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Atypical parkinsonian syndrome – primary progressive freezing gait? Case report

Atypowy zespół parkinsonowski – pierwotne postępujące zatrzymanie chodu? Opis przypadku

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Summary

The diagnosis of atypical parkinsonian syndromes is problematic and may require many years. Similar to Parkinson's disease, it is based on the history of the disease, clinical evaluation, prospective patient's observation and exclusion of secondary parkinsonisms. This paper presents a report of a 59-years-old patient with slowly progressing levodopa unresponsive atypical parkinsonism of 7 years duration, with predominant hypokinesia and early freezing gait, that consist of sudden, episodic motor block due to inability to take steps. The patient fulfills the criteria of primary progressive freezing gait (PPFG), which should be differentiated from other parkinsonian syndromes, mainly progressive supranuclear palsy. The question whether PPFG is a distinct nosological entity or is an initial manifestation of other neurodegenerative disorders remains open.

Key words: atypical parkinsonism, parkinsonism "plus", freezing gait

Streszczenie

Rozpoznawanie atypowych zespołów parkinsonowskich jest problematyczne i może wymagać wielu lat. Podobnie jak w przypadku choroby Parkinsona, opiera się na wywiadzie, obrazie klinicznym, prospektywnej obserwacji chorego i wykluczeniu wtórnych zespołów parkinsonowskich. Praca przedstawia opis 59-letniego pacjenta z powoli postępującym od 7 lat opornym na leczenie dopaminergicznym atypowym zespołem parkinsonowskim, w którym przeważa spowolnienie ruchowe oraz wczesne zatrzymanie chodu, polegające na nagłym, przemijającym bloku ruchowym, związanym z niemożnością dalszego wykonywania kroków. Pacjent spełnia kryteria rozpoznania pierwotnego postępującego zatrzymania chodu (PPFG), które należy różnicować z innymi zespołami parkinsonowskimi, zwłaszcza z postępującym porażeniem ponadjądrowym. Kwestia, czy PPFG stanowi odrębną jednostkę nozologiczną, czy też jest początkowym etapem rozwoju innych chorób neurodegeneracyjnych pozostaje otwarta.

Słowa kluczowe: atypowy zespół parkinsonowski, zespół parkinsonizm „plus”, zatrzymanie chodu

Diagnostics of atypical parkinsonian syndromes, also called parkinsonian syndromes "plus", is, in spite of modern diagnostic methods progress, a clinical challenge. It concerns rare, chronic neurodegenerative diseases of an unknown etiology, unknown causative treatment and often symptomatic treatment of little effectiveness. The terms atypical parkinsonian syndrome and parkinsonian syndrome "plus" are related to the possibility of parkinsonian symptoms occurrence other than typical for idiopathic Parkinson's disease (PD) and additional, nonparkinsonian, symptoms occurrence. The diagnosis of these diseases, similar to PD, is based on the history of the disease, clinical evalua-

tion, prospective patient's observation and exclusion of secondary parkinsonisms. The most difficult moment in differential diagnostics between PD and atypical parkinsonian syndrome, as well as between particular atypical syndromes, is the most often the beginning of the disease. Clinical observation and readiness to verify the diagnosis in the course of the disease is important. In the typical course of PD some symptoms (e.g. escalated posture instability, falls, dementia, visual hallucinations not related with treatment and others) occur in the advanced stage but their early occurrence (in the first 3 years from the onset of the disease) is treated as atypical and should induce diagnostic alertness (1, 2).

One of the symptoms commonly observed in the advanced PD is a phenomenon of freezing of gait, also called motor block. It is a levodopa unresponsive parkinsonian feature, which may be the manifestation of the off time and is defined as a sudden, transient inability to continue walking, inability to “move the feet from the ground”. It occurs mainly with change in the walking direction, walking through narrow spaces, avoiding obstacles and so on. It is often accompanied by festination, postural instability, falls and bradykinesia/akinesia (difficulty in starting and impoverishment of movement/inability to start movement – which concerns different types of movement, not only walking). The symptom yields by itself after a while but it may be made easier by sensorial associations or accessory objects (3).

Freezing of gait may also occur in atypical parkinsonian syndromes, e.g. progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD) and in many secondary brain diseases: in vascular parkinsonism, normotensive hydrocephalus, in frontal lobe tumor and others (3, 4).

The following report is to present the case of the patient with slowly progressive parkinsonian syndrome, in which hypokinesia and early (in the second year of the disease) freezing of gait are predominant.

A 59-year-old male with higher education running his own company stays under care of Outpatient's Clinic of Department of Neurology and Epileptology of Centre of Postgraduate Medical Education in Warsaw due to gradually progressing gait disorder and slowness of movements. The disease started 7 years ago, in the 52 year of age, with a slight slowing in walking, speech and writing and impoverishment of mimics. At the beginning the patient was suspected of depression and treated with venlafaxine by the psychiatrist but occurrence of festination in the first year of the disease caused the diagnostics to widen. In the physical examination parkinsonian syndrome was then diagnosed with predominance of walking disturbance with periodic festination (especially in initiation of walking, while turn back and in limited space) and movement slowing with micrographia.

In the second year of the disease there was gait freezing and then postural instability as well as slightly stooped posture. In the brain magnetic resonance imaging there were discrete lesions of vascular origin in the subcortical white matter on both sides – with no progress in the following examinations. Wilson's disease was excluded. In the next years there were more accompanying diseases: type II diabetes five years ago and arterial hypertension and hypercholesterolemia two years ago.

Since the parkinsonian syndrome diagnosis there were a few attempts of levodopa treatment (in the maximum daily dose 600 mg) also with piribedil and amantadine. Every time the patient stopped the treatment after a few weeks/months with no improvement. A year ago he was taking 2 mg/day of ropinirole and 20 mg/day of paroxetine for a few months but with no satisfactory effect. The patient systematically undergoes motor and orthophonic rehabilitation.

The progress of the disease is slow and the patient remains independent and professionally active beside the treatment ineffectiveness. After 7 years of the disease gait disorder and hypokinesia are still dominant. Walking is slow, the steps are relatively large, the patient takes his feet off the ground and has no arm swing. Festination and freezing of gait occur often, the posture is unstable, the silhouette slightly stooped. Motor slowing is generalized and what mostly attracts attention is masked face and quiet, monotonous and often blurred speech. All movements have lower amplitude but difficulties in starting the movement, often the inability to start it, concern only walking. There is a slight, plastic rigidity in either upper or lower limbs, the most intense in the right lower limb. There is no tremor or other unintentional movements.

Some authors describing cases of long-term and progressive freezing of gait since the onset of the disease with other accompanying parkinsonian symptoms mildly expressed treat such clinical course of the disease as a separate syndrome (5-8). In order to standardize the nomenclature and encourage physicians to take it into consideration in differential diagnosis Factor et al. redefined the term “syndrome of primary progressive freezing of gait (PPFG)” in 2002 (8).

These authors, for about 5 years, observed a group of 30 patients (including 16 males) with progressive atypical parkinsonian syndrome (the onset of the disease at the age from 56 to 86) in whom freezing of gait was an early (in 60% the first) and dominant symptom. Among the accompanying symptoms (slightly expressed) the authors most often described bradykinesia, micrographia, masked face, stooped posture, muscle rigidity, symmetric hyperreflexia, rarely – speech disorder, tremor (postural or kinetic), cognitive dysfunction, extensor plantar response, dysphagia, upgaze impairment. Postural instability and falls occurred in the described patients after 3 years of the disease or later and dopaminergic treatment (levodopa, dopamine agonists) was ineffective (8).

Until now it is not defined whether and what kind of neuropathological lesions would be characteristic for PPFG. It is suspected that pathology could concern frontoparietal cortical regions, frontosubcortical pathways, globus pallidus, caudate nucleus – that would, however, require further research (7-11). As mentioned, freezing of gait is a levodopa unresponsive symptom no matter whether it is due to PD or atypical parkinsonian syndrome. It seems that bilateral deep stimulation of pedunculopontine tegmental nuclei (cholinergic pathway) could have a beneficial influence not only on freezing of gait in the advanced PD but also in PPFG (12-14). There are single reports on PPFG treated with MAO-B inhibitors (selegiline and rasagiline) and serotonin reuptake inhibitor (duloxetine) with positive effect (15-17).

Factor et al. proposed the following clinical diagnostic criteria indicating PPFG: 1) early freezing of gait (in first

3 years since the onset of the disease); 2) exclusion of secondary character of symptoms; 3) exclusion of clinical diagnosis of PD and other defined atypical parkinsonian syndromes; 4) lack of data from clinical evaluation, neuroimaging and laboratory tests suggesting another diagnosis; 5) lack of dyskinesia and motor fluctuations due to levodopa treatment (8). The reported patient in his course of the disease fulfils these criteria.

PPFG should be differentiated from PD, vascular, post anoxic and toxic parkinsonism, with frontal lobe tumor, normotensive hydrocephalus and other atypical parkinsonian syndromes, in which freezing of gait occurs (mainly PSP but also MSA, CBD, dementia with Lewy bodies and other rare neurodegenerative disorders). In particular PD form that manifests in pure akinesia – occur-

ring in patients with good response to levodopa and rather in the later stage of the disease (18, 19) – and the syndrome of pure akinesia with gait freezing (PAGF)(20-22) should be remembered. PAGF is a form of PSP in which ocular disorders (supranuclear gaze palsy, eyelid opening apraxia, blepharospasm) occur in the further course of the disease. Compta et al. described two patients fulfilling PPFG criteria for many years in whom clinical symptoms indicating PSP occurred after 8 and 10 years of the distinct (23).

It seems that the question whether PPFG is a distinct nosological entity or is a first, although lasting for many years (that could last even for most of the time), stage of other neurodegenerative diseases is open. Further observations of presented patients will allow confirming or excluding initial diagnosis of PPFG.

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