunction of the brainstem, cerebellum, superior colliculus, basal ganglia, and/or cerebral hemispheres. Two groups of saccadic intrusions have been identified by the presence or absence of an intersaccadic interval, which is a period that usually lasts 180–200 ms between sequential saccades.[1] Saccadic intrusions without a normal intersaccadic interval include ocular flutter and opsoclonus. Ocular flutter consists of back-to-back horizontal conjugate saccades without an intersaccadic interval. Opsoclonus is similar to ocular flutter; however, it is multidirectional.[2,3] Ocular flutter/opsoclonus, in adults, may be a manifestation of a paraneoplastic or parainfectious condition though, uncommonly, it may be caused by a structural lesion (e.g., pontine hemorrhage or multiple sclerosis) or drug intoxication.[2,4]

Phencyclidine (PCP) is a synthetic dissociative drug originally developed as a general anesthetic. PCP causes feelings of detachment from the environment and self. It was used as a general anesthetic agent in 1926.[5] However, PCP has emerged as a substance of abuse and is currently a controlled substance. There were 75,538 emergency department visits in 2011 in the United States due to PCP toxicity. This was up to 400% from 2005 (14,825).[6] PCP toxicity has been poorly reported in the South Asian region.

Herein, we report a rare case of a young patient presenting with ocular flutter and opsoclonus due to PCP toxicity.

Case Report

A 21-year-old male presented with a 3-day history of intermittent headache, generalized ill health, and altered behavior (aggressiveness and agitation). The patient was not on prior medication including neuroleptics. Before admission, his level of consciousness deteriorated and he developed generalized seizures. His Glasgow Coma Scale was 10/15 on admission. He had diaphoresis, hypersalivation, and at times ocular flutter and at times opsoclonus [Video 1] with a tachycardia (140–160 beats/min), increased blood pressure (BP 170/100 mmHg), and an elevated body temperature of 40°C. There was no demonstrable rigidity arguing against a diagnosis of neuroleptic malignant syndrome.[7]

His liver enzymes were deranged (aspartate aminotransferase [AST] 350 international units per liter [IU/l] and alanine aminotransferase [ALT] 153 IU/l), and creatine kinase (CK) was 40,000 μg/l suggestive of rhabdomyolysis. Noncontrast computed tomography brain was normal. Electroencephalogram demonstrated generalized delta activity, suggestive of encephalopathy/generalized cerebral dysfunction. Septic screen was negative and cerebrospinal fluid analysis was normal. Urine for toxicological screening was positive for PCP.

He was started on empirical antibiotics and supportive care with fluid resuscitation and measures to reduce the hyperpyrexia. Therapeutic strategies such as urinary alkalization and mannitol were also commenced to manage the rhabdomyolysis.

Despite the treatment, our patient rapidly deteriorated. His CK levels increased to 152,000 μg/l within 24 h and his renal functions declined rapidly. Unfortunately, the patient succumbed to acute renal failure secondary to rhabdomyolysis.

Discussion

Ocular flutter/opsoclonus is a disorder of ocular motility seen during fixation, smooth pursuit, convergence, and during sleep.[2] This needs to be distinguished from nystagmus. A slow eye movement takes the eye off the target in nystagmus while a saccade takes the eye off the target in ocular flutter and opsoclonus.[2]

Ocular flutter/opsoclonus is rarely caused by drugs and toxins. This association has been reported in drugs/toxins such as cocaine, phenytoin, lithium, amitriptyline, and more recently venlafaxine.[2,8,9]

PCP intoxication shares many features with overdoses of cocaine, amphetamines, anticholinergic agents, hallucinogens, and withdrawal from benzodiazepines. It is soluble in lipid, water, and alcohol. Thus, the volume of distribution in the body is large (6.2 L/kg).[5] Therefore, the effects vary depending on several factors including body habitus and alcohol ingestion.[5] In an averagely built person, sedation and loss of inhibition along with

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Submission: 23.04.2018 **Revision:** 12.07.2018
Acceptance: 13.07.2018 **Published:** 25.10.2019

DOI: 10.4103/aian.AIAN_174_18

various other manifestations such as dysarthria, aggressive behavior, staring episodes, nystagmus, ataxia, hyperthermia rhabdomyolysis, and seizures tend to occur with ingestions of 1–5 mg.[5] Doses of 5–10 mg may induce acute schizophrenia, psychosis, visual and auditory hallucinations, and catatonia.[5] Doses more than 10 mg lead to coma and death.[5] Most of these features were present in our patient who rapidly progressed to coma and death, suggesting that he would have taken a large amount of the drug. Horizontal, vertical, or rotatory nystagmus is often reported with PCP toxicity;[5] however, ocular flutter/opsoclonus have been poorly described.

PCP increases glutamate transmission, inhibits gamma-aminobutyric acid (GABA)-ergic output, decreases dopamine and norepinephrine uptake, and increases the dopamine and norepinephrine levels by stimulating the enzyme tyrosine hydroxylase.[5] Two hypotheses have been proposed for the pathogenesis of ocular flutter and opsoclonus. The first suggests a transient disinhibition of omnipause neurons in the nucleus raphe interpositus (RIP) of caudal pons, which normally have an inhibitory influence on excitation burst neurons in the paramedian pontine reticular formation.[2,10] The second suggests disinhibition of cerebellar fastigial nucleus (FN) located in the anterior vermis, which plays an essential role in saccadic and smooth pursuit eye movements.[2,11] Both the RIP and FN are mainly glutamatergic and GABAergic and therefore are possibly disinhibited by the effects of high doses of PCP on glutamate and GABA receptors, which would have resulted in this patient's ocular flutter and opsoclonus.

The confirmative test for suspected PCP toxicity is a qualitative chromatographic or immunologic urine drug screen, since 9% of the active drug is excreted directly by the kidneys.[5] Thus, PCP toxicity was confirmed in our patient.

Conclusion

PCP is a paradoxical drug that produces central nervous system depression and peripheral and central nervous system stimulation. Due to its euphoric effects, we are beginning to note PCP's street popularity as a recreational drug, making it important for medical professionals to be aware of the clinical features and complications of its toxicity. This case highlights a rare cause of toxic ocular flutter/opsoclonus and attempts to postulate its pathogenesis. Moreover, our report is the first case of PCP intoxication in Sri Lanka and one of the few documented reports in the South Asian region. For this reason, this case represents a significant worrisome alarm about the spread of this substance in this region. Clinicians thus should be aware of its clinical presentation to be better prepared for treating such patients.

Acknowledgments

We would like to acknowledge the patient, who was kind enough to give her consent to publish this material.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's guardian has given consent for patient's images and other clinical information to be reported in the journal. The patient's guardian understands that the name and initials of the patient will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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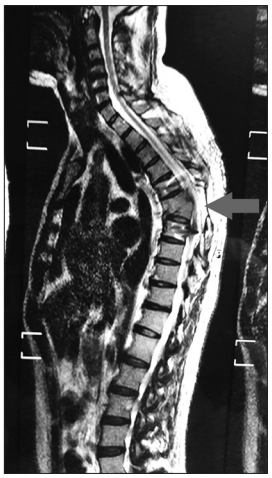
Supplementary Data



Supplementary Figure 1: T2-weighted magnetic resonance imaging sagittal view showing collapse of D6–D7 vertebrae with partial fusion of posterior element of vertebral bodies along with spinal cord atrophy (arrow)

Supplementary Figure 2: T2-weighted magnetic resonance imaging axial view showing collapse of D6–D7 vertebrae with partial fusion of posterior element of vertebral bodies along with spinal cord atrophy (arrow)