CASE REPORT

Transient Daily Episodes of Vision Loss Due to Parkinson's Disease

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ABSTRACT

Visual complaints are common in Parkinson's disease (PD), but transient visual loss has not previously been defined as a feature of parkinsonian-related disease. We report a patient with recurrent daily episodes of transient and disabling visual loss due to PD-related non-motor fluctuation. During his visit, he experienced one such episode, which allowed for close observation and examination during and after the visual loss. Implications for localization of the visual loss are reviewed in the context of visual pathway disturbances in PD.

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Introduction

Parkinson's disease (PD) commonly results in visual disturbances that are not always recognized by clinicians as related to PD neurodegeneration. Efferent visual pathway dysfunction includes abnormal eye movements (such as convergence insufficiency), decreased blink rate, and eyelid retraction, and common clinical manifestations of these disturbances are double vision, inability to perform near tasks (i.e. read), and severe dry eye.¹ Alterations in afferent visual pathway function, from the retina to the cerebral cortex, include diminished contrast sensitivity, colour vision impairment, and visuospatial and visuoperceptual impairment.² Increasing attention is being paid to non-motor symptoms (NMS) in PD, because they contribute to significant disability and decreased quality of life.³ Fluctuations in NMS or non-motor fluctuations (NMF) occur more frequently in dopamine-treated patients with motor fluctuations, but they also occur independently and can result in greater disability.⁴ Other than visual hallucinations and diplopia, visual symptoms are often overlooked in investigations of NMS and NMF.⁴ Here, we report a patient with PD and mild cognitive impairment (MCI) with NMF that include multiple daily episodes of disabling visual symptoms that we serendipitously witnessed during a neuro-ophthalmologic evaluation. Implications regarding

mechanism and localization are discussed. The patient provided written, informed consent to allow for reporting of findings.

Case report

A 75-year-old man with a 7-year history of PD presented for neuro-ophthalmic consultation with complaints of disabling visual symptoms for 10 months. The patient's initial manifestations of PD included tremor (right greater than left), bradykinesia, and gait instability. Four months prior, he sought an outside evaluation for second opinion and a dopamine transporter (DaT) single photo emission computerized tomography scan was completed. Results revealed asymmetric DaT activity (see Figure 1). The patient's NMS included cloudy thinking, memory loss, mood changes (anxiety, depression), constipation, Rapid Eye Movement (REM) sleep behavioural disorder, and mild dysphagia. His motor symptoms were responsive to carbidopa/levodopa and other dopaminergic therapies. Due to his concern for "dependence" on medications and side effects, however, he frequently stopped and/or changed his medications. Around the time he began to experience disabling visual symptoms, he abruptly discontinued all medications for the treatment of PD for 3

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Figure 1. The patient's dopamine transporter SPECT (single photo emission computerized tomography) scan revealing asymmetric dopamine transporter activity in the striatum. There is decreased activity on the left resulting in a circular or oval striatal shape (see arrow), consistent with patient's parkinsonian signs and symptoms of right greater than left motor dysfunction.

months. Eventually, he restarted carbidopa/levodopa, and 2 months prior to presentation, he was instructed to take carbidopa/levodopa 25/100 four times a day. He admitted that he missed one or two doses per day on occasion.

His past medical history included well-controlled hypertension, pre-diabetes, obstructive sleep apnoea, and open-angle glaucoma. Past surgical history was remarkable for cataract extraction with intraocular lens placement in both eyes and successful trans-sphenoidal pituitary resection 2 years prior that was performed after incidental discovery of a pituitary macroadenoma with no evidence (by MRI, examination, or visual field testing) of visual pathway compromise. In addition to carbidopa/levodopa, his medications included artificial tears and latanoprost eye drops, aspirin, metformin, omeprazole, levothyroxine, simvastatin, losartan, calcium, and vitamin D3 supplementation. For 12 months prior to pituitary resection, the patient was monitored by neuro-ophthalmology. At his final monitoring visit, he had normal visual acuity, normal extraocular eye movements, and bilateral dry eye. Fundus examination revealed bilateral optic nerve cupping and threshold visual field perimetry was consistent with early stage glaucoma. Dry eye treatment and continued care for glaucoma was recommended. The patient underwent an uneventful pituitary tumour resection without consequence.

Upon return to neuro-ophthalmology (3.5 years later), he complained of multiple daily, disabling, and transient episodes of visual loss for 10 months. Episodes began with blurred vision in his right eye, then immediate "glare" and bilateral vision loss

that often occurred shortly after waking in the morning. Duration ranged from 20 min to 3 h. He consulted with his optometrist for several months and several prescription lenses were prescribed but not helpful. As a result, he fired his optometrist of several years. Brain MRI 5 months prior was stable with a previously noted remote cerebellar lacune and no recurrence of his pituitary tumour. At that time, he scored 24 of 30 points on a Montreal Cognitive Assessment with memory impairment (3/5 points), language and verbal fluency impairment (0/3 points), and mildly impaired clock drawing (2/3 points, see Figure 2).

Figure 2. Clock drawing by patient to indicate 10 min after 11, which revealed mild difficulty with spatial distribution of number placement and repetition of the number 6.

On neuro-ophthalmic examination, his visual acuities were 20/30 and 20/20 with normal colour vision and confrontational visual field testing. (With refraction at a separate visit 2 weeks later, he was 20/20 both eyes.) He had saccadic pursuits, normal binocular convergence, and no evidence of dry eye. Fundus examination was unchanged. Shortly after the examination, he began to experience the precise visual change that led him to seek help. Symptoms peaked by 1 min, and his vision decreased to count fingers at 2 feet in both eyes. Pupil and motility examinations were unchanged. Simultaneously, he developed facial flushing, of which he was unaware. With questioning, he reported feeling “ill-at-ease” with mild nausea and dry mouth. He remained alert and oriented and had normal conversational language function, allowing him to describe all symptoms. No cognitive fluctuation was evident. His blood pressure and pulse were at baseline and normal, and PD motor signs were unchanged. His last dose of carbidopa/levodopa was 7 h prior. He agreed to take his next dose, and 20 min later, his vision was 20/30 both eyes. Facial flushing, nausea, and dry mouth resolved. Thirty-five minutes from onset, he was asymptomatic except for mild residual anxiety. Previously, he attributed the non-visual symptoms during the fluctuation to incapacitating visual loss. Counselling regarding appropriate timing of carbidopa/levodopa and education regarding NMF was provided at the visit. On follow-up, his symptoms had not changed and he noted that he had not been consistent with taking his medications, but he agreed to a trial of such. With a follow-up phone call, the patient admitted to missing doses and he again agreed to established scheduled dosing to assess whether there was any impact on the transient visual loss episodes.

Discussion

We were afforded a rare opportunity to witness a transient and severe fluctuation in *afferent* visual function in a patient with PD-MCI that occurred in association with anxiety, facial flushing, nausea, and dry mouth. All symptoms improved after carbidopa/levodopa, although it is unknown whether symptoms would have resolved as quickly without treatment. The mechanism and localization of the

patient's *afferent* visual pathway fluctuation is unknown, but several factors can be considered. First, normal neuronal function along the afferent visual pathway, from the retina, to the thalamus, and to the cerebral cortex, relies upon appropriate dopaminergic and cholinergic transmission in each of these regions,^{5–7} and altered dopaminergic and cholinergic activity in visual afferent pathways in PD and PD Dementia have been observed.^{6,7} Next, in early PD there are changes in visual afferent connectivity and a loss of function and/or atrophy involving neurons in the retina, thalamus, and visual cortex.^{8,9} These alterations worsen with progressive cognitive impairment, particularly in the thalamocortical pathways. Retinal morphologic and electrophysiological alterations are well-documented in both visually asymptomatic and symptomatic patients with PD and PD-MCI.^{10,11} Hypometabolism in the occipital and parietal regions are common findings in PD, and these changes increase in the presence of cognitive impairment in PD.¹² Consequently, transient failure of dopamine transmission in the retina, with a relative imbalance in cholinergic transmission, in the setting of morphological and functional changes along the entire afferent visual pathway, could be responsible for our patient's transient vision loss during a NMF. The patient's associated glaucoma, with its evident degeneration of optic nerves that terminate in the lateral geniculate nucleus of the thalamus, could have increased the likelihood of neuronal or synaptic failure in our patient. With review of the literature, we did not find a relationship between latanoprost use and changes to dopaminergic transmission. The patient had been using latanoprost, a selective prostaglandin receptor agonist, for over 3 years without significant side effects and there was no relationship between dosing and the onset of his visual loss. The differential includes bilateral retinal ischaemia due to vasospasm. During the event, a non-dilated direct ophthalmoscopic examination with visualization of optic nerve head and macula only occurred. There were no changes to the examination, albeit the vasculature outside of the nerve head and macula was not fully visualized. However, we believe that bilateral retinal

vasospasm was unlikely given other symptoms that he experienced and 10 months of recurrent episodes that could last up to 3 h by his report.

In summary, we believe that the cause of our patient's daily, transient episodes of vision loss was *afferent* visual pathway failure that began in the retina during a NMF, and underlying glaucoma and MCI increased the likelihood of transient visual failure in our patient for reasons discussed. Since this type of visual loss has not been documented during an examination of this type, contributing factors and frequency of this type of visual pathway failure in PD are unknown.

The *Parkinson's Disease Society of the United Kingdom Non-Motor Symptoms Questionnaire*,¹³ frequently employed to capture and study NMS and NMF, is an excellent instrument to measure NMSs in PD and includes two vision-specific questions related to double vision and visual hallucinations. We recommend broadening survey questions to include symptoms related to afferent visual function (i.e. visual clarity, colour and contrast sensitivity, visual perception, visuospatial function, visuomotion perception). By doing so, clinicians can consider the full spectrum of NMF in PD and treat appropriately to improve quality of life given the detrimental effects that NMF, particularly visual symptoms, have upon quality of life. Unfortunately, we have not been able to determine if our patient's symptoms decreased with improved treatment compliance despite discussions regarding such at two visits. Lastly, our patient's findings demonstrate that further exploration of mechanisms of transient neuronal failure, particularly at the level of the thalamus as proposed by Delli Pizzi and colleagues,⁶ are worthwhile to pursue and could shed light on the cause of cognitive fluctuations in Parkinson's Disease Dementia and Lewy Body Dementia, which are poorly understood.

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Consent

The patient described gave written consent for the inclusion of the material pertaining to them and we have fully anonymized them.

Disclosure of interest

The authors declare that there are no conflicts of interest. The authors alone are responsible for the writing and content of the article.

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