Transient hemiparesis—a rare complication of phenytoin toxicity

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Summary

A 31-year-old man on phenytoin for post-traumatic epilepsy developed transient hemiparesis contralateral to the injury. This appeared to have been precipitated by phenytoin intoxication. A possible mechanism for focal neurological deficit occurring in brain-damaged patients on phenytoin is discussed.

KEY WORDS: epilepsy, phenytoin, hemiparesis.

Introduction

The common neurological manifestations of phenytoin toxicity are nystagmus, ataxia and dysarthria. Rarely, phenytoin toxicity may result in mental changes and focal neurological signs (Levy and Fenichel, 1965) such as unilateral choreoathetosis (Reynolds, 1975) hemihyperaesthesia (Reynolds and Travers, 1974) and progressive hemiparesis (Morris, Fischer and Bergin, 1956). These focal signs apparently occur more often in patients with an underlying brain damage and the mechanisms remain unknown.

A patient is reported who was on chronic phenytoin therapy for post-traumatic epilepsy and in whom phenytoin toxicity induced transient hemiparesis contralateral to the brain injury.

Case report

A 31-year-old man was admitted to hospital with ataxia, headache and mental confusion of 4 days duration. Five years previously, he had sustained damage to the left temporo-parietal area and subsequently developed post-traumatic focal epilepsy documented on electroencephalogram (EEG). This had been controlled on phenytoin, 300 mg daily, for the past 5 years and no side effects or toxic effects were recorded in his out-patient notes.

Seven days before admission, during a confusional episode, he ingested accidentally a large number of phenytoin tablets. Three days later, he became progressively weak and unsteady and required hospitalisation. There was no history of loss of consciousness or a focal seizure before admission.

On examination, he was drowsy, had coarse horizontal and vertical nystagmus, titubation of the head and trunk, slurred speech and marked truncal ataxia. There was no papilloedema. He had a dense right-sided hemiparesis and upper motor neurone facial palsy and increased tendon jerks and positive Babinski response on that side. Hoffmann's reflex was positive on the right side. Abdominal reflexes were absent bilaterally. There was no sensory loss and no signs of meningeal irritation.

General examination was unremarkable and revealed a blood pressure of 110/70 mmHg. Laboratory investigations including full blood count, blood glucose, serum biochemical estimations, liver enzymes, syphilis serology, coagulation profile, antinuclear antibodies, thyroid studies, and erythrocyte sedimentation rate were normal or negative. Chest and skull roentgenograms were unremarkable. Serum alcohol levels were in normal range. Computed tomographic (CT) scan of the brain, including a contrast study was normal. Serum phenytoin level was 134 $\mu\text{mol/litre}$ (therapeutic range 40–70 $\mu\text{mol/litre}$).

Phenytoin was discontinued for 10 days and the patient's condition gradually improved; the confusion cleared, the hemiparesis and cerebellar signs receded and serum phenytoin levels dropped to 76 $\mu\text{mol/litre}$. Treatment with phenytoin was reinstated at 200 mg daily and serum levels maintained in the therapeutic range (40–60 $\mu\text{mol/litre}$). The patient was discharged 3 weeks after admission with no neurological deficit.

Discussion

Since the introduction of phenytoin as a major anticonvulsant agent in 1938 (Meritt and Putnam, 1938), only few reports have appeared in the literature describing transient hemiparesis during phenytoin toxicity (Morris *et al.*, 1956; Findler and Lavy, 1979). In those cases, as in our case, the patients had suffered some form of brain damage before phenytoin administration, and the hemiparesis was contra-

lateral to the injury. In all cases, discontinuation of phenytoin resulted in gradual resolution of the focal neurological deficits.

Our patient was well-controlled and free of toxic effects of phenytoin for 5 years before admission. It is therefore reasonable to assume that the ingestion of high dosage of phenytoin precipitated the development of the hemiparesis and the cerebellar signs, since there was no evidence for a structural brain lesion and no evidence for a post-ictal phenomenon.

The pathophysiology of the transient focal motor deficit in brain-damaged patients on phenytoin is not well understood. It is known that the small inhibitory interneurons utilising gamma-aminobutyric acid (GABA) as a transmitter are particularly sensitive to anoxic and metabolic damage, both of which are operative in central nervous system trauma. Selective loss of these neurones would be expected to result in compensatory supersensitivity of GABA-receptors in the damaged area. Phenytoin is known to act, in part at least, by facilitating GABA-ergic transmission (Lust, Goldberg and Passonneau, 1975). Consequently, administration of phenytoin in high dosage to a patient with focal cerebral damage could result in a selective depression of those neurones postsynap-

tic to the supersensitive GABA receptors in the damaged area.

Whatever the precise mechanism may be, the development of focal neurological deficit in brain-damaged patients on phenytoin may pose diagnostic problems. It is suggested that phenytoin be stopped and serum levels measured in such patients before other more invasive procedures are adopted.

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