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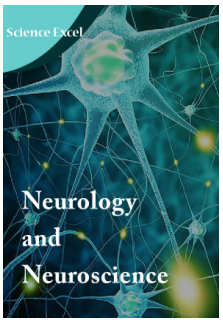

A Criminal Case of Hypersexuality and Parkinson's Disease

Zhou Ke[1], Peter CL Chow[2], Wendy Ko[3], SC Lim[3]

[1]*Senior Resident in Geriatric Medicine, Changi General Hospital, Singapore.*
[2]*Clinical Fellow,Department of Geriatric Medicine, Changi General Hospital, Singapore.*
[3]*Senior Consultant Geriatrician, Changi General Hospital, Singapore.*

*Correspondence
Si Ching LIM. .
Senior Consultant, Department of Geriatric Medicine, Changi General Hospital, Singapore.

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Abstract

Parkinson's Disease (PD) is a neurodegenerative disease which has a combination of motor and non-motor symptoms. The non-motor symptoms pre-dates the appearance of motor symptoms which reflect the deposition of alpha synuclein in regions of the brain which interfered with dopaminergic pathways. Sexual dysfunction is common in PD and hypersexuality is a known impulse control disorder (ICD) secondary to dopaminergic treatment. Hypersexuality as a prodrome to motor symptoms associated with sexual dysfunction is not well described. Consequences of hypersexuality which resulted in criminal acts may not be pardoned based on medical grounds alone.

Introduction

Parkinson's Disease (PD) is the second commonest major neurodegenerative disorder, second only to Alzheimer's Disease. PD presents with non-motor and motor symptoms. In the prodromal phase of PD, non-motor symptoms like constipation, anosmia, rapid eye movement (REM) sleep disorders may precede the onset of motor symptoms by 10-15 years. Hypersexuality has not been described as one of the prodromal symptoms of PD, although it is well recognised as part of impulse control disorder (ICD) associated with dopaminergic drugs used in the treatment of PD.

Hypersexuality has been described as a recurrent, intense and excessive preoccupation with sexual urges, fantasies and behaviour which an individual struggle to control. The objectively observed clinical symptom include high frequency of sexual activity. Subjectively the individual experience uncontrollable urges and fantasies which result in adverse life consequences and psychological distress or impairment. Among the adverse consequences of hypersexuality related behaviour, sexually transmitted diseases like HIV, relationship disharmony, social isolation, loss of income, legal violations and unwanted pregnancies may cause distress and harm not only to the individual but also their sexual partners. Hence, hypersexuality is commonly associated with depression and anxiety [1-3].

This paper described the clinical features of hypersexuality, prior to onset of motor symptoms of PD which became a criminal case. Medical legal arguments of appropriateness of criminal charges for an individual who got to the wrong side of the law due to his medical illness. Can the case be counter argued with insanity to get him off the hook?

Case Presentation

Mr. C, a man in his mid-60s, was referred to the geriatric medicine clinic for evaluation of cognitive impairment, mood disorder, unsteady gait and tremor. He was scheduled to attend a court hearing for sexual harassment which took place 2 years prior to clinic consultation.

While in clinic, he also complained of tremor affecting both lower limbs, low mood and increasing forgetfulness. His medical history was notable for Type 2 diabetes which was well-controlled with oral hypoglycemic agents, and intermediate-risk prostate cancer, for which he underwent prostatectomy with no evidence of recurrence on annual prostate-specific antigen (PSA) surveillance. There was no significant family history of PD or psychiatric conditions. His medication regimen included only his diabetes treatment; he did not take other over the counter medications, supplements, or alternative therapies.

Approximately two years prior to his clinic consultation, Mr. C was charged with sexually molestation while at work leading to his dismissal. He was noted to be quieter and depressed since the incident. His sexual interests and demands completely ceased and he stopped watching pornography. Gradually, his family also observed a decline in his memory, necessitating assistance with some

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of the instrumental activities of daily living (iADLs), such as medication management and finances, though maintained independence in all basic activities of daily living (bADLs).

Chronologically, his wife noted a heightened interest in sexual behaviour 4 years prior to clinic consultation, followed by onset of tremor affecting his distal left lower limb which appeared a year later; which progressively progressed to involve all four limbs. The tremor was more prominently on the left. The progression of events was shown on Figure 1.

His wife described heightened increase in surfing the internet for pornography and masturbation but was unsure if he seeked relief from commercial sex workers. His wife, overwhelmed by work and domestic responsibilities, usually rejected his sexual demands. On the occasions that she reluctantly consented to intercourse; intercourse never did happen due to Mr. C's erectile dysfunction. No other disinhibited behavior or changes in affect were observed. Despite these personal issues and onset of tremor, Mr. C continued to perform effectively as a bus driver for persons living with mental disabilities.

At the first clinic visit, when asked about the sexual harassment incident, he still had good insight into the incident where he described a sudden desire to touch the female passenger in the bus seated 2 rows behind him. He then approached the passenger, touched her chest and private parts. He stopped only when someone outside shouted for him to stop. After the incident, he recalled being interviewed by the police and admitted he had touched the female passenger inappropriately.

On physical examination in clinic, Mr. C was observed to be hypomimic. Neurological examination showed normal cranial nerves, presence of bradykinesia, more pronounced on the left upper and lower limbs, than on the right side. Cogwheel rigidity was observed in the left upper limb. Power was 5 for all muscle groups. Tone was increased in all 4 limbs, knee and ankle reflexes were absent on both sides, with an extensor Babinski on the left. The patient's gait was stooped and slow, with absence of arm swing on the left side. The gait stance was normal, with no shuffling, freezing or festination. He was walking independently without walking aid. There were no gaze abnormalities, nor frontal lobe release signs. There was no postural drop in BP on standing from lying position. There were no other abnormalities detected on examination of the other systems.

At his first clinic consultation, Psychometric screening yielded the following results:

- Geriatric Depression Scale (GDS) 7/15
- Mini-Mental State Examination (MMSE) 21/30
- Montreal Cognitive Assessment (MOCA) 15/30
- A formal neuropsychological evaluation revealed deficits in attention, information processing speed, and verbal fluency, along with mild deficits in learning and memory.

The provisional diagnosis in clinic after his first consultation was major depression with cognitive impairment, idiopathic Parkinson's disease and probable dementia.

Over the next year, (PD post diagnosis year 4) his stability declined, culminating in a fall that caused a left proximal humeral fracture. The fracture was surgically fixed and he was sent to a step down care facility for slow stream rehabilitation. Post-rehabilitation, he regained community ambulation with the aid of a quad stick.

Investigations

Basic blood investigations taken after the first clinic visit were all unremarkable and within normal ranges. Serum free Thyroxine 11.5 pmol/L, Thyroid stmulating hormone, serum 0.967 mu/L, serum folate 7.36 nmol/L, serum vitamin B12 372 pmol/L, corrected calcium 2.23 mmol/L.

Magnetic Resonance Imaging (MRI) nigrosome series showed loss of the nigrosome-1 on the SMWI images. Findings were in keeping with nigral cell loss and clinical suspicion for Parkinsonism. The MRPI was within normal limits and there was no relative volume loss or abnormal signal in the cerebellum and deep nuclei is seen. In addition, patchy FLAIR hyperintensities in the periventricular and subcortical white matter with beginning confluency likely representing chronic microvascular ischaemic changes was noted. There was mild cerebral involutional changes which were deemed appropriate for age. In summary, the MRI imaging confirmed features of Parkinson Disease with no imaging evidence of atypical Parkinsonism is seen. There was background chronic microvascular ischaemic changes seen.

Differential Diagnosis

Parkinson Disease

The asymmetrical nature of the Parkinsonian symptoms and the positive response to dopaminergic treatment support the diagnosis of Parkinson's disease. The MRI nigrosome finding was helpful to confirm diagnosis of idiopathic PD, even though the presentation of tremor which started in his lower limb was unusual.

Hypersexuality as a prodrome to PD?

The patient exhibited hypersexuality approximately 9 months prior to the onset of motor symptoms, suggesting these as potential prodromal symptoms.

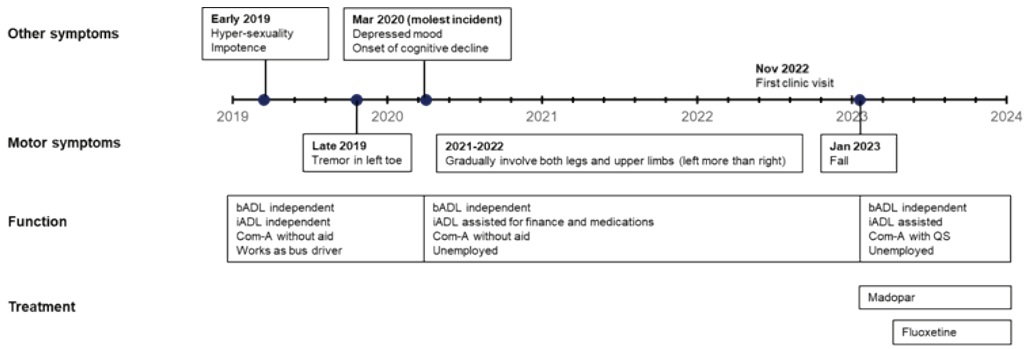

Figure 1. *Timeline of key events.*

Importantly, there was no evidence of alternative conditions that could be associated with hypersexuality, such as bipolar disorder, substance abuse, or behavioural and psychological symptoms of dementia (BPSD).

Depression

The onset of depression after the sexual harassment incident was likely precipitated by his dismissal from work, impending legal actions for his sexual harassment case, loss of respect from his colleagues, friends and family; on the background of an increased risk of depression due to the underlying PD. Intriguingly, the onset of depression and probably its associated psychomotor retardation led to a reduction of his hypersexuality symptoms.

Mild dementia

His spouse complained of increasing difficulties managing his instrumental activities of daily living such as assistance with medications and financial management. The onset of depression preceded the cognitive symptoms and may have contributed to the cognitive impairment.

Management

Mr. C was started on anticholinergic in March 2022 for tremor predominant PD but developed anticholinergic side effects with no improvement in motor symptoms, hence anticholinergic was discontinued and he was started on Madopar (50mg Levodopa + 12.5mg Benserazide) 62.5mg TDS, which was subsequently increased to 125mg TDS after three months due to suboptimal response.

He was referred to psychiatrist for a formal assessment of his mental status especially pertaining to his mental capacity at the time when he harassed his victim sexually. The psychiatrist concurred with geriatrician's diagnoses of major depression and mild dementia. He was started on Fluoxetine (SSRI) for management of depression. The psychiatrist was of the opinion that he had insight and mental capacity when he intentionally offended the victim sexually.

Outcome and Follow-up

Mr. C was followed up in clinic to review function, response to treatment for PD and depression. Since anticholinergic treatment started in March 2022, he remained independent and community ambulant. He requested for phosphodiesterase inhibitor in September 2022 for erectile dysfunction, which did not improve satisfactorily. His wife reported modest improvement in tremor and bradykinesia with Madopar. Importantly, hypersexuality did not recur with the initiation of Madopar.

His depression did not fully respond to fluoxetine after a trial of 2 years and was changed to Duloxetine (SNRI). Duloxetine was the preferred antidepressant since he had concomitant neuropathic pain due to vertebral fracture sustained after a fall. His mood subsequently improved, but cognition continued to decline, albeit gradually over the years.

Discussion

PD is the second commonest major neurodegenerative disorder after Alzheimer's Disease. Prior to the onset of motor symptoms, alpha synuclein has been shown to be present in midbrain which progressively involve other areas of the brain and spinal cord, spreading to involve other organs like the GI tract (causing constipation), Olfactory nerve (causing hyposmia), depression, Rapid eye movement behavioural disorder (RBD). These non-motor symptoms predate the onset of motor symptoms by up to 10-15 years [4].

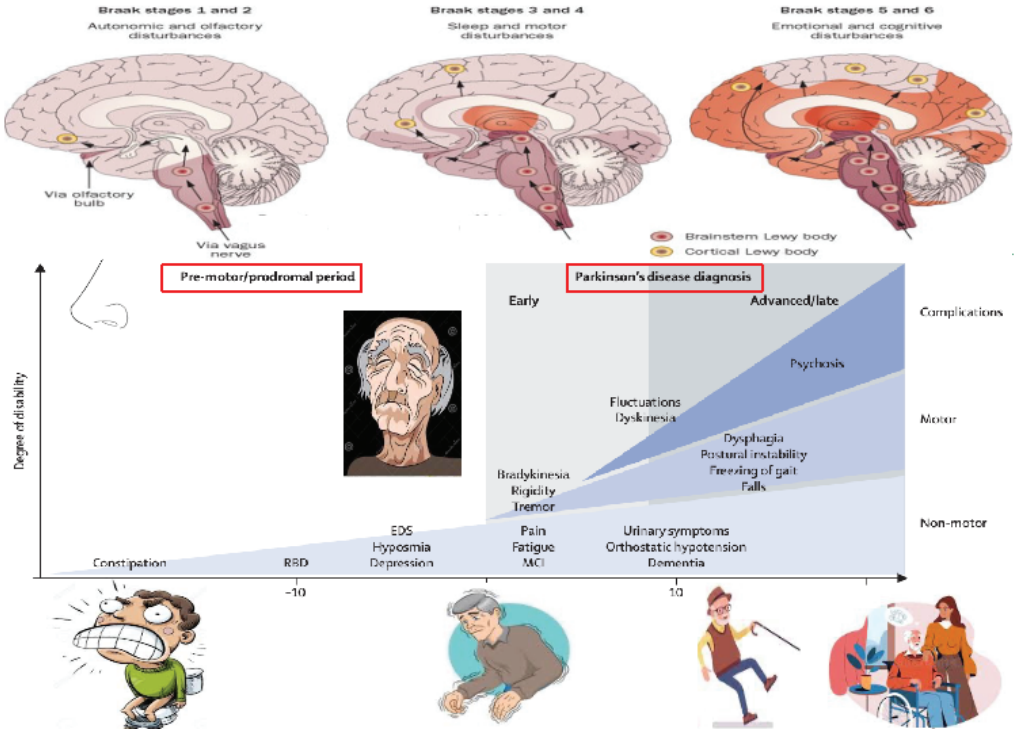

Figure 2. *Disease progression and symptoms of PD. (Braak 2004)*

The cardinal motor symptoms of PD are resting tremor, rigidity and bradykinesia [5]. Clinical diagnosis of PD is usually made based on the appearance of these motor symptoms. However, it is increasingly recognized that non-motor symptoms precede motor symptoms by many years [5]. Non-motor symptoms of PD are often underreported, and may include neuropsychiatric symptoms, sleep disorders, autonomic symptoms including sexual dysfunction, gastrointestinal symptoms, sensory and other symptoms (Table 1) [6]. With progression of PD, therapeutic window of madopar gets narrower and patients develop motor complications like dyskinesia, autonomic dysfunction progresses causing orthostatic hypotension, urinary symptoms, postural instability causing falls and dementia are both late complications of PD (see Figure 2).

Hypersexuality is classified as an ICD along with typical examples like gambling, compulsive eating, compulsive shopping etc. In PD, ICD is typically associated with treatment with dopamine agonists with an estimated prevalence of 3.5-7.2% [7,8]. Hypersexuality is characterised by an increase in sexual interest, arousal and behaviour which are out of keeping with premorbid personality. Hypersexuality is commonly reported among persons with neurodegenerative diseases and is distressing for the person, their caregivers and healthcare workers. Features of hypersexuality like preoccupation with sexual thoughts, frequent demands and desires for sexual practice, which may include use of sexual phone lines, internet pornography or contact with commercial sex workers may lead to distress and disharmony for the person and his sexual partner. For this particular case, his spouse reported features of hypersexuality which was different from his premorbid personality and behaviour pattern. The heightened interest and excessive demands caused unhappiness and stress for the spouse due to the mismatch in demand and interest. Hypersexuality in neurodegenerative disorders often leads to caregiver burden resulting in institutionalisation [9]. Within institution settings like hospital and long-term residential care, sexual disinhibition is a challenge for the healthcare workers and may result in elder abuse. Reported qualitative changes in hypersexuality in PD also included transvestism, paraphilias and gender identity disorders. These cases however, were reported after initiation of PD treatment, with patients denying the onset of symptoms prior to treatment [10-13].

Sexual dysfunction in PD is one of the most under-recognized non-motor symptoms. Studies have demonstrated a high prevalence of decreased libido, orgasmic dysfunction and erectile dysfunction (ED) in patients with PD [14]. The cause for sexual dysfunction is due to autonomic dysfunction due to loss of dopaminergic neurones. Mr C hypersexuality was limited by sexual dysfunction as his spouse reported ED on the occasions that she consented to intercourse, and this had caused much frustration for them both. The possible causes of ED in this case could be due to autonomic dysfunction caused by diabetes mellitus and PD. One of the earlier non-motor manifestations of PD is autonomic dysfunction which is generally mild in idiopathic PD compared to the other Parkinson Plus syndromes like Multisystem atrophy (MSA) [15]. Treatment with anticholinergic like Benztropine for PD may also contribute to ED.

Hypersexuality in PD is typically associated with long-term dopaminergic therapy. Dopamine receptor agonists, the most implicated class of medications, is associated with 2-3.5 times increased odds of the development of ICDs [16]. In addition, other risk factors include younger onset of disease, male gender and higher doses of dopaminergic agent [17]. Pathogenesis of hypersexuality is not currently well understood. Studies have suggested that aberrations in the structures or circuit linked to behaviour mediations, such as the frontal-subcortical, temporal, or limbic system could contribute to the development of hypersexuality [18]. The central dopaminergic pathway also has been postulated to influence sexual function and plays a role in the increase or decline in libido [10]. Dopamine in the mesolimbic area is implicated in drug addiction and has a role in regulation of sexuality. Hypersexuality has also been described among lesions of prefrontal cortex associated with general loss of impulse control [19,20].

In cases of hypersexuality in context of dopaminergic therapy, it has been hypothesized that the pulsatile stimulation of the dopaminergic reward system results in secondary changes after an initial degenerative process [14]. Another

Table 1. *Non-motor symptoms of Parkinson's Disease [3]*

Neuropsychiatric symptoms	Sleep disorders	Autonomic symptoms	Gastrointestinal symptoms	Sensory symptoms	Other symptoms
Depression Apathy Anxiety Anhedonia Attention deficit Psychosis-hallucinations, illusion, delusions Dementia Obsessional behaviour (usually drug induced) Repetitive behaviour Confusion Delirium Panic attacks	Restless legs syndrome Periodic limb movements Rapid eye movement (REM) sleep behaviour disorder Non REM-sleep related movement disorders Excessive daytime somnolence with sleep attacks Vivid dreams Insomnia Sleep disordered breathing	Bladder disturbances-Urgency, nocturia, frequency. Sweating Orthostatic hypotension Coat-hanger syndrome Pain Sexual dysfunction Hypersexuality (likely drug induced) Erectile dysfunction Dry eyes	Dribbling of saliva Ageusia Dysphagia and choking Reflux Vomiting Nausea Constipation Unsatisfactory voiding of bowel Faecal incontinence	Pain Paraesthesia Olfactory disturbance	Fatigue Diplopia Blurred vision Seborrhoea Weight gain / loss (possibly drug induced)

hypothesis described denervation hypersensitivity leading to an augmented excitatory effect of the exogenous dopaminergic agent [14]. However, the pathophysiology of hypersexuality in PD as a prodromal non-motor symptom prior to prescription of dopaminergic use remained unexplained.

Hypersexuality and Criminal Law

Mr C was unfortunately caught and brought to a criminal proceeding for him touching a mentally handicap female inappropriately when he was the driver of the bus she was on. This conviction of sexual offence follows the common law approach in criminal law because Singapore is a common law jurisdiction where judgements handed down by the courts are one of the sources of law. Specifically, there is a statutory Penal Code 1871 [21] spelling out the definition and punishment for a wide range of actions which are classified as criminal offenses such as assault, sexual offence, rape, wrongful hurt, murder etc. Mr C had insight at that time, as he remembered he consciously wanted to touch the passenger for sexual gratification, which was consistent with the statement he gave the police. He then proceeded to sit down next to the passenger and touched her breasts and genitals until he was stopped by another person outside the bus who shouted for him to stop.

These two elements of intention and action comprise the general principle of criminal law in common law jurisdiction of mens rea and actus reus - mens rea refers to the offender's mental state at the time of the crime, whereas actus reus relates to the physical act of committing a crime [22]. He was prosecuted for his indecent act and was imprisoned as his actions were intentional and he insulted the modesty of his victim.

One of the defences used in the English criminal law is insanity [23] or a state of unsoundness of mind (in Singapore law) [24]. This argument was not be applicable for Mr C since he clearly remembered and expressed his intention of wanting to touch his victim for sexual gratification. Furthermore, the victim was mentally disabled and probably did not understand what his actions implied; therefore, it was unlikely that Mr C could establish she consented to his actions [25].

He was referred for formal psychiatric assessment before the trial and was certified as mentally fit at the time when he was caught violating his victim's modesty. The same argument by his psychiatrist was that he remembered his full intentions prior to committing the act, yet he still went ahead knowing his actions were wrongful. Even with the diagnosis of hypersexuality as the non-motor prodromal symptom of PD, he did not have any other medical conditions like dementia, delirium or psychosis to certify him as mentally unsound. Even though hypersexuality as an early symptom of PD without prescription of dopaminergic drugs, has not been reported, this could not be used as an argument to pardon his actions as his intentions at the time was clearly wrong. Furthermore, even though PD is associated with dementia risk, it is a late complication for PD patients. Mr C was still working as a competent bus driver, hence he clearly did not have cognitive impairment. The lack of exposure to dopaminergic drugs ruled out ICD like hypersexuality which is well documented for PD patients.

Therefore, insanity or unsound mind is not applicable as a defence to get him off the prosecution. The symptoms of hypersexuality should have been brought for earlier medical assessment and management to avoid this unfortunate incident.

In common law, when the actus reus were fulfilled, in the setting of mental incapacity (like dementia or under the influence of substance use) criminal prosecution for violation of modesty would be acquitted on the grounds of unsoundness of mind. In that case, the sentencing shall not be imprisonment but referral for psychiatric treatment [26].

Management of hypersexuality is challenging for the patients and caregivers. Medications for management of hypersexuality are prescribed off-label and evidence is weak. The choice of medications include SSRI, Naltrexone, antipsychotics, mood stabiliser, beta blockers, alpha reductase inhibitors where the effects include interfering with libido, erectile dysfunction and ejaculation [27,28]. For PD patients with hypersexuality on dopamine agonist or high dose levodopa, it is recommended to try to reduce the dose. Switching dopamine agonist for levodopa may be helpful [29].

Conclusion

This case presents the first case of hypersexuality as an initial non motor prodromal symptom of PD. The change in sexual behaviour was uncharacteristic of his premorbid behaviour and the patient had no evidence of comorbid psychiatric conditions, cognitive impairment, other neurological conditions, or drug use that could be attributed to the development of hypersexuality. The pathophysiology of PD and hypersexuality is complex and not well-understood. This case describes hypersexuality as a non-motor prodromal symptom of PD which unfortunately, led to criminal prosecution.

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