J Neurol (2006) 253 [Suppl 7]: VII/17–VII/20
DOI 10.1007/s00415-006-7005-4

Fusako Yokochi

Lateral flexion in Parkinson's disease and Pisa syndrome

Abstract Various types of abnormal posture are observed in Parkinson's disease (PD). Lateral flexion is very common and frequent among them. The clinical characteristics of lateral flexion in PD vary and are classified into two types, the chronic and subchronic types. The chronic type of lateral flexion in PD appears subclinically and worsens, which is related to the laterality of parkinsonian symptoms and the progression of the disease. The subchronic type of lateral flexion in PD develops subacutely and worsens rapidly in several months. An atypical and rare type of tonic truncal dystonia, Pisa syndrome, may be induced following the intake of neuroleptics. The clinical features of the subchronic type of lateral flexion in PD are similar to those of Pisa syndrome. Differences between lateral flexion in PD and Pisa syndrome are described.

Key words Parkinson's disease · lateral flexion posture · Pisa syndrome · dopamine agonist · oblique sign

F. Yokochi, M.D., Ph.D.
Department of Neurology
Tokyo Metropolitan Neurological Hospital
2-1-16 Musashidai, Fuchu
Tokyo, 184-0032, Japan
E-Mail: fyokochi-tmnh@umin.ac.jp

Introduction

An abnormal posture is a very common symptom of Parkinson's disease (PD). Parkinsonian posture is characterized by a flexed posture of the trunk and extremities, as described in an essay written by Dr. James Parkinson. Abnormal postures in PD are observed in the entire body, namely, flexion to the anterior, lateral or anterolateral parts of the trunk, neck flexion, flexion of the extremities, and abnormal postures of the hands, fingers and toes such as thalamic hand or hammer toe. The abnormal posture presented in this paper is limited to lateral flexion, which I describe on the basis of published reports and my clinical observation. Lateral flexion is a very common clinical observation, but there are few published reports on this abnormal posture. There was no specific name for this symptom, but recently, the term Pisa syndrome has sometimes been used for a similar symptom in PD. The term Pisa syndrome was originally used to refer to a symptom caused by psychiatric drugs, which I describe later.

Lateral flexion in Parkinson's disease

In 1975, Duvoisin and Marsden described lateral flexion as the scoliosis of parkinsonism [1, 2], characterized by a lateral deviation of the spine and a corresponding tendency to lean to one side. They analyzed the relationship between the direction of postural deviation and the laterality of symptoms in 20 nonoperated patients with parkinsonism. Sixteen patients had scoliosis contralateral to the side of initial symptoms, three patients had ipsilateral scoliosis and one patient had no scoliosis. The direction of postural deviation correlated significantly with the initial and major symptoms of parkinsonism, and the concavity of scoliosis was contralateral to the side of initial and major symptoms. They did not discuss the effects of antiparkinsonian drugs on abnormal postures.

Duvoisin and Marsden reported a very high frequency (95%) of lateral flexion in PD. To confirm the frequency and awareness of lateral flexion in PD, patients with PD were analyzed. Fifteen consecutive patients, consisting of nine women and six men with a mean age of 66.6(7.7) years and a mean illness duration of 14.3(8.0) years, examined in the outpatient clinic par-

JON 7005

ticipated in the study. There were four patients at Hohen-Yahr stage II, nine at stage III, and two at stage IV. All of the patients were treated with antiparkinsonian drugs and not operated on. The two types of posture on standing viewed from the back were photographed for each patient. One was the patient's natural posture and the other was the posture after correction by a neurologist. Each patient was asked whether he/she felt that he/she was leaning in the corrected posture. Twelve of the fifteen patients (80 %) had lateral flexion. All of the patients felt that they were leaning toward the contralateral side following the correction of their posture. Only four of the twelve patients who had abnormal postures had simple lateral flexion and the remaining eight patients had a combination of lateral flexion and forward flexion. Therefore, the abnormal postures of almost all parkinsonian patients are complex, not only for lateral flexion, but also for forward flexion. Almost all of the patients were not themselves aware of their abnormal postures.

Furukawa reported the oblique sign (naname sign) of PD, which means the leaning of the trunk on sitting, an oblique supine posture on lying down, or an indeterminate posture in many situations [3]. Patients with the oblique sign keep their postures indeterminate. Apparently, it is difficult to maintain this posture. Furukawa studied the awareness of the oblique sign in patients with PD in terms of the position of the trunk using a chair that changed the angle of the body from the supine to the sitting position [4]. The patients were instructed to determine whether they were in the vertical or horizontal position without a visual guide. Under the condition that the position was changed from supine (horizontal: 180 degrees) to sitting (vertical: 90 degrees), he/she had to determine the position in which he/she felt the angle was 90 degrees. Control subjects felt that they were in a vertical position in the range of 110–100 degrees, but parkinsonian patients with the oblique sign felt that they were in a vertical position at a more obtuse angle than the control subject. Under the condition that the position was changed from sitting to supine, control subjects felt that they were in a horizontal position in the range of 155–160 degrees, whereas parkinsonian patients with the oblique sign felt that they were in a horizontal position at smaller angles, at which the position was similar to a half-sitting position. This study showed that the judgment of vertical and horizontal positions was affected in patients with PD.

The disturbance in awareness of an abnormal position of the body in patients with PD might involve a disturbance in body schema or body image. Body schema means the image of one's own body in space [5]. All of the moment-to-moment postural changes are memorized one by one and the postural change in progress is compared with a posture memorized previously and the determined position is recognized as the body image in normal subjects. However, it is hypothesized that patients with PD memorize an abnormal body image, resulting in chronic and progressive disturbance in posture. It was suggested that the abnormal position of the body in space and the disturbance in its awareness in PD result from the disorders in the memory of the body image. In a study to determine the relationship between body size and the width of a door shown on a screen, the ability to determine body position in space was found to be disturbed in patients with hemiparkinsonism [6]. The disturbance in the ability to determine body position in space in PD appears not only as a result of a progressive abnormal posture, but also as a disorder caused by PD [7].

Pisa syndrome

Pisa syndrome is an atypical acute or tardive dystonia called pleurothotonus or drug-induced pleurothotonus, which is a very rare adverse event associated with neuroleptic treatment. The typical clinical feature is tonic truncal dystonia with a slight backward rotation without dystonia in other parts of the body. Ekbom et al. [8] reported a new dystonic syndrome associated with butyrophenone therapy. An acute syndrome in three elderly women with presenile dementia appeared as a side effect of treatment with methylperone or haloperidol. In each patient, a tonic flexion of the trunk to one side was observed. A slight rotation of the trunk in the sagittal plane was noted. The rotation was enhanced with walking and the patients tended to turn in a direction opposite to their intended path. The symptoms were reversible and were improved by anticholinergic drugs.

The prevalence of Pisa syndrome in a psychogeriatric population over a five-year period was analyzed by Yassa et al. [9], which was 8.3 %, with 9.3 % in women and 6.4 % in men. In a multicenter drug safety surveillance project [10], Pisa syndrome was observed in 17 among 45,000 psychiatric patients and the prevalence was 0.04 %. Risk factors were a history of previous treatment with conventional neuroleptics, female gender, old age, and organic brain disorders.

Drugs reported to induce Pisa syndrome are typical and atypical antipsychotics, tricyclic antidepressants, selective serotonin reuptake inhibitors, cholinesterase inhibitors, antiemetics, lithium carbonate, benzodiazepines and tiapride [11]. Suzuki et al. [12] studied the clinical characteristics of 24 patients with drug-induced Pisa syndrome, which included responders and nonresponders to anticholinergic drugs. However, no significant differences in gender, age, psychiatric diagnosis, direction of extrapyramidal symptoms, or organic brain changes were noted between the responders and nonresponders.

Generally, Pisa syndrome is treated with anticholin-

ergic drugs or the reduction of the dose of neuroleptics. The significant improvement in the symptoms of Pisa syndrome following the withdrawal of antipsychotic drugs differentiates this syndrome from tardive dystonia.

It is suggested that a cholinegic-dopaminergic imbalance, or the interactions among noradrenaline, serotonin and dopamine are involved in the development of drug-induced Pisa syndrome [13].

Is abnormal posture in Parkinson's disease similar to Pisa Syndrome?

An abnormal posture observed in PD is caused not only by the worsening of the disease or the distribution of symptoms, but also by antiparkinsonian drugs. The administration of a dopamine agonist sometimes induces abnormal postures such as the drop neck, forward flexion or lateral flexion of the body. The development of Pisa syndrome in a patient with PD during treatment with Pergolide [14] or Pramipexole [15] was reported. One patient had been treated with Pergolide for more than one year before developing Pisa syndrome, which was improved and reversed by only the withdrawal of Pergolide. On the other hand, Pisa syndrome induced by Pramipexole showed no improvement following the withdrawal of this dopaminergic medication for one week. I have encountered patients who developed this syndrome during the administration of another dopamine agonist. This suggests that these symptoms are not characteristically induced by a particular dopamine agonist.

In the advanced stage of PD, the stiffness of the trunk and neck worsens gradually. In this stage or in patients treated with antiparkinsonian drugs, rigidity in extremities is attenuated, but rigidity in the trunk, which is difficult to treat with antiparkinsonian drugs, is severe. The distribution of symptoms in PD varies in each patient; but generally, neck and trunk stiffness becomes severe in the advanced stage. Trunk stiffness is caused by rigidity and deformities in the spine, and by many other factors. Rigidity is a characteristic feature of abnormal postures in PD. On the other hand, Pisa syndrome induced by neuroleptics is characterized not by trunk rigidity, but by dystonia in trunk muscles.

Abnormal postures with lateral flexion in PD are classified into two types on the basis of the pattern of appearance: chronic and subchronic. The chronic type of lateral flexion in PD appears subclinically and worsens gradually; such worsening is related to the progression of the disease. The subchronic type of lateral flexion in PD is observed in cases reported by Cannas et al. [14] and Gambarin et al. [15] and seems to show similar symptoms with those of Pisa syndrome. The severity of this lateral flexion progresses in a few months and this abnormal posture becomes marked. The administration of a dopamine agonist sometimes causes truncal dystonia as reported previously [14, 15]. In a patient with the subchronic type of lateral flexion, the asymmetry of the paraspinal muscles is prominent, as shown in the figure. The volume of the paraspinal muscles contralateral to the side of lateral flexion is larger than that of those ipsilateral to the side of this abnormal posture and this pathological enlargement of the muscles might be a sign caused by dystonia. This finding indicates that this postural abnormality in patients with PD have a component of dystonia in addition to that of rigidity. The initial development of lateral flexion is subclinical, but its progression is rapid. This type of lateral flexion has a neurological condition similar to one of the neurological conditions of Pisa syndrome. Anticholinergic drugs do not improve this type of lateral flexion in PD. There is no doubt that Pisa syndrome and the subchronic type of lateral flexion in PD are not the same owing to the existence of truncal rigidity in PD. Neuroleptics have a function of acting on neurotransmitters in the brain, and antiparkinsonian drugs do as well. In a study of rats with hemiparkinsonism induced by a unilateral injection of 6-hydroxydopamine into the ventralis tegmenti, a strong

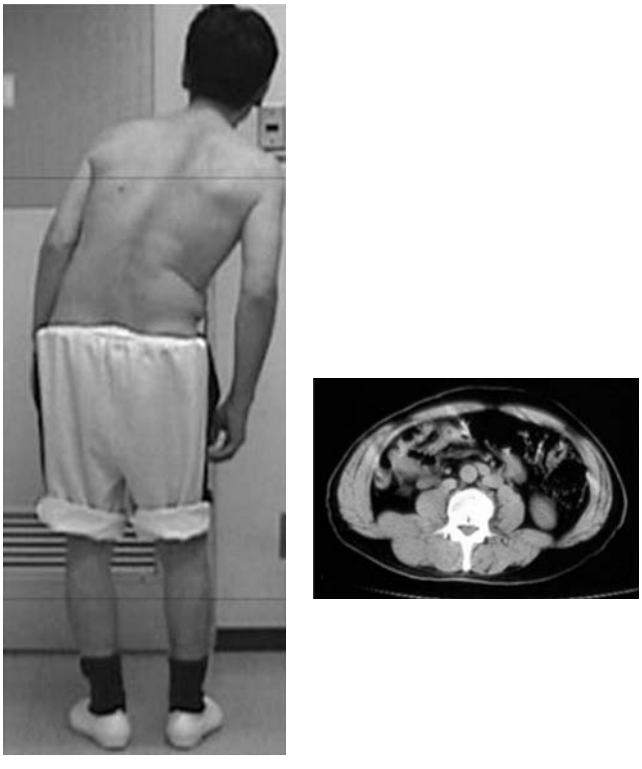

Fig. 1 Subchronic type of lateral flexion similar to Pisa syndrome. Sixty-year-old patient with PD and illness duration of seven years. Lateral flexion to the right and forward developed 1 year ago. His medication was 300 mg of levodopa/DCI, 150 mg of amantadine and 1.5 mg of pramipexole. A computed tomographic image shows a larger volume of the left paraspinal muscle than that of the right paraspinal muscle, which was contralateral to the lateral flexion

ipsilateral deviation and a scoliosis-like skeletal deformity were observed, and the severity of this scoliosis was closely related to a decrease in extracellular striatal dopamine level measured by microdialysis [16]. The term Pisa syndrome should not be indiscriminately used for all cases of lateral flexion in PD, and the type of lateral flexion in PD should be carefully observed.

Treatment of lateral flexion in Parkinson's disease

Lateral flexion in PD is a difficult symptom to treat with antiparkinsonian drugs. Preventing the development and progression of lateral flexion is the most important aim, which is difficult to realize. To treat the subchronic type of lateral flexion, it should be determined whether drugs lead to the development of this type of lateral flexion. A dopamine agonist administered before the development of lateral flexion should be discontinued or the dopamine agonist may need to be changed. Deep brain stimulation can effectively treat abnormal postures including lateral flexion and forward flexion. However, if lateral flexion induces deformities in the spine, it is impossible to treat deformities in the spine by deep brain stimulation. The decision to treat by deep brain stimulation must be made before abnormal posture becomes irreversible.

References

1. Duvoisin RC, Marsden CD (1975) Note on the scoliosis of Parkinsonism. J Neurol Neurosurg Psychiatry 38(8): 787–793
2. Marsden CD, Duvoisin R (1980) Scoliosis and Parkinson's disease. Arch Neurol 37(4):253–254
3. Furukawa T (1986) The oblique signs of Parkinsonism. Neurol Med 25:11–13
4. Furukawa T, Okiyama R, Tsukagoshi H (1989) Oblique sign of Parkisonism. Clin Neurol 29:1603
5. Furukawa T (2001) Body schema. Neurol Med 54:472–478
6. DLee AC, Harris JP, Atkinson EA, Fowler MS (2001) Disruption of estimation of body-scaled aperture width in Hemiparkinson's disease. Neuropsychologia 39(10):1097–1104
7. DProctor F, Riklan M, Cooper IS et al. (1964) Judgment of visual and postural vertical by parkinsonian patients. Neurology 14:287–293
8. Ekbom K, Lindholm H, Ljungberg L (1972) New dystonic syndrome associated with butyrophenone therapy. Z Neurol 202(2):94–103
9. Yassa R, Nastase C, Cvejic J et al. (1991) The Pisa syndrome (or pleurothotonus): prevalence in a psychogeriatric population. Biol Psychiatry 29(9): 942–945
10. Stubner S, Padberg F, Grohmann R et al. (2000) Pisa syndrome (pleurothotonus): report of a multicenter drug safety surveillance project. J Clin Psychiatry 61(8):569–574
11. Suzuki T, Matsuzaka H (2002) Drug-induced Pisa syndrome (pleurothotonus): epidemiology and management. CNS Drugs 16(3):165–174
12. Suzuki T, Hori T, Baba A et al. (1999) Effectiveness of anticholinergics and neuroleptic dose reduction on neuroleptic-induced pleurothotonus (the Pisa syndrome). J Clin Psychopharm 19(3):277–280
13. Villarejo A, Camacho A, Garcia-Ramos R et al. (2003) Cholinergic-dopaminergic imbalance in Pisa syndrome. Clin Neuropharmacol 26(3):119–121
14. Cannas A, Solla P, Floris G et al. (2005) Reversible Pisa syndrome in Parkinson's disease during treatment with Pergolide: a case report. Clin Neuropharm 28(5):252
15. Gambarin M, Antonini A, Moretto G et al. (2006) Pisa syndrome without neuroleptic exposure in a patient with Parkinson's disease: case report. Mov Disord 21(2):270–273
16. Herrera-Marschitz M, Utsumi H, Ungerstedt U (1990) Scoliosis in rats with experimentally-induced hemiparkinsonism: dependence upon striatal dopamine denervation. J Neurol Neurosurg Psychiatry 53(1):39–43