Treatment for Late-Onset Obsessive-Compulsive Disorder with Parkinsonism

Arunlata Agarwal, M.D.
Devdutta Biswas, M.D.
Raja Sadhu, M.D.

Dysfunction of the basal ganglia and frontal subcortical structures occurs in both obsessive-compulsive disorder and parkinsonism. Treatment of obsessive-compulsive disorder with parkinsonism is a therapeutic challenge, especially in old age as selective serotonin reuptake inhibitors may aggravate motor symptoms and worsen clinical conditions. The authors present a series of patients with late onset obsessive-compulsive disorder demonstrating improvement in obsessive-compulsive disorder as well as parkinsonian signs.

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An association of obsessive-compulsive disorder (OCD) with movement disorders (e.g., Tourette's syndrome, Huntington's disease, and Sydenham's chorea) has been noted since the recognition of the latter.[1] The association of obsessive-compulsive disorder with parkinsonism was recognized during the encephalitis lethargica pandemic in 1917 when its occurrence temporarily provided insight on the importance of the basal ganglia and subcortical structures in movement disorders and OCD.[2,3] Although neurology and psychiatry were distancing themselves from each other, it was recognized that disorders affecting the brain were not always clinically expressed in only one of these specialties.[1] In the next few decades, neurology focused more on neurobiology and evolved along a parallel yet completely separate line from psychiatry, which took a more biopsychological approach to understanding the human brain.[4] The development of structural and functional imaging in the 1980s led to a new era and provided an impetus for the reunification of the neurosciences. A spate of imaging studies in OCD ensued, which demonstrated evidence of the dysfunction of basal ganglia, especially caudate and frontal subcortical structures.[5–9]

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Drs. Agarwal and Biswas are affiliated with the Department Of Psychiatry at Maulana Azad Medical College and G.B. Pant Hospital in New Delhi; Dr. Sadhu is affiliated with the Department Of Psychiatry, All India Institute of Medical Sciences in New Delhi. Address correspondence to A.L. Agarwal, M.D., D-5, M.A.M.C. Campus, New Delhi- 110002, India; dralagrawal@hotmail.com (e-mail).

On the basis of these data, several authors have advanced models of basal ganglia thalamocortical circuits in which behavior is modulated by filtering irrelevant thoughts. Dysfunction of these circuits has been proposed in the pathogenesis of OCD.[10–12] From 1988 onward, case reports of basal ganglia lesions (diagnosed radiologically) associated with OCD were reported by several authors.[13–20] These reports spurred studies exploring the prevalence of anxiety disorders,[21–23] especially OCD, in Parkinson's disease.[24–27] The studies were conducted on patients with established Parkinson's disease, but the results conflicted—some authors reported association[22,24,26] and some reported a lack of association.[25,27]

Despite recognizing for nearly a century the possible association between OCD and parkinsonism, treatment needs of this special group remain relatively unexplored. Common therapeutic strategies for OCD like serotonin reuptake inhibitors (SSRIs) might aggravate motor symptoms by stimulating 5-HT2 receptors and inhibiting dopamine release in the basal ganglia.[28–33] On the other hand, L-dopa for parkinsonism is reported to aggravate compulsive and impulsive symptoms.[34–36] Patients exhibiting both obsessive and parkinsonian features thus provide a therapeutic challenge for the clinician. A few studies have demonstrated the safety and efficacy of tricyclic antidepressants in depression with parkinsonism but have not clearly commented on the effect on motor features.[37–40] OCD with parkinsonism, however, has not been satisfactorily addressed.

We present a naturalistic follow-up study of a group of late-onset OCD patients exhibiting parkinsonian signs who demonstrated a response to clomipramine, which might be considered a viable option for such patients.

METHOD

The patients were seen in the psychiatry clinic of a superspecialty tertiary care hospital in India over a span of 1 year. The hospital serves as the culmination point for many chronic and difficult-to-treat cases. This paper describes 10 patients who were diagnosed with OCD according to ICD-10 criteria and who showed parkinsonian signs (not deemed to be the effect of drugs). Two OCD patients without parkinsonian signs and one who did not undergo investigations were excluded from the study. Patients were rated on the Yale-Brown Obsessive Compulsive Scale, a 10-item scale that rates severity of obsessive-compulsive symptoms,[41] and the Webster Scale for severity of parkinsonian features (bradykinesia, rigidity, gait, arm swing, tremor, and facial expression).[42] We obtained cardiology, prostate, and glaucoma tests and clearance for starting tricyclic antidepressants. Patients were started on a regimen of clomipramine following the principle of starting low and going slow, and the dose was titrated on the basis of clinical improvement and tolerability. We periodically rated the patients on the Visual Analogue Scale, the Yale-Brown Obsessive-Compulsive Scale, and the Webster Scale through December 2006.

RESULTS

The sociodemographic and clinical profile of patients are summarized in Table 1. Table 2 demonstrates past treatment history. All patients had late age of onset for OCD, and most had demonstrable basal ganglia/frontal subcortical lesions. Table 3 shows patients' robust and early responses to low doses of clomipramine.

DISCUSSION

This case series is notable as it presents a large series of patients presenting with late-onset obsessive-compulsive disorder exhibiting parkinsonian signs, with demonstrable lesions in the basal ganglia and/or frontal subcortical structures on MRI. All patients consulted a psychiatrist due to dysfunction resulting from OCD, and motor signs were elicited on evaluation. Potential confounding factors were avoided as their obsessive symptoms were not L-dopa induced, nor were motor signs antipsychotic induced (patient 9, with history of antipsychotic treatment, had a 6 month drug-free interval before baseline assessment). The cases support the view that lesions of the basal ganglia could account for OCD as well as parkinsonism. Recognition of behavioral as well as motor features is essential, as such patients present a diagnostic and therapeutic challenge. A diagnosis of late-onset OCD with parkinsonism is often shrouded in therapeutic nihilism as several authors have observed limited response to psychotropic medication[20] and aggravation of motor symptoms with SSRIs.[28–33] Our case study gives us reason to be hopeful, as all patients (including past nonresponders to SSRIs)

TABLE 1. Sociodemographic and Clinical Profiles

Patient	Age/ Sex	Onset OCD (years)	Obsession/Compulsion	Parkinsonian Signs	MRI	Cardiac Status	Prostate Status
1	65/M	63	Day-to-day events; preplanning; impulsivity; excessive list making (YBOCS 12)	Left pill rolling; arm swing less; mask face (Webster 6)	Left frontal periventricular; lacunar infarct	ECG normal; ECHO normal	Gr II
2	65/M	60	Fear might harm self; fear will act on impulse; concern with disease; impulsivity; mental compulsion (YBOCS 25)	Cogwheel rigidity; R>L; tremor (Webster 4)	B/L lacunar infarct in subcortical region	ECG normal; ECHO normal	Normal
3	63/M	58	Past conversation; sleep state mispercep; mental compulsion (YBOCS 14)	L perioral movement; rigidity (Webster 2)	Normal	ECG LVH; ECHO normal	Gr I
4	64/M	61	Intrusive nonsense sound/word/ music (YBOCS 9)	R rigidity; tremor; mask face (Webster 7)	Lacunar infarct R basal ganglia	ECG normal; ECHO normal	Normal
5	75/M	60	Day-to-day events; preplanning; impulsivity; need to repeat (YBOCS 24)	Imbalance; tremor; cogwheel rigidity (Webster 9)	Lacunar infarct B/L frontal and parietal	ECG mild; ECHO Mild LV	Prostate surgery done
6	65/M	65	Day-to-day events; checking compulsions (YBOCS 15)	Gait imbalance (Webster 4)	Lacunar infarct B/L periventricular	ECG LBBB	Gr III
7	60/M	60	Day to day events; checking compulsions (YBOCS 24)	Cogwheel rigidity; tremor R>L (Webster 6)	Cystic encephalomalacia; left frontal	ECG normal	Gr I
8	42/M	41	Compulsive movement; bruxism; obsessions of death (YBOCS 23)	Left tremor (Webster 4)	Lacunar infarct R periventricular caudate and basal ganglia	Treatment for RHD	Normal
9	68/M	68	Contamination obsession; fear of doing something embarrassing; bruxism; involuntary vocalization; suicidal impulses (YBOCS 26)	Cogwheel rigidity; arm swing less; short steps; stooped; posture (Webster 7)	Lacunar infarct R caudate and basal ganglia and L parietal infarct	ECG LAD; ECHO normal	Gr II
10	60/F	56	Obsession of contamination; cleaning/washing (YBOCS 28)	Cogwheel rigidity; B/L DTR; imbalance (Webster 6)	Lacunar infarct L putamen	ECG normal; ECHO Mod LV abnormal	—

YBOCS = Yale-Brown Obsessive Compulsive Scale; R/L = right/left; B/L = bilateral; DTR = deep tendon reflexes; ECHO = echocardiogram; LV = left ventricular; LBBB = left bundle branch block; LAD = left axis deviation; RDH = rheumatic heart disease; Gr = grade

showed an early and robust response to low doses of clomipramine without significant adverse effects. A concomitant decline in the Webster score was an added benefit. Sedative and anxiolytic effects of clomipramine obviated the need for benzodiazepines in all except two cases, avoiding drug interactions and the adverse cognitive effects of benzodiazepines noted in parkinsonism. Although our study is limited by the narrow population

TABLE 2. Past Treatment History

Patient	Past Diagnosis	Treatment and Dosage	Duration of Past Medication	Response
1	Depression	Mirtazapine (15 mg)	4 weeks	No response
2	Depression	All SSRI; all SNRI; adequate doses	3 years	No response
3	Panic disorder	Venlafaxine (75 mg)	2 years	80% (adverse effects)
4	Panic disorder	Mianserin (40 mg)	1 year	50%
5	Depression	Mianserin; Sertraline	3 years	25%
6	—	—	—	—
7	Depression	Mirtazapine (30 mg); Citalopram (10 mg)	4 weeks	No response
8	Migraine + depression	Valproate (1000 mg) + Fluoxetine (40 mg)	1 year	No response
9	Psychosis	Citalopram, Risperidone	6 months	Worsening
10	Recurrent depressive disorder	Carbamazepine	10 years	Developed OCD while on medication

OCD = obsessive-compulsive disorder; SNRI = serotonin-norepinephrine reuptake inhibators; SSRI = selective serotonin reuptake inhibators

TABLE 3. Treatment Response to Clomipramine

Patient	Maximum Dose	Scale	Baseline	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 32
1	62.5 mg	VAS		60%	75%	75%	75%	100%	100%	
		YBOCS	12	6	4	4	4	0	0	
		Webster	6	4	4	4	4	4	4	
2	62.5 mg	VAS		40%	40%	60%	80%	90%	100%	100%
		YBOCS	25	20	20	15	9	6	0	0
		Webster	4	2	2	1	1	1	1	1
3	37.5 mg	VAS		60%	90%	90%	90%	90%	90%	100%
		YBOCS	14	8	4	4	4	4	4	0
		Webster	2	1	1	1	1	1	1	1
4	62.5 mg	VAS		50%	80%	90%	95%	100%	100%	100%
		YBOCS	9	6	4	1	1	0	0	0
		Webster	7	2	2	1	0	0	0	0
5	12.5 mg	VAS		25%	30%	50%	60%	60%	75%	
		YBOCS	24	20						
		Webster	9	7						
6	12.5 mg	VAS		50%	75%	75%				
		YBOCS	15	9	5	5				
		Webster	4	3	2	2				
7	75 mg	VAS		20%	20%	20%	40%			
		YBOCS	24	22	22	20	18			
		Webster	6	5	5	4	4			
8	75 mg	VAS		20%	50%		100%			
		YBOCS	23	18	13		4			
		Webster	4	2	2		1			
9	50 mg	VAS			40%		75%			
		YBOCS	26		18					
		Webster	7		5					
10	50 mg	VAS		25%		50%				
		YBOCS	28	22						
		Webster	6	5						

VAS = Visual Analogue Scale; YBOCS = Yale-Brown Obsessive Compulsive Scale

sample, it indicates a need for evolution of therapeutic strategies that address both behavioral and motor components of obsessive-compulsive disorder with basal ganglia lesions.

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