ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 08 | August - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CHRONIC PHENYTOIN TOXICITY INDUCED ORGANICITY AND VITAMIN D DEFICIENCY: A CASE REPORT

Toxicology

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ABSTRACT

Phenytoin-induced organicity along with vitamin D deficiency is a rare adverse drug reaction that is observed upon long-term usage of phenytoin. We present a case of a 35-year-old female who presented with seizures, nausea, vomiting, irritability, mild gingival hypertrophy, and altered sensorium. Based on her clinical presentation a provisional diagnosis of meningoencephalitis was made. However, after further evaluation, it was observed that the patient has epilepsy and had been taking antiepileptics (phenytoin 100 mg/BD) for the previous 30 years, and based on her condition she was diagnosed with chronic phenytoin toxicity. The patient's condition improved after phenytoin withdrawal but, she remained irritable, so she was referred to a psychiatrist, and they determined that she had developed organicity and treated her accordingly. After 3 weeks of phenytoin withdrawal, the complete recovery of the patient was observed. We decided to report this case because of the uncommon presentation of this rare intoxication.

KEYWORDS

Phenytoin Toxicity, Organicity, Vitamin D deficiency, mild gingival hypertrophy

INTRODUCTION

Phenytoin is a commonly used antiepileptic drug for a range of seizure disorders, except for absence seizure[1]. Neurotoxic effects may differ depending on concentration[2]. Long-term dose-dependent neurological adverse reactions of phenytoin treatment include cerebellar atrophy, cerebral atrophy, and brain stem atrophy[3]. The phrase "organicity" describes hallucinations or delusions that develop in a patient who has recently experienced a brain function malfunction. Toxic metabolic disorders, drug overdose, intoxication, and vitamin deficiency, which influence a variety of physiological systems, could be the reason for this abnormality[4]. Here we report a case of chronic phenytoin toxicity leading to organicity with vitamin D deficiency.

CASE REPORT

A 35-year-old female patient was presented with chief complaints of seizure activity of 2 episodes, loss of appetite, and 4 episodes of non-projectile vomiting, with a previous medical history of generalized tonic-clonic seizures and had been on oral antiepileptics- phenytoin (100mg BD) for the past 30 years. She was admitted to the hospital two months ago with the chief complaints of seizures, fever, loss of appetite, vomiting, difficulty walking, and they mentioned that she had not taken phenytoin for four days before symptoms appeared, symptomatic treatment was given and levetiracetam (500mg BD) was started to reduce the seizure activity, with this treatment patient was seizure-free, so she continued the medication.

On examination, the patient was found to be moderately built and nourished, consciously disoriented, and has altered sensorium for the past two days with drowsiness and irrelevant talk [Figure 1].

Figure1- Patient presenting with mild gingival hypertrophy, irritability, and disorientation

So, the physician suspected her of meningoencephalitis and advised her to test ADA-CSF levels, CT scan, MRI scan, and biochemical parameters. Her ADA-CSF levels were found to be within the normal range of 3 U/L, CT scan and MRI scan were also normal, and abnormalities observed in biochemical parameters are mentioned in [Table 1]. Based on the patient clinical presentations, and past medication history she was diagnosed with chronic phenytoin toxicity.

Table 1- Abnormalities observed in her biochemical parameters

Test	Observed range	Normal range
Vitamin B12	>2000 pg/ml	190-950 pg/ml
25-OH vitamin D (Total)	13.91 ng/ml	Deficiency- < 20 ng/ml
Calcium	7.23 mg/dl	8.8-10.6 mg/dl
Haemoglobin A1c levels	5.2%	4 -5.6%
Folate	2.5 ng/ml	2.7-17 ng/ml
Serum phenytoin level	>> 40 µg/ml	10-20 µg/ml

Her treatment procedure was started with acyclovir and ceftriaxone as she was suspected of meningoencephalitis. As her ADA-CSF levels reports are normal, acyclovir and ceftriaxone doses were reduced and continued until her serum phenytoin reports are evaluated, Phenytoin dose was reduced to 100mg OD and continued for one 1week and discontinued, and symptomatic treatment was started as mentioned in below [Table 2]. After phenytoin withdrawal, her vomiting stopped, but the patient was still drowsy, disoriented, and irritated for which she was made an appointment with the psychiatrist and a diagnosis was made that she was suffering from organicity, as there are no signs and symptoms of psychiatric illness so, she was treated accordingly with counseling therapy. After 3 weeks of discharge, the patient recovered from the symptoms of drowsiness, and irritability, and the patient was found to be oriented.

Table 2-Table showing the drugs used during hospital admission

Drugs prescribed	Generic name	Dose	Frequency	Route of administration
Inj. Monocef	Ceftriaxone	2gm 1gm	BD BD	Intravenous
Inj. Acyclovir	Acyclovir	500mg 500mg	BD OD	Intravenous
Tab. Levipil	Levetiracetam	500mg	BD	Oral
Tab. Eptoin	Phenytoin	100mg	OD	Oral
Tab. Folvite	Folic Acid	5mg	OD	Oral
Inj. Zofer	Ondansetron	4mg	BD	Intravenous
Human insulin Regular	Human insulin Regular	According to GRBS		Sub Cutaneous
Inj. Pan	Pantoprazole	40mg	OD	Intravenous
Tab. Shelcal-500	Calcium and vitamin D3	500mg and 250 IU	OD	Oral

DISCUSSION

Phenytoin is the first-line medicine for treating GTCS, and it is the

most widely prescribed prescription. The severity of phenytoin toxicity is determined by the drug's mode of administration, duration, and exposure. If serum phenytoin levels are between 10 and 40 µg/ml, symptoms such as nystagmus, nausea, vomiting, gingival hypertrophy, ataxia, and slurred speech are observed; if serum phenytoin levels are > 40 µg/ml, symptoms such as lethargy, disorientation, depression, cognitive impairment changes, confusion, and coma are observed. Phenytoin has effects on intellectual functions and behavioural changes during long-term use[5,6].

There have been previous reports of phenytoin adverse effects manifesting in a variety of psychiatric diseases. Organicity (organic brain damage) induced by phenytoin intoxication, has only been described in a few cases. The American Psychiatric Association defines organic brain syndrome as a disturbance of orientation, memory, cognition, judgment, and affect caused by diffuse brain tissue deterioration. The source of the disorientation is sometimes obvious, such as in alcohol- or drug-intoxicated patients, the head-injured patient[7,8]. Organic brain damage is also commonly caused by vitamin b12, folate, and vitamin D deficiencies, which can exacerbate depressive symptoms. However, once the patient begins to take supplements, the condition improves. Most commonly used AEDs are proven to lower serum folate and vitamin B12 levels, and also lower vitamin D levels, which can cause depression, panic disorder, and phobias[9]. In our case, the patient had been on phenytoin for a long time, which resulted in high serum phenytoin levels, which led to vitamin D and folate deficiency. Although organic brain damage with phenytoin overdose is uncommon, vitamin D and folate insufficiency are major determinants of organic brain damage. Because organicity isn't associated with any neurological symptoms, the patient has not treated with antipsychotics, which could exacerbate the problem, and instead was given counselling. Organicity is assumed to be caused by phenytoin toxicity, as symptoms subsided when phenytoin levels decreased.

CONCLUSION

In this case report, we observed how long-term phenytoin use causes vitamin B12, folate, and vitamin D deficiencies, and how these deficiencies hasten the organic brain damage (organicity) caused by phenytoin toxicity. This case report does not imply that long-term use of phenytoin will result in toxicity and organicity, but the appearance of such conditions must be handled with appropriate management therapy, and withdrawal of phenytoin at the appropriate time may help to improve the patient's quality of life.

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