

페니토인 사용에 따른 소뇌 위축 사례

A case of phenytoin-induced cerebellar atrophy

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Abstract

Cerebellar atrophy was found that a patient was taking oral phenytoin for 3 years. 53 years old female patient with General tonic clonic(GTC) type seizure was prescribed phenytoin. In the process, she developed ataxic gait, dysarthria. Brain magnetic resonance imaging(MRI) finding was revealed differential diagnosis cerebellar atrophy. She was prescribed epileptol instead of phenytoin. But leukopenia, thrombocytopenia occurred. As a result, phenytoin restarted. Development of medical state decreased abuse of anticonvulsants. Considering various convulsive disorders, we must give attention to using anticonvulsants.

1. Introduction

Cerebellar atrophy may occur in phenytoin-exposed patients. Cerebellar degeneration after chronic phenytoin therapy was reported by McLain et al. in 1980[1]. Cerebellar atrophy occurring in patients with chronic epilepsy is considered either to be a sequel of cumulative seizure-mediated cell loss or a side effect of phenytoin treatment but there is little neuropathological data regarding the distribution of this cerebellar damage[2]. Del Negro A et al. reported that although there is a possibility that repeated seizures contribute to cerebellar damage, long term exposure to phenytoin, particularly in high doses and toxic serum levels, cause cerebellar atrophy[3]. Cerebellar atrophy was found that a patient was taking oral phenytoin for 3 years. The author reported and reviewed literature about cerebellar atrophy related to phenytoin. To our knowledge, there have been few reported cases similar to this patient in Korea.

2. Case Report

The author reported a case of a patient that developed gait disturbance and dysarthria while on oral phenytoin. This 53 years old female patient have been GTC type seizure and medicated phenytoin for 3 years. She admitted to our hospital for gait disturbance, dysarthria that started on April, 2007. She medicated

phenytoin 100 mg 3 times daily and its dosage increased 150 mg 3 times daily after GTC tye seizure with loss of conscious on Feb., 2008. Brain CT scanning was none specific findings. She admitted to complain general weakness, dizziness, vomiting, asphyxia and dysphagia. the patient reported Glasgow coma scale 14, pupil size 2.0/2.0 mm, generalized motor weakness grade 4. Brain MRI studies at that time differential diagnosis cerebellar astrphy. She referred for Rehabilitation department, which evaluated Myasthenia gravis. But EMG(electro myelography) and NCV(nerve conduction velocity) study conclusion was that there is no definite electrophysiologic evidence of neuropathy(including Guillain-Barre syndrome).

On March 19, 2008. she checked serum phenytoin level of 78 ug/mL, which above the therapeutic level 10-20 ug/mL. the patient showed general weakness, vomiting, dizziness, dysphagia. Phenytoin toxicity was impressed, so phenytoin tapering out and switched epileptol 100 mg 2 times per day.

On Jun 11, Laboratory data revealed that was serum WBC $1.8 \times 10^3/uL$, Platelet count $125 \times 10^3/uL$, epileptol discontinued and then phenytoin restarted 100 mg 3 times daily treatment for leukocytopenia, thrombocytopenia. On Jun 19, Seizure was provoked GTC type during 30 seconds and vital sign stabled. Serum WBC $2.6 \times 10^3/uL$ elevated. She was discharged on Aug 6.

On Sep. 19, she repeated gait disturbance, dysarthria

and readmitted while serum phenytoin level checked 16 ug/mL that is normal range. On Oct. 1, she added on indenol 10 mg 1 time per day, rivotril 0.5 mg 1time per day and rehabilitation training for observed ataxic gait.

3. Discussion

Through the findings of the above, our patients diagnosed phenytoin induced cerebellar atrophy and then tapering out phenytoin. But epileptol instead of using phenytoin was encompassed leukocytopenia, thrombocytopenia. at last epileptol discontinued and restarted phenytoin for seizure control.

Phenytoin is one of the first line antiepileptic drugs for many epileptic syndromes. Its high efficacy and low cost makes it widely used. As other antiepileptics, it has various side effects, especially when blood levels are too high[4]. In the study of mechanisms of cerebellar atrophy, the purkinje cells and granule cells are the main target of toxic agents. Purkinje cells are one of the largest neurons in the brain and are sensitive to ischemia, bilirubin, ethanol, and diphenylhydantoin[2]. But Crooks et al. persisted that it is unlikely that this drug acts alone in inducing the Purkinje cell loss.

There have been reports of cerebellar atrophy following both acute and chronic phenytoin overdose and De marcos et al. reported correlation between cerebellar volume reduction and time of exposure to phenytoin. Cerebellar atrophy is frequently associated with long-term use of phenytoin. Although duration of epilepsy may have an influence in the cerebellar atrophy, this is clearly less important than the time of exposure to phenytoin.[5]. sixty-six patients studied and had their computerized tomographies analyzed for cerebellar atrophy. Of the 66 patients studied, 18 had moderate/severe atrophy, 16 had mild atrophy and 33 were considered to be normal. The patients with moderate/severe atrophy were those with higher exposure to phenytoin. This study resulted that although there is a possibility that repeated seizures contribute to cerebellar damage, long term exposure to phenytoin, particularly in high doses and toxic serum levels, cause cerebellar atrophy[3].

4. Conclusion

In our case the patient developed cerebellar atrophy as a result of phenytoin toxicity from overdosing,

although the duration of overdose is unclear. Brain images were cerebellar atrophy but is not sure. Our patient showed ataxic gait, We were medication adjusted with indenol, rivotril and rehabilitation training.

We can learn the importance of maintaining therapeutic levels by blood monitoring, to decrease the possibility of developing permanent cerebellar dysfunction.

■ 참고 문헌 ■

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