What I learned from my patients

Irene Litvan, M.D.

This lecture will consist on video case presentations and group discussion of patients with atypical parkinsonian disorders. Discussions will focus on phenomenology, clinical, and pathologic diagnoses. Stress will be placed on clues for the diagnoses and differential diagnosis based on evidence-based knowledge. This syllabus summarizes main concepts.

The atypical parkinsonian disorders are defined by the presence of akinesia (hypokinesia and/or bradykinesia) with tremor, rigidity or postural instability and the presence of features that are not usually observed in Parkinson's disease.

Features suggestive of an atypical parkinsonian disorder include:

- Limited or No Dopaminergic Response
- Early Postural Instability/Falls
- Rapid Progression (Wheelchair Sign)
- Supranuclear Gaze Palsy / Saccade Abnormalities
- Early or Severe Autonomic Features
- Cerebellar Signs
- Early Prominent Dysphagia/Dysarthria
- Lower Motor Neuron / Pyramidal Signs
- Ideomotor Apraxia, Aphasia or Sensory Neglect
- Early Well-formed Hallucinations Unrelated to Rx
- Early Cortical or Severe Frontal Dementia

The atypical parkinsonian disorders include progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD), vascular Parkinsonism (VaP), dementia with Lewy Bodies (DLB), and other rarer disorders. Listed below are the diagnostic criteria or commonly used features to diagnose these disorders.

Possible NINDS-SPSP PSP-Richardson Syndrome	
• **Gradually progressive disorder**	
• **Onset age 40 or later**	
• **No evidence of other disease that could explain features**	
OR	
Supranuclear vertical gaze palsy	**Slowing of saccades**
	Prominent postural instability with falls within 1st year of onset

In addition to the typical, PSP-Richardson syndrome, PSP also presents with other phenotypes: Recently developed criteria that still require validation, may allow the diagnosis of these phenotypes (see Hoeglinger et al., 2017, for diagnostic criteria).

- PSP-Parkinsonism (less than 1/3 of patients)
- Pure Akinesia Freezing of Gait
- Frontal dementia
- Corticobasal Syndrome

Among the atypical parkinsonian syndromes, CBD is probably the most challenging disorder to diagnose antemortem. It can present with multiple phenotypes but none of them is specific enough to lead to an unequivocal diagnosis. The classic clinical presentation is the corticobasal syndrome (CBS), which typically presents as an asymmetric parkinsonism with a variable combination of ideomotor apraxia, rigidity, myoclonus and dystonia, often associated with the presence of an alien limb phenomenon. Recently, a new set of diagnostic criteria has been developed that needs validation (see Armstrong et al., 2013 for further diagnostic criteria details). The underlying pathology of the CBS is in approximately 50% of the cases CBD, but PSP, Alzheimer disease and frontotemporal dementia are also frequent.

Multiple system atrophy is the most common atypical parkinsonian disorder after PSP. It presents with two major phenotypes: MSA-Parkinsonism and MSA-Cerebellar, although most patients develop both, parkinsonism and cerebellar features (see Gilman et al., 1998, for diagnostic criteria details).

Multiple system atrophy (MSA)		
• **Gradually progressive disorder**		
• **Onset age 30 or later**		
• **Autonomic failure:**		
Orthostatic Hypotension		
Urinary problems: urgency, frequency, nocturia, and urge incontinence		
Erectile disturbances		
	&	
Parkinsonism (MSA-P)	**OR**	**Cerebellar (MSA-C)**
Akinesia, rigidity, tremor, post. Instability		Gait/limb ataxia, speech problem

MSA-P
• Parkinsonism benefits from L-dopa in 30% of pts
• Orofacial/craniocervical dyskinesias/dystonia in 50%
• All problems to develop may take 5 years
• Differential diagnosis with PSP & PD

MSA-C
• Gait ataxia

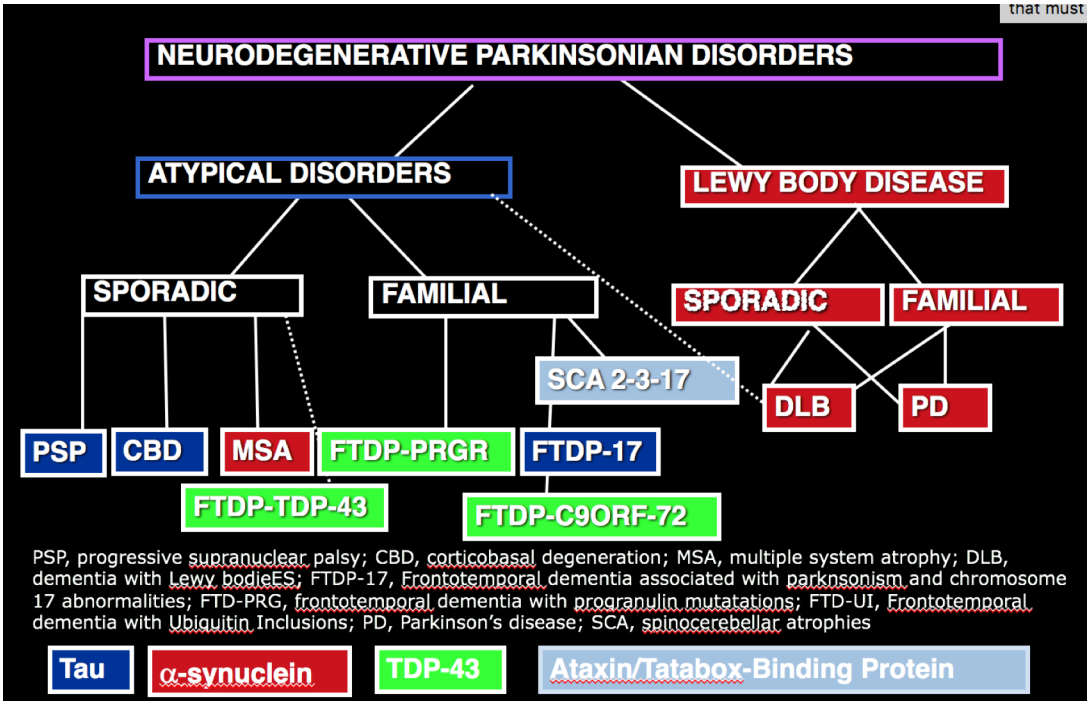
- Cerebellar tremor
- Scanning speech
- Usually develop non-cerebellar problems
- Differential diagnosis with idiopathic late onset cerebellar ataxia

Differences between PSP and MSA
• Early, severe autonomic dysfunction
• Cerebellar limb and speech dysfunction
• Supranuclear vertical gaze palsy/slowing of vertical saccades

Vascular parkinsonism is not very frequent, approximately 2.5-5% of all cases of parkinsonism. Usually presents as a lower boy parkinsonism, and may have additional cerebrovascular features.

Vascular Parkinsonism
• Secondary Parkinsonism due to ischemic Cerebrovascular disease
• Lower body parkinsonism
• Postural instability and falls; short shuffling wider base of stance & variable stride length (parkinsonian-ataxic gait)
• Frequent pyramidal signs
• Early subcortical dementia.
• Diffuse white matter lesions and/or strategic subcortical infarcts

In addition to a nosological classification, nowadays we also use a molecular classification of the neurodegenerative parkinsonian disorders. PSP and CBD are classified as tauopathies, whereas PD, DLB and MSA as synucleinopathies. The



molecular classification if very relevant, as novel experimental biological therapies are directed to inhibit the aggregation or spread of tau or alpha-synuclein.

An early and accurate diagnosis of the atypical parkinsonian disorders is important for appropriate management, prognosis and clinical research. Management requires an interdisciplinary team and a personalized approach Although at present, at present there are no disease modifying therapies available, extensive research is being conducted (see clinicaltrials.gov).

Key aspects of non-surgical management

1. **Comprehensive and personalized interdisciplinary team approach**
2. **Non-Pharmacologic**
   - Physical Therapy (i.e., freezing, prevention of falls, learn how to use weighted walkers)
   - Swallowing techniques (i.e., thickeners, PEG)
   - Speech therapy (i.e., LSVT-LOUD, amplifiers)
   - Occupational Therapy (i.e., transfer)
   - Supportive Therapy/Education
   - Social Worker


Weighted Walker

3**. Pharmacologic**
   - Motor: dopaminergic therapy (e.g., Levodopa/carbidopa, dopamine agonists, MAO-inhibitors)
   - Orthostatic hypotension: Na, fludrocortisone, midrodrine, droxidopa
   - Neurogenic bladder: (e.g., solifenacin, mirabegron)
   - Antidepressants
   - Gastroparesis
   - Myoclonus (i.e., clonazepam)

Thickener

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