West Syndrome Associated with Administration of a Histamine H₁ Antagonist, Oxatomide

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Summary: We report a 4-month-old female infant who developed West syndrome eleven days after administration of a histamine H₁ antagonist, oxatomide, for atopic dermatitis. It has been reported that some histamine H₁ antagonists induce seizures in epileptic patients. The age, the interval between oxatomide administration, and the onset of West syndrome and its clinical course were similar to two previously reported 3-month-old infants with West syndrome associated with ketotifen administration. We should be cautious in using the histamine H₁ antagonists, oxatomide and ketotifen, in young infants because such agents could potentially disturb the anticonvulsive central histaminergic system.

Key words West syndrome, histamine H₁ antagonist, oxatomide

INTRODUCTION

The central histaminergic neuron system plays an important role in the inhibition of convulsions in young infants. Some anti-allergic agents acts as histamine H₁ antagonists and may induce epileptic seizures. We present the first case of West syndrome following the administration of a histamine H₁ antagonist, oxatomide, and discuss its possible association with the occurrence of West syndrome.

CASE REPORT

A 4-month-old female infant was admitted to Kurume University Hospital because of tonic spasms. The pregnancy and delivery were uneventful. She was born at term with a birth weight of 2760 g. She had facial eczema from 1 month of age. At four months of age, she was diagnosed as having atopic dermatitis and was administered oxatomide (1 mg/kg/day) by a pediatrician. She became sleepy immediately after oxatomide administration. The parents noticed that she became irritable 8 days after taking oxatomide. She developed symmetrical tonic spasms 11 days after oxatomide medication. Oxatomide was discontinued on the day the seizures had started. During tonic spasms, her neck and arms were flexed with her legs extended. This condition was repetitive and occurred 2-3 times a day, with each series consisting of 30-50 spasms. On admission, her physical features and development were normal except for mild atopic dermatitis around her mouth. The laboratory examinations were normal including TORCH titers. An interictal EEG showed hypsarrhythmia (Fig. 1). MRI and Tc[99 m]-ECD SPECT was normal. Her seizures were not controlled by vitamin B6 (20 mg/kg/day) and valproic acid (25 mg/kg/day) but were well controlled by ACTH therapy in 3 days. Interictal EEG normalized after 1 week of ACTH therapy (Fig. 2). She is now 2 years old and has been seizure-free while being administered valproic acid. Her development is normal.
DISCUSSION

It has been shown in animal studies that the central histaminergic neuron system works via the action of the histamine H1 receptor [1]. Classical anti-histaminics such as diphenhydramine, methapyrilene, tripelennamine, and pyranisamine have all been associated with convulsions, especially in children under...
2 years of age [2]. For young infants, the histaminergic system, developmentally an older neuron system than the gamma-aminobutyric acid (GABA) system, is important as an inhibitory system of convulsions. Thus, histamine H₁ antagonists might induce seizures. Yokoyama et al. [3] reported the effects of H₁ antagonists and found that H₁ antagonists increased the number of seizures in young mice. Furthermore, they reported that centrally-acting histamine H₁ antagonists such as pyrilamine, ketotifen, and d-chlorpheniramine increased the duration of all the convulsive phases in 21- and 30-day-old mice, but did not increase those in 42-day-old mice [4].

The clinical course of our case was very similar to those of 2 cases of 3-month-old boys reported by Yasuhara et al. [5], who developed West syndrome 8 to 10 days after ketotifen administration. We speculate that oxatomide, one of the H₁ antagonists, may be also associated with West syndrome. We should be cautious in using the histamine H₁ antagonists, oxatomide and ketotifen, in young infants because they could potentially disturb the central histaminergic system and induce convulsions.

REFERENCES