

Phenytoin Toxic Encephalopathy

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Phenytoin is a commonly used anticonvulsant. The availability of highly concentrated suspensions of phenytoin and the low toxicity threshold frequently results in phenytoin toxicity. Toxic encephalopathy is a less frequent side effect(1,2) and may often mimic a degenerative neurological disease(3). We report this unusual presentation of chronic phenytoin intoxication.

Case Report

A 2-year-old girl, weighing 10 kg, presented to this hospital with a 3-day-history of gradually progressive inability to walk, stand or sit up and deterioration in sensorium. She was receiving one teaspoonful of phenytoin suspension daily (5 ml = 125 mg, i.e., 12.5 mg/kg/day) for generalized tonic clonic seizures since the last 16 months. The seizures had not recurred and the child was apparently well till 3 days prior to admission. She had a normal neonatal and development history and no family history of seizures.

She was admitted in a local hospital

for 3 days, where anti-tuberculous drugs (INH, rifampicin, streptomycin) were empirically started inspite of a normal CSF examination. The patient's symptoms worsened and she was referred to us for further management.

At admission, the pulse rate was 96/min with a regular rhythm, respiratory rate was 26/min, blood pressure was 100/40 mm Hg and she was afebrile. There was no pallor, edema, icterus, gingival hypertrophy or significant lymphadenopathy. The liver was palpable 1 cm below the costal margin. The patient was disoriented and stuporous; she was able to localise deep pain. The extraocular movements were absent and the pupils were equal and reacting to light. There was no nystagmus, and fundus examination was normal. Motor system examination revealed generalized hypotonia, brisk tendon reflexes and Grade 4 power in all muscles. Plantars were bilaterally extensor and there were no signs of meningeal irritation.

A clinical diagnosis of phenytoin toxic encephalopathy was considered. The levels of phenytoin were 40.6 mg/ml (upper limit of normal 15 mg/ml). The level of serum creatinine were 0.63 mg/dl, SGOT 49 IU/l, SGPT 37 IU/l and the prothrombin time was 14 seconds. The electrocardiogram was normal and the CSF examination showed 9 lymphocytes/cu mm, protein 23 mg/dl and sugar 35 mg/dl. The electroencephalogram showed bilateral diffuse slowing of background activity.

She was treated with intravenous fluids over the next 48 hours. The child recovered and was recognizing her parents at 5 days. During recovery she became ataxic which recovered completely at 10 days.

On follow-up at 2 months, she was normal and on phenobarbitone 4-5 mg/kg/day as a single night dose.

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Discussion

Acute phenytoin intoxication generally causes cerebellar or vestibular symptoms(4,5); occasionally cerebellar atrophy may occur(6). In chronic intoxication there may be more diffuse neurologic dysfunction(4). The classical signs of ataxia and nystagmus may be difficult to identify in young children, and a diffuse slowing of electroencephalogram(7), inability to walk, marked hypotonia, altered sensorium and normal or brisk reflexes have been described in phenytoin intoxication(3). Apart from a hypersensitivity angitis presenting as a pseudo-degenerative disease(2,3), phenytoin encephalopathy, as described above, may occasionally occur(1).

The serum phenytoin levels may not accurately reflect total phenytoin levels since there is a high degree of protein and tissue binding. Levels less than 15 mg/ml are usually not associated with side effects(1). Diuresis, dialysis (hemo or peritoneal) and exchange transfusions are not useful in reversing the symptoms of phenytoin toxicity. The clinical management includes stoppage of the drug, resuscitation, oral activated charcoal, catharsis, intensive care and at discharge, psychiatric counselling and restarting properly dosed anticonvulsants(7,8).

Addition of drugs to phenytoin therapy must be made with knowledge of potential drug interactions. INH is a powerful inhibitor of phenytoin metabolism(9,10). It is not clear whether a 3-day therapy with INH in this case led to increased symptoms of toxicity.

This report highlights the importance of unusual presentations of chronic phenytoin intoxication and drug interactions especially while on multitherapy regimens (e.g., tubercular meningitis, uncontrolled seizures). There is a need for small

strength phenytoin tablets to avoid the available highly concentrated suspensions of phenytoin. These suspensions require to be well shaken and dispensed using standard measures.

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