CEREBELLAR ATROPHY FOLLOWING ACUTE PHENYOIN INTOXICATION

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SUMMARY
A 25-year-old woman was admitted to our hospital with encephalopathy and clinical signs of cerebellar dysfunction. She had recently received an overdose of phenytoin. On admission, plasma phenytoin level was high (50 µg/ml, therapeutic range 10-20 µg/ml). Magnetic resonance imaging showed no signs of cerebellar atrophy. The patient’s neurological condition improved rapidly after withdrawal of phenytoin. Eight months later, the neurological examination disclosed minimal cerebellar disorders and magnetic resonance imaging showed cerebellar atrophy. Cerebellar atrophy due to acute phenytoin intoxication is very unusual but few cases have been reported. The present clinical and radiological findings suggest that short-term phenytoin overdose alone may cause cerebellar atrophy.

Key words: cerebellar atrophy, phenytoin, intoxication.

INTRODUCTION
Acute intoxication of phenytoin leads to cerebellar symptoms including nystagmus, diplopia, dysarthria and ataxia [1]. The clinical signs of cerebellar dysfunction is usually disappear when reduction or withdrawal of the drug [2]. Occasionally, irreversible cerebellar signs due to cerebellar atrophy has been reported for the patients who have been treated with phenytoin chronically [3]. Several case reports suggest that short time intoxication of phenytoin can lead to cerebellar atrophy [4].

We describe here a patient with epilepsy who has developed encephalopathy and clinical signs of cerebellar dysfunction associated with progressive cerebellar atrophy after acute phenytoin intoxication.

CASE REPORT
A 25-year-old woman was admitted to our hospital with confusion, urinary incontinence and severe ataxia. She was unable to sit or stand. She had tonic-clonic seizures for 20 years. She had been treated with phenytoin 300 mg/day for 10 years. Twenty-five days before admission, she has started to take phenytoin because of increased frequency seizure. As a result of, she was receiving
phenytoin 600 mg/day on admission. At this time neurological examination showed clouding of consciousness and cerebellar dysfunction including ataxia in trunk and all extremities, nystagmus, diplopia, dysarthria, bilateral dysmetria, dysdiadochokinesia, intention tremor and titubation of head. Plasma phenytoin level was 50 µg/ml (therapeutic range, 10-20 µg/ml). Whole blood count, serum electrolytes, renal and liver function tests, serum glucose level, serum folate and B₁₂ levels were normal. Electrocardiography, cerebro spinal fluid analysis and magnetic resonance (MR) were normal (figure 1). Electroencephalography (EEG) showed bilateral theta and delta waves. The dose of phenytoin was reduced rapidly, and carbamazepin 600 mg/day was started. Phenytoin treatment entirely was withdrawn within a week. The patient’s neurological condition was improved rapidly after withdrawal of phenytoin. When the patient discharge from the hospital 20 days after the admission, she had dysarthria, bilateral dysmetria, dysdiadochokinesia, intention tremor, ataxic gait without support. Eight months later, clinical assessment showed near-normal cognitive function. The clinical findings of cerebellar dysfunction (dysarthria, bilateral dysmetria, dysdiadochokinesia, intention tremor, ataxic gait) improved markedly. At this time, MR revealed hemispheral and vermal atrophy and, enlargement of superior cerebellar cisterna, fourth ventricle, cisterna magna (figure 2a). 15 months later, neurologic examination findings was not change, but degree of cerebellar atrophy was more severe (figure 2b). In the last examination (at 28 months after the admission), severity of clinical findings was still unchanged, but cerebellar atrophy on MR was more pronounced than previous one. (figures 2c, 2d).

DISCUSSION

Cerebellar dysfunction is a common manifestation of acute phenytoin intoxication. Clinical findings are usually reversible with discontinuation of the drug. The patients recover without neurologic sequelae [10]. Cerebellar atrophy due to acute phenytoin intoxication is very unusual, but a few case have been reported [1, 2, 6, 7, 9].

The cause of the cerebellar atrophy in patients who treated with phenytoin is controversial. Some authors claimed that hypoxia resulting from epileptic seizures is mainly responsible for the cerebellar degeneration [3, 5, 11]. However, cerebellar atrophy developed in patients who suffered to phenytoin intoxication and they have not have any epileptic seizure [1, 2]. In 1958, Utterback et al. reported degeneration of purkinje cells of cerebellum following phenytoin intoxication [11]. Masur et al. [1] the first time showed cerebellar atrophy on MR in a case who had a single intoxication.

Pathological lesions and anatomical structures in posterior fossa were easily determined by MR today. We determined cerebellar atrophy on MR for a long-time. But, she had not showed cerebellar findings previously and had normal MR on admission. After phenytoin was discontinued, clinical findings of cerebellar dysfunction is regressed but cerebellar atrophy on MR was progressed. On 28 months after the admission, the patient had slight clinical findings of cerebellar dysfunction and pronounced cerebellar atrophy on MR. The present clinical and radiological findings suggest that short-time phenytoin overdosage alone may cause cerebellar atrophy.
FIG. 2. — a and b: T1-weighted sagittal images showing vermian atrophy and enlargement of superior cerebellar cisterna, fourth ventricle and cisterna magna. Fig. b shows more severe cerebellar atrophy than figure a.

c and d: T1-weighted sagittal image (c) and T1-weighted coronal image (d) showing more pronounced cerebellar atrophy compared with figures a and b.

FIG. 2. — a et b : IRM pondérée en T1 montrant une atrophie vermienne, un élargissement de la citerne cérébelleuse supérieure, du quatrième ventricule, et de la grande citerne. L’atrophie est plus sévère sur la figure a que la figure b.

c et d : IRM coupe sagittale pondérée en T1 (c) et coupe coronale pondérée en T1 (d) montrant une atrophie cérébelleuse plus prononcée par rapport aux figures 2a et 2b.
REFERENCES


