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A case report on phenytoin toxicity

KEYWORDS

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A 43 year old female presented to VSGH with complain of giddiness,difficulty in maintaining gait and irrelevant talking since 10 days.Patient was a known case of epilepsy(GTCS) and on regular treatment as per relatives. Patient had a history of left cerebral ischaemia sometimes back but she was not on any anti platelet drug for the same.On examination temperature was normal.Pulse was 98/min BP was 150/84 mm Hg.Spot RBS was 260 mg%. Detailed examination of respiratory system and cardiovascular system did not yield any useful information.

Detailed CNS examination carried out by neurologist. Patient was conscious,oriented and following verbal command . Speech was otherwise normal except for mild slurring.Bilaterally pupils were reacting normally to light.

Power	Left upper limb	Left lower limb	Right upper limb	Right lower limb
Proximal	5/5	5/5	4/5	4-/5
Distal	5/5	5/5	4/5	4-/5

Tone was normal in all 4 limbs.

Deep tendon reflexes were as follows:

	Biceps	Triceps	Supinator	Knee	Ankle
Left	++	++	++	++	++
Right	++	++	++	+++	+++

Plantars were flexor both sides.

Cerebellar tests were performed .

Finger nose test showed over shooting bilaterally.

Knee-heel test was also abnormal bilaterally.

Patient had vertical nystagmus.

During the examination simultaneous history taking continued and patient's relatives were asked about drug details of antiepileptics.They showed the bottle of eptoin(100 mg) and said again that patient is on regular treatment.This time it is asked that what do they mean by regular treatment?Relative's said that patient is taking 3 tablets(300mg) thrice daily.

Relatives were asked to show the prescription which has mentioned dose as 0-0-3(3 tablets at bed time)so,patient was taking higher than required dose and was not attending clinic for refill prescription.So,from the history and clinical examination provisional diagnosis of eptoin toxicity made and patient advised to undergo further investigations along with routine investigations such as serum eptoin level,CSF examination and MRI brain.Patient is asked to withheld eptoin with immediate effect and to resume therapy for stroke(antiplatelets and statin)which was prescribed earlier but not taken by patient.Patient is also prescribed valproate as an antiepileptic in appropriate dose and repeatedly explained the dose of the same by doctor or nursing staff.

Hb 12.7 gm% Bilirubin-0.5 mg%

Total WBC count 16000/cumm Sodium-140 mmol/L

Platelet=2.46lacs/cumm Potasium-3.4mmol/L

Creatinine=0.68mg% Calcium-9 mg%(ioinic-1.12mmol/L)

Phenytoin level>40 mcg/ml(normal therapeutic level-10-20mcg/ml)

MRI brain and CSF were normal for acute changes.

So,investigations confirmed the diagnosis of phenytoin toxicity and further recovery of patient was uneventful.

Patient was discharged after few days with improvement in clinical parameters.

Discussion:

Phenytoin is a commonly prescribed antiepileptic drug for the management of GTCS and prophylactically after neurosurgery and intraparenchymal haemorrhage.Apart from its use as an anticonvulsant it is also being used as anti arrhythmic agent,in treatment digoxin toxicity and trigeminal neuralgia(not the drug of choice). It is included in WHO's list of list of essential medicine.Due to its saturation pharmacokinetics(zero order kinetics)it has a very narrow therapeutic range and carries a special risk of dose related toxicity. Various large scale studies are conducted in India and abroad have showed following as the causes for phenytoin toxicity.

Causes:

- Excessive self medication
- Misunderstanding of prescription order(as seen in this case)
- Probable drug interactions

Common symptoms include unsteady gait,dizziness,vertigo,nausea/vomiting,general weakness,drowsiness,slurring of speech.vertical nystagmus,diplopia,sedation can also occur.It can lead to

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hyperglycemia.

Eptoin may accumulate in cerebral and cerebellar cortex over the period of time which cause atrophy.The degree of cortical atrophy caused by phenytoin depends on the duration and not on the dose.

Side effects seen on therapeutic level includes gum hypertrophy,bleeding upon probing the gums,increased gingival exudates,haematological effects such as megaloblastic anaemia(all these can be prevented by giving simultaneous high doses of folic acid).

It is also associated with increased risk of suicide,hypertrichosis,purple glove syndrome,hirsuitism and coarsening of facial features.Phenytoin can also cause drug induced lupus.Phenytoin therapy is also linked to life threatening skin reaction such as steven Johnson syndrome and toxic epidermal necrolysis(TEN).These conditions are linked with HLA B1502.These allele is almost exlusively seen in Asians including Indians.Phenytoin is also associated with induction of reversible Ig A deficiency.

Drug interactions:
Phenytoin is an inducer of CYP3A4 and CYP2C19 families of enzmes which responsible for hepatic degradation of various drugs.Warfarin and trimethoprim increase the phenytoin level by inhibiting its metabolism.

Conclusion:
Acute phenytoin toxicity is somewhat under diagnosed problem which can be easily diagnosed with classical clinical features and can be confirmed by serum phenytoin level and with temporary withdrawl of drug and supportive care can be managed well and causes no mortality and has very good outcome.however unsteady gait increases the chances of fall.

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