Multiple System Atrophy

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Introduction

Multiple System Atrophy (MSA)Multiple System Atrophy (MSA) is a rare and progressive neurodegenerative disorder that affects various parts of the nervous system. Classified as a "Parkinson Plus" syndrome due to its overlap of symptoms with Parkinson's disease.

MSA is characterized by a combination of motor dysfunction, autonomic disturbances, and other neurological symptoms.

Epidemiology

- Incidence _0.6 cases per 100,000 per year
- Prevalence -4 to 5 cases 100,000individual per ye
- The average age of onset in MSA is around 52.5 to 55 years
- The disease can exhibit a progression that varies in duration , lasting anywhere from 1 to 18 years.

Etiology

- Sporadic
- COQ2 Gene

mutations resulting in loss of function lead to CoQ deficiency, leading to increased mitochondrial oxidative stress and reduced ATP synthesis.

- SNCA gene (also known as α-synuclein

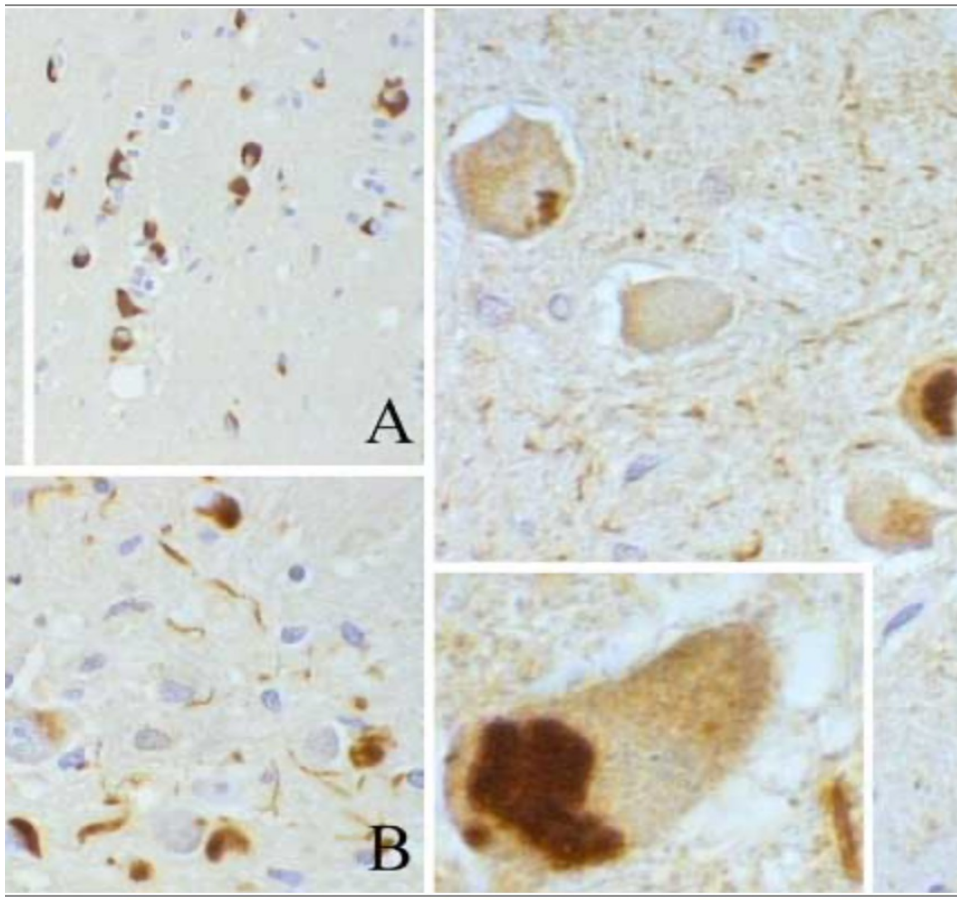
Responsible for producing Alpha -synuclein protein, mainly found in neurons' presynaptic terminals.

This protein plays a vital role in synaptic transmission.

Inflammation-related genes

Neuroinflammation has been suggested as a potential mechanism involved in the development of MSA.

Due to microglial activation and the release of cytokines and chemokines, it is thought that proinflammatory circumstances may hasten the aggregation of alpha-synuclein and lead to Oligodendroglia apoptosis.

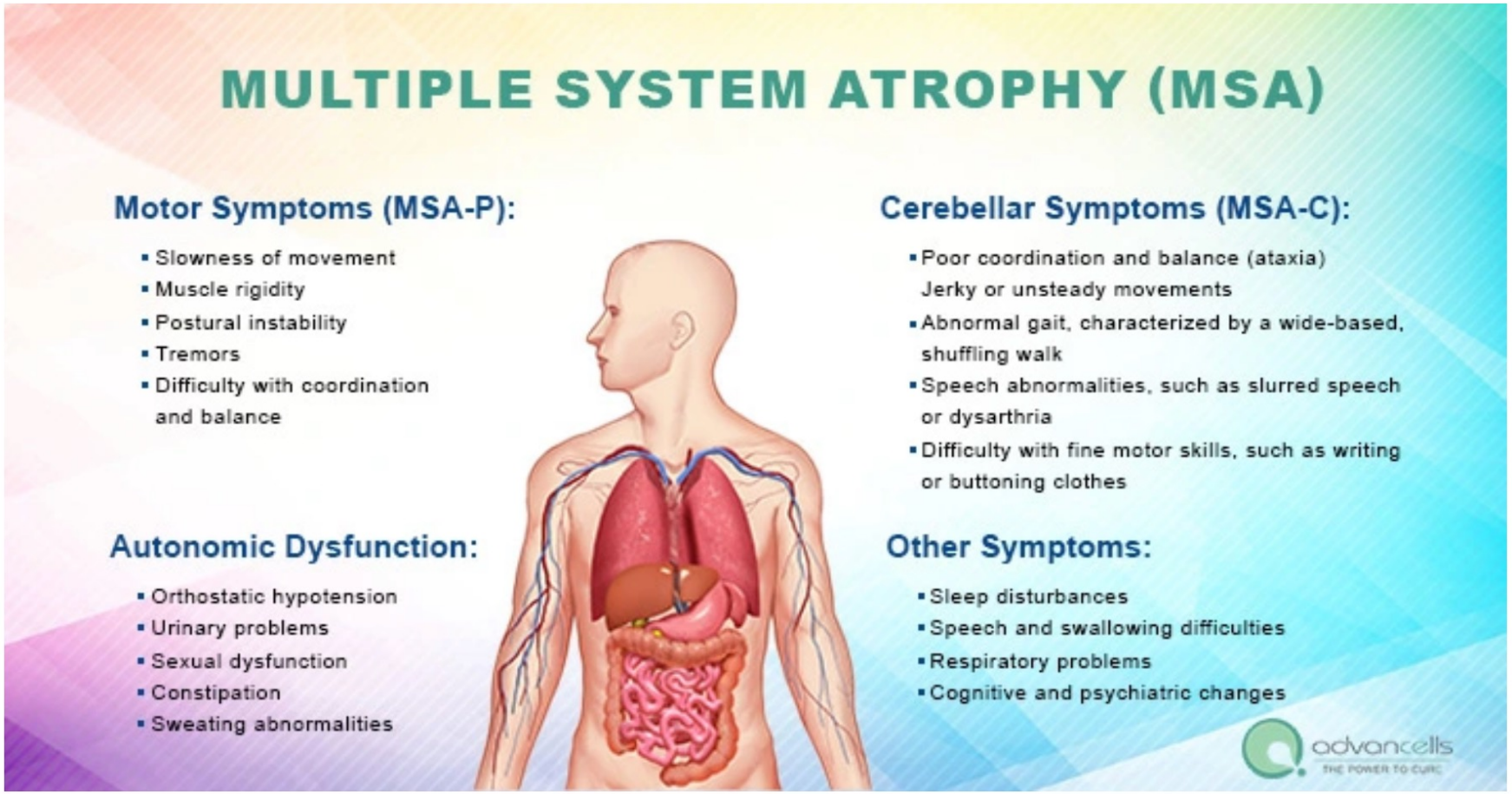


lein positive neural and glial inclusions in MSA (Image court
, Mayo Clinic, Jacksonville FL, USA).

- Alpha-synuclein

  accumulates in the Oligodendroglia cells ,Oligodendroglia cytoplasmic inclusions

Clinical presentation



Progression

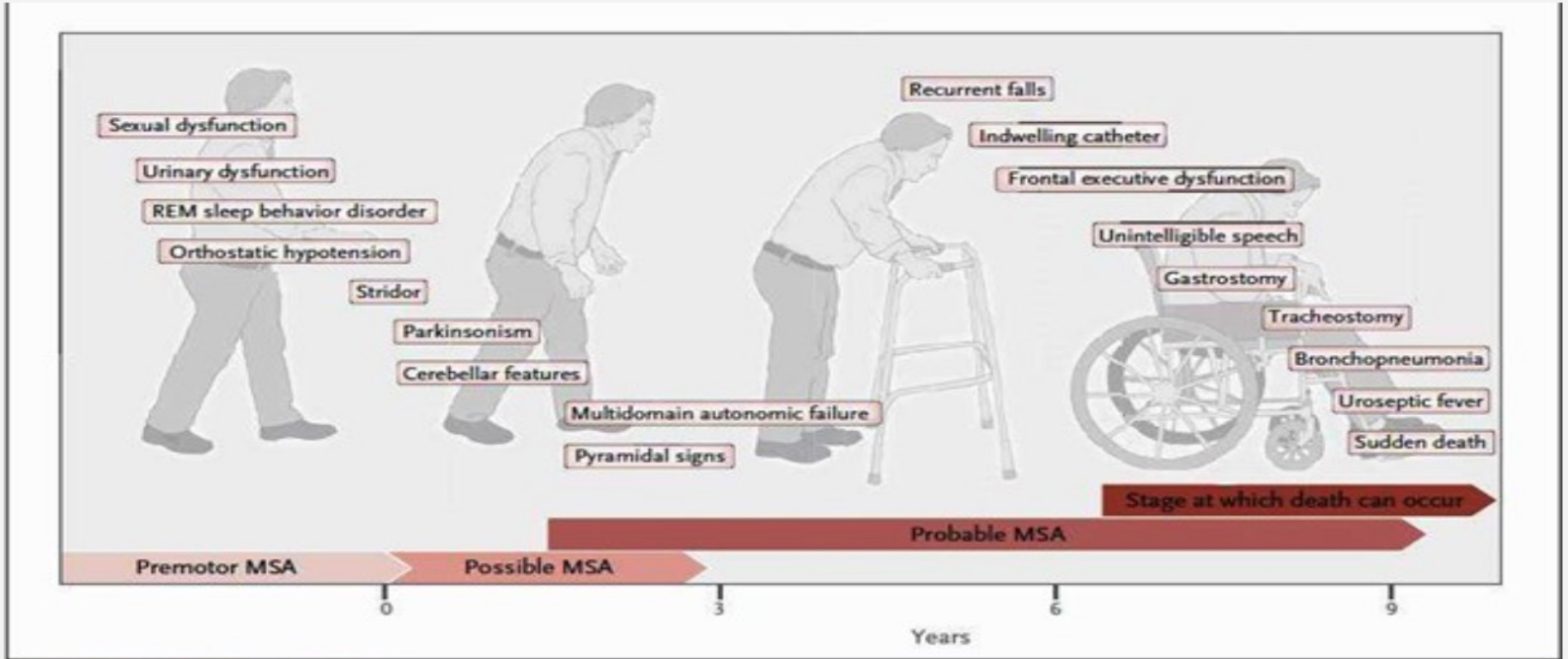
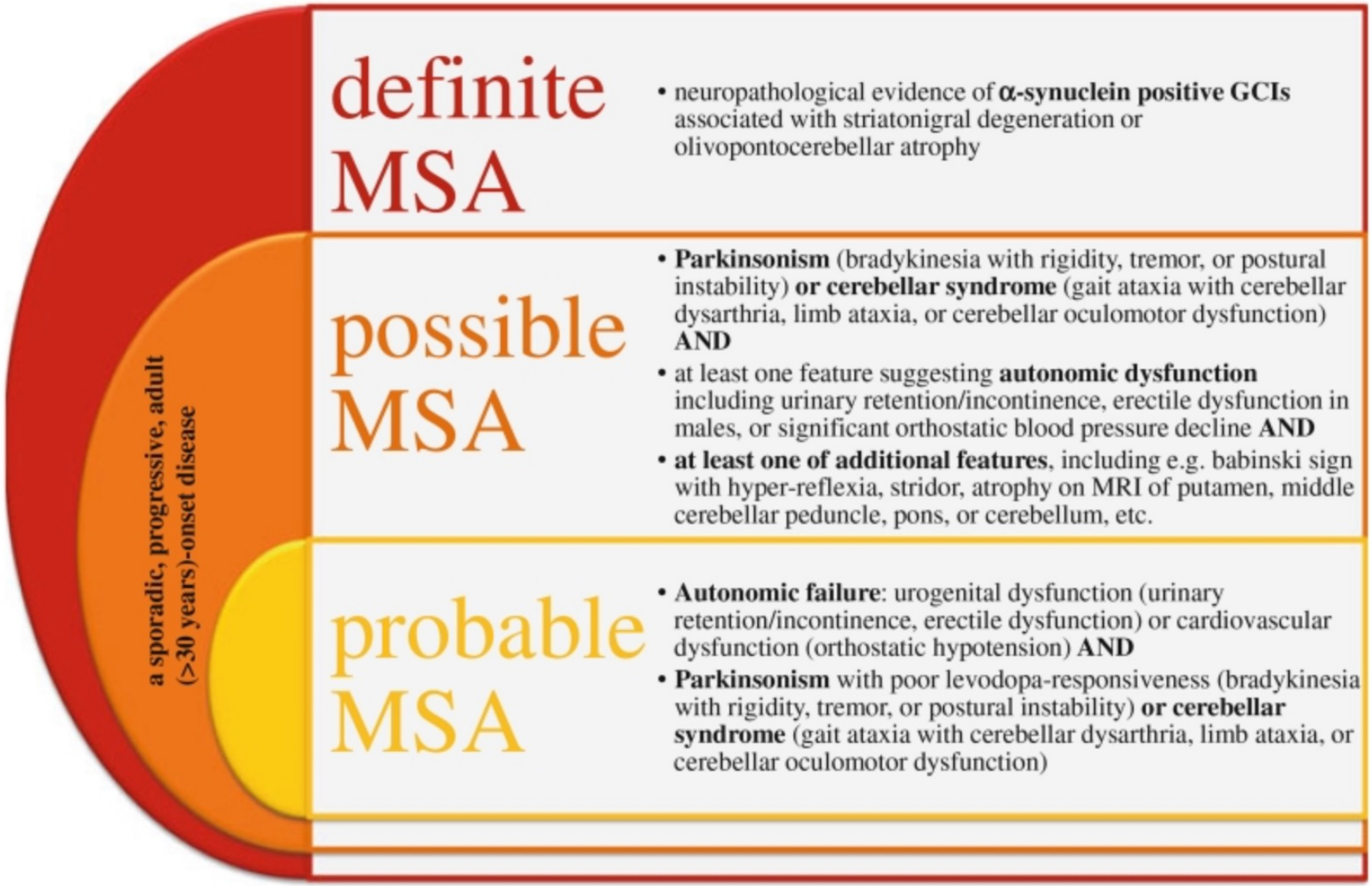


Figure 3. Natural History of MSA.
The premotor phase of MSA can last for months to years. Year 0 denotes the time of onset of motor symptoms. A diagnosis of definite MSA is not possible until the postmortem examination is performed.

Fanciulli, Alessandra, and Gregor K Wenning. "Multiple-system atrophy." The New England journal of medicine vol. 372,14 (2015): 1375-6. doi:10.1056/NEJMc1501657

Diagnosis

- .Diagnosing multiple system can be difficult because its symptoms can resemble those of other movement disorders .
- . Its diagnosis relies on clinical features , medical history , Neurological examination , and the exclusion of other conditions.
- . The diagnostic criteria of MSA involve four level of certainty.



Consensus statement and criteria for the clinical diagnosis of MSA adapted from Gilman et al. (2008). Three different categories of increasing certainty were established to ease the diagnosis of MSA for clinicians. These include: possible, probable, and definite MSA which can be diagnosed by means of specific clinical features and postmortem neuropathological examination

Clinical features that provide support for the diagnosis of Multiple System Atrophy (MSA) include:

Supportive clinical features	
Motor ▪ Rapid progression within 3 years of motor onset ▪ Moderate to severe postural instability within 3 years of motor onset ▪ Craniocervical dystonia induced/exacerbated by levodopa in absence of limb dyskinesia ▪ Severe speech impairment within 3 years of motor onset ▪ Severe dysphagia within 3 years of motor onset ▪ Unexplained Babinski ▪ Jerky myoclonic postural or kinetic tremor ▪ Postural deformities (eg, anterocollis, laterocollis, camptocormia)	**Nonmotor** ▪ Stridor ▪ Inspiratory sighs ▪ Cold discolored hands and feet ▪ Erectile dysfunction (before age 60 years for c.e.) ▪ Pathologic laughter or crying

Exclusion features

- *Not being able to smell anything during an olfactory test without any clear reason.*
- Onset after age 75
- ×Family history of ataxia or parkinsonism
- White matter lesions suggesting multiple sclerosis
- Hallucinations not induced by drug
- Significant neuropathy
- Classic pill-rolling rest tremor

Additional tests can be performed to further evaluate and diagnose

- MRI finding
- Atrophy of putamen, middle cerebellar peduncle, pons or cerebellum and Striatonigral degeneration.
- . Hot cross bun

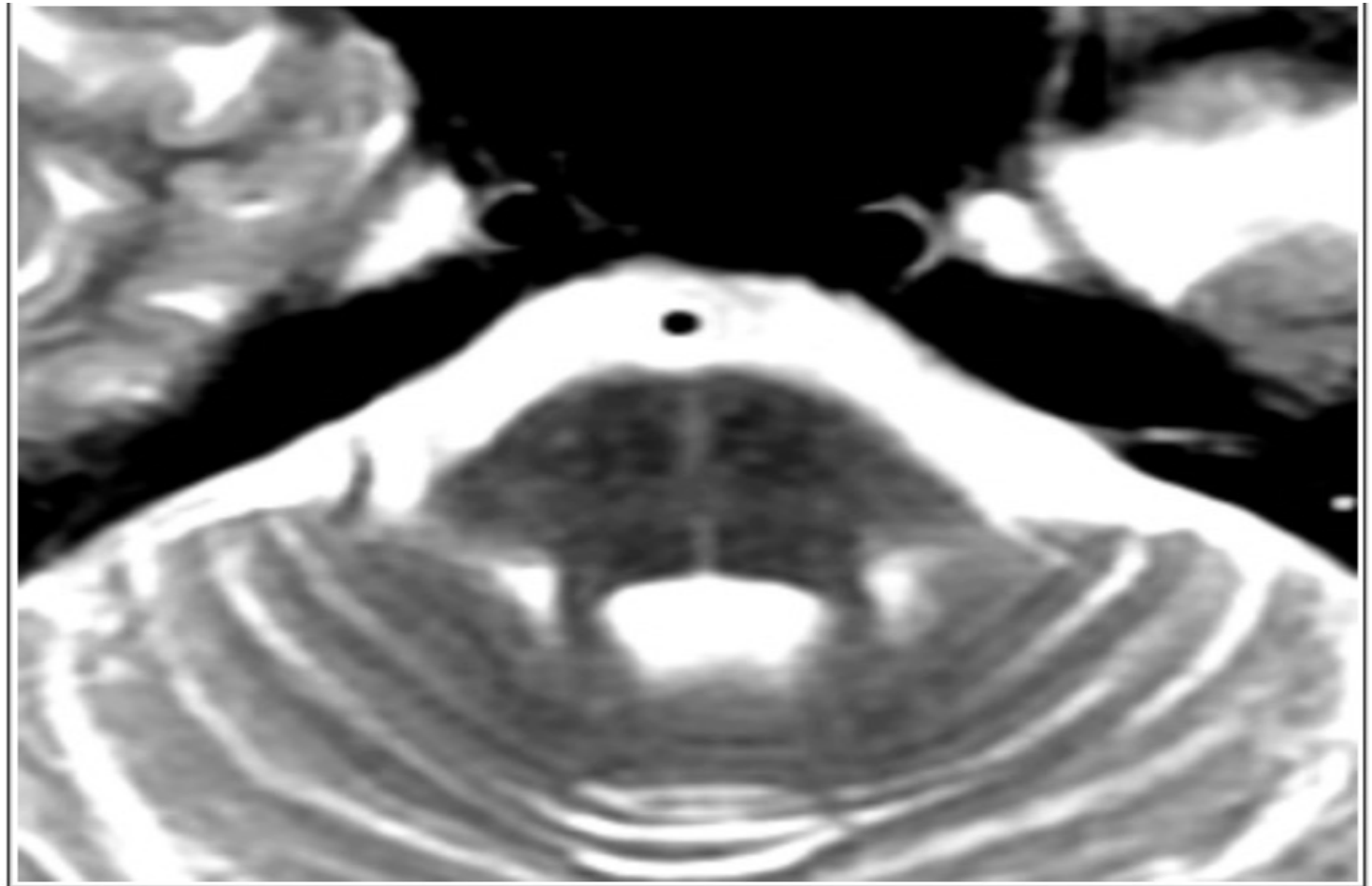


Figure 2: "hot cross bun" sign seen in pons on T2 MRI. (c) Timothy C. Hain, M.D.

Autonomic function Test

- Evaluate the degree or level of dysfunction in both the parasympathetic and sympathetic nervous system
- pupillary and sweating responses,
- -genitourinary and rectal responses.

Ultrasonography

- Incomplete bladder emptying of greater than 100ml can be observed

123I-metaiodobenzylguanidine (MIBG) SPECT scan

- Differentiate Lewy body diseases (Parkinson's disease, Lewy body dementia, and pure autonomic failure) with significant abnormalities from MSA with a normal scan

Differential Diagnosis

Progressive supranuclear palsy

- Slowed eye movements in the vertical direction and difficulty in moving the eyes upward or downward.
- Changes in thinking and speaking , particularly having trouble speaking fluently due to frontal lobe issues.

Corticobasal ganglionic degeneration

- involuntary and uneven movements in one or more limbs and alien limb

Dementia with Lewy bodies

- Fluctuating consciousness and cognitive changes, including visual hallucinations, are unrelated to L-dopa treatment.

Pure Autonomic failure

- solely exhibits symptoms related to autonomic failure.

Management

.There are currently no available treatments to slow down the progression of Multiple System Atrophy (MSA) or cure the condition.

.There are symptomatic drugs which can alleviate the symptoms of MSA.

_**Motor**

Parkinsonian Type _ Levodopa

Dystonia _ Botulinum injection

Therapy

_myoclonus or action tremor

clonazepam, gabapentin, buspirone

_Sleep Disorder

Melatonin

Clonazepam

CPAP

Tracheostomy

_Mood Disorders

SRRI

_Genitourinary

Antimuscarinic

Desmopressin

Cholinergic

Botox

_Erectile dysfunction

Sildenafil

_Orthostatic Hypotension Treatment

Compression Stock

Increase Salt intake

Midodrine

Fludrocortisone