Treatment of Neuroleptic-Induced Tardive Dystonia with Dantrolene: A Case Report

Shigeru MORISHITA, Kanemune MATSUSHITA, Jun EBATA, Shuichiro HARADA, Masanari KIRIYAMA and Shozo AOKI

Department of Psychiatry, Kawasaki Medical School, Kurashiki 701-0192, Japan

Accepted for publication on March 1, 2000

ABSTRACT. We present a case of neuroleptic-induced tardive dystonia in a male schizophrenia in which treatment with dantrolene was associated with improvement. The dystonia appeared 12 months after the patient had began neuroleptic treatment. He did not respond to anticholinergic or other medications, so dantrolene was added to the regimen. After the patient had taken 50 mg of oral dantrolene, his cervical dystonia improved. Dantrolene may be beneficial in the treatment of some patients with tardive dystonia, but further research is necessary.

Key words: tardive dystonia — neurolepties — dantrolene — side effect

It has been recognized that neuroleptics can cause persistent dystonia.[1] The medications generally used to treat it are botulinum toxin, anticholinergics, benzodiazepines, baclofen, carbamazepine, tetrabenazine, and diphenhydramine. However, results have been mostly disappointing.[2] Otsuki *et al*[3] reported improvement of a case of tardive dystonia with dantrolene. We also present here a case with refractory neuroleptic-induced tardive dystonia in whom administration of dantrolene appear to have produced a improvement of symptoms.

CASE REPORT

Patient is a 36-year-old single male with no family history of Parkinson's disease or other neurological diseases. At the age of 34, he developed a schizophrenic paranoid type condition with auditory hallucination of an accusatory nature, paranoid delusions, and aggressive behavior. He showed no evidence of organic disease. He was treated with oral neuroleptics (bromperidol 6 mg/day, risperidone 6 mg/day). His psychotic symptoms soon improved, but the neuroleptics were continued. After 12 months of this treatment, he showed moderate to severe cervical dystonia with involuntary twisting and turning of the neck. The main movement disorder was a rotational torticollis which involved a rotation of the chin around the longitudinal axis towards the shoulder. His walk was disturbed because of abnormal posture. Rigidity, tremor and oral dyskinesia were not present. A diagnosis of neuroleptic-induced tardive cervical dystonia was made by Burke's criteria.[4] The dosage of neuroleptics was decreased and carbamazepine 600 mg/day, biperiden 3 mg/day, and clonazepam 4 mg/day were added to treat

森下 茂，松下兼宗，江幡 淳，原田修一郎，桐山正成，青木省三

the cervical dystonia. After three months of treatment with these drugs, the cervical dystonia had not improved. Therefore all the neuroleptics were stopped. However, he noted that his cervical dystonia was unchanged after approximately nine months. At the age of 36, he experienced a relapse of schizophrenia with paranoid delusions and aggressive behavior. He was admitted to the hospital and neuroleptics (zotepine 200 mg/day) were started. After one month, his psychotic symptoms had improved, but his cervical dystonia became worse and worse. Carbamazepine 600 mg/day and clonazepam 4 mg/day were continued and biperiden was increased to 12 mg/day. There was no improvement within two months. Oral dantrolene, 50 mg/day, was added to the regimen in an attempt to potentiate the antidystonia's effect. Over a period of one month he reported feeling a little better and two months later he reported that the frequency of rotational torticollis had decreased and he could control movement of his neck to the right position for a long time. For the following three months he had a little dystonia, but he was able to maintain a normal posture and walk.

DISCUSSION

Tardive dystonia is a neurological syndrome consisting primarily of abnormal motor movement (torticollis, retrocollis, opisthotonus and oculogyric crises) of the body and limbs. Symptoms usually begin insidiously, with patients complaining of a 'pulling' or 'drawing' movement or an involuntary twisting or jerking movement, generally slow, which may affect the limbs, trunk, neck, or head. A wide variety of abnormal head and neck postures may be assumed. Deviations may occur in any single plane or a combination of directions in which the head may voluntarily move. Rotational torticollis is a rotation of the chin around the longitudinal axis towards the shoulder while laterocollis is a rotation of the head in the coronal plane, with the ear moved towards the shoulder. Anterocollis and retrocollis are rotations of the head in the sagittal plane. The former involves movement of the chin towards the chest and the latter involves elevation of the chin and movement of the occiput towards the back. There may also be sagittal or lateral deviation of the base of the neck from the midline. The most common component of complex deviations is cervical rotational torticollis, followed by head tilt, retrocollis and anterocollis. These effects can all occur after the administration of neuroleptics. High-potency neuroleptics often produce dystonia.[1] The pathophysiology of tardive dystonia is not known.

This case was diagnosed as tardive dystonia according to Burke's criteria: 1) the presence of chronic dystonia, 2) a history of antipsychotic drug treatment preceding or concurrent with the onset of dystonia, 3) exclusion of known causes of secondary dystonia by appropriate clinical and laboratory elevation, and 4) a negative family history for dystonia.[4]

No treatment for tardive dystonia has been established. Botulinum toxin, anticholinergics, benzodiazepine, baclofen, carbamazepine, tetrabenazine and diphenhydramine have been reported to be helpful,[2] but it is difficult to treat tardive dystonia. This case responded to dantrolene. Dantrolene is a peripheral muscle relaxing agent which reduces contraction of skeletal muscle by direct action on excitation-contraction coupling, apparently by decreasing

the amount of calcium released from the sarcoplasmic reticulum.[5] Although dantrolene depresses the central nervous system, it does not appear to produce antispastic effects by actions on neurons.[6] Dantrolene diminishes the force of electrically-induced twitches in man without altering muscle action potentials, and it reduces reflexes more than voluntary contraction.[7] The latter effect appears to be due to preferential actions on "fast" as compared to "slow" skeletal muscle fibers. It does not affect neuromuscular transmission, nor does it change the electrical properties of skeletal muscle membranes.[8]

In patients with upper motoneuron lesions, spasticity is generally diminished by treatment with dantrolene, and functional capacity is often improved. It is also effective in alleviating the signs of malignant hyperthermia. Although the mechanism of dantrolene is presently unknown, it seems that a decrease in the amount of calcium release from the sarcoplasmic reticulum[5] is related to improvement of muscle contraction on these disorders.

Otsuki *et al* reported improvement of a case of tardive dystonia with dantrolene and they supposed that its mechanism was related to amine metabolism in the central nervous system.[3] Yamawaki *et al*[9,10] reported the possible central effect of dantrolene. The central effect of dantrolene may, at least in part, be associated with therapeutic effect of tardive dystonia. In the present case, the use of dantrolene was associated with improvement in the patient's symptoms. This is, to our knowledge, the second report of the therapeutic effect of dantrolene on tardive dystonia. Although the neurochemical mechanism of dantrolene on tardive dystonia is clearly unknown, the findings in this case suggest that dantrolene has therapeutic effect. We feel that this case warrants further investigation of dantrolene in the treatment of neuroleptic-induced tardive dystonia.

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