CASE REPORT

Park sleep: a non-motor dominant Parkinson's disease phenotype

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SUMMARY

A 69-year-old man was evaluated in our neurology department, for a presumed diagnosis of 'night-time seizures'; however, this diagnosis was quickly dismissed after the patient (and his wife) described how he 'acted out' and talked throughout his dreams, without any seizure-like activity. This problem had been present for ~10 years. An EEG ruled out epilepsy. The patient also described a 10-year history of constipation, loss of smell and 'frequent collapses'. These symptoms fit in with the recently published criteria of 'prodromal Parkinson's Disease' and prompted a formal assessment for Parkinson's disease (PD). He had no tremor. A subtle festinating gait pattern and a 2-finger tremor in the right hand were noted. The diagnosis of PD was confirmed by a dopamine transporter scan. Clinically, this is one—Park sleep: rapid eye movement sleep behaviour disorder subtype—of 7 different non-motor dominant PD phenotypes recently described.

BACKGROUND

This case reflects the importance of recognising the early—prodromal or non-motor symptoms (NMS) of Parkinson's disease (PD). It highlights the benefit of identifying the early non-motor (NM) features of PD, in order to treat promptly and reduce the multiple morbidities of this disease. Moreover, it describes one—rapid eye movement (REM)—sleep disorder subtype—of seven recently postulated phenotypes of NM predominant PD.

CASE PRESENTATION

A 69-year-old man was referred to our neurology outpatient clinic, with a presumed diagnosis of 'night-time seizures'. However, after detailed clinical history-taking, it became evident that epilepsy was not this patient's diagnosis. He and his wife described a 10-year history of basically four symptoms, which started almost simultaneously. The main symptom was described as an 'exaggerated and realistic acting out' of his dreams: talking loudly, moving aggressively (suffering several injuries as a consequence), falling from the bed and even breaking his wrist on one occasion. This led the patient and his wife to sleep in separate beds. The second symptom presented was severe constipation; even with daily use of a laxative, he had (on average) only one bowel movement per week. Third, he noted that he was incapable of smelling usual scents and foods. Finally, his fourth symptom was recurrent episodes of collapse, which usually corresponded to drops in his blood pressure. Importantly, throughout those 10 years, no obvious

motor symptom was noted. His wife mentioned that, more recently, during the past year, she started to note that the patient was 'dragging' his feet; however, the patient denied tremor, rigidity or slowness of movement.

Both the patient and his wife also mentioned that his overall cognitive capacity was deteriorating. For example, he was struggling to do the household accounting, something routine for him. Additionally, he was losing the ability to read a book for more than 15 min (because everything 'became a blur') and found it difficult to recall recent events of his day. This cognitive decline was subtle but, however, increasingly worrisome for the patient and his wife.

Unfortunately, these symptoms had not been taken seriously throughout the previous 10 years. They were treated as separated, isolated symptoms and were regarded individually. They were never considered as part of one single diagnostic entity.

Physical examination revealed a mild resting and positional tremor of the first two fingers of his right hand. No other tremor was noted. A subtle festinating gait was evident after walking short distances, as was a mild stooped posture. No postural imbalance was seen. Strength was 5/5 in all the limbs and no rigidity was noted. The patient had cogwheel rigidity in both upper limbs. Reflexes were diminished in all four limbs. Neither cerebellar signs nor cranial nerve palsies were identified.

Owing to the predominance of NMS in the setting of possible PD, a presumptive diagnosis of 'prodromal Parkinson's Disease' was made, which prompted pertinent investigations, including a brain MRI, dopamine transporter (DAT) scan, complete blood tests (including thyroid function tests, toxins, heavy metals, antibodies and vitamin B₁₂) and lumbar puncture. The brain MRI showed mild-to-moderate frontal lobe atrophy, no atrophy in brainstem or cerebellum and no signs of previous strokes or small vessel disease. However, it did show (figure 1) a low signal in basal ganglia in T2-fluid attenuated inversion recovery, very suggestive of PD. All blood investigations were normal as was the lumbar puncture. Importantly although, the DAT scan was abnormal, revealing a symmetrical loss of uptake in both putamina with relatively preserved uptake in the caudate nucleus.

Following the DAT scan results, a diagnosis of NM-predominant PD was made, specifically, of REM-sleep subtype. Treatment with Madopar 62.5 mg three times a day was given and improvement was noted soon after ~1 week of treatment. The dose was then increased to four times a day

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Figure 1 (T2-fluid attenuated inversion recovery): low signal in bilateral basal ganglia, suggestive of Parkinson's disease.

with no side effects noted and continuous improvement. Mainly, the improvement was noted in the gait pattern, mobility of the lower limbs and of the discrete resting tremor of the first two fingers of the right hand. Moreover, the NMS were treated accordingly (interestingly, some of this patient's NMS such as constipation and depression, improved after starting Madopar); Clonazepam was prescribed for the REM-sleep disorder and it proved to be helpful as the patient (and his wife), when returning to clinic, stated that this treatment had reduced the frequency of acting out episodes at night. His constipation was also treated with lactulose and it, too, provided relief. Overall, once the diagnosis was made, with the correct treatment the patient presented a very good response.

INVESTIGATIONS

- ▶ Brain MRI
- ▶ DAT scan
- ▶ Blood tests including antibodies for vasculitis, toxins, heavy metals and cultures.
- ▶ Lumbar puncture: proteins, cellular count and glucose normal. Normal pressure.

DIFFERENTIAL DIAGNOSIS

- ▶ Vascular PD
- ▶ REM-sleep disorder

TREATMENT

- ▶ Levodopa 62.5 mg four times a day. Laxatives for constipation and blood pressure control.
- ▶ Clonazepam for REM-sleep disorder.
- ▶ Physiotherapy and occupational management.

OUTCOME AND FOLLOW-UP

The patient responded very well to Levodopa and he currently continues on a steady dose. Interestingly, his NMS have also improved after starting levodopa. Mainly, his constipation improved and the acting out of his dreams also reduced.

DISCUSSION

NMS subtyping in PD is a new concept. Much effort has taken place to incorporate NMS into the motor-predominant diagnostic criteria (UK-Parkinson Disease-Brain Bank Criteria). The objective is to ensure that the prodromal—NM—phase of PD is promptly detected and adequately diagnosed not as independent or unrelated symptoms but, rather, as part of PD. Hence, if this

is obtained, the morbidity and mortality of patients with PD will greatly improve.

To this day, essentially six different NMS dominant clinical phenotypes within PD, mainly in the early and untreated phase, have been proposed on clinical observation:

- ▶ Park cognitive
- ▶ Park apathy
- ▶ Park depression/anxiety
- ▶ Park sleep
- ▶ Park pain
- ▶ Park autonomic

Of these six subtypes, this patient presented Park sleep: REM-sleep behaviour disorder subtype. The REM-sleep behaviour disorder subtype of PD has several important characteristics:

- ▶ Symmetric disease onset;
- ▶ Autonomic dysfunction—prone to higher prevalence and severity of orthostatic hypotension;
- ▶ Higher rate of depression;
- ▶ Visual hallucinations;
- ▶ Male gender;
- ▶ Non-tremor dominant subtype/akinetic rigid syndrome, lower total Unified Parkinson's Disease Rating Scale (UPDRS) score accounted for by tremor;
- ▶ Increased frequency of falls;
- ▶ Impairment of colour vision.

Our patient, besides being male and having a predominant REM disturbance, suffered from autonomic dysfunction, a low-scoring UPDRS, altered colour vision and several falls.¹

Excessive daytime sleepiness and involuntary dozing affects up to 50% of patients with PD and could be a preclinical marker.² REM behaviour disorder (RBD) occurs in about a third of patients with PD and represents a parasomnia characterised by loss of the normal skeletal muscle atonic during

Learning points

- ▶ Prodromal Parkinson's disease (PD) is characterised by multiple non-motor symptoms, mainly constipation, anosmia, rapid eye movement-sleep disorder and autonomic dysfunction.
- ▶ There are essentially seven different non-motor phenotypes: (1) Park cognitive, (2) Park apathy, (3) Park depression/anxiety, (4) Park sleep, (5) Park pain, (6) Park autonomic and (7) Park fatigue. Any one of these particular phenotypes or subtypes can be the dominant manifestation in a patient with PD.
- ▶ Dopamine transporter scan imaging is useful for diagnosis of prodromal PD.
- ▶ The diagnosis of PD is now being approached differently: as a disease not restricted to the central nervous system but, rather, as a disease that—according to pathological discoveries—extends to the peripheral nervous system and enteric nervous system, among other systems. This extension enables a more specific and detailed group of PD phenotypes.
- ▶ The UK-Parkinson Disease-Brain Bank Criteria (UKPDBBC) only consider the motor aspects for diagnosis. However, in view of recent publications and discoveries, the UKPDBBC falls short of diagnosing the newly described non-motor predominant cases of PD. Hence, new criteria and diagnostic algorithms are needed.

REM-sleep, thus enabling patients to physically enact their dreams, which can often be vivid or unpleasant;³ Vocalisations (talking, shouting and vocal threats) and abnormal movements (arm or leg jerks, falling out of bed and violent assaults) are commonly reported by partners. In patients with isolated RBD, imaging studies have indicated a small but significant symmetrical reduction in striatal dopaminergic uptake, which may be suggestive of preclinical PD.⁴ Speculation is that RBD could arise because of the degeneration of lower brainstem nuclei, including the pedunculopontine and subcoeruleal nucleus, characteristics consistent with Braak stages 1 and 2.⁵

Undoubtedly, the incorporation of NMS in PD diagnosis is exciting and inspiring because it implies that timely treatment will improve morbidity and mortality.

Competing interests None declared.

Patient consent Obtained.

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