파킨슨병 및 이상운동 질환

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학습목표

- 병동에 입원하는 파킨슨증 환자의 진단과 치료
- 응급실에서 만나는 이상운동질환 환자의 진단과 치료

Hoehn & Yahr staging

Stage 0 : no sign of disease
Stage 1 : unilateral disease
Stage 1.5 : unilateral plus axial
Stage 2 : mild bilateral, without postural imbalance
Stage 2.5 : mild bilateral, with recovery on pull test
Stage 3 : moderate bilateral, with postural imbalance, independent
Stage 4 : severe, still able to walk unassisted
Stage 5 : wheelchair-bound, bed-ridden

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파킨슨증 parkinsonism

- 서동증 bradykinesia
- 안정시 진전 resting tremor
- 강직 rigidity
- 보행/자세 장애 postural imbalance/gait disturbance

파킨슨병 Parkinson disease

- 파킨슨증
- Asymmetric onset, course
- Response to levodopa

PD

UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria

Step 1 Diagnosis of Parkinsonian syndrome
- Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive actions)
- And at least one of the following:
  - muscular rigidity
  - 4–6 Hz rest tremor
  - postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction.

Step 2 Exclusion criteria for Parkinson's disease
- History of repeated strokes with stepwise progression of parkinsonian features
- History of repeated head injury
- History of definite encephalitis
- Oculogyric crises
- Neuroleptic treatment at onset of symptoms
- More than one affected relative
- Sustained remission
- Strictly unilateral features after 3 years
- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Early severe dementia with disturbances of memory, language, and praxis
- Babinski sign
- Presence of cerebral tumour or communicating hydrocephalus on CT scan
- Negative response to large doses of levodopa (if malabsorption excluded)
- MPTP exposure

Step 3 Supportive prospective positive criteria for Parkinson's disease
(Three or more required for diagnosis of definite Parkinson's disease)
- Unilateral onset
- Rest tremor present
- Progressive disorder
- Persistent asymmetry affecting side of onset most
- Excellent response (70–100%) to levodopa
- Severe levodopa-induced chorea
- Levodopa response for 5 years or more
- Clinical course of 10 years or more

MSA

- Second consensus statement on the diagnosis of multiple system atrophy

Table 1 Criteria for the diagnosis of probable MSA

A sporadic, progressive, adult (>30 y)–onset disease characterized by
• Autonomic failure involving urinary incontinence (inability to control the release of urine from the bladder, with erectile dysfunction in males) or an orthostatic decrease of blood pressure within 3 min of standing by at least 30 mm Hg systolic or 15 mm Hg diastolic *and*
• Poorly levodopa-responsive parkinsonism (bradykinesia with rigidity, tremor, or postural instability) *or*
• A cerebellar syndrome (gait ataxia with cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction)

Table 2 Criteria for possible MSA

A sporadic, progressive, adult (>30 y)–onset disease characterized by
• Parkinsonism (bradykinesia with rigidity, tremor, or postural instability) *or*
• A cerebellar syndrome (gait ataxia with cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction) *and*
• At least one feature suggesting autonomic dysfunction (otherwise unexplained urinary urgency, frequency or incomplete bladder emptying, erectile dysfunction in males, or significant orthostatic blood pressure decline that does not meet the level required in probable MSA) *and*
• At least one of the additional features shown in table 3

Table 3 Additional features of possible MSA

Possible MSA-P or MSA-C
• Babinski sign with hyperreflexia
• Stridor
Possible MSA-P
• Rapidly progressive parkinsonism
• Poor response to levodopa
• Postural instability within 3 y of motor onset
• Gait ataxia, cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction
• Dysphagia within 5 y of motor onset
• Atrophy on MRI of putamen, middle cerebellar peduncle, pons, or cerebellum
• Hypometabolism on FDG-PET in putamen, brainstem, or cerebellum
Possible MSA-C
• Parkinsonism (bradykinesia and rigidity)
• Atrophy on MRI of putamen, middle cerebellar peduncle, or pons
• Hypometabolism on FDG-PET in putamen
• Presynaptic nigrostriatal dopaminergic denervation on SPECT or PET

MSA = multiple system atrophy; MSA-P = MSA with predominant parkinsonism; MSA-C = MSA with predominant cerebellar ataxia; FDG = [$^{1.8}$F]fluorodeoxyglucose.

Table 4 Features supporting (red flags) and not supporting a diagnosis of MSA

Supporting features	Nonsupporting features
• Orofacial dystonia	• Classic pill-rolling rest tremor
• Disproportionate antecollis	• Clinically significant neuropathy
• Camptocormia (severe anterior flexion of the spine) and/or Pisa syndrome (severe lateral flexion of the spine)	• Hallucinations not induced by drugs
• Contractures of hands or feet	• Onset after age 75 y
• Inspiratory sighs	• Family history of ataxia or parkinsonism
• Severe dysphonia	• Dementia (on DSM-IV)
• Severe dysarthria	• White matter lesions suggesting multiple sclerosis
• New or increased snoring	
• Cold hands and feet	
• Pathologic laughter or crying	
• Jerky, myoclonic postural/action tremor	

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Clinical Criteria for the Diagnosis of Progressive Supranuclear Palsy
National Institute for Neurological Disorders and Society for PSP (NINDS-SPSP)

PSP	Mandatory Inclusion Criteria	Mandatory Exclusion Criteria	Supportive Criteria
Possible	•Gradually progressive disorder •Onset at age 40 or later	•Recent history of encephalitis •Alien limb syndrome, cortical sensory deficits, focal frontal or temporoparietal atrophy	•Symmetric akinesia or rigidity, proximal more than distal •Abnormal neck posture, especially retrocollis
	•*Either* vertical (upward or downward gaze) supranuclear palsy[a] or both slowing of vertical saccades and prominent postural instability with tendency to fall[b] in the first year of disease onset	•Hallucinations or delusions unrelated to dopaminergic therapy •Cortical dementia of Alzheimer's type (severe amnesia and aphasia or agnosia, according to NINCDS-ADRA criteria)	•Poor or absent response of parkinsonism to levodopa therapy •Early dysphagia and dysarthria
	•No evidence of other diseases that could explain the foregoing features, as indicated by mandatory exclusion criteria	•Prominent, early cerebellar symptoms or prominent, early unexplained dysautonomia (marked hypotension and urinary disturbances)	•Early onset of cognitive impairment including at least two of the following: apathy, impairment in abstract thought, decreased verbal fluency, utilization or imitation behavior, or frontal release signs
Probable	•Gradually progressive disorder •Onset at age 40 or later	•Severe asymmetric parkinsonian signs (i.e. bradykinesia)	
	•Vertical (upward or downward gaze) supranuclear palsy[a] *and* prominent postural instability with tendency to fall[b] in the first year of disease onset	•Neuroradiologic evidence of relevant structural abnormality (i.e. basal ganglia or brainstem infarcts, lobar atrophy)	
	•No evidence of other diseases that could explain the foregoing features, as indicated by mandatory exclusion criteria	•Whipple's disease, confirmed by polymerase chain reaction, if indicated	
Definite[c]	•Clinically probable or possible PSP *and* histopathologic evidence of typical PSP		

[a] Upward gaze is considered abnormal when pursuit or voluntary gaze, or both, have a restriction of at least 50% of the normal range
[b] Tendency to fall is not the same as actual falls, as some patients have caregivers who accompany or catch them, and patients may also be more cautious. (I. Litvan, personal communication, July 25, 2012)
[c] Definite PSP is a clinicopathologic diagnosis

Source: Litvan, I., Agid, Y., Calne, D., Campbell, G., Dubois, B., Duvoisin, R. C.,... Zee, D. S. (1996). Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): Report of the NINDS-SPSP international workshop. *Neurology 47*(1):1-9.

입원환자 중 가장 위험한 잠재적 중환은?

- 강의 시간에 공개 예정.^^

Acute parkinsonism

- Infectious, postinfectious: postencephalitic parkinsonism of von Economo, postvaccinal, viral (Coxackie, HIV, Epstin-Barr, influenza, Japanese B encephalitis, poliovirus, postmeasles)
- Autoimmune: systemic lupus erythematosis
- Medication: dopamine receptor blocker, neuroleptic malignant syndrome, serotonin syndrome
- Toxic: CO, methanol, MPTP
- Structural: stroke, hydrocephalus, central and extra-pontine myelinolysis, tumor
- Psychiatric: conversion, obsessive-compulsive disorder, catatonia, malingering

Neuroleptic malignant syndrome

- Neuroleptic drugs
- Hyperthermia > 38 ℃, rigidity, tremor, myoclonus, stupor or delirium, tachycardia or labile blood pressure, dyspnea, diaphoresis, sialorrhea, incontinence, dysarthria, dysphagia
- Creatine phosphokinase ↑, leukocytosis, metabolic acidosis
- Rhabdomyolysis, renal failure, cardiac arrest

Treatment guideline

- Discontinue neuroleptic
- Supportive care
- Diazepam, lorazepam
- Dopaminergic drugs, amatadine
- Dantrolene
- Electroconvulsive therapy

Vocal cord abductor paralysis in MSA

- Loud snoring, tachypnea
- Daytime stridor in advanced stage
- Inspiratory hollow of the suprasternal recess
- Paralytic: denervation of laryngeal abductor muscle
- Nonparalytic: increased laryngeal muscle tone
- Aggravated during sleep, related to aspiration
- Tx: continuous positive airway pressure with a nasal mask, tracheostomy

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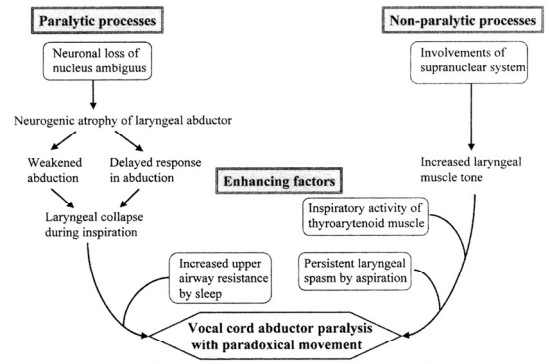

Vocal cord abductor paralysis vs sleep apnea syndrome

- Sound from larynx
- Position change, not effective
- Daytime stridor, present
- Sleep apnea, present, but often tachypneic
- To REM sleep, not related

- Sound from pharynx
- Position change, effective
- Daytime stridor, absent
- Sleep apnea, present
- To REM sleep, closer relationship

Hemiballism-hemichorea

- Stroke, basal ganglia, rarely subcortical
- Nonketotic hyperglycemia

- Focal basal ganglia lesions: tumor, cryptococcal granuloma, toxoplasmosis, tuberculoma, vascular malformation, multiple sclerosis
- systemic lupus erythematosis, Bechet's disease
- Hypoglycemia
- Sydenham's chorea
- Head injury
- Levodopa

Poststreptococcal disorders

- Sydenham's chorea: F>M, chorea, OCD
- PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections): tics, OCD
- Poststreptococcal acute disseminated encephalomyelitis: dystonia, tremor, rigidity
- Poststreptococcal myoclonus: myoclonus
- Poststreptococcal striatal necrosis: dystonia, tremor, rigidity
- Poststreptococcal paroxysmal dystonic choreoathetosis: dystonia, chorea

Serotonin syndrome

- Serotonin ↑: moclobemide, selegiline, cocaine, amphetamine, SSRI, tramadol, venlafaxine, buspirone, sumatriptan, lithium, levodopa, dopamine agonists, amantadine
- Confusion, agitation, hallucination, coma
- Hyperthermia, diaphoresis, tachycardia, hypertension
- Myoclonus, legs, hyperreflexia, rigidity, tremor, ataxia

Treatment guideline

- Discontinue serotonergic drugs
- Supportive care
- Cooling
- Neuromuscular blocking and mechanical ventilation
- Diazepam, lorazepam

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Serotonin syndrome vs neuroleptic malignant syndrome

• Acute	• Gradually in days to weeks
• Improves in < 24 h	• Slower to resolve (10 days)
• Hyperthermia 45%	• Hyperthermia > 90%
• Altered mentality 50%	• Altered mentality > 90%
• Autonomic dysfunction 50-90%	• Autonomic dysfunction > 90%
• Rigidity 50%	• Rigidity > 90%
• Leukocytosis 11%	• Leukocytosis > 90%
• Increased CK 15%	• Increased CK > 90%
• Increased GOT, GPT 8%	• Increased GOT, GPT > 75%
• Hyperreflexia very common	• Hyperreflexia rare
• Myoclonus very common	• Myoclonus rare
• Dopaminergic drugs, exacerbate conditions	• Dopaminergic drugs, improve conditions
• Serotonin antagonists, improve conditions	• Serotonin antagonists, no effect