



Early Remission in Focal Tardive Dystonia Associated with the Use of Neuroleptic Medication: A Rare Case Report and Review of Literature

Gulsen Aykol¹, Neslihan Cansel²

¹ Physical Medicine and Rehabilitation, Private Sevgi Medical Centre, Malatya, Turkey

² Psychiatry, Private Gözde Academy Hospital, Malatya, Turkey

Abstract

Tardive dystonia is a movement disorder which develops with twisting of one part of the body or abnormal posture because of severe muscle contractions. The most important factor in the occurrence of tardive dystonia is the use of antipsychotic medication. Tardive dystonia associated with long-term use of antipsychotic drugs may be focal, segmental or generalised. When tardive dystonia has occurred once, there is a tendency for it to be permanent and complete recovery is rare. The aim of this paper was to present a case of neuroleptic drug-associated tardive dystonia with focal involvement where early remission was observed and thus draw attention to the necessity of considering physical therapy approaches in addition to medication in the treatment choices.

Key Words: Tardive dystonia, neuroleptic, early remission, physical therapy

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Corresponding Author: Gülşen Aykol, Physical Therapy and Rehabilitation, Private Sevgi Medical Center, Malatya, Turkey.

E-mail: gaykol@hotmail.com

Phone: +90 422 324 4646

Introduction

Tardive dystonia induced by antipsychotic medication, which may affect the extremities, trunk or facial region, is characterised by generally slow, involuntary twisting movements, which may be regional or general.

Medications are among the most common reasons of movement disorders and are invariably considered in the evaluation of movement disorders. The most common medications which lead directly to movement disorders are neuroleptic (antipsychotic) medications.

In addition to antipsychotic medications, tardive dystonia may also be caused by levodopa, bromocriptine, metoclopramide, fenfluramine, flecainide, ergot alkaloids, anticonvulsants and calcium channel blockers [1].

Classic antipsychotics (1st generation, old) affect the mesolimbic and mesocortical regions of the central nervous system. The effects are generally shown with dopaminergic block. Tardive dyskinesia, parkinsonism, tardive dystonia and akathisia are based on the side effects of antipsychotic medication on the extrapyramidal system. Movement disorders are thought to originate from excessive sensitivity of the dopamine receptors in the basal ganglia as post-synaptic dopamine receptor blockage is extended with neuroleptics. Extrapyramidal symptoms caused by neuroleptic drugs often do not conform after the treatment and sometimes result in unsuccessful treatment.

Several studies have reported the development of tardive dystonia in the field of long-term antipsychotic treatment to be mean 2.7% with a tendency for male gender [2]. The occurrence of tardive dystonia is generally within the first year of the use of antipsychotic drug use.

Despite different treatment approaches, full recovery is rarely seen. Age, psychopathology, the dosage of antipsychotic drug therapy and duration of exposure to the drug and extrapyramidal symptoms have been accepted as risk factors, but have not yet been fully defined [3].

Although tardive dystonia developing after long-term antipsychotic therapy may be focal, segmental or generalised, it starts most often in the cranial and cervical regions [4].

A specific, widespread, succesful treatment for dystonia has not yet been found. As the evaluation and treatment of movement disorders is usually applied in neurology clinics, physical therapy applications are not usually given any place in the treatment choices [5]. There have been no objective data of the benefit and specificity of rehabilitation applications for these syndromes [6].

Case

A 59-year old, single, female housewife presented at the psychiatry outpatient clinic with complaints of increased hallucinations, hearing voices, disordered speech and behaviour, and involuntary, painless, twisting movements in both hands and fingers which had been ongoing for 3 months. The history revealed that the patient, who was being followed up for a 6-year history of schizophrenia, had been started on therapy of 10 mg/day haloperidol and 200 mg/15 days zuclopenthixol (depot) 6 months previously with continuaaation of the previous therapy of 6 mg/day biperiden. The medications had been taken regularly by the patient, who had a history of involuntary movements, perinatal stress, head trauma and peripheral injuries. There was no family history of movement disorders.

As the schizophrenia symptoms had increased and dystonia was determined in both hands, a full blood count, routine biochemistry and thyroid function tests were applied in respect of movement disorders differential diagnosis. The test results were all evaluated as normal. In the cranial and cervical MR examination and neurological examination, no findings were determined to explain dystonia. Tardive dystonia associated with haloperidol and zuclopenthixol use was considered so the haloperidol and zuclopenthixol treatment was terminated. The schizophrenia symptoms of the patient were exacerbated and treatment of 10mg/day olanzapine and 25mg/15 days risperidone (depot) was started with continuation of 6 mg/day biperiden. At a follow-up examination at the psychiatry outpatient clinic 1 month later, as the schizophrenia complaints were determined to have improved, the olanzapine dose was increased to 15mg/day with continuation of risperidone and biperiden at the same dose. As the tardive dystonia in both hands was continuing in the same way, physical therapy was recommended.

The patient presented at the outpatient clinic with complaints of twisting in the hands which had been ongoing for 4 months and she could not grasp with either hand. Therefore, she was unable to meet her personal care needs of dressing, washing and food preparation without assistance. There were involuntary, painless abnormal twisting movements in both hands. On physical examination, with both forearms in pronation, excessive flexion was observed in both wrists and all the finger joints. In the sensory examination, the deep tendon reflexes were evaluated as normal and no tremors were observed. Based on the clinical history and physical examination of the patient, who had normal test results, a physical therapy programme was started of 1 hour per day, 5 days per week for 6 weeks on the diagnosis of focal hand dystonia associated with neuroleptic drug use. At each session, the same physiotherapist applied passive range of movement exercises to both wrists and all the finger joints and slow, mild stretching exercises up to the pain threshold. From the third week, proprioceptive neuro-muscular facilitation (PNF) exercises were added to the programme. The patient was fully compliant with the physical therapy programme. Olanzapine and risperidone treatment was re-started and the previous biperiden treatment was continued regularly. After 30 sessions of the physical therapy programme, the abnormal, involuntary, twisting, crooked movements in both hands were observed to have fully recovered.

Discussion

In this case, the tardive dystonia which was seen was related to the use of haloperidol and long-lasting effect zuclopenthixol, and by terminating the classic antipsychotics used by the patient, the treatment was continued with olanzapine, which has fewer extrapyramidal side-effects, and risperidone, which has a long-lasting effect. When the medication was changed, although the schizophrenia symptoms subsided, the abnormal twisting in both hands continued and as the patient was unable to meet her daily needs and undertake personal care, she was admitted to a physical therapy programme with the aim of regaining hand functions.

Dystonia is a movement disorder characterised by involuntary, chronic and repeated muscle contractions, which lead to temporary or permanent abnormal posture, often with twisting and

turning features. To be able to perform appropriate motor behaviours or to maintain a certain posture, the simultaneous and co-ordinated working against each other of agonist and antagonist muscles results in contractions and extensions.

In addition to antipsychotic medications, tardive dystonia may also be caused by levodopa, bromocriptine, metoclopramide, fenfluramine, flecainide, ergot alkaloids, anticonvulsants and calcium channel blockers [1].

In patients treated long term with 1st generation (classic, typical) antipsychotic drugs, movement disorders caused by the drugs have been reported at levels of 50-75%. In a prospective study of 209 patients using antipsychotic drugs for 1 year with a 4-year follow-up period, tardive dyskinesia was determined at 28.4%, parkinsonism at 56.2%, akathisia at 4.6% and tardive dystonia at 5.7% [7]. It was reported that two thirds of the participants developed at least one movement disorder. In the same study it was determined that the incidence of tardive dyskinesia, tardive dystonia and parkinsonism increased with advancing age, whereas akathisia decreased. In a review of 13 studies by Van Harten and Kahn, the prevalence of tardive dystonia was calculated as mean 5.3% [8].

Contrary to what was hoped of them, atypical (2nd generation, new) antipsychotic drugs carry the risk of movement disorders. In 11 long term studies conducted with 2nd generation neuroleptic drugs (except for clozapine), it was reported that there was a lower risk of the development of movement disorders associated with atypical antipsychotics than with classic neuroleptics [9].

Antipsychotic drugs with a long-lasting effect (injectable, depot) have been shown to decrease the rate of recurrence and length of hospital stay in the treatment of schizophrenia although an increase has been seen in the spread and severity of extrapyramidal symptoms. New generation antipsychotics are tolerated better than typical antipsychotics, although high rates of non-conformity are still seen [10]. This has resulted in the treatment continuing after 6 months at the level of 57% of patients treated with atypical neuroleptics as outpatients [11].

In a study by Brugnoli et al, the frequency of extrapyramidal side-effects was found to be 32 % for typical antipsychotics with long-lasting effects and 30% for typical oral antipsychotic drugs. In the same study, the values determined for new generation drugs were determined as

16% for risperidone, 10% for quetiapine, 9% for clozapine, and 8% for olanzapine. Extrapyramidal symptoms at the 12th month were found to be at a significantly high level for classic neuroleptics in that study [12]. In the case reported here, the extrapyramidal side-effects were high from the use of the classic neuroleptics, haloperidol and depot zuclopenthixol. As olanzapine and depot risperidone are atypical antipsychotics, there is a lower risk of movement disorders.

In a study by Vasilyeva et al comparing extrapyramidal side-effects of risperidone with typical antipsychotic drugs such as haloperidol and phenothiazine in elderly patients aged over 65 years, it was determined that patients using risperidone were at lower risk [13].

Lencer et al reported that the duration of usage strongly affected the development of extrapyramidal symptoms (parkinsonism, akathisia, some sub-groups including acute dystonic reaction) [3].

Depending on the area of the body affected, tardive dystonia may be observed with focal, segmental or generalised involvement. Cervical dystonia is the most commonly seen type of focal dystonia, followed by blepharospasm. Oromandibular dystonia, Meigs syndrome (eyelid and mouth region involvement together), hemifacial spasm, laryngeal dystonia, pharyngeal dystonia and hand cramps are other types of focal dystonia.

Extremity dystonia is a movement disorder characterised by abnormal posture in the extremities with twisting and repeated movements of the extremity muscles leading to excessive, disproportional, long-lasting, involuntary muscle contractures. Extremity dystonia can be observed in the form of focal (limited to one region of the body) when only the arms or legs are affected, segmental (at least two adjacent muscle groups are affected) when the arms and neck or trunk and legs are affected, hemidystonia (half the body) or generalised. It may be primary (idiopathic) or emerge secondary to other diseases.

The incidence of extremity dystonia not related to activity is rare and is generally of a secondary source, often seen together with axial and cervical dystonia, becoming a continuous dystonic posture as the disease progresses.

Focal hand dystonia generally starts with impaired fine control, with complex motor activities such as writing and playing a musical instrument triggering muscle spasms and over time less

specific movements are affected. Clinically, spasms caused by excessive activity in the muscle group, abnormal crooked postures and irregular tremors may be seen. In most patients, when writing, the pen is held tightly and there is an abnormal hand and arm position. As the disease progresses, motor control becomes more difficult. The rate of continuity and control of the movement are impaired. Symptoms improve with rest and recur with activity. In more severe cases, dystonia is seen at rest.

In focal hand dystonia, most primary sensory evaluations such as reflexes, touch, pain and vibration are normal. In dystonia not related to activity, pain may be the main symptom. In patients with secondary dystonia, other abnormalities may be determined, such as rigidity, impaired balance, changes in reflexes, weakness and limited eye movements (findings indicating Parkinson's disease, stroke or other neurodegenerative diseases).

The diagnosis of focal hand dystonia is based on clinical findings. Electrophysiological tests are not diagnostic. In the differential diagnosis, apart from medication side-effects, evaluation must be made for Parkinson's disease, stroke, neurodegenerative diseases, neuropathies, radiculopathies, plexopathies, complex regional pain syndrome, repetitive stress injuries, focal seizure, thoracic outlet syndrome and psychogenic movement disorders [14]. If there is suspicion of radiculopathy or peripheral neuropathy, muscular or nerve disease must be excluded with EMG.

When hand dystonia progresses, it may spread towards the proximal muscles of the same or the contralateral extremity and it has been reported that within 8 years (range, 2-32 years) of the onset of symptoms, it may advance to a generalised form [15]. Spontaneous remission is rare. Although tardive dystonia is considered a chronic disorder, spontaneous recovery has been reported. Neuroleptic-associated tardive dystonia has been observed to develop at any time from 4 days to 23 years (mean 6.2 ± 5.1 years). Remission has been reported in tardive dystonia in a period varying from 1 month to 9 years after terminating neuroleptic drugs after a mean usage period of 5.2 years (range, 1-12 years). In a study of 107 cases with an 8.5-year follow-up period, recovery was determined in 15 patients (14%; 7 full recovery, 8 partial), improvement was seen in 42 (39%) and in 50 patients (47%) the course of the dystonia was observed to worsen or there were no changes [2].

In patients where remission is seen, the duration of exposure to dopamine receptor antagonists has been found to be significantly shorter compared to patients with permanent tardive dystonia. The chance of remission has been observed to be higher in tardive dystonia which has developed associated with a drug usage period of 10 years or less and the possibility of remission is low when patients have been exposed to dopamine receptor antagonist medications for more than 10 years. In the same study, it was determined that in patients exposed to dopamine receptor antagonists at a younger age, generalised involvement was determined more frequently than focal or segmental involvement [2].

As tardive dystonia which develops associated with drug use is iatrogenic, the ideal approach seems to be using the lowest effective dose of antipsychotic medication only when there are absolute indications and selecting new generation antipsychotic drugs which have fewer side-effects. In addition, in the follow-up examinations of patients using antipsychotic drugs, attention should be paid not only to clinical symptoms but also to extrapyramidal side-effects such as tardive dystonia.

In the treatment of drug-associated tardive dystonia, firstly the antipsychotic medication which is thought to have caused the dystonia should be terminated. There is no consensus on the treatment for tardive dystonia, but improvement may be seen with anticholinergic medication. It has been reported that dopamine antagonist drugs such as reserpine and tetrabenazine, in addition to clonazepam have beneficial effects on dystonic symptoms. Baclofen is generally effective in extremity dystonia. Atypical neuroleptics such as clozapine and olanzapine are used in focal or generalised dystonia resistant to other drug treatments. Successful results have sometimes been reported from the use of atypical neuroleptics, such as clozapine and olanzapine in the treatment of focal or generalised dystonia [16]. Olanzapine, which is an atypical neuroleptic, is known to have a lower rate of extrapyramidal side-effects compared to classic neuroleptics. While success has been reported in several cases in the treatment of tardive dystonia, cases have also been reported where tardive dystonia has developed associated with the use of olanzapine [17]. Botulinum toxin injection and intrathecal baclofen are accepted as safe and effective alternative treatment methods for dystonia.

The efficacy of physical therapy methods such as soft tissue mobilisation, cervical muscle strengthening and stretching exercises and the application of an orthosis, have not been

investigated in detail. Physical therapy applications must be personalised appropriately to the specific problems of each patient. In the treatment of extremity dystonia, the main objective is functional improvement and correction of abnormal posture. Opening a dystonic hand provides patient comfort and hand hygiene [18].

There is limited amount of data available on the subject of the effectiveness of physical therapy in the treatment of dystonia. Nevertheless, two small randomised, controlled studies have shown the beneficial effects of physical therapy on the daily living activities of dystonia cases [19, 20]. In those studies, where boulinum toxin injection together with physical therapy was compared with botulinum toxin injection alone, it was reported that a significant difference was observed in pain and disability in the combined treatment group. In the case presented here, joint range of movement was restricted because of long-term lack of movement associated with dystonia in the hands. In both hands, there was shortening of the muscle length in the flexor muscle group, loss of flexibility and limited range of joint movement, associated with remaining in the same position for long periods of time. Passive EHA exercises were applied to increase the range of joint movement. With stretching exercises, it was aimed to provide lengthening by stretching the dystonic muscle (Golgi tendon reflex helped loosening in the dystonic muscle). It was aimed to increase the capability, functional capacity and muscle strength of both hands with PNF exercises.

Electroconvulsive therapy (ECT) is one of the alternative methods which has been applied in the treatment of tardive dystonia. In a retrospective study by Yasui-Furukori et al of 18 patients, the response rate to ECT was determined as 39% in the treatment of tardive dystonia and tardive dyskinesia. Although, ECT is an effective method in the treatment of tardive dystonia and dyskinesia, this effect has been reported to be at a mild level [21].

Botulinum toxin injections should be considered as a treatment choice for focal tardive dystonia which has not responded to medical treatment. It is injected to the affected muscle or muscle group under EMG guidance. It has been reported that the maximum effect is observed 2-4 weeks after the injection and in subsequent weeks the effect decreases and symptoms return. As the effect is reduced after a mean of 3 months, it has been emphasised that it is necessary to repeat the injections on average every 3-4 months [18].

In this report, the case was presented of a patient with tardive dystonia who benefitted from physical therapy applications together with olanzapine and risperidone treatment for focal hand dystonia which developed associated with the use of antipsychotic medication. When cases in literature which have spontaneously recovered are taken into consideration, there is seen to be a need for further studies examining the importance of collaboration between departments in the treatment of movement disorders and the efficacy of physical therapy applications.

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