

Parkinson's Disease and Look-alikes

SV Khadilkar

A plethora of extrapyramidal disorders is encountered in the clinics of neurologists and physicians and form an important category of neurological disorders having a potential for disease modification. Amongst the degenerative extrapyramidal diseases, Parkinson's disease [PD] is perhaps the most common and best described disease. The disease often presents asymmetrically and has four main components of rest tremor, rigidity, bradykinesia and alterations of postural reflexes. Patients with idiopathic PD respond well to dopaminergic medications. There are other diseases that share features with Parkinson's disease [the look-alikes] but are much different in their pathogenesis and natural history, often proving resistant to therapy.

The diagnosis of these conditions is almost completely clinical with some clues from the radiology and when facilities are available, by genetics. Hence it is important for us to be aware of the clinical differentiating features of these diseases. The clinicians need to know of progressive supranuclear palsy [PSP or Steele Richardson Olzewsky syndrome], corticobasal ganglionic degeneration [CBGD] and multiple system atrophy [MSA]. PSP presents with early falls. Most patients experience falls within the first one or two years of the illness. The examination shows a startled look, severe limitation of the ocular movements, erect posture and axial rigidity. The ocular abnormality consists of supranuclear gaze restriction in vertical direction. Upgaze is affected more commonly but the downgaze restriction is more specific to PSP. These patients tend to get disabled rapidly and get limited benefit from use of dopaminergic medications. CBGD is less common. It is a complex neurobehavioral disorder characterized by insidious onset and gradually progressive cerebrocortical and extrapyramidal dysfunction. The presentation is strikingly asymmetrical with a useless hand, cortical sensory loss, apraxias and the alien limb phenomenon. Akinesia, rigidity, postural instability, limb dystonia, tremor and stimulus sensitive myoclonus accompany.

MSA is another Parkinson look-alike. The term MSA was introduced in 1969 and cases previously reported as striatonigral degeneration, olivopontocerebellar atrophy, Shy Drager syndrome and idiopathic orthostatic hypotension are probably examples of the same disease.¹ In 1998, diagnostic criteria for MSA got formulated.² MSA is a sporadic neurodegenerative disorder characterized clinically by combination of parkinsonian, autonomic, cerebellar or pyramidal symptoms and signs.

Table 1

Motor :

Orofacial dystonia

Pisa syndrome

Disproportionate antecollis

Jerky tremor

Dysarthria

Non-motor:

Autonomic dysfunction

Abnormal respiration

REM sleep behavior disorder

Cold hands/feet Raynaud's phenomenon

Emotionality

Head, Department of Neurology, Grant Medical College and Sir JJ Group of Hospitals, Mumbai

Pathologically, there is cell loss, gliosis and glial cytoplasmic inclusions in several brain and spinal cord structures. In the late nineties, alpha synuclein was found to be a sensitive marker of the inclusion pathology and MSA is now firmly established as alpha synucleinopathy.³ The condition may present with cerebellar dominant symptoms and signs [MSA-C] or may have prominent extrapyramidal features [MSA-P]. In MSA-P, misdiagnosis with PD is common.⁴ MSA manifests in middle age, affects both sexes equally and progresses relentlessly. The mean survival is 6-9 years. In general, patients respond poorly to Levodopa, or have transient response and this is perhaps the most important clue to differentiate them from idiopathic PD. In addition, following red flags help the clinician in the differential diagnosis.¹¹

Pisa syndrome refers to axial dystonia with severe tonic lateral flexion of the trunk. Disproportionate antecollis often is seen as chin on chest, where as flexion attitude of rest of the body is minimal.

The autonomic nervous system is affected early in the disease and orthostatic hypotension, urogenital and gastrointestinal symptoms accompany the motor disorder in almost half of the patients at the onset of disease. The early appearance of these symptoms is striking. In this issue of the journal, Swaminath et al⁵ have elegantly described the differences in the urogenital symptoms in a cohort of MSA and PD patients which are very helpful to the clinician. The treatment of MSA is largely symptomatic with Levodopa, Amantadine and Dopa agonists used for the motor symptoms. Botulinum toxin has been used for severe dystonia. Orthostatic hypotension is often helped by head up tilt of bed at night, elastic stockings, increased salt intake, Fludrocortisone, Ephedrine or Midodrine. For post prandial hypotension, Octreotide has been used 30 min before meals. Nocturnal polyuria responds to Desmopressin. For the detrusor hyperreflexia, Oxybutynin can be used and some patients have to go on to self intermittent catheterization when the residual urine exceeds 100 ml. Physiotherapy, speech therapy and rehabilitation become more important as the disease progresses.

Thus, it is important for the internist to be aware of the look-alikes of Parkinson's disease like PSP, CBGD and MSA and to make the clinical differentiation for better management of these patients.

References

1. Wenning G, Geser F. Diagnosis of multiple system atrophy: an Update. *ACNR* 2004; 3: 5-9.
2. Gilman S, Low P, Quinn N, Albanese A, Ben-Shlomo Y, Fowler CJ et al. Consensus statement on the diagnosis of multiple system atrophy. *Clin Auton Res* 1998; 8:359-362.
3. Dickson DW, Liu W, Hardy J, Fairer M, Mehta N, Uitti R et al. Widespread alterations of alpha-synuclein in multiple system atrophy. *Am J Pathol* 1999; 155:1241-1251.
4. Wenning GK, Ben Shlomo Y, Magalhaes M, Daniel SE, Quinn NP. Clinical features and natural history of multiple system atrophy. An Analysis of 100 cases. *Brain* 1994; 117 (Pt 4):835-845.
5. Pazhayannur V Swaminath, Mona Ragothaman, Suma Koshy, Nagaraja Sarangmath, Mohan Adhyam, DK Subbakrishna, Christopher J Mathias, Uday B Muthane. Urogenital Symptoms in Parkinson's Disease and Multiple System Atrophy-Parkinsonism: At Onset and Later. *JAPI* 2010;58:86-90.