TREATMENT OF SEVERE CONSTIPATION IMPROVES PARKINSON'S DISEASE (PD) SYMPTOMS

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1. INTRODUCTION

Constipation is common in idiopathic PD, a bradykinetic disorder which affects motor skills, speech and other functions. While constipation frequently appears with age, studies show that PD patients have a significantly higher onset rate than that of controls (28-61% vs 6-33%).[1,2,3] Literature suggests that constipation appears as a very early symptom of PD due to Lewy bodies affecting the dorsal vagal nucleus and myenteric plexus.[4] It is also a common belief that PD medication, especially anti-cholinergic drugs[4], may be the cause of constipation in PD patients, although recent studies have shown that constipation may precede PD by up to 10 years[5]. These study findings have led to the hypothesis that constipation may be a risk factor in developing PD[5]. One such hypothesis points to a neurotoxin in bowel flora that contributes to the progression of this disease[6]. We report intriguing observations in one PD patient treated for constipation using a novel approach.

CONFLICT OF INTEREST STATEMENT

T J Borody has a pecuniary interest in the Centre for Digestive Diseases.

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2. CASE

A 73y old man with a 4y history of severe constipation and PD presented with constipation developing shortly after the PD diagnosis in 2004. He reported bloating with 1-2 stools/week requiring high doses of docusate sodium and psyllium husks. He exhibited marked pillrolling hand tremor, micrographia, positive glabellar tap reflex and cogwheel rigidity while on carbidopa/levodopa combination. Patient was not taking anti-cholinergic medication for his PD symptoms.

He started a combination of vancomycin, metronidazole and colchicine for his treatment-resistant constipation in May 2008. His PD medication and dosage remained unchanged. At 21 days he reported his constipation to be markedly improved defecating daily with ease and no bloating. He also noticed a dramatic improvement in his Parkinsons symptoms with visible decrease in tremor commencing from about 10 days into therapy. By November 2008 and March 2009 on continuous therapy he reported 1 stool/d, no persistent tremors and there was no detectable cogwheel rigidity with absence of glabellar tap reflex. By May 2009 the patient reported a single episode of tremor which lasted 5 minutes. He is continuing 800mg metronidazole, 1g vancomycin and 1mg colchicine daily. In March 2009, after observation of PD symptom improvement, carbidopa/levodopa was reduced which resulted in occasional tremor 'attacks'. A low dose of carbidopa/levodopa was continued.

3. DISCUSSION

PD, being a neurodegenerative disorder, often presents with a myriad of symptoms. Along with the 4 major PD symptoms (tremor, rigidity, bradykinesia/akinesia, postural instability) PD patients often suffer from various other secondary symptoms, including gastrointestinal symptoms.[7] Although the mechanism is unknown, constipation is common among PD patients.[8]

4. DISCUSSION

Constipation in PD patients is notoriously difficult to treat.[9] This case report not only shows successful treatment of constipation, previously generally unachievable with current best therapies, but also an unexpected and dramatic symptom reduction in PD. It may be a clue to the causality in a subset of PD patients. Treatment-resistant constipation may be a preceding marker of PD perhaps related to the underlying pathophysiologic process.[5]

It has been hypothesised that pathogenic material from the gastric mucosa could possibly be the origin of PD.[10] It is Braak *et al.*'s[10] contention that an unidentified toxin from the intestine may be passing through the gastric mucosa and being retrogradely transported via the vagus nerve axons, which causes the vagus nerve neuron damage typical of PD.

In addition to this, bacterial and fungal toxins have been shown to inhibit proteasomes resulting in PD-like syndrome in rat models[6]. Injection of *Nocardia asteroides* (NA) into mice resulted in PD-like syndrome and NA genes were demonstrated in brain tissue of PD patients[11]. Vancomycin originated from *Nocardia orientalis* and may be acting in the gut flora to suppress a related pathogen's release of its toxins and may help uncover the riddle of PD. Such simple therapy may improve quality of life in many patients with PD.

5. POINTS TO PONDER

- Constipation could become an important secondary symptom that can now be managed better in PD patients.
- In light of these observations, should we be looking at possible bacterial origins of PD?
- Is PD becoming more of a "syndrome" where subsets of patients can be characterised by different causes of the disease (eg. Pneumonia can be caused by various pathogens)?

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