
بسم الله الرحمن الرحيم

Continuum
LIFELONG LEARNING IN NEUROLOGY®
AMERICAN ACADEMY OF NEUROLOGY.

Neurologic Manifestations of Gastrointestinal and Nutritional Disorders

Deficiencies of vit B1,B3, B6, B9, B12, D, A, E, Selenium, Copper

IBDs(Ulcerative colitis and crohn disease), Celiac disease

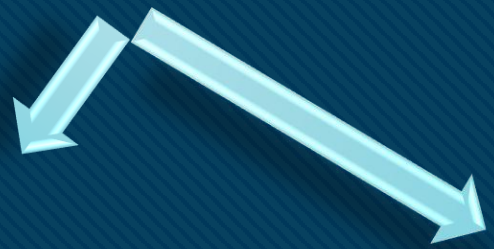
Hepatic Encephalopathy, Acquired Hepatocerebral Degeneration, Wilson Disease, Whipple disease

1.Hepatic Encephalopathy

عدم توانايي كبد در تبديل آمونياك به اوره و در ادامه دفع اوره

افزايش آمونياك خون

تضعيف CNS



مرحله نهايي انسفالوپاتي با علايم
از دست دادن هوشياري، تشنج و
كماي غير قابل برگشت

مرحله ابتدايي انسفالوپاتي
با علايم كاهش هوشياري،
گيجي و بي قراري

Hepatic Encephalopathy

Can be present in patient:

- Other end-organ effect
- Abnormal medication metabolism
- Condition that caused the liver disease

Covert encephalopathy
to
overt and disabling
neurologic dysfunction

Hepatic Encephalopathy previously portosystemic encephalopathy

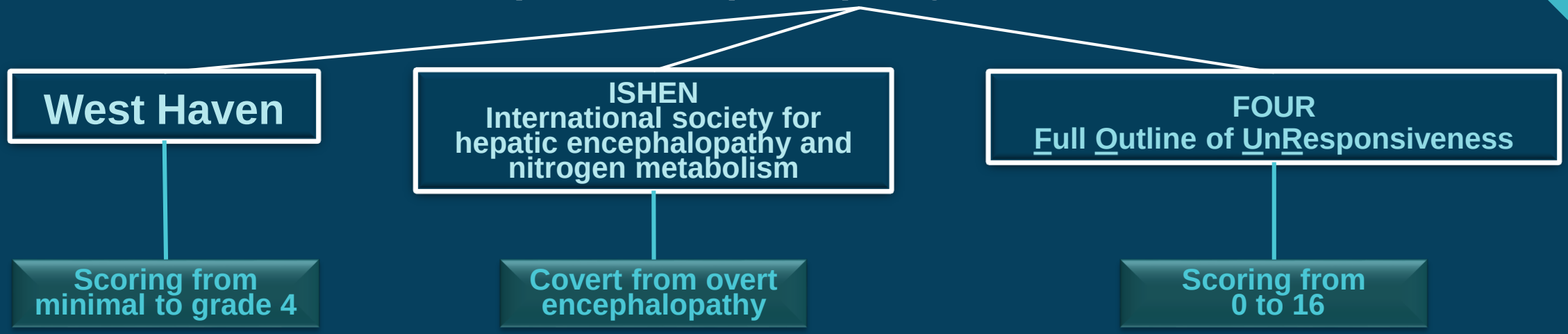
After a patient experiences an episode of clinical encephalopathy, recurrence is typical

Hepatic Encephalopathy

Previously thought to be reversible, recent studies have found evidence of permanent neurologic damage

- ✓ Initiate acute treatment
- ✓ Prophylaxis
- ✓ Avoidance of triggers

Hepatic Encephalopathy classification



Hepatic Encephalopathy

- Asterixis video
- Ataxia 1

TABLE 2-7 Comparative Grading and Progression of Hepatic Encephalopathy

International Society for Hepatic Encephalopathy and Nitrogen Metabolism	West Haven Criteria	Full Outline of Unresponsiveness Score	Clinical severity	Mental status examination	Physical examination
None	0	16	Normal	Normal	Normal
Covert	Minimal	16	No clinical findings Abnormalities only evident on neuropsychometric or neurophysiologic testing Abnormal EEG, evoked potentials Psychometric Hepatic Encephalopathy Score, number connection test, inhibitory control test	Normal	Normal
	Grade 1	16	Clinical findings detectable but inconsistently present and not obvious	Detectable changes from baseline in wakefulness, awareness, or attentiveness; behavior or mood including anxiety or euphoria; cognition or processing including simple calculations	Normal
Overt	Grade 2	15 to 8	Clinical findings consistently present, but variable type	Obvious changes including somnolent and apathetic; inappropriate behavior or mood; disoriented, lethargic, or confused	Asterixis, dysarthria
	Grade 3	15 to 8	Severe	Obtunded or stuporous	Ataxia, nystagmus
	Grade 4	7 to 0	Coma	No response to pain or stimulation	Pyramidal dysfunction, rigidity

Diagnosis of Hepatic Encephalopathy

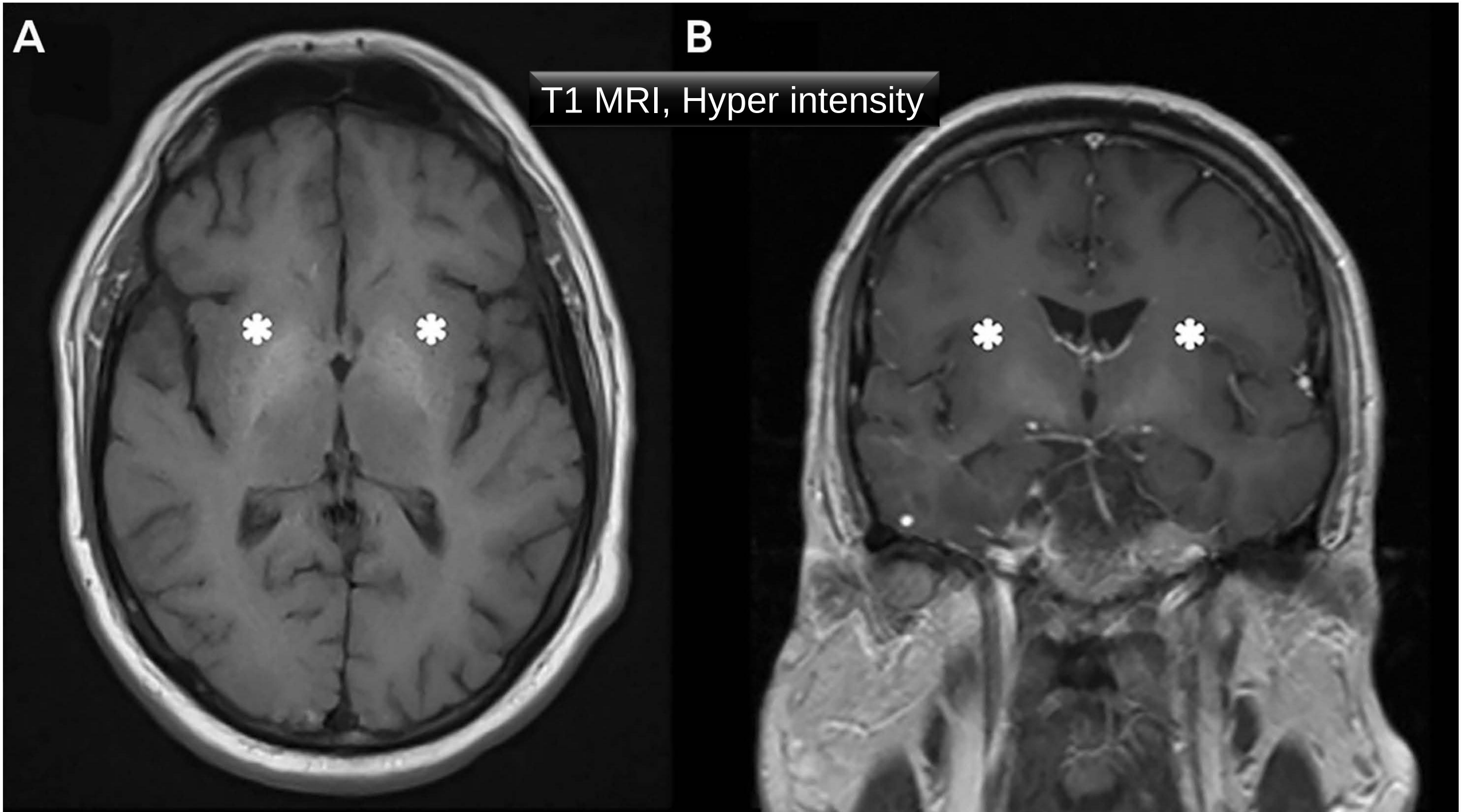
Is clinical

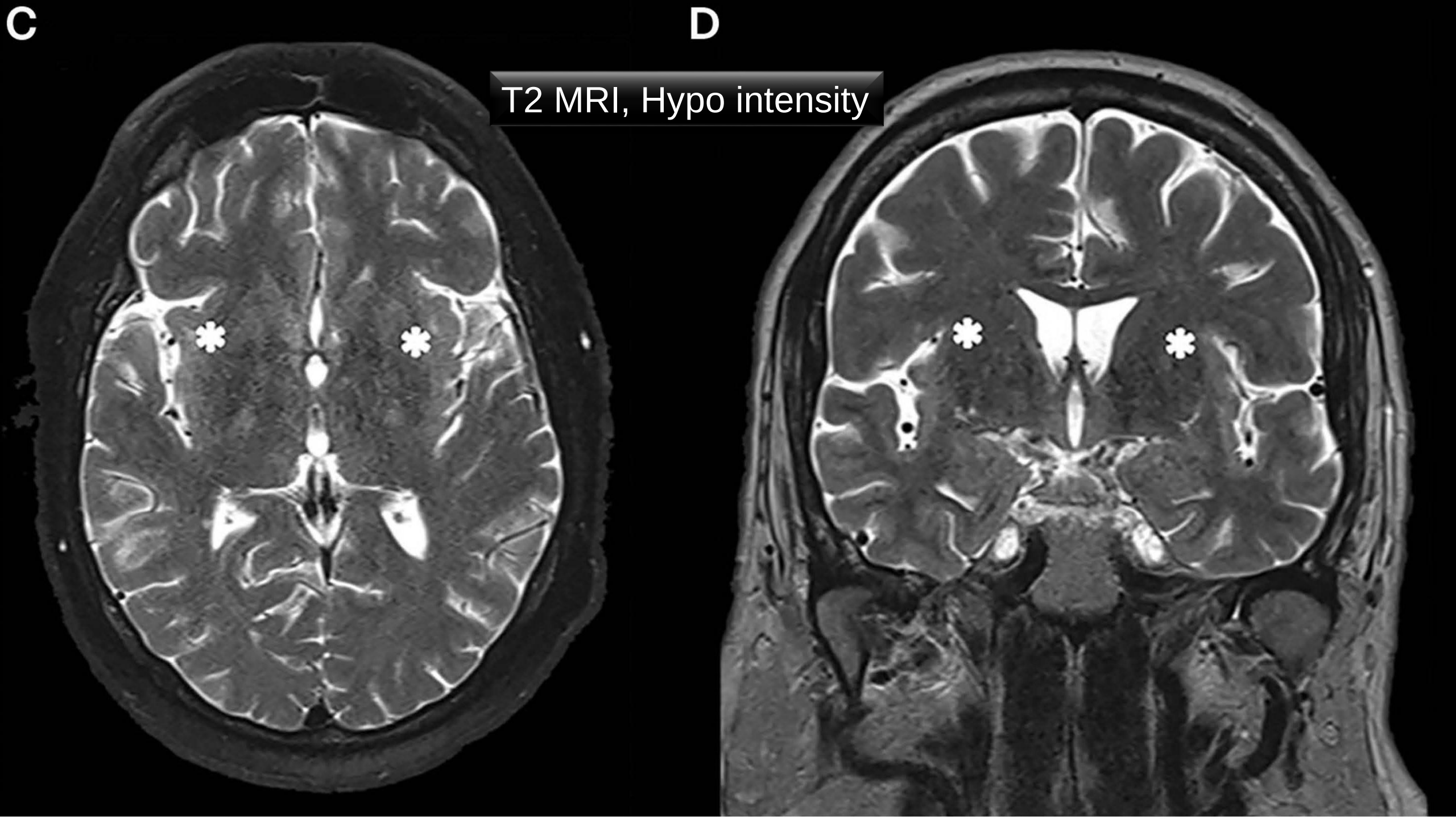
No single test, including ammonia level

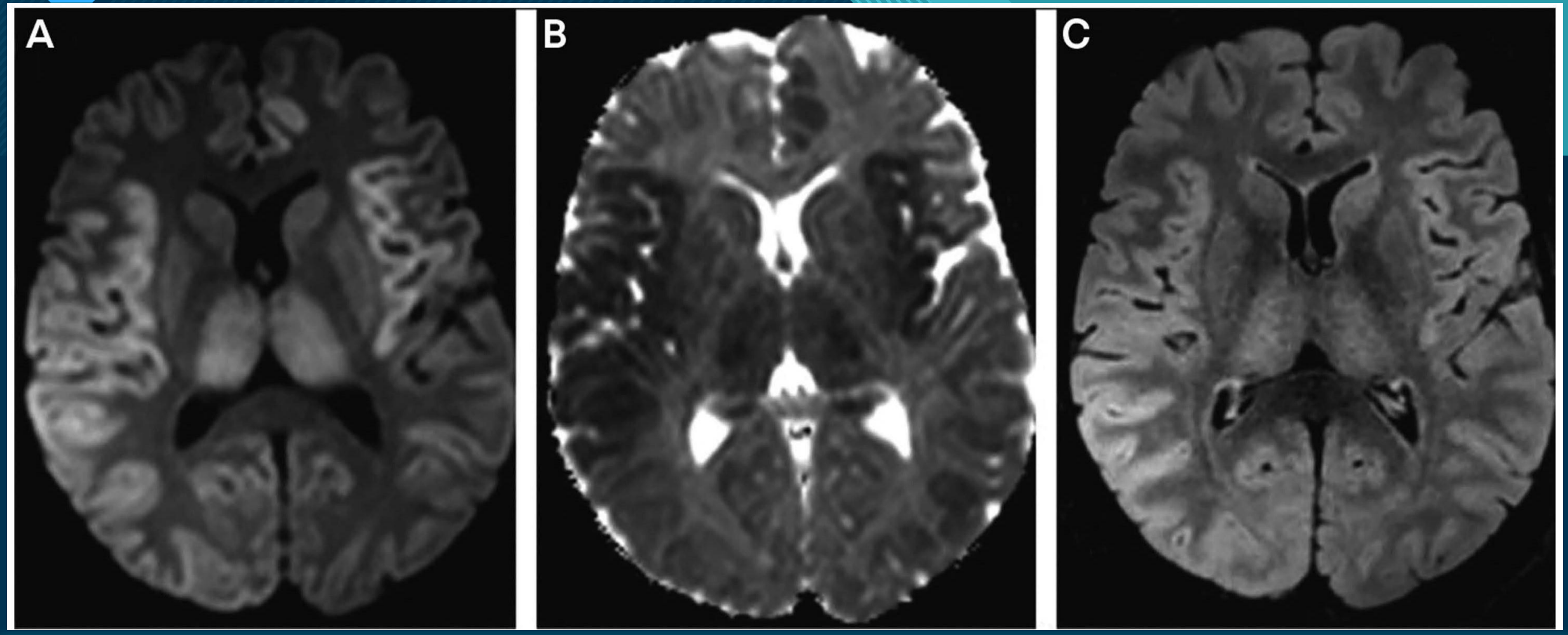
Often shows generalized slowing and triphasic wave

Brain CT is insensitive, Except in severe cases in which cerebral edema

MRI may be show change consistent with chronic hepatic disease or Hepatocerebral degeneration


A
B
T1 MRI, Hyper intensity


C
D
T2 MRI, Hypo intensity



Brain MRI findings in hyperammonemic encephalopathy. Axial brain MRI showing diffusion-weighted (*A*), apparent diffusion coefficient (*B*), and fluid-attenuated inversion recovery (FLAIR) (*C*) changes in the cortical ribbon and thalami. Note the predilection for the insular cortex.

2.Acquired Hepatocerebral Degeneration

- Wilson disease
- Non Wilson disease

Is a chronic irreversible neurologic condition seen in patient with chronic liver disease that manifests as combination of movement and neuropsychiatric disorders

Hepatic Encephalopathy	Acquired Hepatocerebral Degeneration
More common episode	Uncommon
Non progressive	progressive
Decrease level of consequences	Not associated to L.O.C
Asterixis and myoclonus is less common	Asterixis and myoclonus is common
	Movement disorders(Parkinson and ataxia-plus) are most common
	Resting tremor is rare, kinetic tremor is common
	Dystonia, dyskinesia, myelopathy and chorea have been reported
	Frontal lobe dysfunction and memory impairment

2.Acquired Hepatocerebral Degeneration

- **Note:**

♠ Pathophysiology and why only a fraction of patient with chronic liver disease develop this complication are not completely understand

♣ incidence, nature, duration and severity of the liver disease

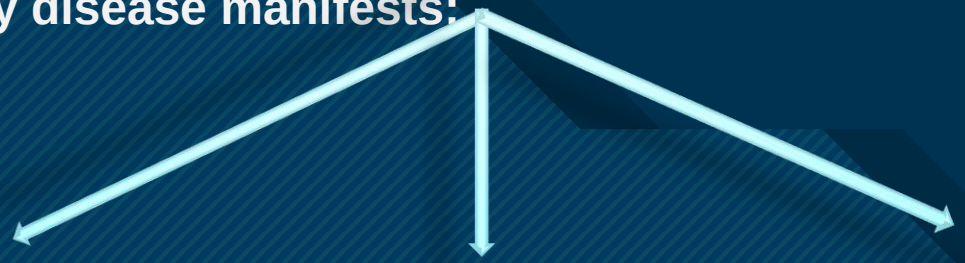
♥ Accumulation of manganese

♦ Manganese transporters are highly expressed in basal ganglia, which may explain why these areas are particularly vulnerable and why blood manganese levels are not reliable marker

3.Wilson disease

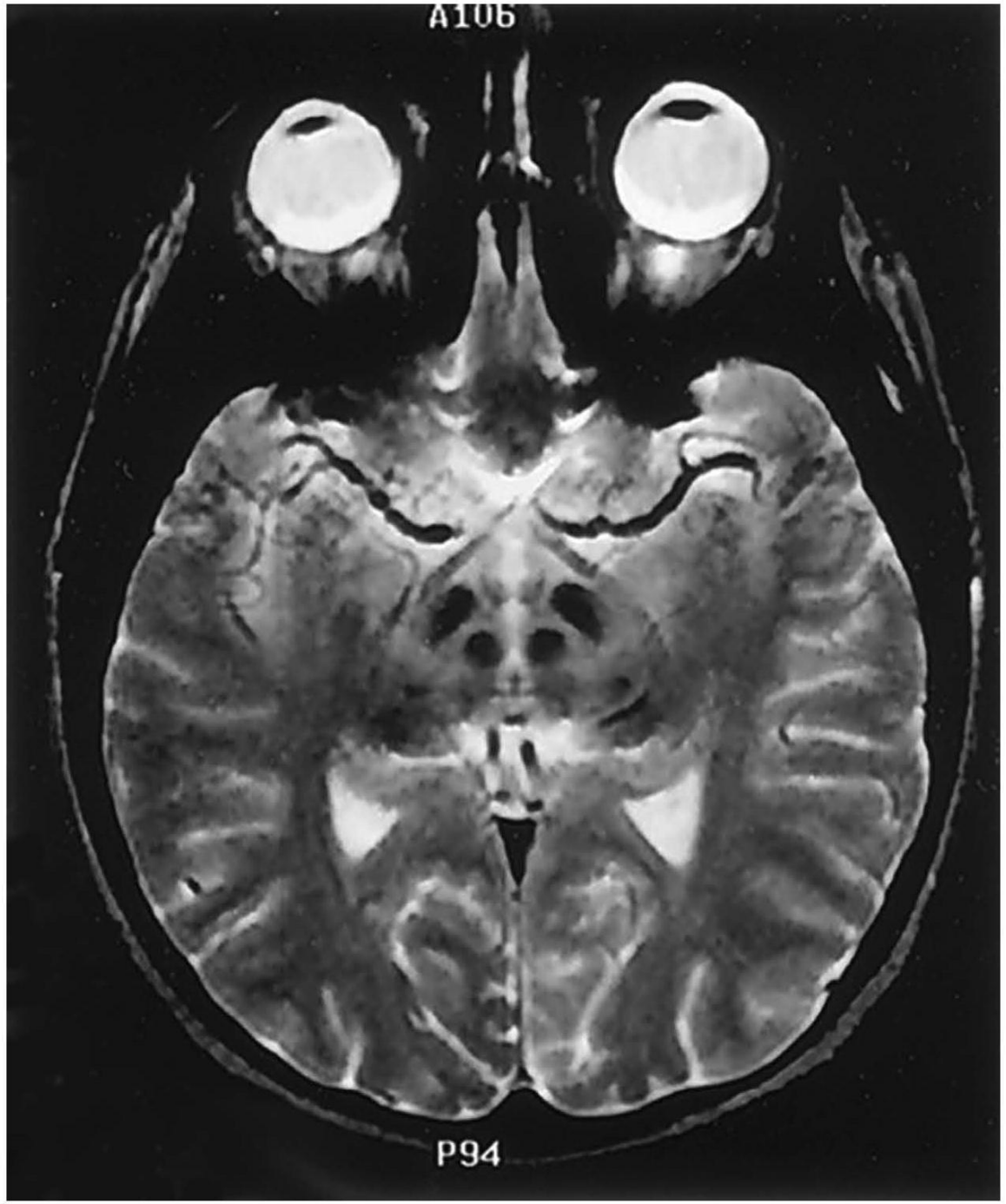
Is a rare type of Hepatocerebral degeneration due to a mutation in the ATP7B gene on chromosome 13 that encodes for the cupper-binding protein ceruloplasmin

Clinically disease manifests:

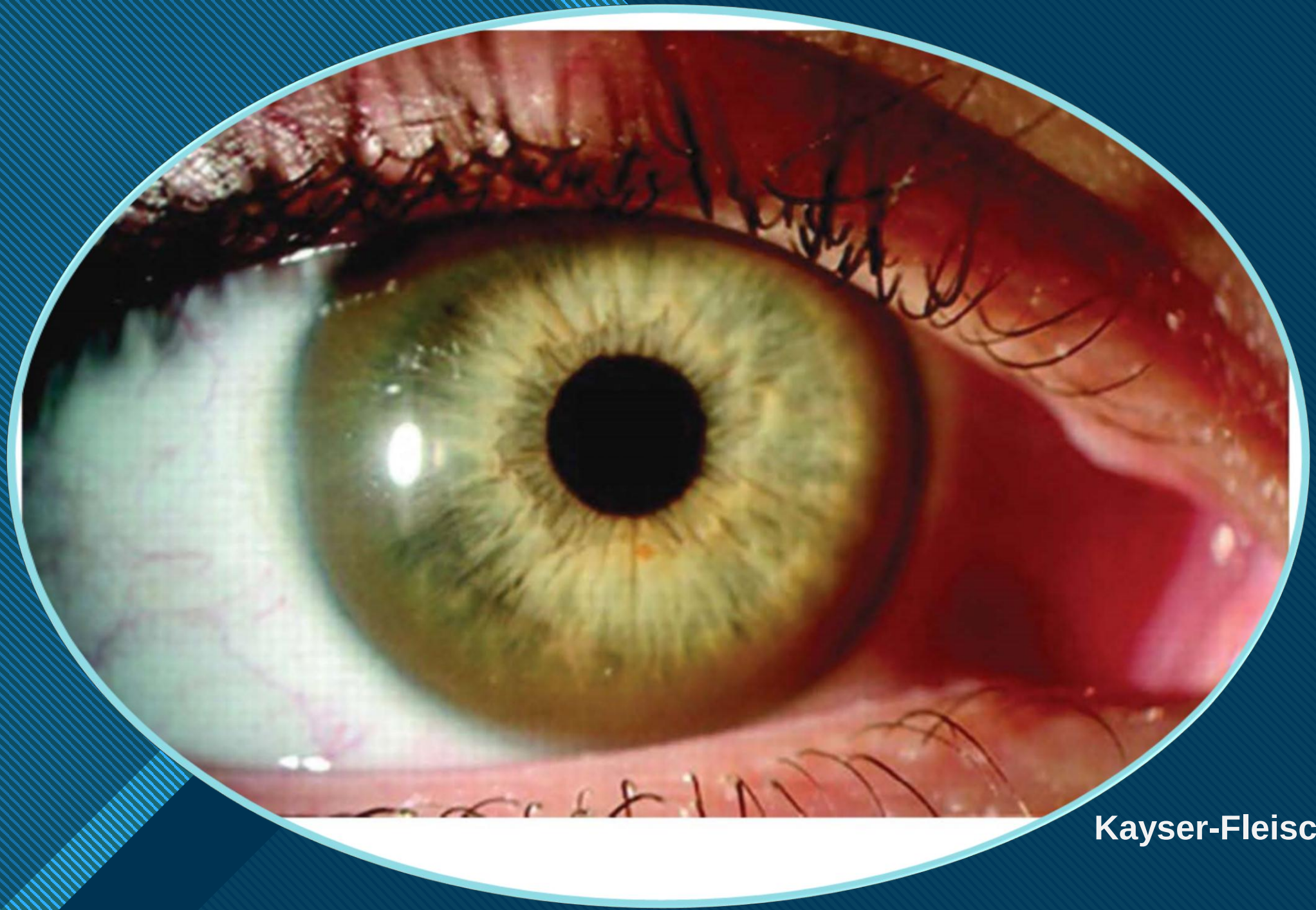


psychiatric	hepatic problem	neurologic
Non specific mood, anxiety and behavioral disorder	Very widely from asymptomatic stenosis to acute liver failure	Most often movement disorder: tremor, dystonia and ataxia. Wing-beating tremor and facial dystonia of risus sardonicus. Kayser-Fleischer ring


Kayser-
Fleischer ring
Cardiac
Renal tubular
dysfunction
Arthritis
CNS disorders
Behavioral changes
Dystonia
Dysarthria
Excessive salivation
Dysphagia
Mask-like facies
Hepatomegaly
Jaundice
Acute hepatitis
Fulminant hepatic failure
Cirrhosis
Wilson's Disease



Face of the giant panda sign in Wilson disease. Axial MRI of the brain in Wilson disease demonstrating the face of the giant panda sign. Increased T2 hyperintensity is seen in the midbrain tegmentum. The red nuclei and substantia nigra are unaltered and resemble the eyes and ears of a giant panda.



Kayser-Fleischer ring

Leipzig criteria

Criteria	Result	Points
Kayser-Fleisher rings	Present	2
	Absent	0
Neurologic symptoms or brain MRI findings	Severe	2
	Mild	1
	Absent	0
Serum ceruloplasmin level	<0.1 g/L	2
	0.1-0.2 g/L	1
	Normal (>0.2 g/L)	0
Coombs-negative hemolytic anemia	Present	1
	Absent	0
Liver copper	>4 µmol/g	2
	0.8-4 µmol/g	1
	Normal (<0.8 µmol/g)	-1
	Rhodamine-positive granules	1
Urinary copper	>2× upper limits of normal	2
	1-2× upper limits of normal	1
	Normal	0
Genetics	Mutation on both chromosomes	4
	Mutation on one chromosome	1
	Normal	0
	Diagnosis	**Total score**
	Established	4 or more
	Possible, additional evaluation needed	2-3
	Very unlikely	0-1

Wilson disease treatment

Drug: D-penicillamine or Trientine

Diet: low- copper diet

Competitive: zinc salts

4.Whipple disease

Tropheryma whipplei gram positive bacillus

Tetrad: Arthralgia, abdominal pain, diarrhea and weight loss

Neurologic manifestation in 10-40%

CNS involvement is common, 50-90%

In 2022 large systemic review of CNS whipple disease:

- Supranuclear ophthalmoplegia 42%
- Disorder of sleep 38%
- Myoclonus 19%
- Myorhytmia 23%
- Ataxia and nystagmus are common

Myorhytmia video

Diagnosis of Whipple disease

1.Whipple Tetrad

2.Identification of T.Whipplei duodenal biopsy

3.In CNS manifestation LP: (PCR+)

Mild to moderate increase of WBC and Protein

4.Brain MRI do not have uniquely identifying

In 2022 large review :

- Normal MRI 11%
- Single nonspecific parenchymal lesion 14%
- Multifocal lesion 56%
- Meningeal involvement 3%
- Spinal cord involvement 1.4%

CONCLUSION

Gastrointestinal and neurologic diseases have complex interrelationships. These include neurologic syndromes due to poor intake or absorption of nutrients, neurologic manifestations of inflammatory or immune-mediated gastroenteropathies, neurologic disease caused by hepatic insufficiency, and the coexistence of neurologic and gastrointestinal disease resulting from a mutual genetic, degenerative, or infectious etiology.

سپاس فراوان

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