CEREBELLAR ATROPHY FOLLOWING ACUTE PHENYTOIN INTOXICATION

Z. ALIOĞLU (1), A. SARI (2), S.K. VELIOĞLU (1), M. ÖZMENOĞLU (1)
(1) Department of Neurology, (2) Department of Radiology, Karadeniz Technical University Medical School, Trabzon, Turkey.

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 mg/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].

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 overdosage of phenytoin because of increased frequency seizure. As a result of, she was receiving...
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phenytoin 600 mg/day on admission. At this time neurologica
l examination showed clouding of con-
ciousness and cerebellar dysfunction including ataxia in trunk and all extremities, nystagmus, diplopia, dys-
arthria, bilateral dysmetria, dysdiadochokinesia, in-
tention 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. Electrocar-
diography, cerebro spinal fluid analysis and magne-
tic resonance (MR) were normal (figure 1).
Electroencephalography (EEG) showed bilateral
theta and delta waves. The dose of phenytoin was re-
duced 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, bi-
lateral dysmetria, dysdiadochokinesia, intention tre-
mor, ataxic gait without support. Eight months later,
clinical assessment showed near-normal cognitive
function. The clinical findings of cerebellar dysfunc-
tion (dysarthria, bilateral dysmetria, dysdiadochoki-
nesia, intention tremor, ataxic gait) improved
markedly. At this time, MR revealed hemispheral and
vermal atrophy and, enlargement of superior cer-
bellar cisterna, fourth ventricule, 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 exa-
mination (at 28 months after the admission), severity
of clinical findings was still unchanged, but cerebel-
lar atrophy on MR was more pronounced than pre-
vvious 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 in-
toxication 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 in-
toxication and they have not have any epileptic sei-
zure [1, 2]. In 1958, Utterback et al. reported
degeneration of purkinje cells of cerebellum fol-
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 in a wo-
men patient who exposed short-time phenytoin
overdosage. The patient have been used phenytoin
for a long-time. But, she had not showed cerebellar
findings previously and had normal MR on admis-
sion. After phenytoin was discontinued, clinical fin-
dings 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 pro-
nounced cerebellar atrophy on MR. The present cli-
nical and radiological findings suggest that short-
time phenytoin overdosage alone may cause cerebel-
lar 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.
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REFERENCES


