Severe Contractions in Parkinson's Disease Caused by Immobilization and Lack of Dopaminergic Treatment

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Citation

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Abstract

Four patients in advanced stages of Parkinson's disease developed irreversible limb contractures in the course of acute comorbidity. The most likely reasons for such severe conditions are exacerbation of severe rigidity, dystonic posturing and loss of physiologic movement range following the reduction of dopaminergic medication.. A movement disorder specialist should therefore be consulted for tailoring an adequate treatment plan and appropriate administration of oral levodopa preparations via gastric tube. Further, high frequency physiotherapy should be provided during immobilization periods.

INTRODUCTION

Immobilization is a frequent condition in elderly patients with PD due to surgery after hip fractures, other operations or any acute comorbidity. Usually a deterioration of the general condition is followed by a rehabilitation phase in which the patient tries to begin walking again. Contractures, however, present a major complication which may seriously endanger the patient's independence in activities of daily living.

Few publications refer to contractures in PD patients. In the era before a levodopa/decarboxylase inhibitor was available for treatment of PD, axial and limb deformities were noted as rare but – if occurring – with a typical distribution pattern. Charcot [1] first described deformities of hand and feet similar to those seen in rheumatoid arthritis in 1877, Jackson [2] noted several cases in 1899, which he linked to tetany. Martin [3] and Onaguluchi [4] saw skeletal deformities and hand contractures in post-encephalitic Parkinsonism. Also remission of hand and foot deformities in severely affected PD patients following stereotactic thalamotomy was reported by Bravo [5], Cooper [6] and Gortvai [7]. Fahn and Jankovic [8] identified the dystonic striatal hand with flexion of metacarpophalangeal joints and extension of proximal interphalangeal joints as completely reversible under levodopa treatment. These findings suggest that dopaminergic deficiency, with loss of a physiologic movement pattern, enhanced rigidity and dystonic posturing due to basal ganglia dysequilibrium, are a major cause for the development of the disabling deformities described in the pre-levodopa era.

More recently however, Kyriakides and Hewer [9] described hand contractures similar to those noted by Charcot in three PD patients with ongoing levodopa therapy. Hu and coworkers [10] present 7 cases of limb contractures in advanced PD which were not alleviated by levodopa. Shah and collaborators only recently published on a PD patient suffering a flexion contracture after total knee arthroplasty [11]. Because patients' quality of life and independence in daily activities is threatened by these deformities, it is necessary to further investigate why they evolve.

In our hospital, a specialized center for diagnosing and treating Parkinson patients, we treat about 1500 inpatients with PD annually. 500 to 600 of those patients are in far advanced stages of the disease. Within one year four patients with advanced Parkinson's disease (PD) were admitted to our movement disorder center who showed disabling limb contractures following immobilization. The following case analysis illustrates the clinical picture, therapy regimen, possible origin and follow-up of these four cases to further identify risk factors and preventive strategies.

CASE 1

A 65-year-old woman with PD for 14 years, fluctuations and recurring psychotic episodes beginning 4 years ago, and requiring a wheelchair due to postural instability, was admitted to a general hospital because of aspiration pneumonia with tracheal rupture. She required surgery, artificial respiration for 3 weeks and intensive care

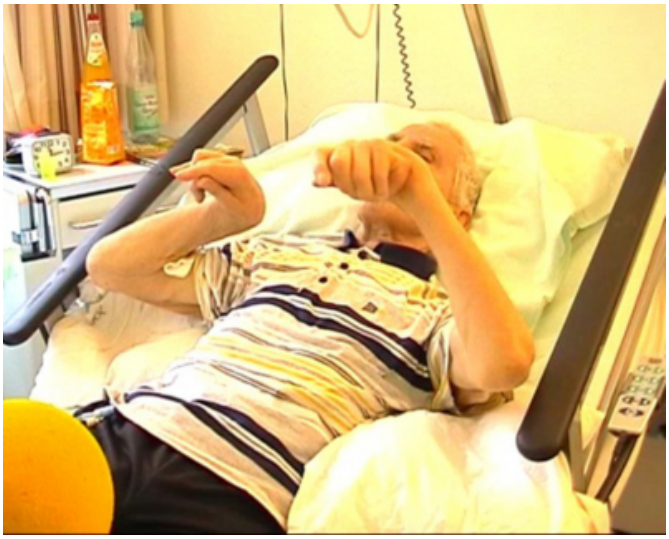
treatment. PD medication was reduced from 12 mg ropinirole plus 175 mg levodopa (total 575 mg levodopa) to 5 mg ropinirole plus 150 mg levodopa (total 316 mg levodopa) at the beginning of the acute phase and was continued at this level for 16 days, then elevated again to the former level. All drugs, liquids and nutrition had to be administered via gastric tube for at least 8 weeks. Upon admission to our hospital, the patient was bedridden, with hips, knees, elbows, wrists, metacarpophalangeal joints and ankles in flexion position. All contractures proved irreversible, the patient remained wheelchair-bound, despite apomorphine applications.

CASE 2

A 77-year-old man with PD for 16 years, fluctuations present for 9 years, but still ambulatory and fully mobile with clozapine treatment due to recurring psychosis, was admitted to a general hospital because of febrile urinary tract infection and psychotic decompensation. After antibiotic treatment and reduction of dopaminergic medication from 675 mg to 400 mg levodopa and 300 mg tolcapone, the patient gradually lost his mobility over a period of 5 months. On admission to our hospital, the patient was severely akinetic, bedridden with both hips, knees, ankles, elbows, wrists and metacarpophalangeal joints in flexion position. After re-establishing sufficient dopaminergic medication (875 mg levodopa plus 4 mg rotigotine transdermal per day) and aided by intensive physiotherapy, the patient became ambulatory again. However both wrists and fingers showed irreversible contractures in flexion position, thus severely limiting the use of both upper limbs (see figure 1).

Figure 1

Figure 1: Case 2: persistent flexion of the distal extremities; partial improvement of the arms to perform some voluntary movements

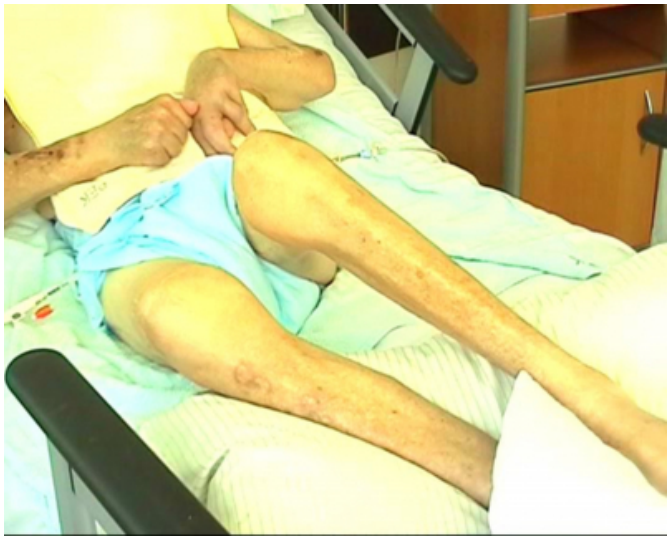


CASE 3

A 78-year-old man with a PD duration of 6 years, with evolving dementia and recurring hallucinations during the last year, suffered a hip fracture by falling. Following surgery in a general hospital the patient could not be remobilized although oral dopaminergic medication was continued at 600 mg levodopa plus 1000 mg entacapone. According to the medical records, medication intake however was highly irregular due to sleepiness reduced capability of cooperation and dysphagia. 4 weeks after surgery the patient received a percutaneous enterogastric tube to reinstate regular medication as well as sufficient intake of liquids and nutrition. Because, further orthopedic rehabilitation failed, the patient was transferred to our center, bedridden with hips, knees, elbows, wrists, metacarpophalangeal joints andankles in flexion position. No improvement was achieved by elevating levodopa therapy as well as physiotherapy. The patient has remained bedridden and totally dependent (see figure 2).

Figure 2

Figure 2: Case 3: Severe contractions of the hands, hips and knees without functional improvement.



CASE 4

A 65-year-old man with PD for 22 years, fluctuations present for 17 years, and apparent cognitive decline, was wheelchair-bound, but able to transfer independently, and needed only minor assistance in day-to-day activities. Due to recurring hallucinations and paranoia in the nursing home, levodopa was reduced stepwise over a period of twelve months from 825 mg to 200 mg plus 150 mg amantadin. In the course of approximately 24 weeks on the low dose treatment, the patient developed dysphagia and became completely bedridden. We saw the patient severely akinetic, dehydrated, hips, knees, elbows, wrists, fingers and ankles in flexion position. The patient was rehydrated, amantadine stopped and quetiapine administered. He was then able to tolerate 900 mg levodopa. Plantar flexion of the ankles and flexion contracture of the left wrist and fingers remained, but the patient regained his ability to aid in transfers, move about in a wheelchair and could eat and drink unaided.

Figure 3

Table 1: Basic Data of Patients with Limb Contractures

Patient gender, age, disease duration	Concomittant disease	Levodopa equivalent dose before / after	Duration of lowered dopaminergic dosage	Final outcome
Case 1 Female, 65 yrs, 14 yrs of PD	Complicated pneumonia with artificial respiration	575 mg/316 mg	16 days	No improvement
Case 2 Male, 77 yrs, 16 yrs of PD	Urinary tract infection, psychosis	675 mg/400 mg	20 weeks	Partial improvement
Case 3 Male, 78 yrs, 6 yrs of PD	Hip fracture	600 mg/600 mg	4 weeks	No improvement
Case 4 Male, 65 yrs, 22 yrs of PD	Psychosis	825 mg/200 mg	24 weeks	Partial improvement

DISCUSSION

During the course of PD, there may be several reasons for reducing, discontinuing or even stopping dopaminergic medication. These causes include 1) concomittant acute infections, cardiovascular or cerebrovascular diseases, 2) drug induced psychosis and 3) surgery. Both the sudden deterioration of the medical condition as well as reduced dopaminergic stimulation result in transient immobilization.

Altogether, we saw four cases of severe, disabling contractures in PD patients within one year. All patients were in advanced stages of the disease, with a disease duration of between 6 and 22 years. Fluctuations and dyskinesias were described in three of the four cases. Two patients suffered cognitive decline and all four patients had a history of recurring psychosis under dopaminergic medication. In three of the four patients acute concomittant diseases necessitated hospital admission and a primarily non-neurologic medical intervention. As a result, dopaminergic medication was either reduced (case 1 & 2) or administered via gastric tube (case 3). In case 4, because of recurring hallucinations levodopa was slowly tapered off over 24 weeks to less than a quarter of the original dose. Excluding other structural or peripheral neurologic causes, the resulting striatal dopaminergic deficit has to be regarded as the main precipitating factor for limb contractures.

In the four cases presented here, contractures developed within 16 days to 24 weeks. Interestingly, contractures took a significantly longer time to develop in those two patients with prolonged levodopa reduction due to psychosis, and these patients were not primarily immobilized (cases 2 & 4), as were the two other patients (cases 1 & 3). Case 1 and 3 were immobilized immediately upon onset of the concomittant disease, and at the same time as irregular intake or application of levodopa/DCI via gastric tube was started. A failure of levodopa resorptionmay be assumed, as formula nutrition containing protein was probably given at the same time.

Levodopa or oral dopamine agonists cannot be administered intravenously. If a patient on oral dopaminergic medication will not or cannot swallow properly due to sleepiness psychotic status or physical incapability, a dopaminergic deficit will result. Medication should therefore be switched to soluble levodopa tablets as a minimum requirement. Levodopa must not be administered together with formula nutrition and a sufficient time should be allowed for gastric emptying and therefore resorption before application of medication. Although non-neurologists may be familiar with intravenous application of amantadine as a form of parenteral PD medication, this drug may not be sufficient to treat PD patients in advanced stages of the disease over a span of several weeks. Furthermore, it will enhance psychosis. Usually only movement disorder specialists are aware of the possibility of continuous subcutaneous apomorphine infusion or intestinal levodopa instillation via special pumps and are capable of titrating the dosage. Applying the non-ergot dopamine agonist rotigotine via transdermal patch may be a future treatment alternative, but may also not be well known among non-neurologists. In order to avoid a prolonged dopaminergic deficit in PD patients whose oral medication intake and / or resorption capability is impaired, these options should be considered, even if only as a transient measure on the intensive care unit or in the perioperative treatment stage.

Progressive degeneration of nigrostriatal neurons with depletion of endogenous dopamine, loss of physiologic storing capacity for decarboxylated levodopa as well as irregular resorption of medication due to reduced gastro-intestinal motility [12,13] are assumed to be responsible for fluctuations of motor performance in advanced stages of PD. It is common knowledge that insufficient exogenous dopaminergic stimulation in advanced stages of the disease will lead to exacerbation of rigidity, akinesia and dystonia with loss of physiologic movement range. Reports on characteristic skeletal deformities in PD patients dating back to a time before the widespread introduction of levodopa/DCI treatment [1,2,3,4,5,6,7] point to a characteristic pattern: flexion of wrists and metacarpophalangeal joints resemble the appearance of rheumatoid arthritis. This clinical picture was coined as “dystonic striatal hand” by Fahn and Jankovic [8], who demonstrated its complete resolution by adequate levodopa administration. Flexion of the knees, a slightly stooped posture with bilateral hip flexion, both arms bent at the elbows – every neurology textbook includes these features in its illustrations of Parkinson's disease. It is therefore reasonable to suggest that insufficient dopaminergic stimulation is the crucial precipitating factor for the development of flexion contractures in PD. The fact that several authors [9,10,11] present cases in which contractures occurred in levodopa-treated PD patients does not necessarily contradict this thesis, as patients were in advanced stages of the disease, suffering from fluctuations and dyskinesia, and no detailed information is given on the possibility of an insufficient dosage of levodopa or a reduced medication intake.

PD patients in advanced stages of the disease and with previous psychosis appear to be especially at risk for developing severe limb contractures. A consultant neurologist, specialized on movement disorders, should support the medical team of the intensive care unit for individual titration and application of dopaminergic medication in advanced PD patients. Furthermore, a physiotherapyist should regularly check the patient's range of limb movements and alert the attending physicians at the first signs of fixed dystonic posturing.

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