Neuroradiology in Toxic & Metabolic Encephalopathy

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Introduction

- Toxic & metabolic → ED, although relatively uncommon.
- Important to recognize → can lead to catastrophic outcome if not rapidly & properly managed.
- **Imaging plays a key role**
  - ***First line modality*** to point the next step investigation
  - Patient with toxic & metabolic disorder frequently ***can not be asked properly*** (confusional state/delirium)
  - Some patients will also not be honest about their drug history

Introduction

- Neuroimaging in toxic & metabolic is quite ***challenging***:
  - Consist of many heterogenous groups of etiology.
  - Majority of cases are also unspecific.
- Toxic & metabolic brain disorders in the literature are usually approached based on the classification of the etiology of the substance
- This approach mixes many different possible imaging manifestation and creates more confusion.

Most common *endogenous metabolic derangement*:

- Hypertensive encephalopathy
- Glucose disorder
- Parathyroid disorder
- Hepatic encephalopathy
- Uremic encephalopathy
- ODS
- Cobalamine deficiency

Major *exogenous causes of toxic encephalopathy*:

- Alcohol related disorder (WE, MBD)
- Industrial agents (methanol, toluene)
- Inhaled gases (carbon monoxide, pesticides)
- Illicit drug use (heroin, cocaine)
- Chemotherapeutic agents (methotrexate, fludarabine, 5-fluorouracil).
- Immunosuppresive agents (cyclosporine)
- Other potentially neurotoxic medications (metronidazole, vigabatrine)

Introduction

- This presentation use a systematic approach based on the **pattern of neuroimaging findings**.*
- This approach is more applicable to our daily clinical practice, because we often see the pattern of image first.
- But, **clinical history** should always be looked, as it points to subjacent toxic and metabolic causes.

*de Oliveira AM, Paulino MV, Vieira APF, McKinney AM, da Rocha AJ, Dos Santos GT, Leite CDC, Godoy LFS, Lucato LT. Imaging Patterns of Toxic and Metabolic Brain Disorders. Radiographics. 2019 Oct;39(6):1672-1695. doi: 10.1148/rg.2019190016. PMID: 31589567.

Pathophysiology of Cerebral Edema in Toxic & Metabolic Brain Disorders

- **Vasogenic Edema**
- **Cytotoxic Edema**
- **Intramyelinic Edema**

→ 3 pathologic process that are commonly related to **toxic & metabolic brain disorders.***

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Pathophysiology of Cerebral Edema in Toxic & Metabolic Brain Disorders

Vasogenic Edema

- Blood-brain barrier disruption by mechanical or chemical insults
- Leakage of fluid from capillaries into the extracellular space
- **Imaging findings:**
  - T2WI & T2 FLAIR hyperintensities.
  - No restricted diffusion on DWI-ADC.
  - WM >> GM

Pathophysiology of Cerebral Edema in Toxic & Metabolic Brain Disorders

Cytotoxic Edema

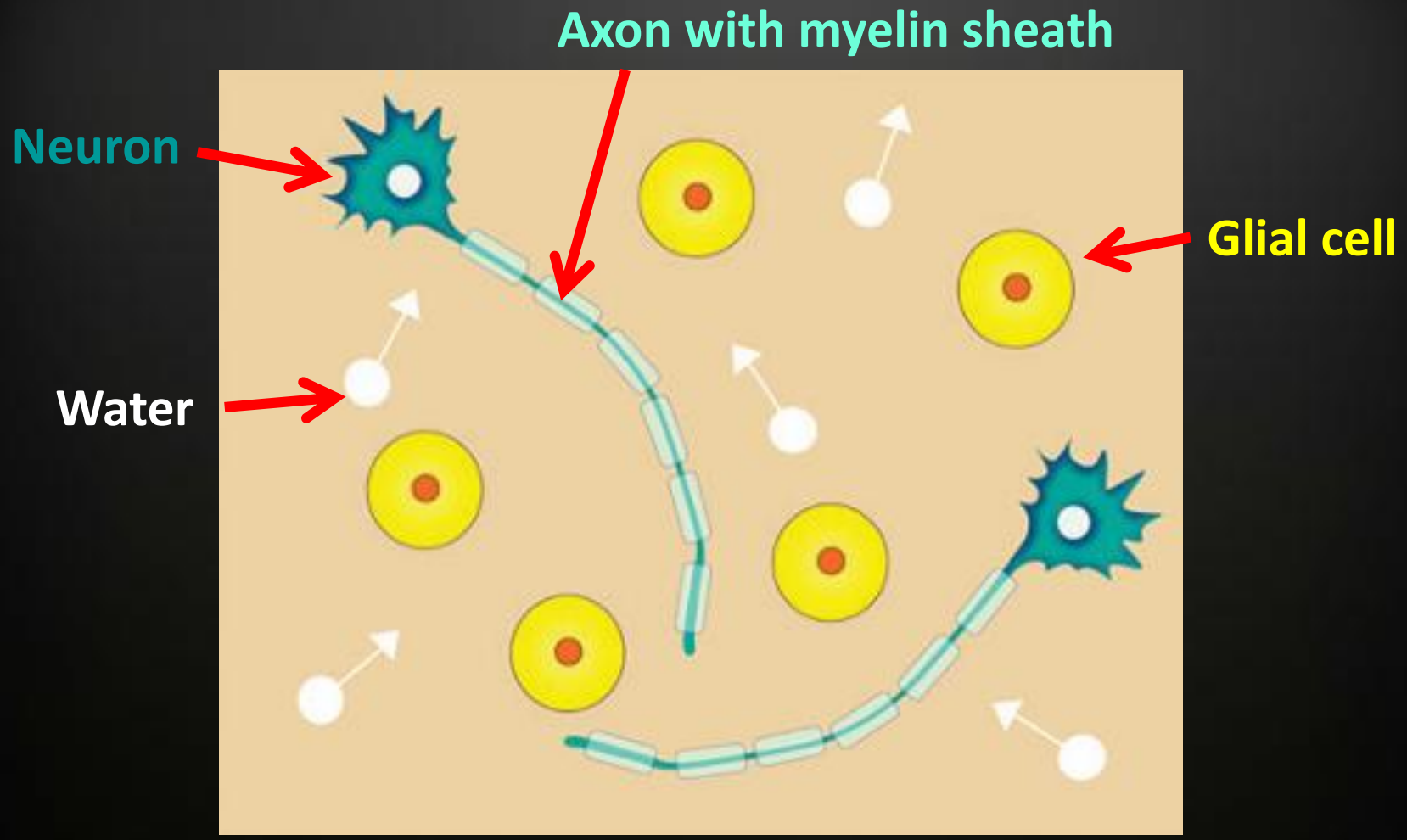
- Extracellular water passes into cells → swell.
- Prior ischemic/hypoxic insults impair mitochondrial function → failure of ion pumps → cellular edema
- Changes are not completely reversible (cell death)
- **Imaging findings:**
  - Restricted diffusion on DWI-ADC.
  - Less changes in T1WI and T2WI
  - GM >> WM

Pathophysiology of Cerebral Edema in Toxic & Metabolic Brain Disorders

Intramyelinic Edema

- Excessive release of exicatory amino acids (glutamate) in the synaptic cleft (excitotoxic brain injury) → cell swelling & subsequent death in the event of ischemia and cell failure with disruption in glutamate reuptake.
- If reuptake of glutamate is maintained → cell swelling and death may not occur → intramyelinic edema
- Changes are reversible
- **Imaging findings:**
  - Reversible restricted diffusion on DWI-ADC.
  - Periventricular WM and splenium CC>>

Normal



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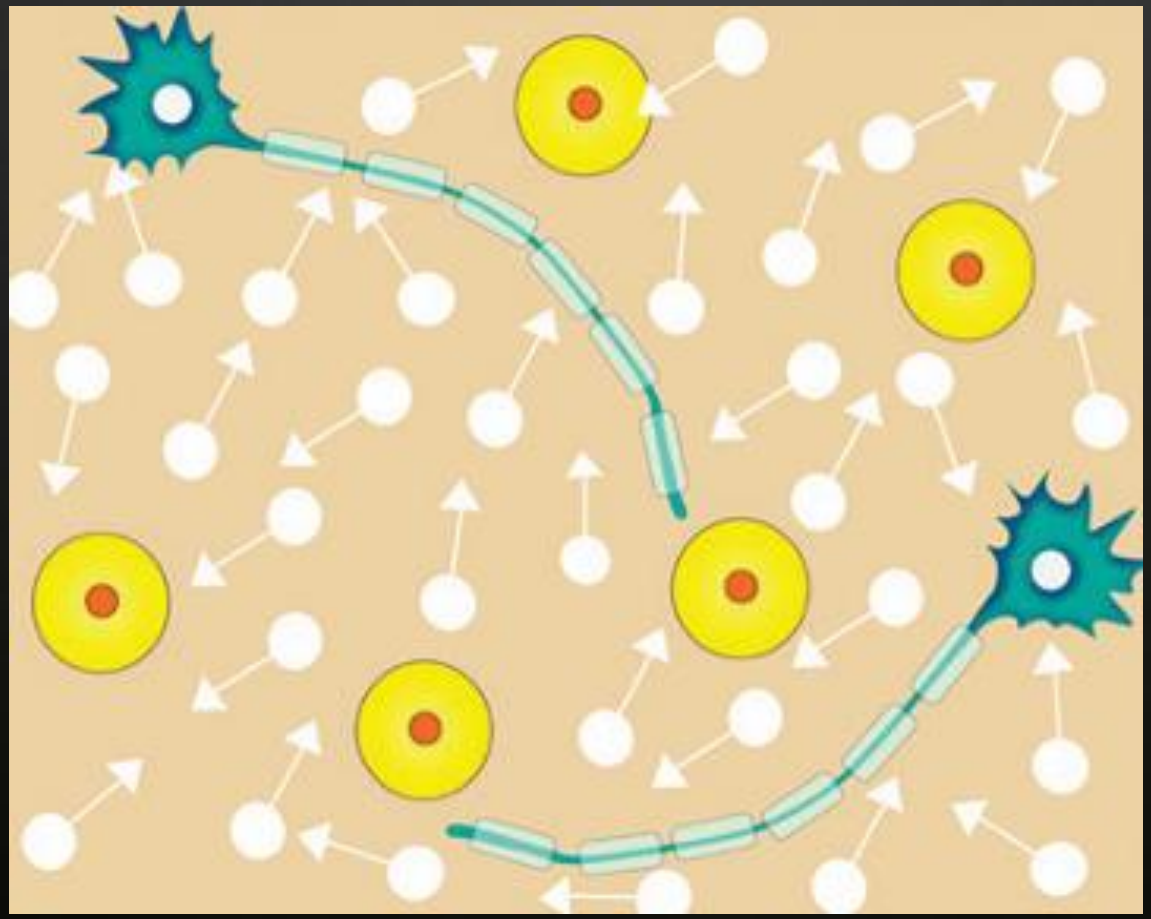
Vasogenic Edema



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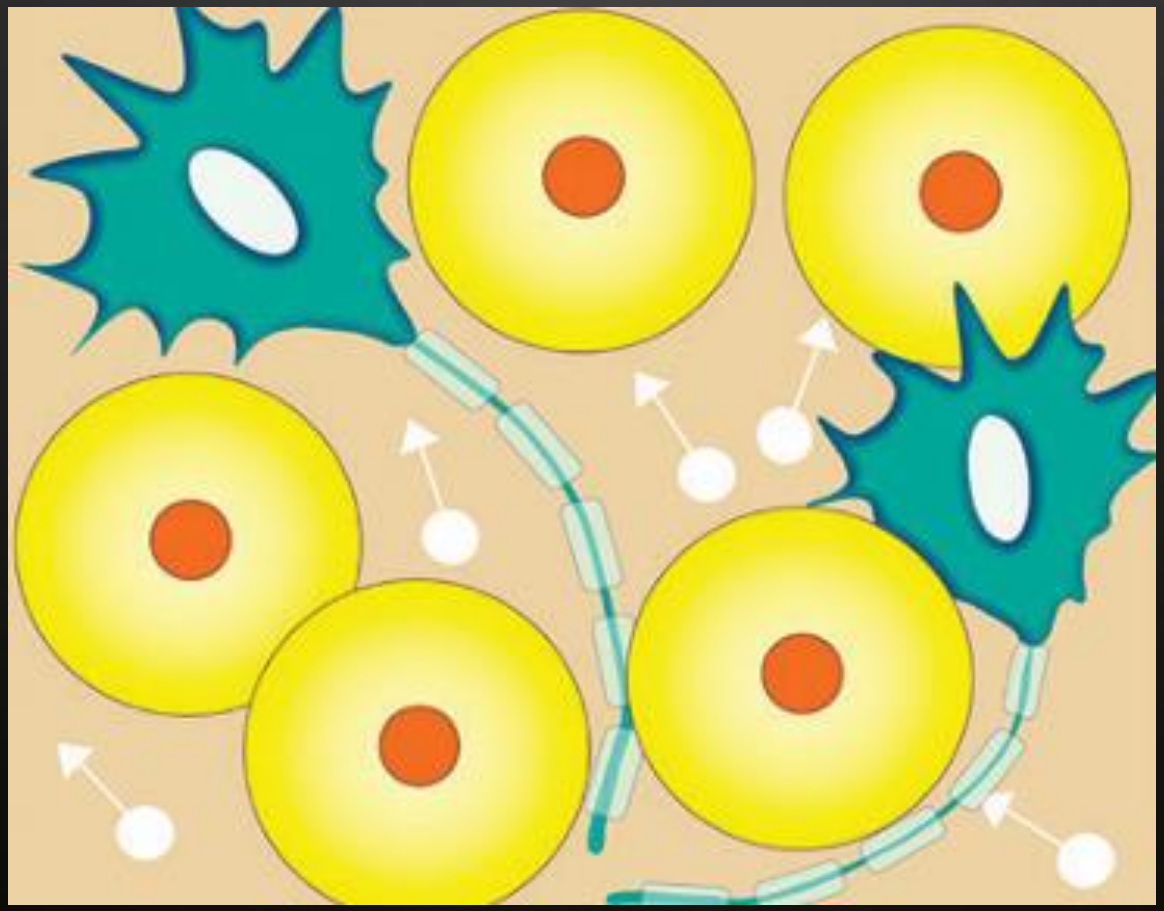
Cytotoxic Edema



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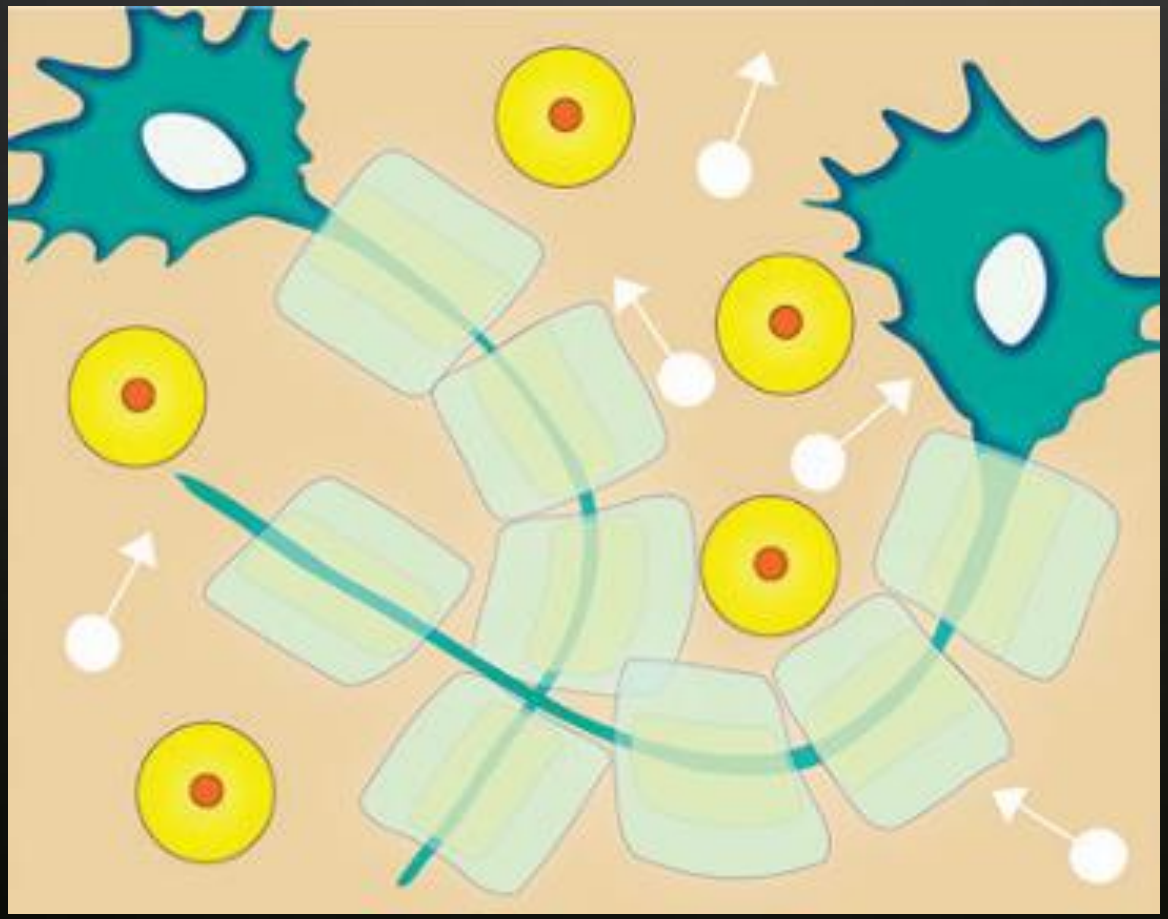
Intramyelinic Edema



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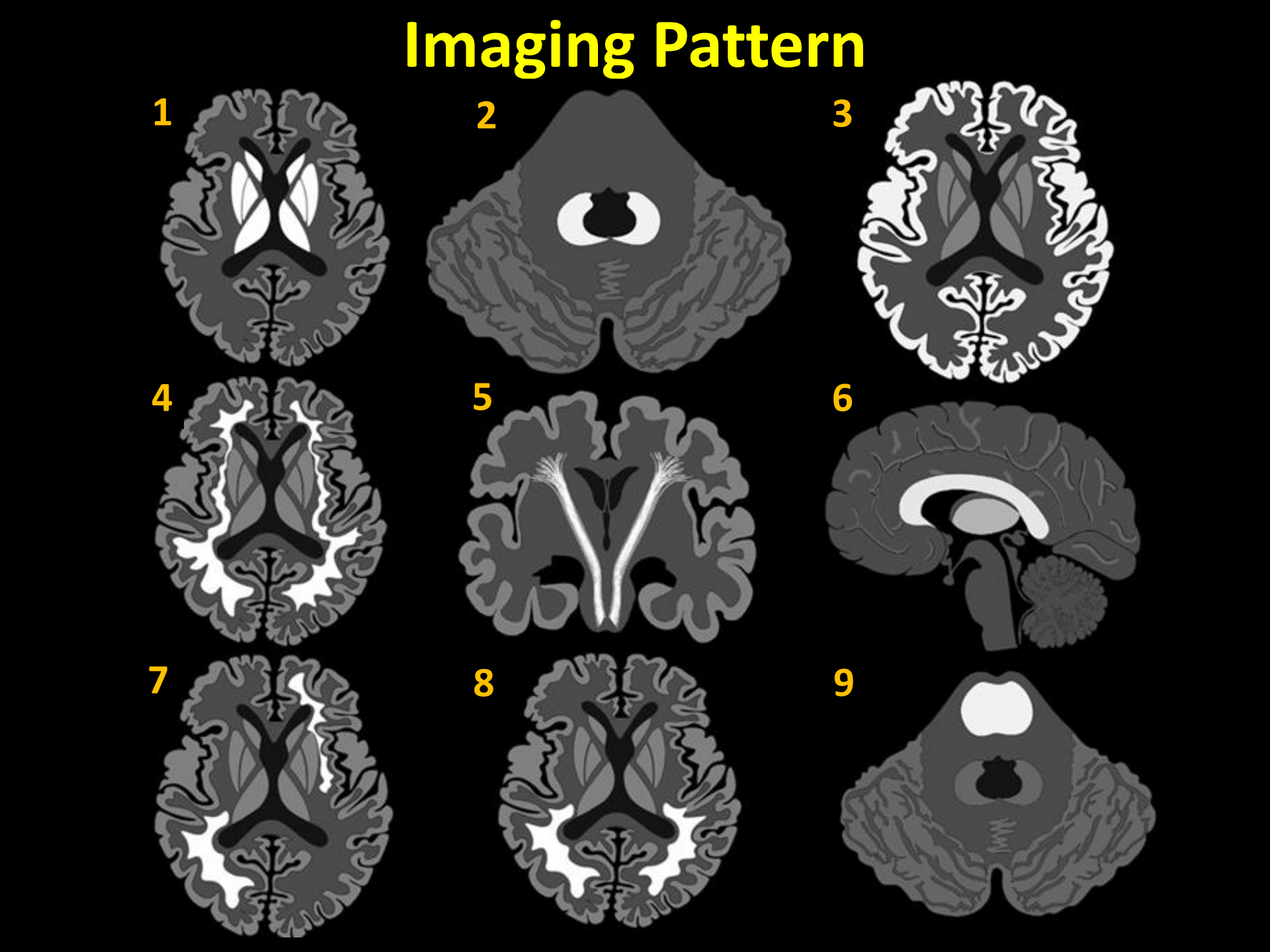
Imaging Pattern



Pattern 1:
Basal Ganglia and/or Thalami Involvement

- Pattern 1a: T2WI & FLAIR Hyperintensity
- Pattern 1b: T2WI Hypointensity
- Pattern 1c: T1WI Hyperintensity

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Wernicke Encephalopathy

- Chronic & frequent alcohol intake
- Can be unrelated to alcohol use (malnutrition):
  - Thiamine deficiencies (Vitamin B1)
  - Hyperemesis
  - Eating disorder
  - Bariatric surgery

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

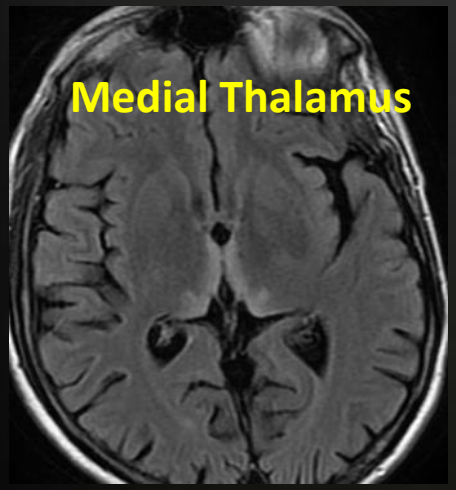
Wernicke Encephalopathy

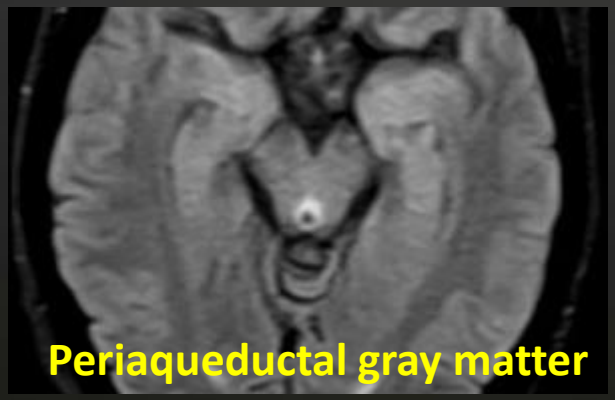
- **Affected sites:**
  - Medial thalami
  - Mammilary bodies
  - Hypothalamus
  - Tectal plate
  - Periaqueductal gray matter
  - Putamina
  - Dorsal pons
  - Cortical involvement (perirolandic)
- **MR findings:**
  - T2WI/T2 FLAIR hyperintense
  - Restricted diffusion on DWI-ADC (acute phase)
  - 50% showing enhancement

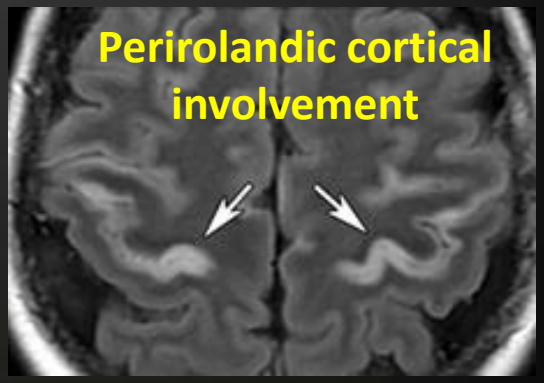
Pattern 1: Basal Ganglia and/or Thalami Involvement

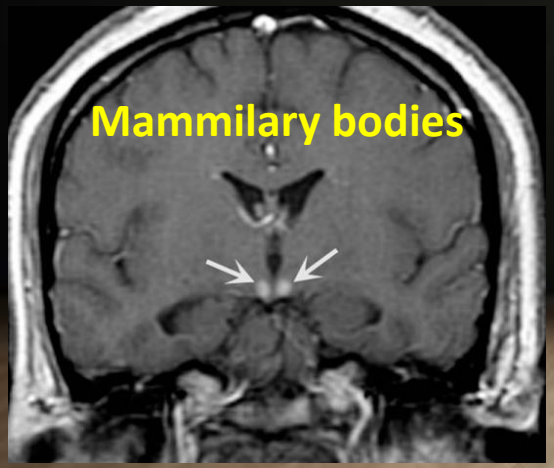
Pattern 1a: T2WI & FLAIR Hyperintensity

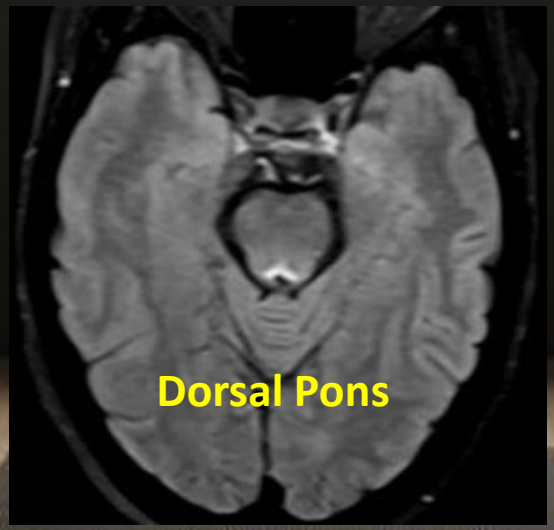
Wernicke Encephalopathy

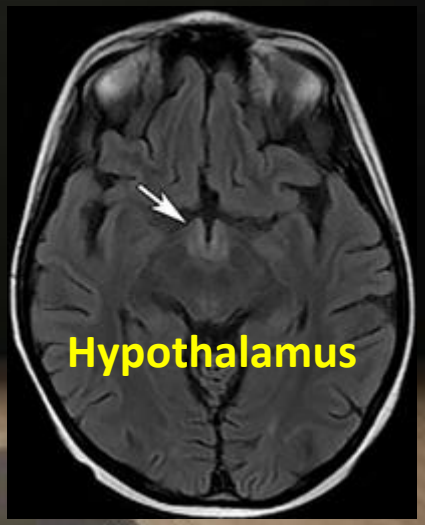








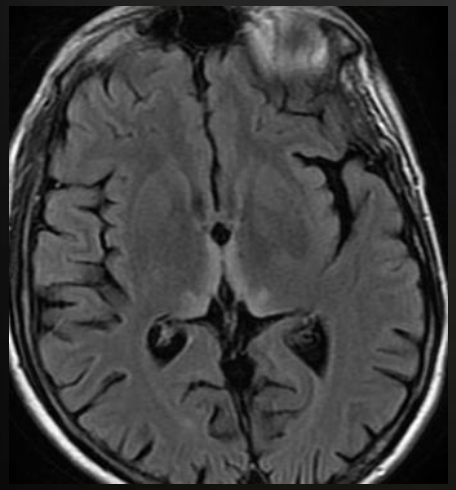
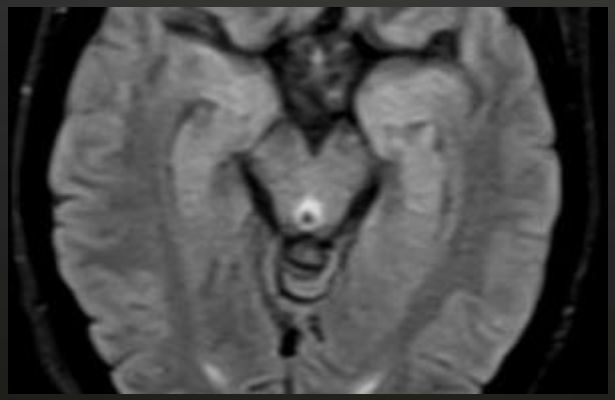
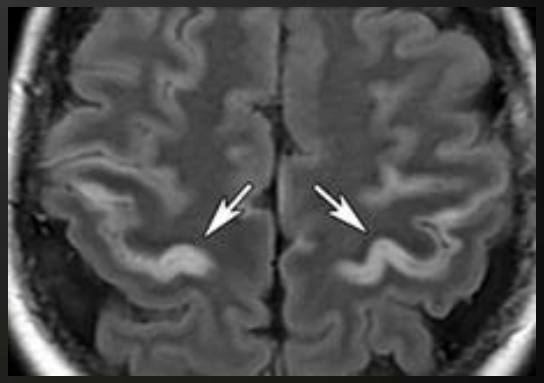
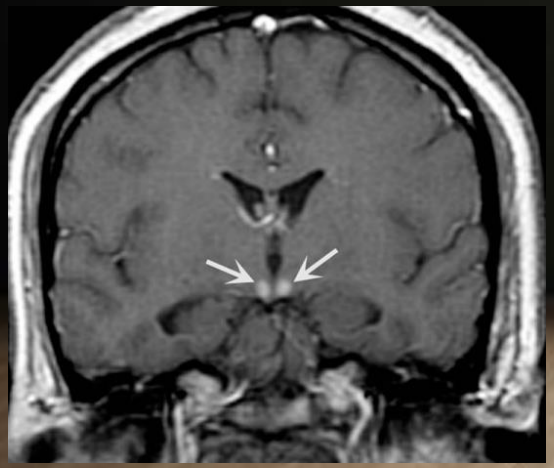
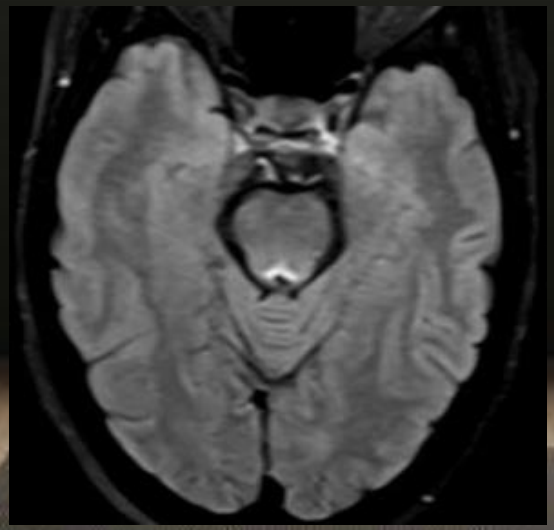
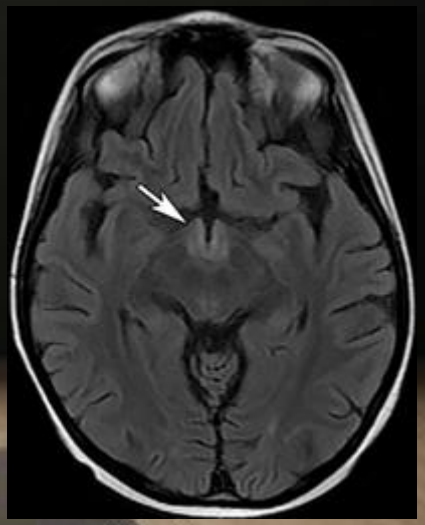




Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Wernicke Encephalopathy


ALCOHOL

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Methanol Poisoning

- Usually be used in solvent, paint removers & gasoline.
- Illicitly be used in alcoholic drink/perfumes.
- Cause severe metabolic acidosis, strong CNS depressant, visual & gastrointestinal disturbances.
- Retina, optic nerve & putamina are particularly vulnerable

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

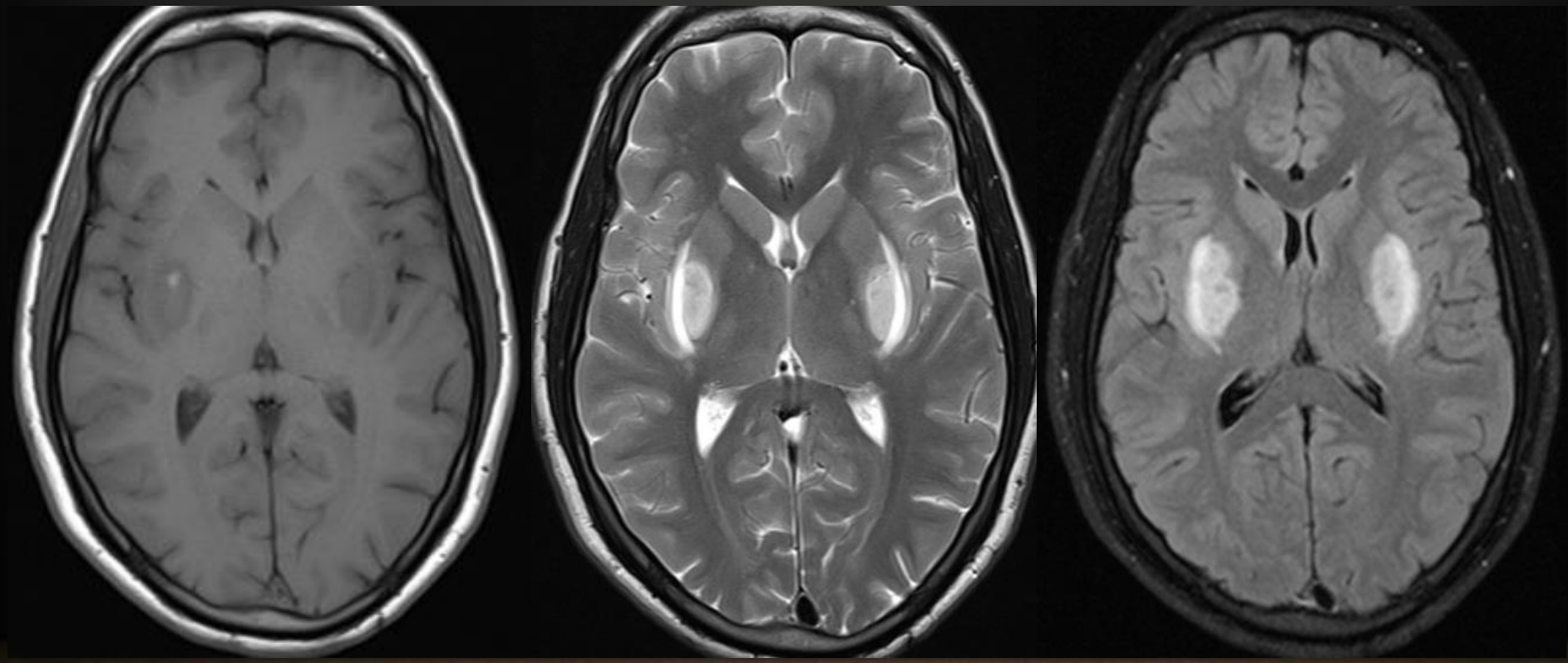
Methanol Poisoning

- **Imaging findings:**
  - Bilateral symmetric putaminal necrosis
  - Relative sparing of the globi pallidi
  - Variable degree of subcortical white matter and cerebellar involvement
  - Optic nerve necrosis.
  - T2WI/T2 FLAIR hyperintensity
  - Hemorrhage (variable intensity according to the phase, susceptibility artefact)

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

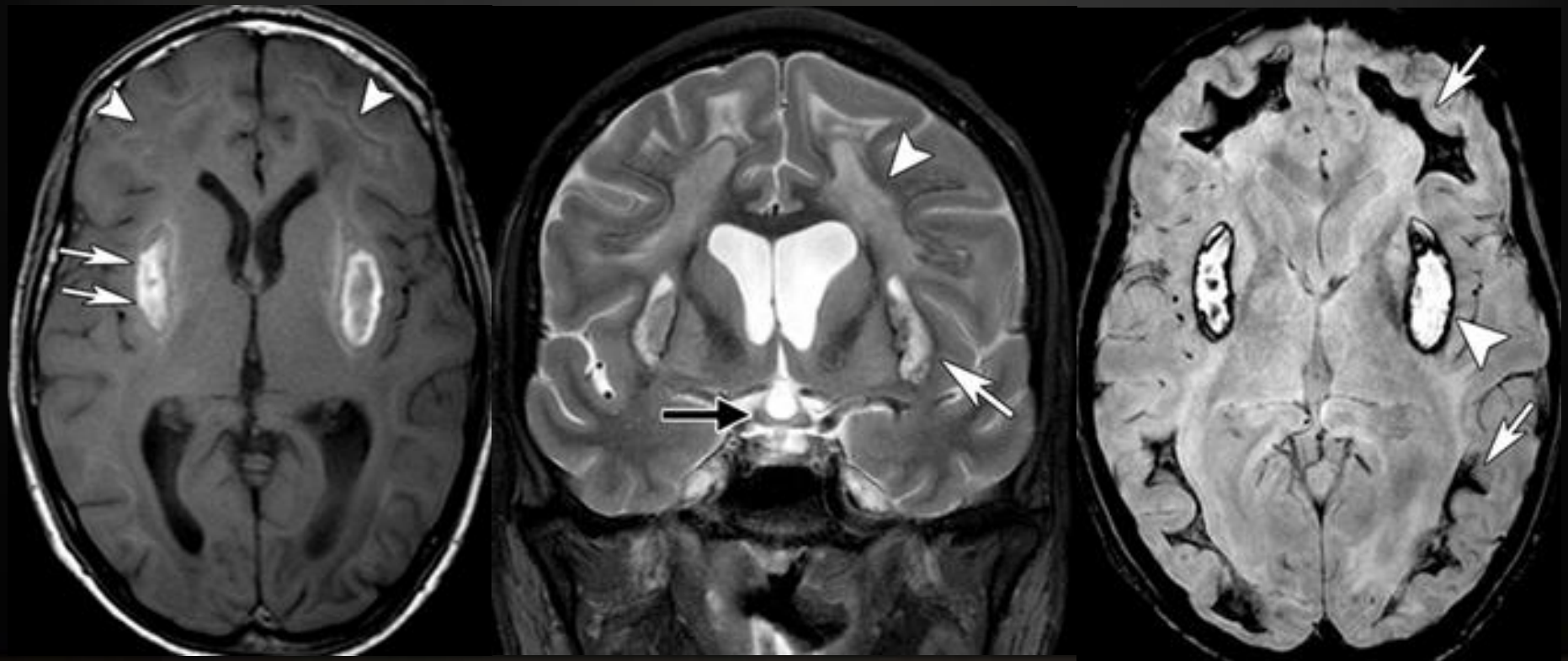
Methanol Poisoning



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Methanol Poisoning



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Methanol Poisoning

Mnemonic:

- Illicit alcohol process usually in ***peripheral***/rural area.
- **Putamen** (***peripheral***/lateral of the lentiform nuclei)

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

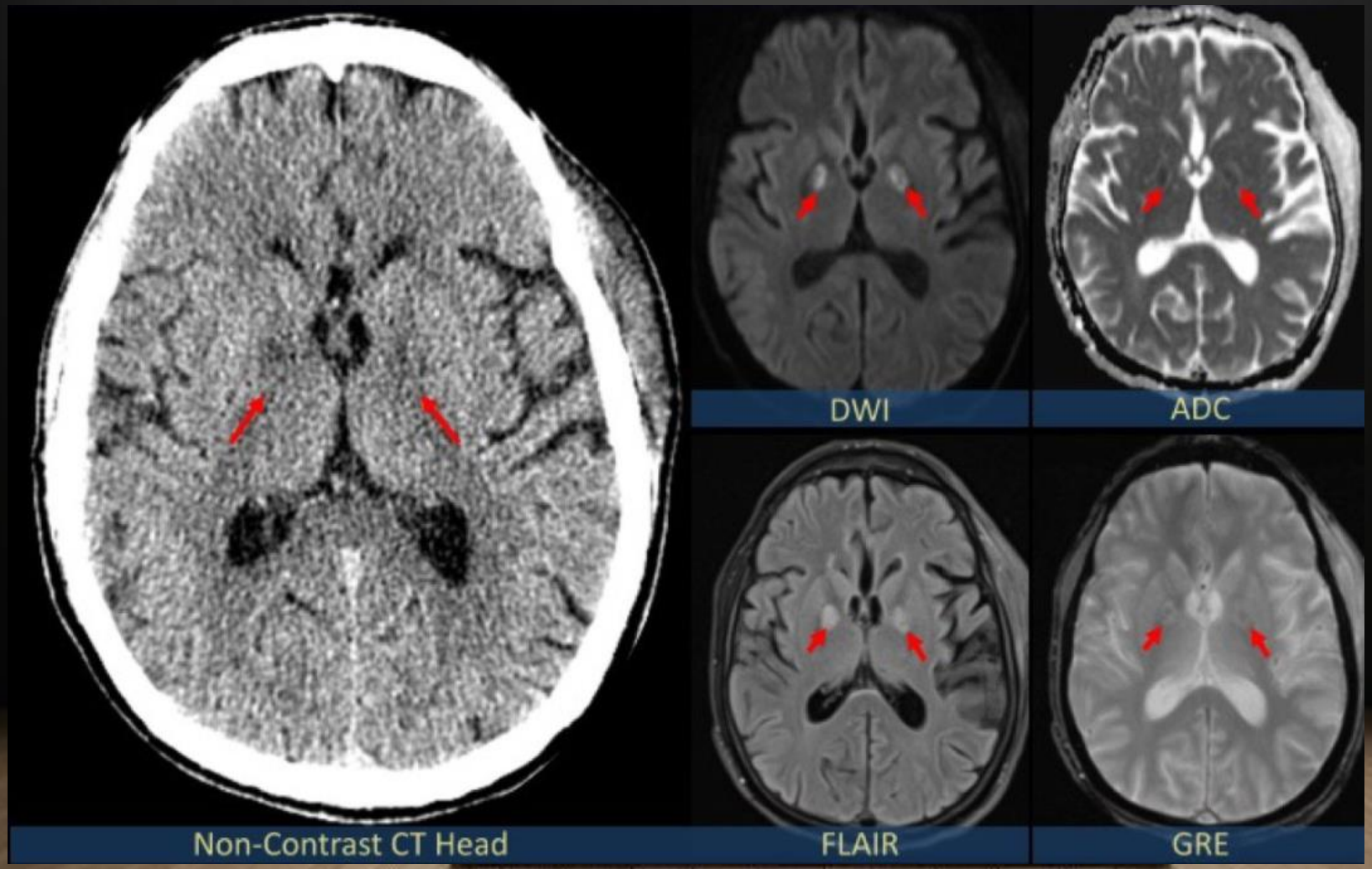
Carbon Monoxide Poisoning

- Odorless and colorless gas
- Most common cause of accidental poisoning (suicide)
- **Imaging findings:**
  - Globus pallidus sensitive to hypoxia:
    - Hypodense on CT
    - Hyperintense on T2WI & T2 FLAIR
    - Restricted diffusion on DWI-ADC
    - Hypointense in T2 GRE if there is haemorrhage.
  - 2nd most commonly affected site: cerebral white matter (1/3 of cases → Pattern 4: Symmetric Periventricular WM).
  - Less common sites: hippocampi, caudate nuclei, putamina, thalami, cerebellum, corpus callosum, cerebral cortex.

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Carbon Monoxide Poisoning



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Carbon Monoxide Poisoning

Mnemonic:

- CO must be taken *inside*/medial.
- **Globus pallidus** (*inside*/medial aspect of the lentiform nuclei)

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Vigabatrin-associated Toxicity

- Vigabatrin: antiepileptic drug for infantile spasms.
- The younger the patient (<1 year old), the higher the risk.
- Frequently asymptomatic course & reversibility through drug discontinuation
- Visual disturbance & movement disorder

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

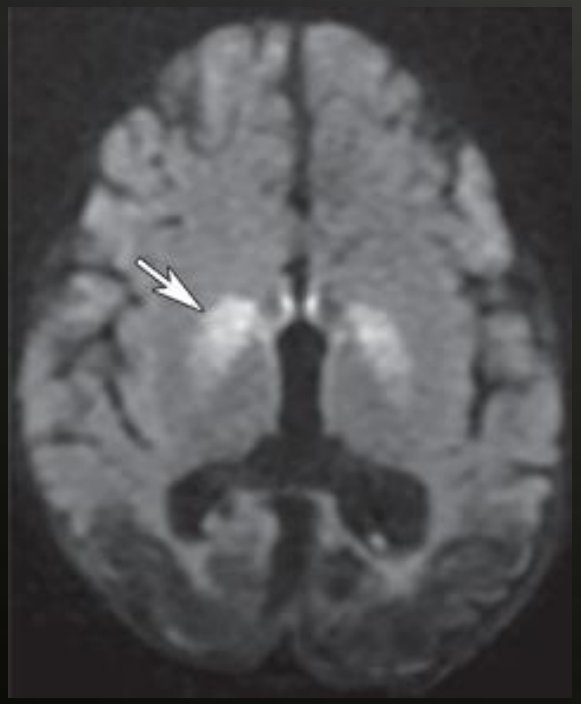
Vigabatrin-associated Toxicity

- **MR findings:**
  - Symmetric restricted diffusion and T2WI&T2 FLAIR hyperintensity in globi pallidi, thalami, dorsal brainstem or dentate nucle.
  - Reversible on vigabatrin withdrawal

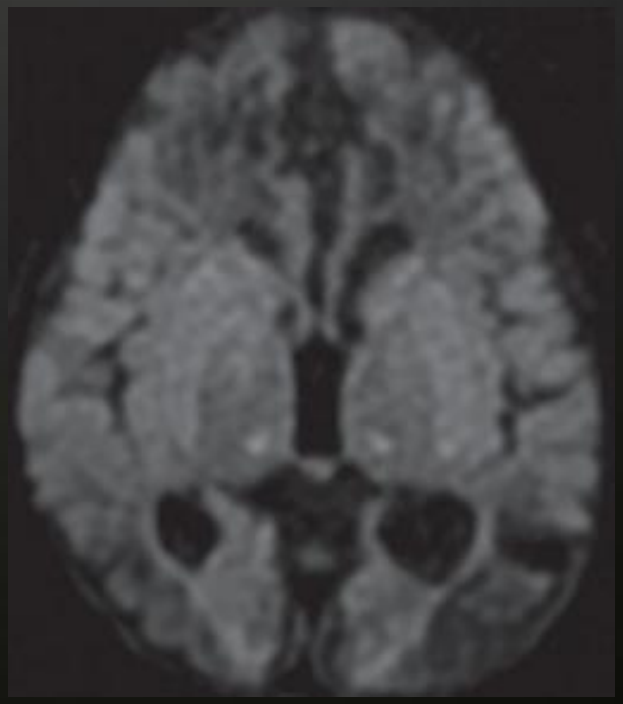
Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Vigabatrin-associated Toxicity



Symmetric restricted diffusion in globi pallidi



Reversible on vigabatrin withdrawal

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

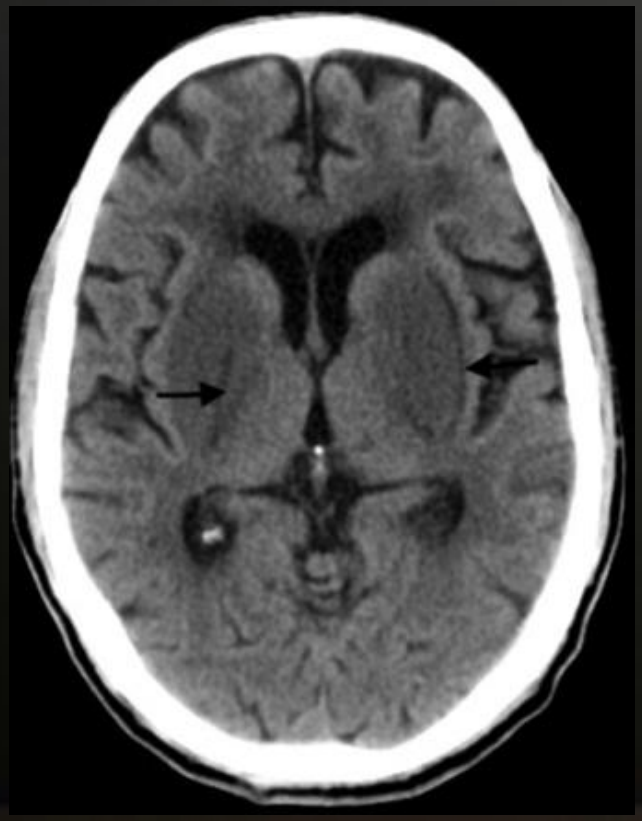
Uremic Encephalopathy

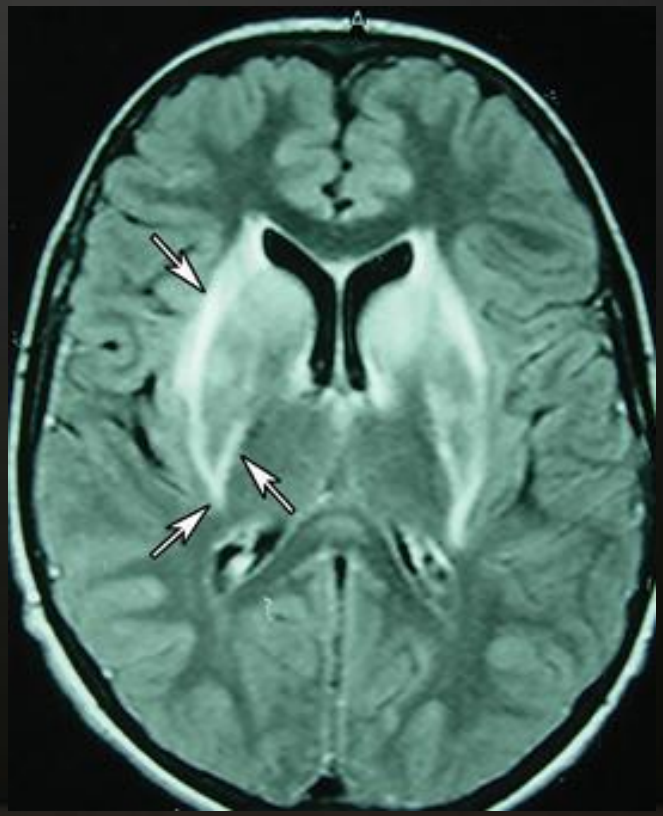
- Metabolic disorder in acute or chronic renal failure.
- Endogenous uremic toxin
- **Imaging finding (unspecific):**
  - Basal ganglia involvement (lentiform fork sign).
  - Cortical subcortical involvement (PRES-like).
  - White matter involvement.

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Uremic Encephalopathy

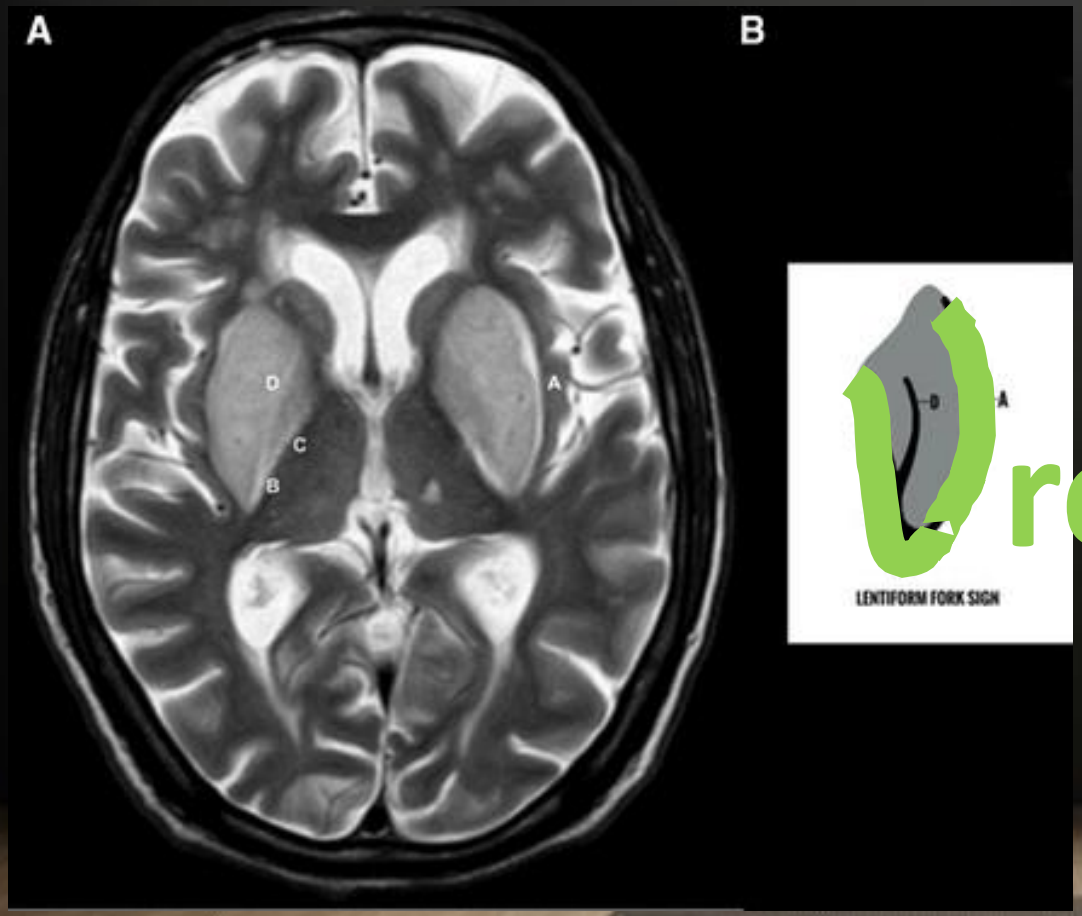




Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1a: T2WI & FLAIR Hyperintensity

Uremic Encephalopathy



A: external capsule
B: internal capsule
C: internal medullary lamina
D: external medullary lamina

Uremic

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity

Toluene Use

- Toluene: component of solvent in glues, paint thinners & ink.
- Clinical & imaging findings → after chronic use (chronic solvent encephalopathy).

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity

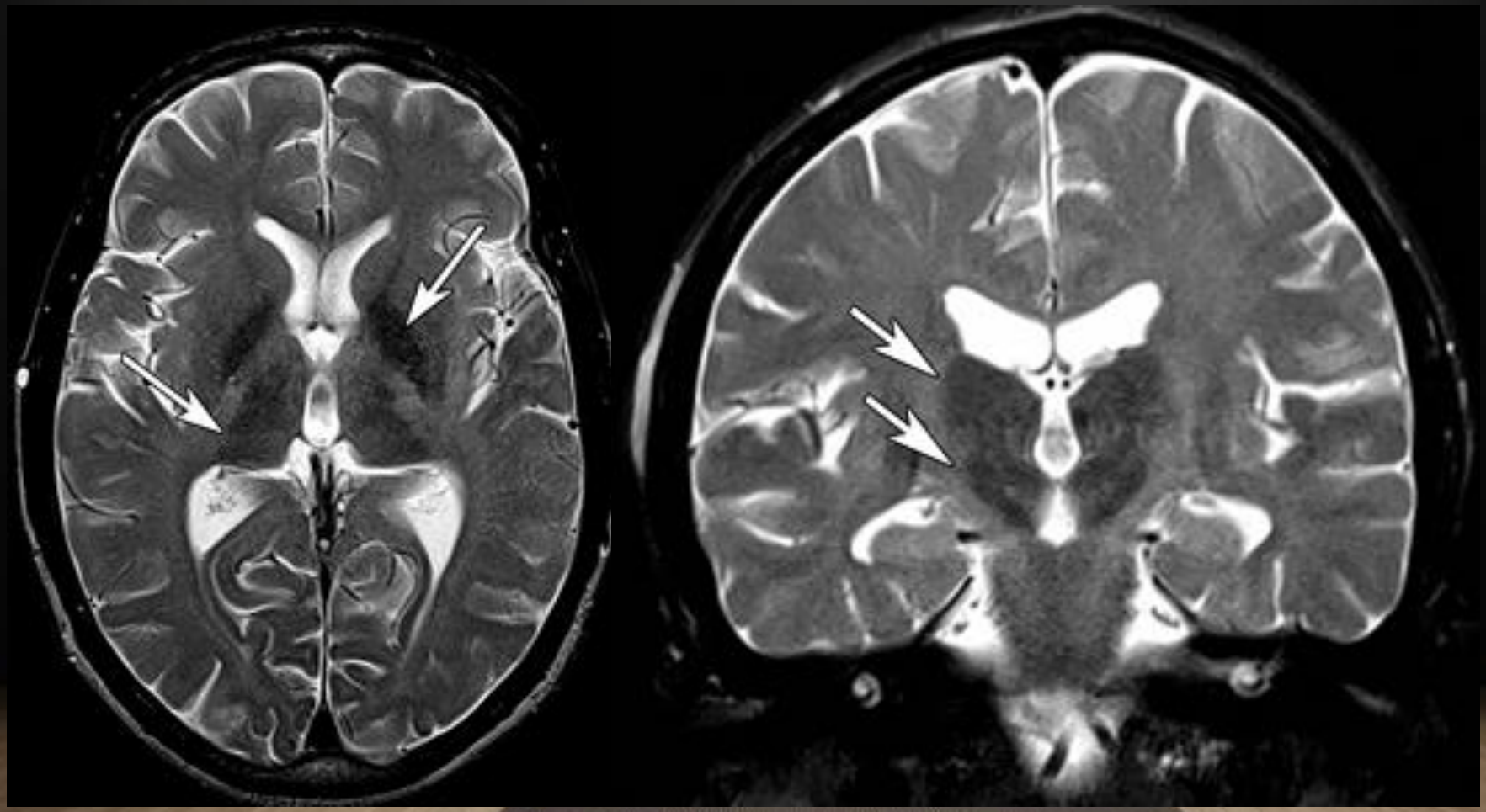
Toluene Use

- Cause severe irreversible cognitive impairment
- **MRI findings:**
  - T2 hypointensity involving basal ganglia, thalami and substantiae nigrae
  - T2 hyperintensity periventricular white matter
  - Cerebral & cerebellar atrophy

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity

Toluene Use



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity

Toluene Use

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity

Parathyroid-Hypofunction Disorder & Hyperparathyroidsm-related Disorders

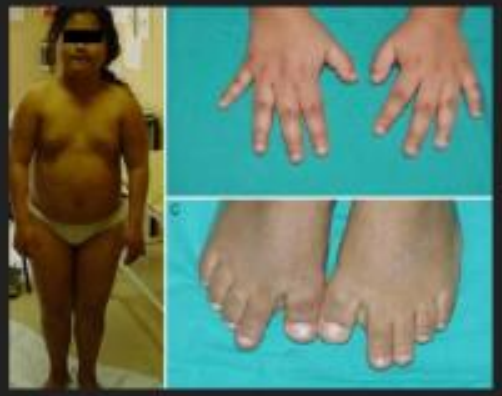
- Parathyroid hypofunction disorder:
  - Hypoparathyroidsm
  - Pseudohypoparathyroidsm
  - Pseudopseudohypoparathyroidsm
- Hyperparathyroidsm:
  - Primary hyperparathyroidism (adenoma, hyperplasia, carcinoma)
  - Secondary hyperparathyroidism (related to chronic renal failure)
- Main imaging findings are the same and are related to calcium deposition in the basal ganglia.

Hypoparathyroidism

Decreased PTH, Low Calcium, High Phosphate.
The main problem - **Hypocalcemia.**
Caused by deficiency of **PTH (P**hosphate **T**rashing **H**ormone which also **increases calcium)**
Seen after surgery or due to autoimmune process or in DiGeorge Syndrome (deletion of 22q11)

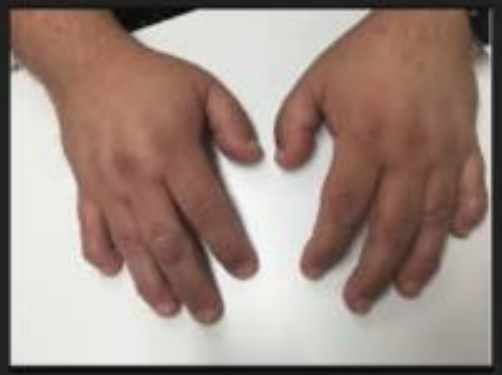
Pseudohypoparathyroidism

Increased PTH, Low Calcium, High Phosphate.
The main problem - **Hypocalcemia + Albright Hereditary Osteodystrophy**
Kidneys and bones do **not respond to the actions of PTH.** Organism **compensatory increases PTH level to increase calcium but fails to do that.** Additionally, it causes **bone abnormalities** known as **Albright Hereditary Osteodystrophy - shortened 4th/5th fingers**, round facies, developmental delay.
Don't confuse with secondary hyperparathyroidism - it has increased creatinine + no finger abnormalities.



Pseudopseudohypoparathyroidism

Normal PTH, Normal Calcium, Normal Phosphate
The main problem - **Albright Hereditary Osteodystrophy**
Mutation in PTH sensing receptors associated protein (GNAS) but **without end-organ resistance to PTH.**
The patient looks the same way as a patient with pseudohypoparathyroidism (shortened 4th and 5th fingers), but labs are completely fine!



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity

Parathyroid-Hypofunction Disorder & Hyperparathyroidsm-related Disorders

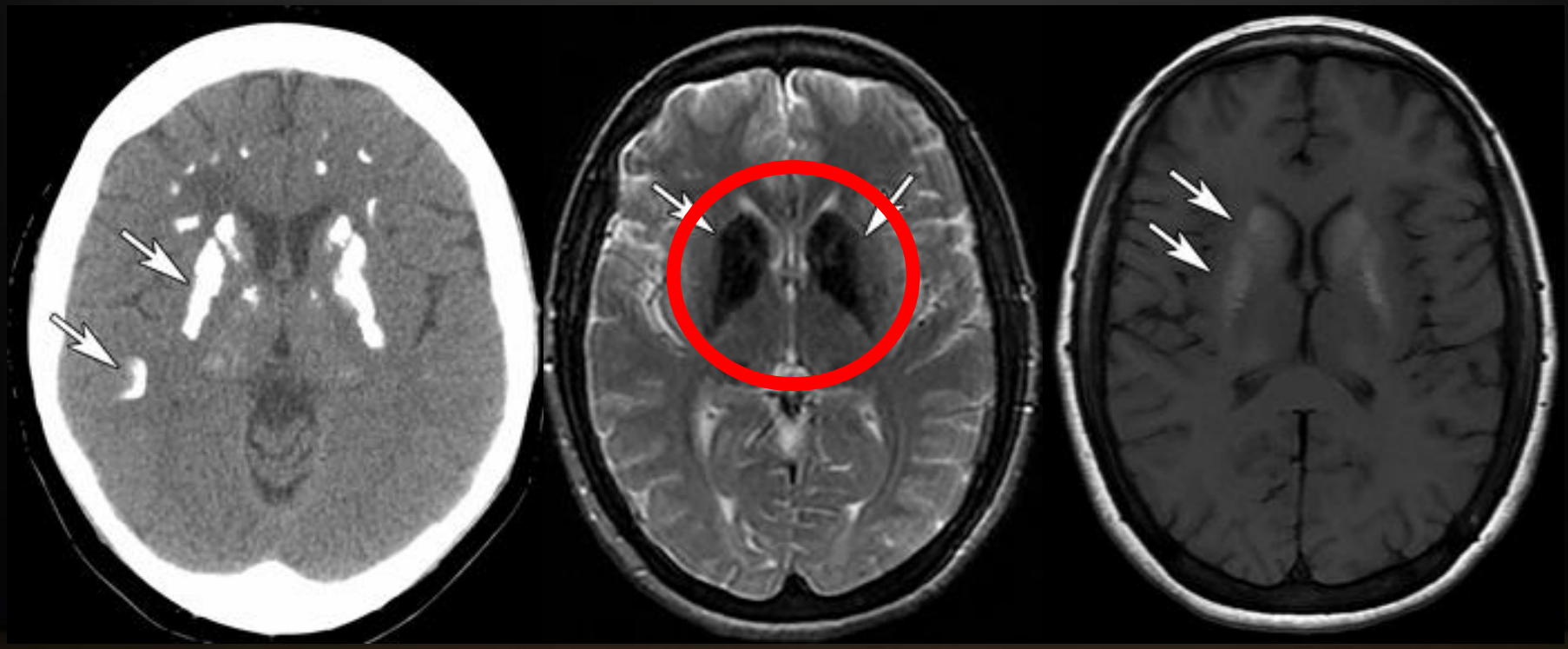
- **Imaging findings:**
  - CT:
    - Coarse bilateral & symmetric calcifications in globi pallidi, putamina & caudate nuclei.
    - Thalami, subcortical white matter & dentate nuclei may also be affected
  - MR:
    - Hyper/hypointensity on T1WI (depend on concentration, surface area and composition of calcification)*.
    - Hypointensity on T2WI
    - Blooming artefact on T2 GRE

*Henkelman, R M; Watts, J F; Kucharczyk, W . (1991). High signal intensity in MR images of calcified brain tissue.. Radiology, 179(1), 199–206. doi:10.1148/radiology.179.1.18487

Pattern 1: Basal Ganglia and/or Thalami Involvement

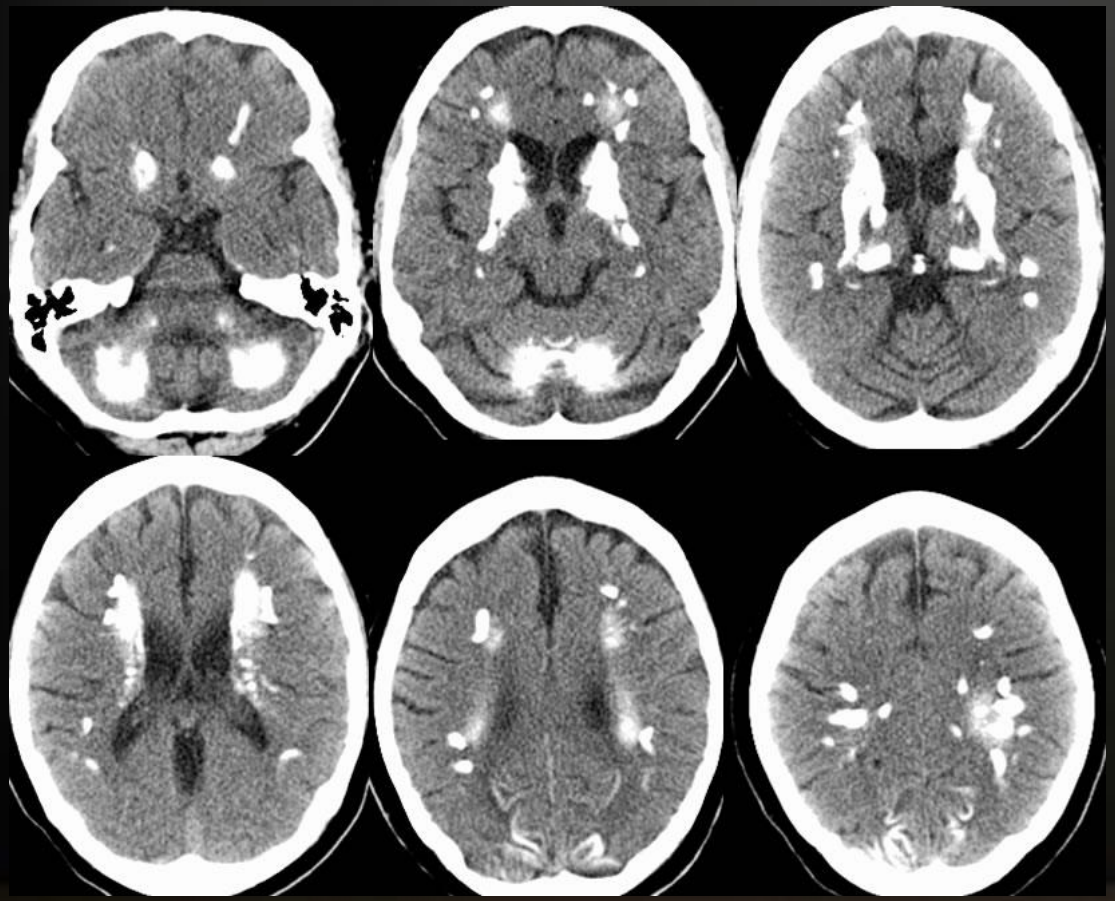
Pattern 1b: T2WI Hypointensity

Parathyroid-Hypofunction Disorder & Hyperparathyroidsm-related Disorders



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1b: T2WI Hypointensity



DDx:

Fahr disease /
Bilateral
Striatopallidodentate
Calcinosis

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

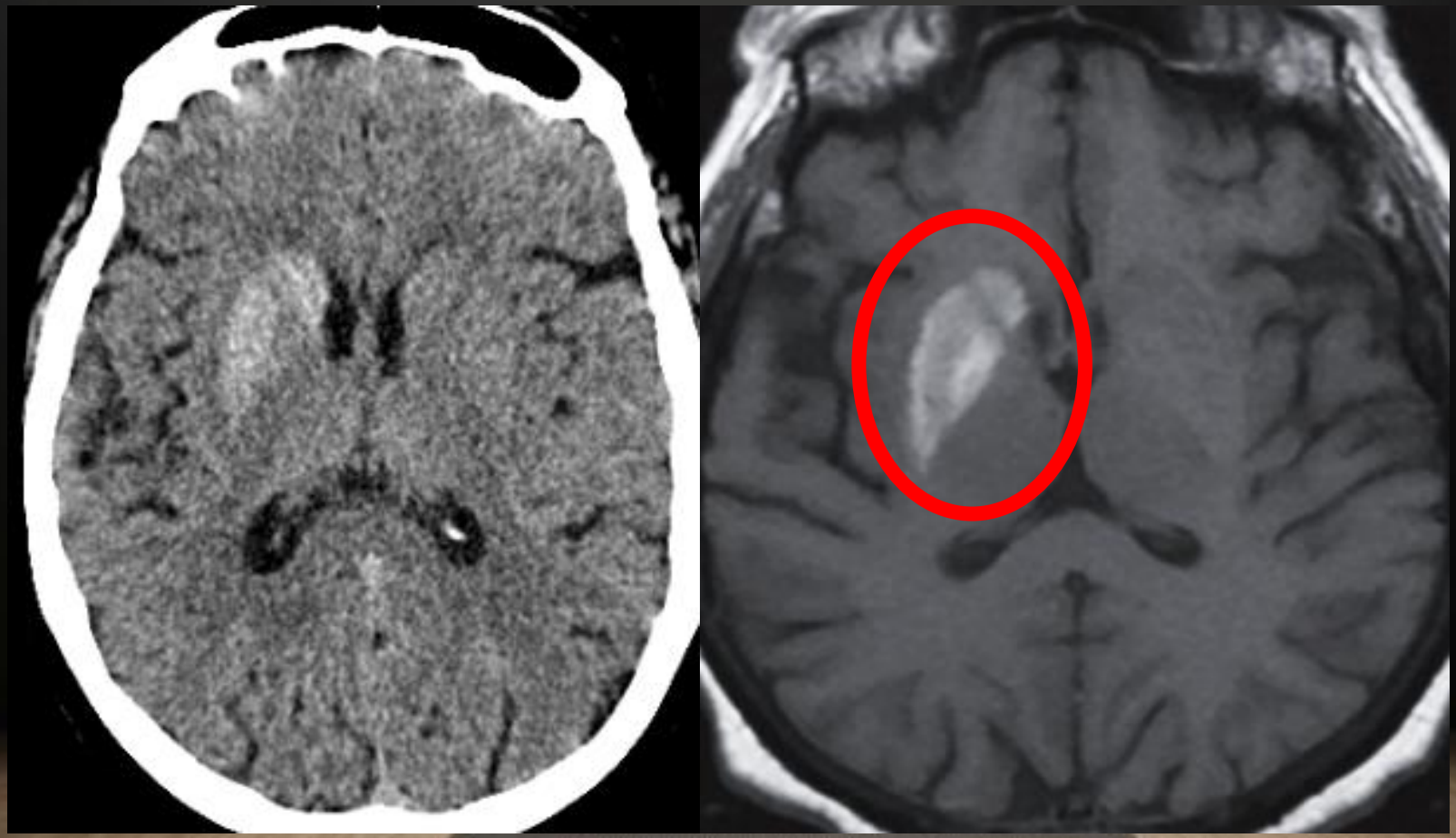
Diabetic Striatopathy

- Hyperglycemia-induced hemichorea-hemiballismus
- **Imaging finding:**
  - Involving striatum
  - Hyperdense on CT
  - Hyperintensity on T1WI
  - Restricted diffusion on DWI-ADC
  - Imaging findings gradually resolve a hyperglycemia correction. However, tend to return to baseline more slov the clinical findings

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

Diabetic Striatopathy



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

Diabetic Striatopathy

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

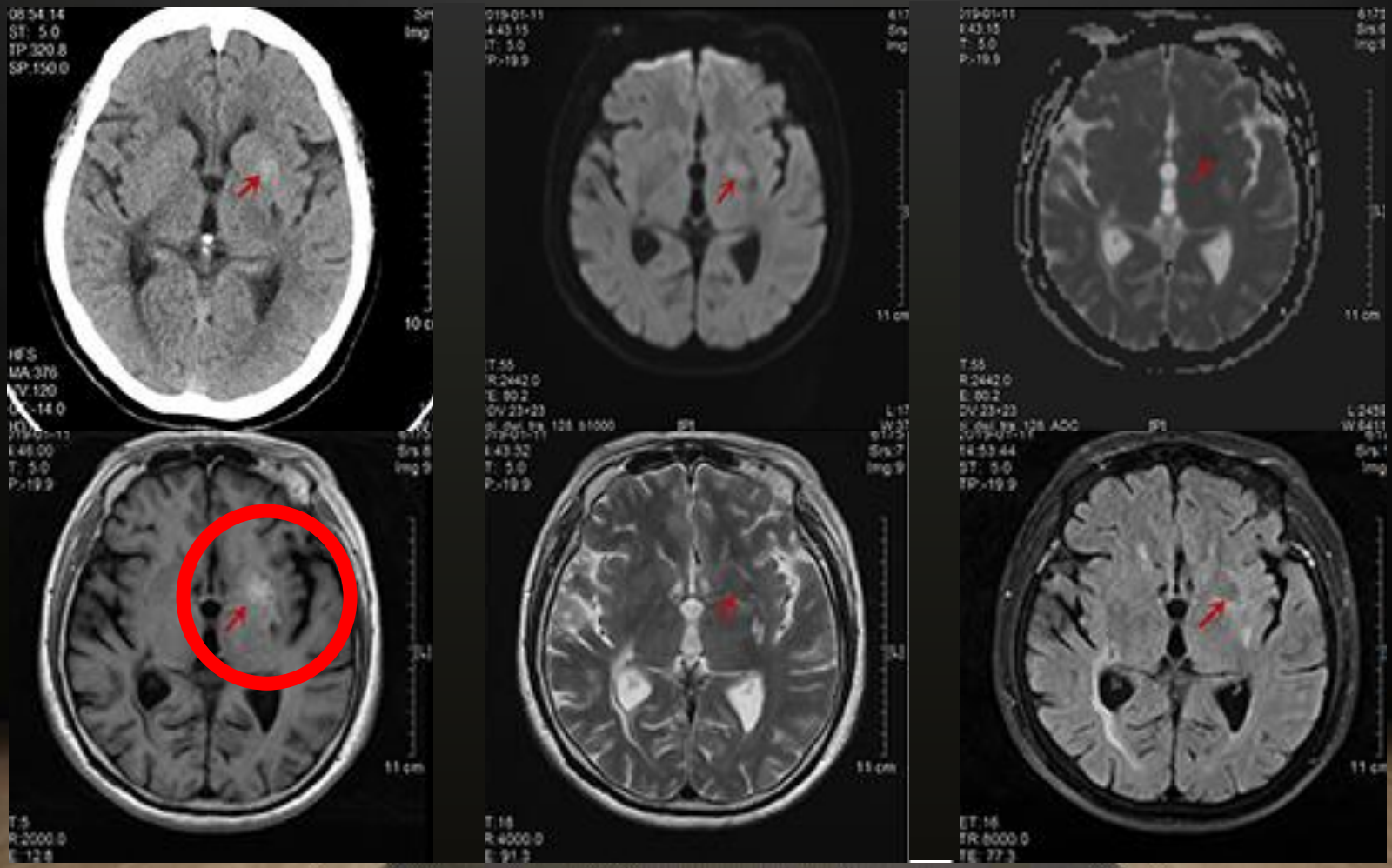
Diabetic Striatopathy

- Acute ischemic injury→reactive swelling &recruitment of astrocytes→gemistocytes.
- Gemistocytes → ↑ intracellular water content → restricted diffusion.
- Also contain ↑ zinc-friendly metalloproteins, iron &copper → ↑ paramagnetic susceptibility & CT density.
- Prominent protein hydration layer & to a lesser extent the metal ions → shortened T1 relaxation time

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

Diabetic Striatopathy



Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

Chronic Hepatic Encephalopathy

- A potentially reversible clinical syndrome that occurs in the context of chronic severe liver dysfunction.
- Neurotoxic substances (manganese) accumulate within brain tissue.

Chemicalinterest / Wikimedia Commons

Manganese can make water appear yellow-ish or brown-ish.

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

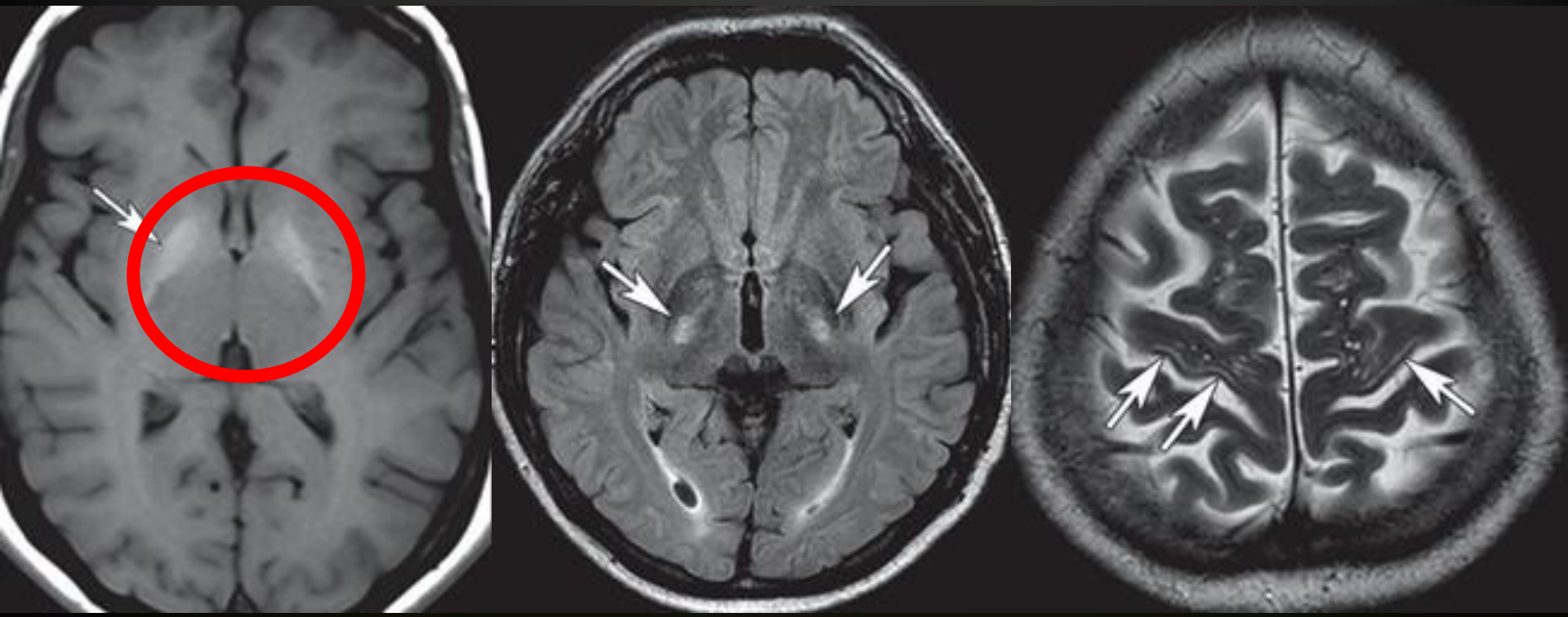
Chronic Hepatic Encephalopathy

- **Imaging findings:**
  - Bilateral & symmetric T1 hyperintensity involving the globi pallidi & substantiae nigrae.
  - After liver transplant, changes can decrease or even disappear, typically normalizing after 1 year.
  - Glutamine-glutamate peak at MR spectroscopy with short echo times, resonating at 2.1–2.4 ppm
  - FLAIR → bilateral vasogenic edema (without restriction at DWI) in cerebral white matter, mainly involving the corticospinal tract.

Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

Chronic Hepatic Encephalopathy

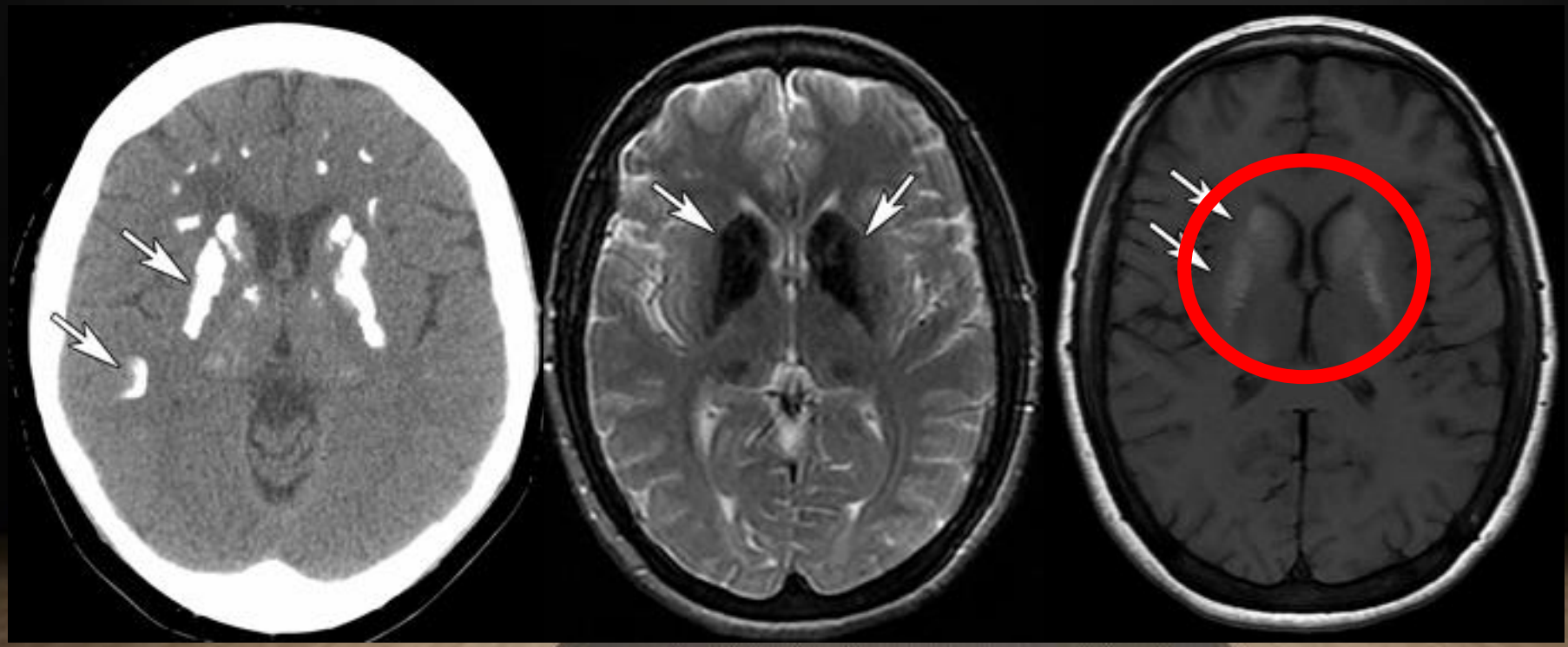


Pattern 1: Basal Ganglia and/or Thalami Involvement

Pattern 1c: T1WI Hyperintensity

Parathyroid-Related Disorders

- T1WI hyperintensities involving the basal ganglia, thalami & dentate nuclei secondary to calcifications



Pattern 2: Dentate Nuclei Involvement

Metronidazole-induced Brain Toxicity

- Metronidazole: antibiotic to treat a wide variety of bacterial & protozoan infections.
- Toxic effect:
  - Usually during prolonged treatment (>25 days, mean 54 days).
  - Shorter period (7 days) have also been reported.
- Present with symptoms of cerebellar dysfunction (dysarthria, ataxia, dysmetria), confusion, seizures

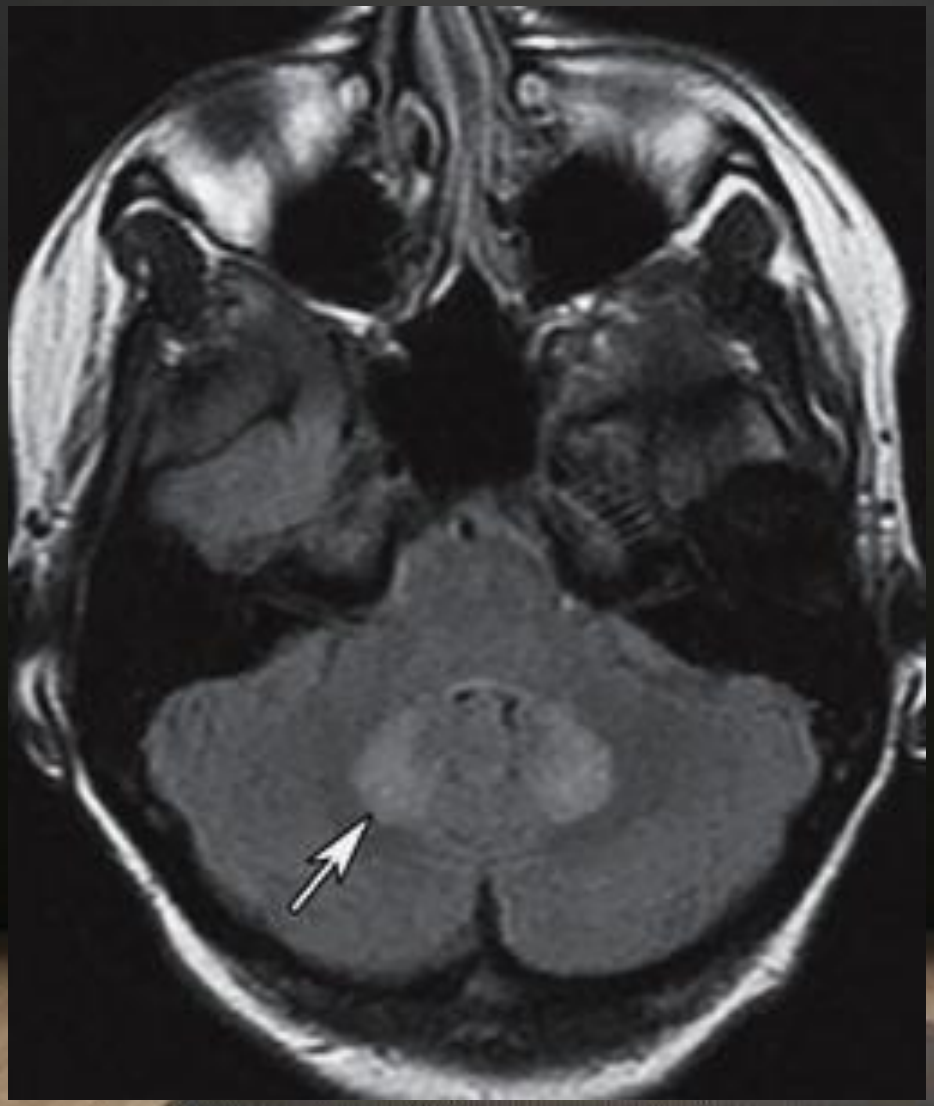
Pattern 2: Dentate Nuclei Involvement

Metronidazole-induced Brain Toxicity

- **MR findings:**
  - Bilateral symmetric lesion in the dentate nuclei of the cerebellum (most commonly involved), followed by tectum, red nucleus, periaqueduct gray matter and dorsal pons.
  - T2WI & T2 FLAIR hyperintensity
  - Lack of enhancement on T1WI+C
  - Some cases : periventricular white matter involvement or affecting splenium.
  - Reversible after discontinuation of the drug
- DDx: isoniazid (in patient with TB treatment)

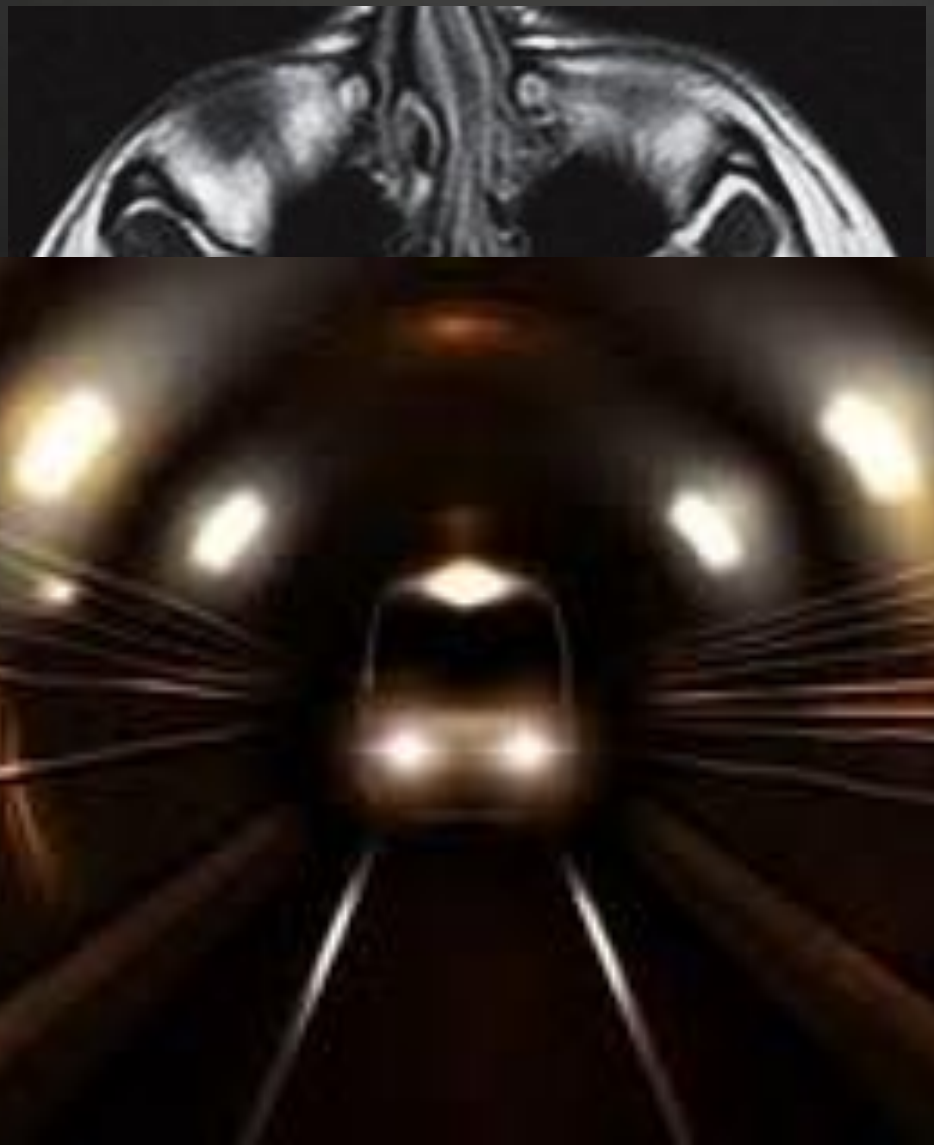
Pattern 2: Dentate Nuclei Involvement

Metronidazole-induced Brain Toxicity



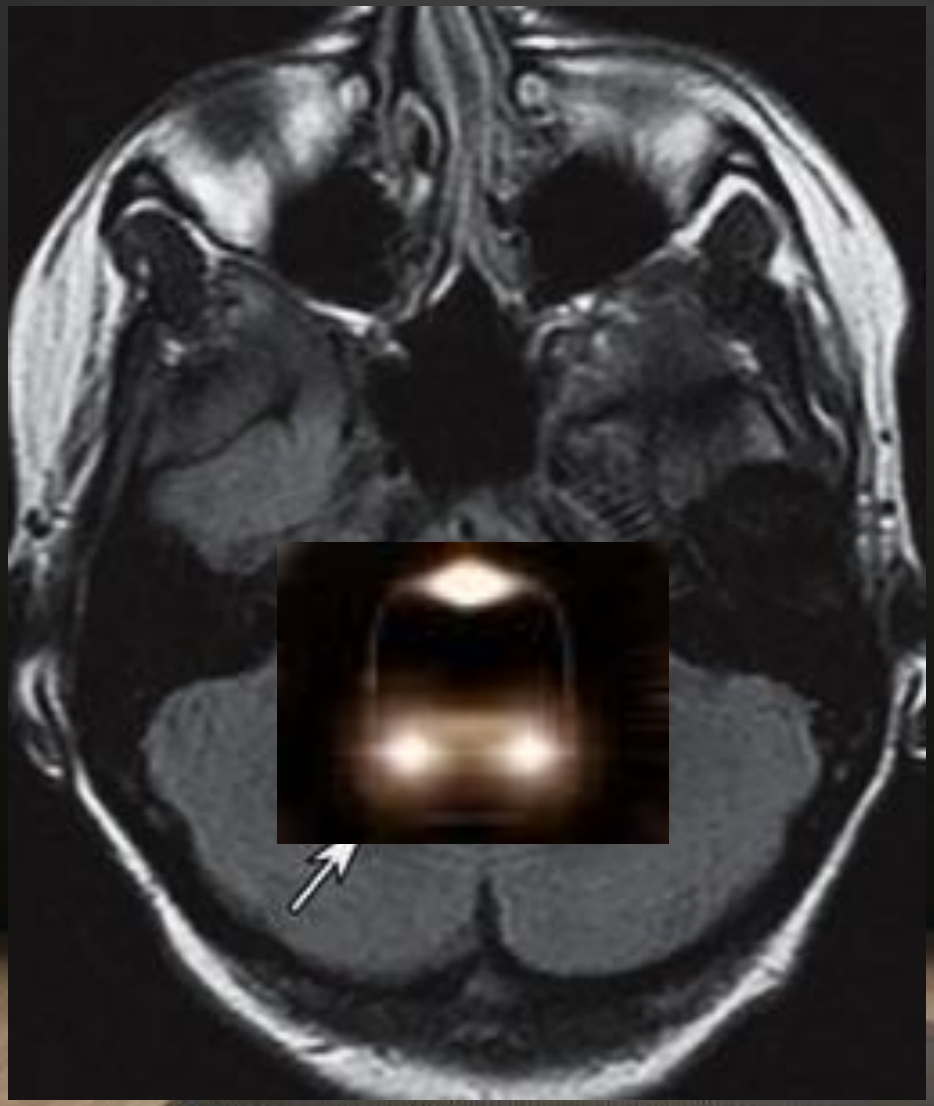
Pattern 2: Dentate Nuclei Involvement

Metronidazole-induced Brain Toxicity



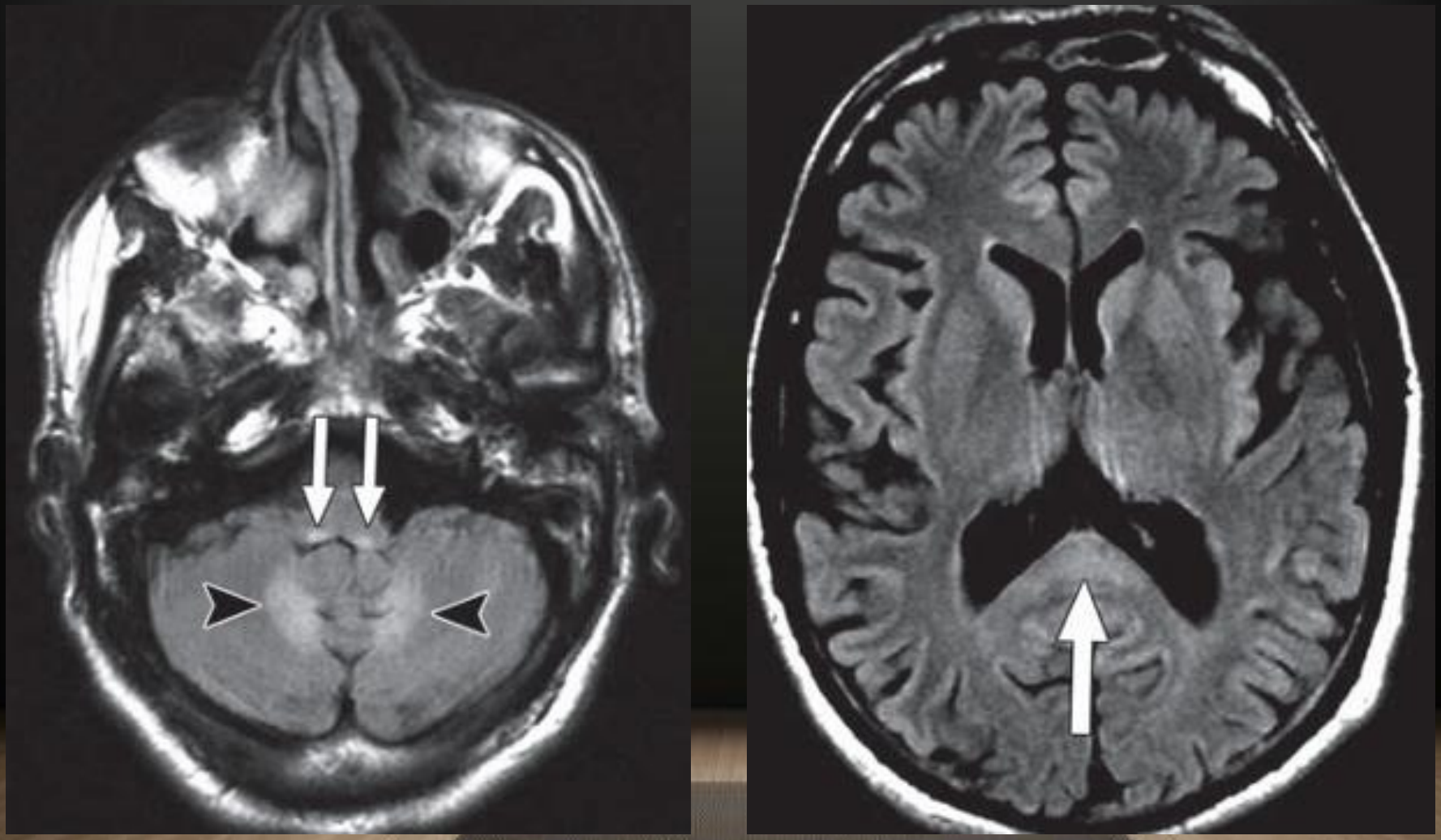
Pattern 2: Dentate Nuclei Involvement

Metronidazole-induced Brain Toxicity



Pattern 2: Dentate Nuclei Involvement

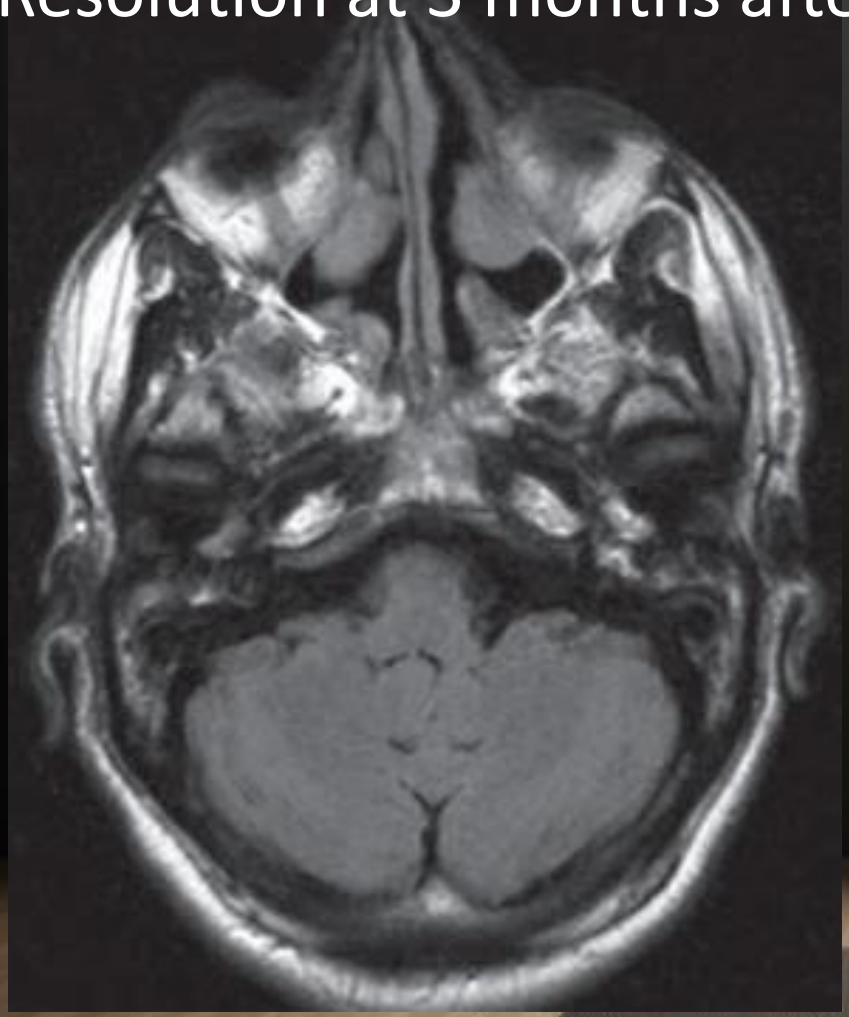
Metronidazole-induced Brain Toxicity

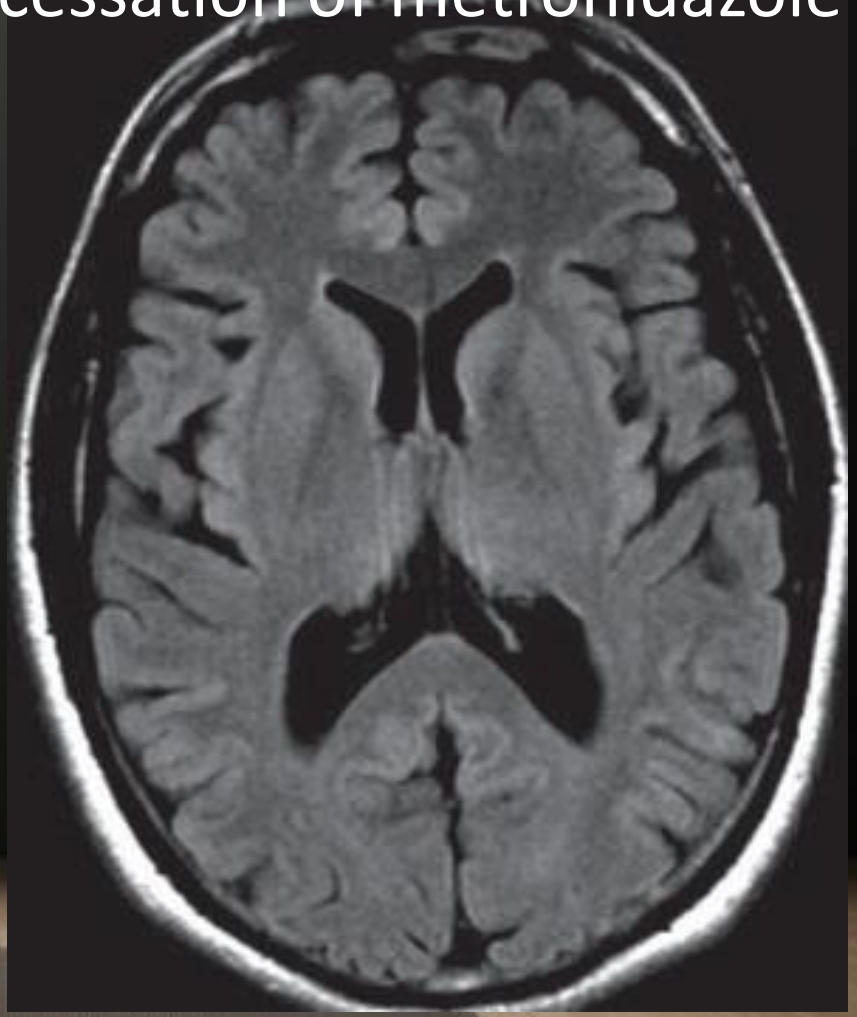


Pattern 2: Dentate Nuclei Involvement

Metronidazole-induced Brain Toxicity

Resolution at 3 months after cessation of metronidazole





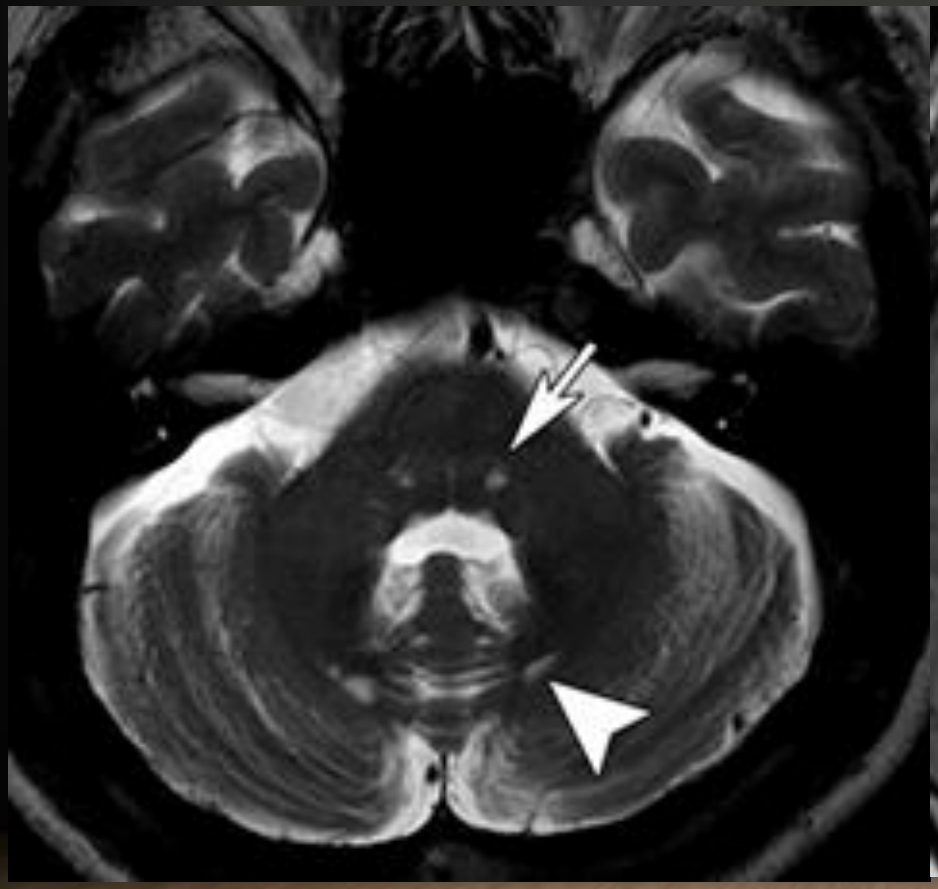
Pattern 2: Dentate Nuclei Involvement

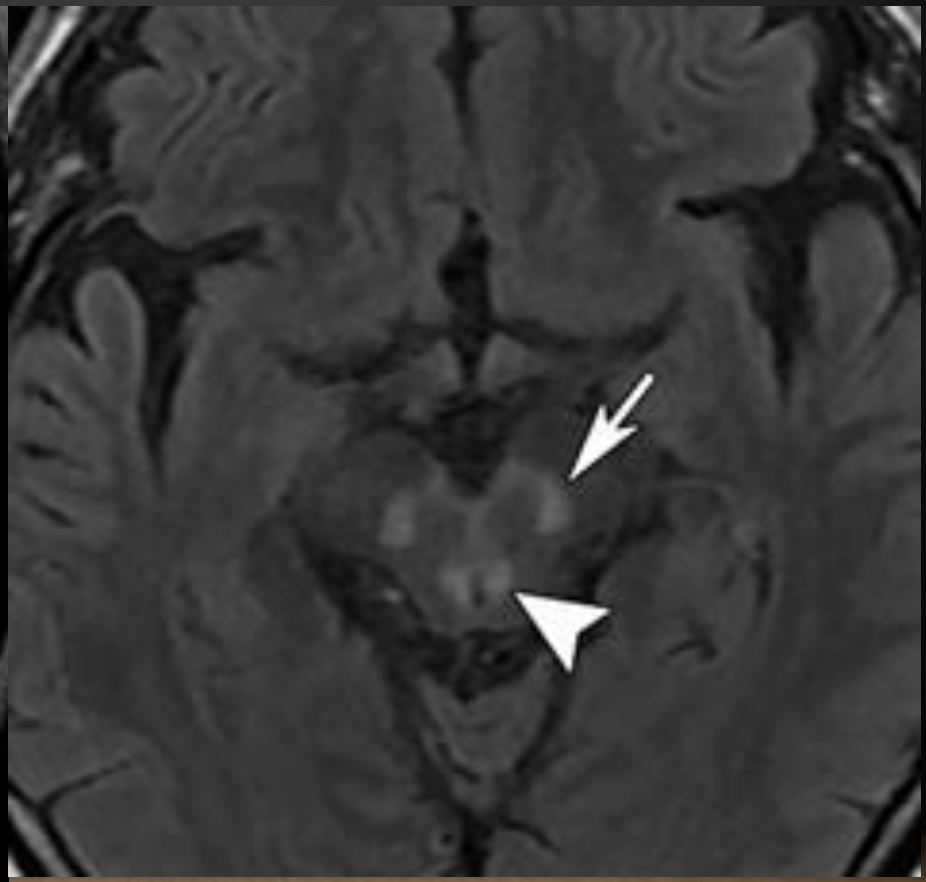
Methyl Bromide-induced Toxicity

- Methyl Bromide : pesticides component
- Involved in toxicity related to directed occupational inhalation in agricultural use
- **MR Imaging:**
  - Bilateral symmetric hyperintensities involving cerebellum (dentate nuclei) and brainstem (periaqueductal midbrain, dorsal pons)
  - Hyperintense on T2WI & T2 FLAIR

Pattern 2: Dentate Nuclei Involvement

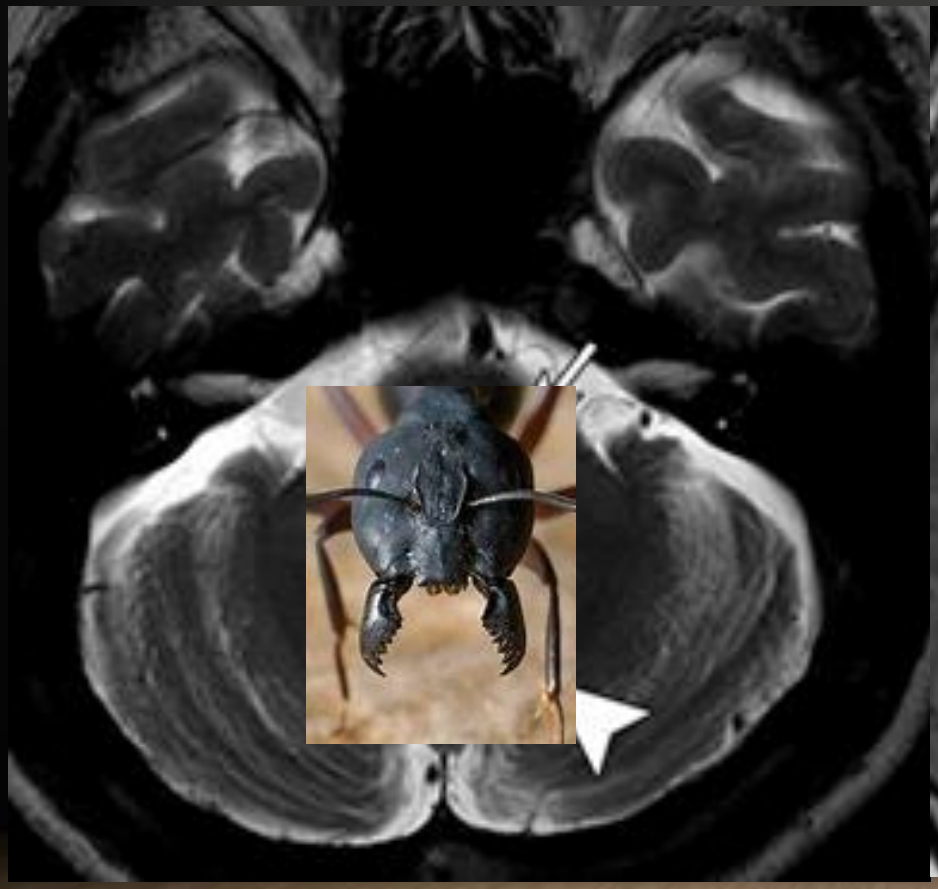
Methyl Bromide-induced Toxicity

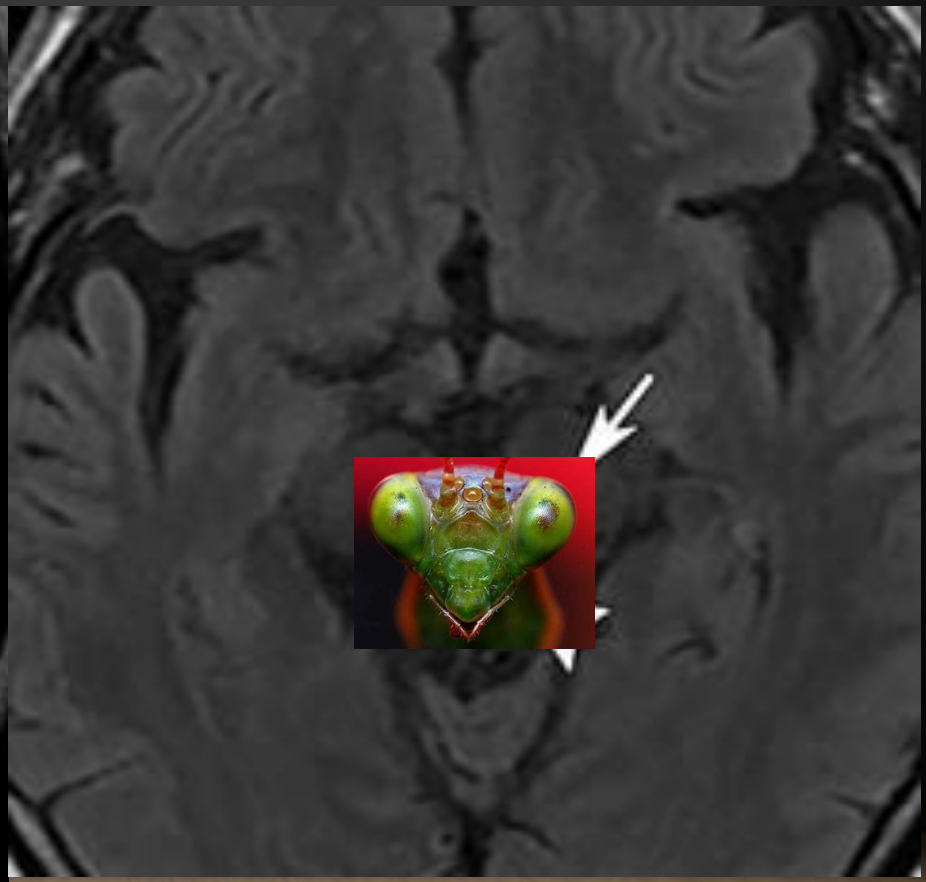




Pattern 2: Dentate Nuclei Involvement

Methyl Bromide-induced Toxicity





Pattern 3: Prominent Cortical Involvement

Adult Hypoglycemic Encephalopathy

- Cause by an imbalance between supply & use of glucose by cerebral cells, leading to brain injury.
- Clinical manifestation: seizures, depressed level of consciousness and even coma.
- Usually in patient with diabetes with undergoing insulin replacement therapy.
- In newborn, the most common cause is maternal diabetes, which usually manifests in the first 3 postnatal days.

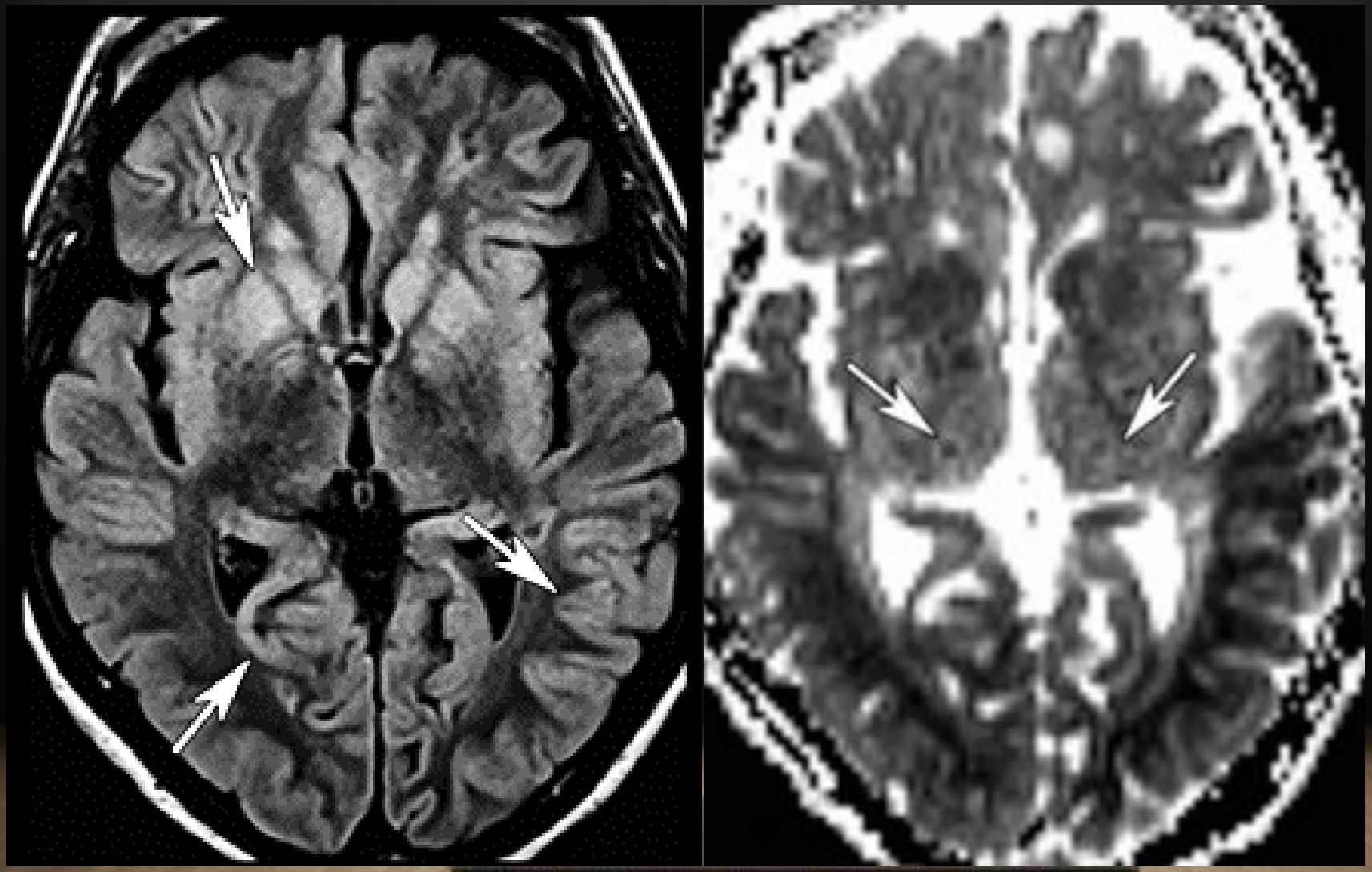
Pattern 3: Prominent Cortical Involvement

Adult Hypoglycemic Encephalopathy

- **Imaging findings:**
  - Symmetric hyperintensities on T2WI & T2 FLAIR and restricted diffusion on DWI-ADC in the gyri of parieto-occipital & temporal region.
  - Basal ganglia can be involved (poor outcomes).
  - Sparing thalami, white matter and cerebellum.
  - **In newborns:** symmetric posterior parieto-occipital GM & WM signal abnormality with diffusion restriction involving the optic radiations and frequently the posterior thalami.
- **Important DDx:** hypoxic ischemic injury (usually involves the thalami and cerebellum).

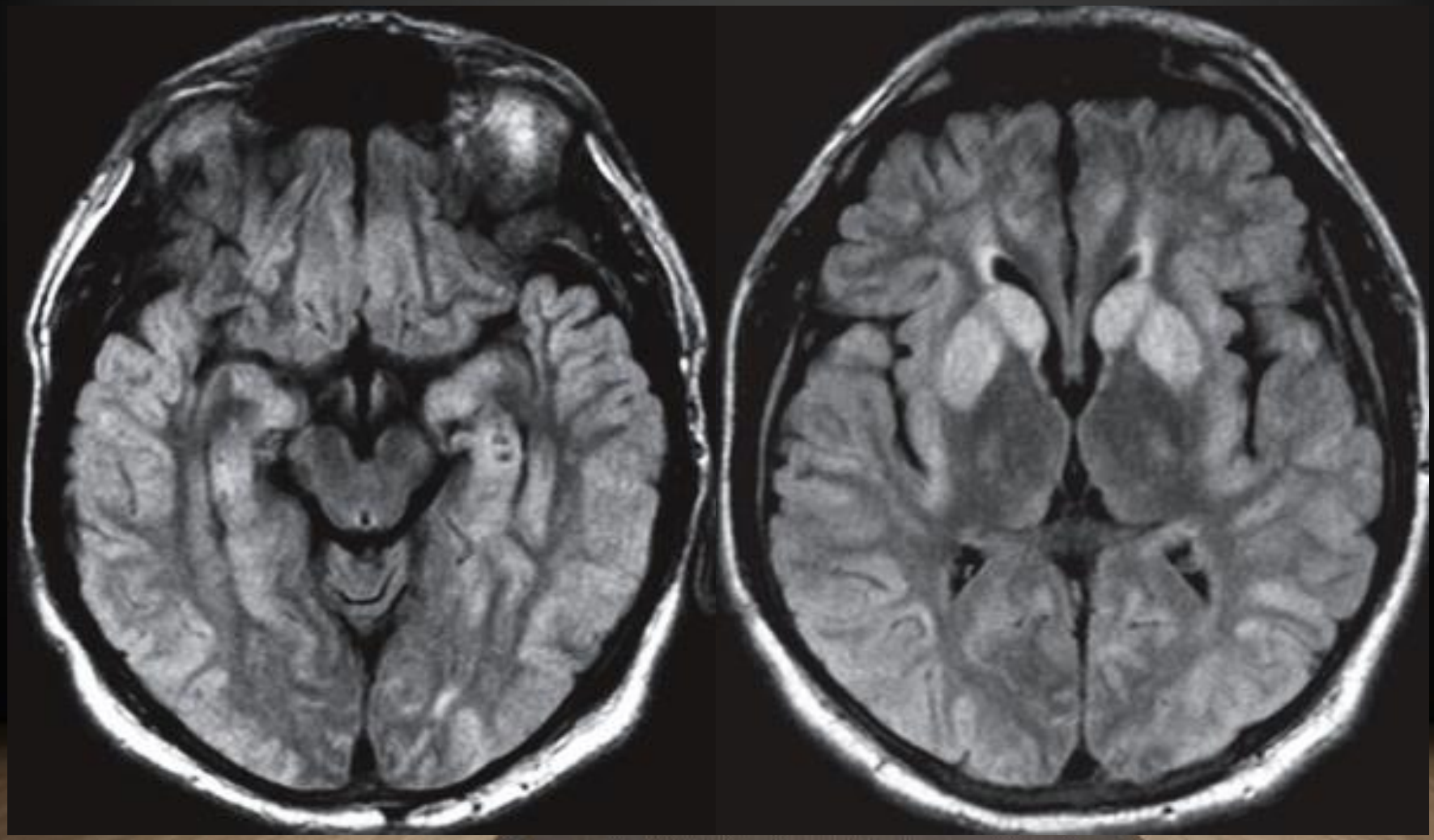
Pattern 3: Prominent Cortical Involvement

Adult Hypoglycemic Encephalopathy



Pattern 3: Prominent Cortical Involvement

Adult Hypoglycemic Encephalopathy



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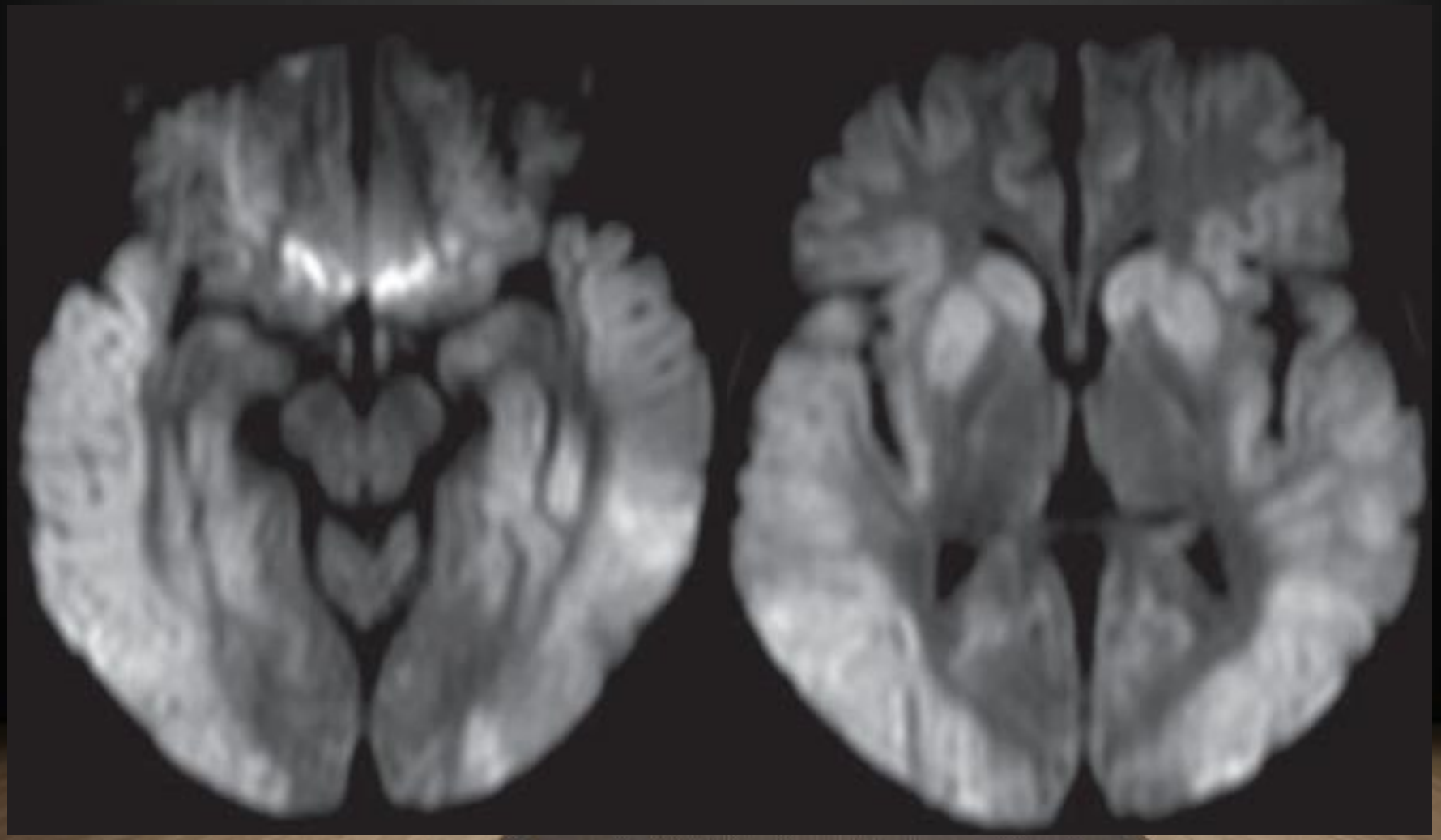
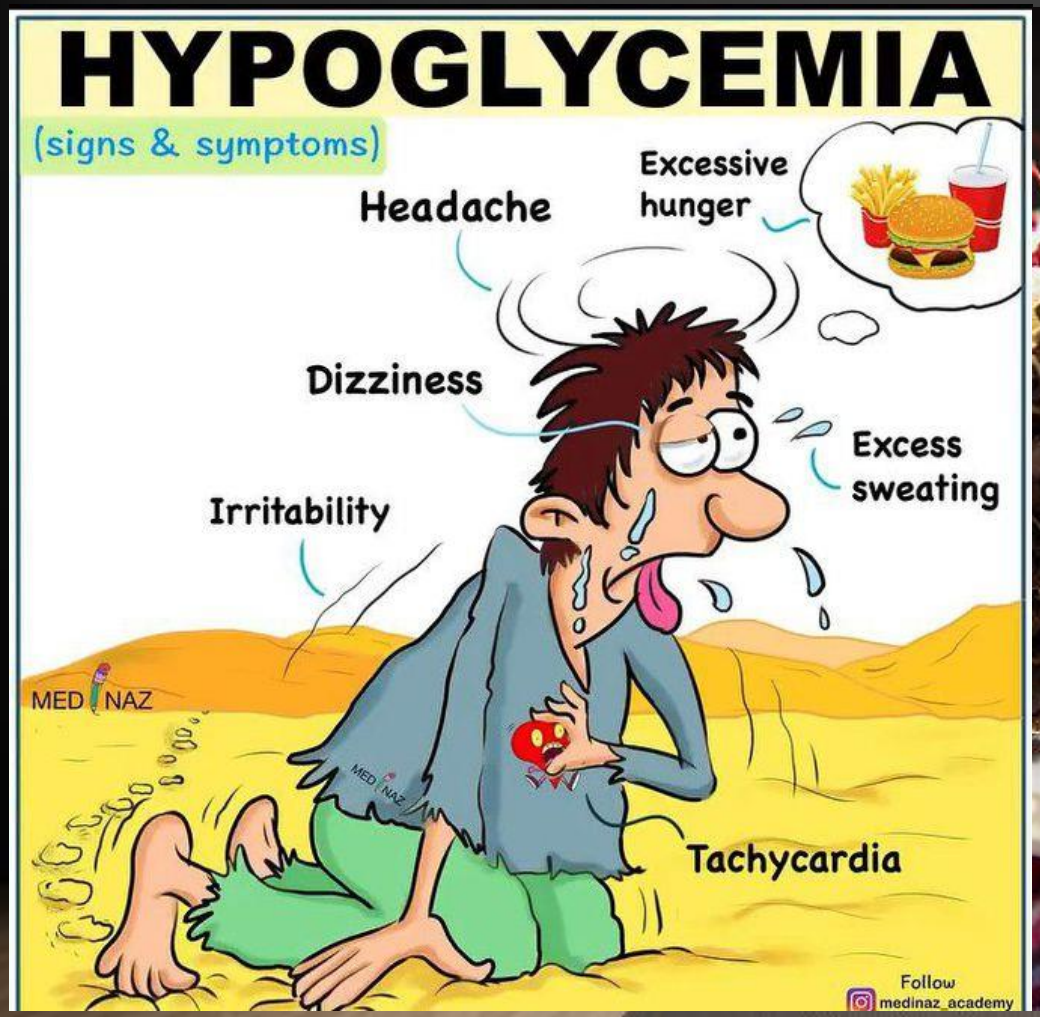
Adult Hypoglycemic Encephalopathy



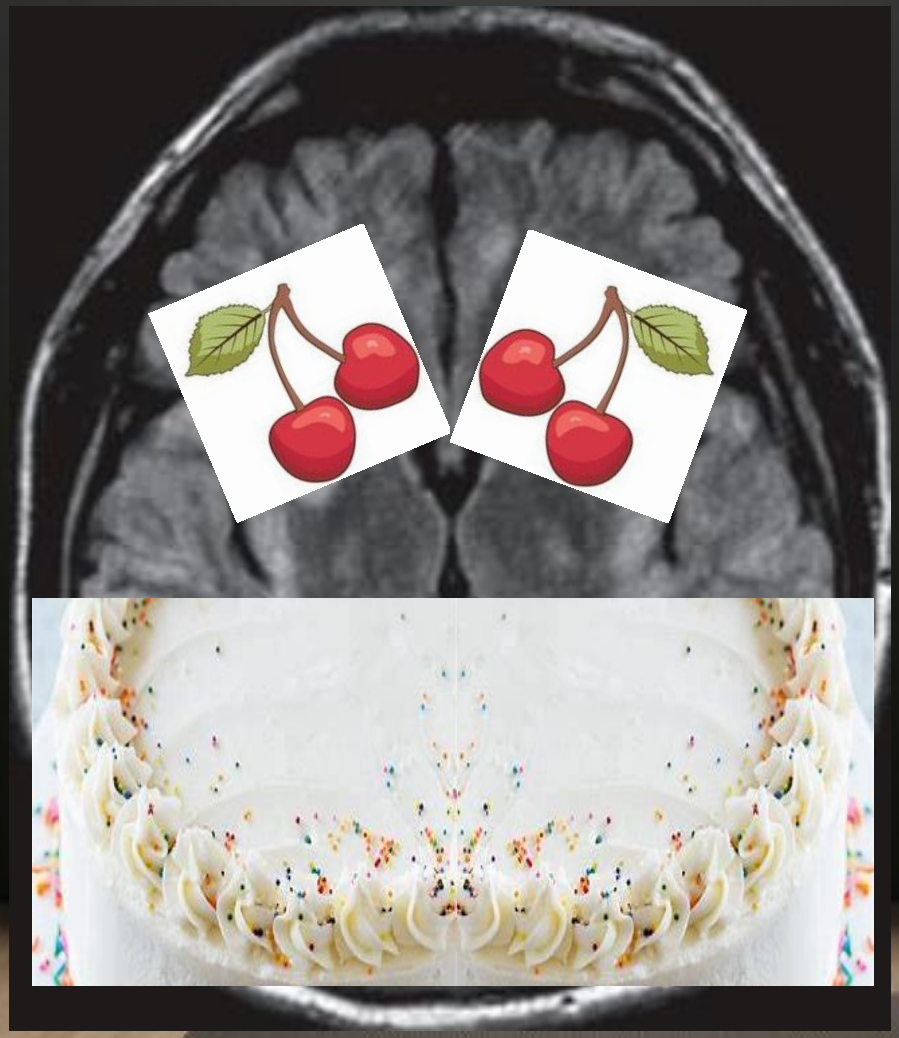
Pattern 3: Prominent Cortical Involvement

Adult Hypoglycemic Encephalopathy



Pattern 3: Prominent Cortical Involvement

Adult Hypoglycemic Encephalopathy



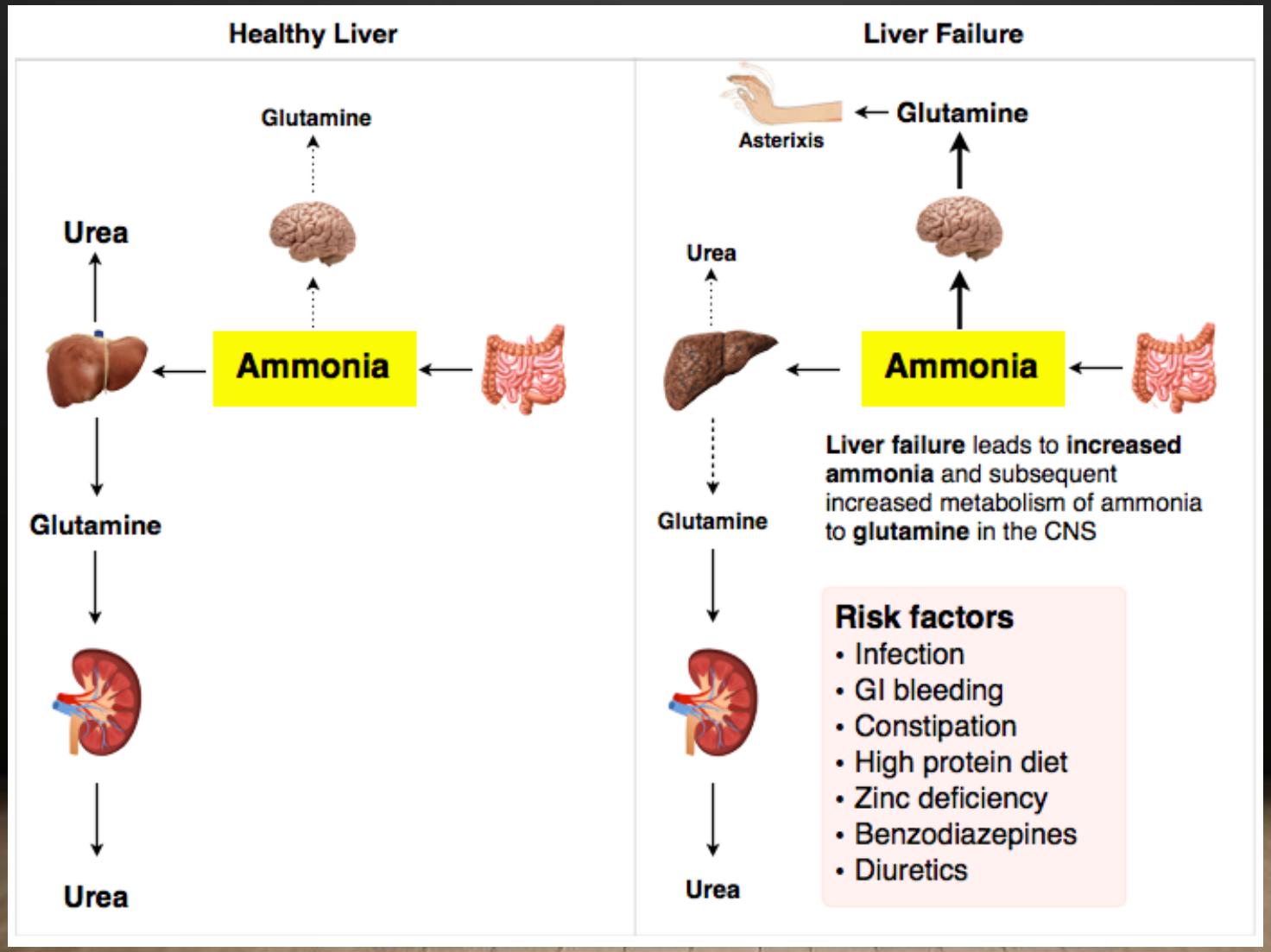
Pattern 3: Prominent Cortical Involvement

Hyperammonemic Encephalopathy & AHE

- Caused by hyperammonemia
  - Direct toxic effect to the brain
  - Osmotic imbalance
- Cause of hyperammonemia:
  - Acute liver failure / AHE (acute hepatic encephalopathy)
  - Drug toxicities (valproate, acetaminophen).
  - Sepsis
  - Bone marrow transplant
  - Parenteral nutrition

Pattern 3: Prominent Cortical Involvement

Hyperammonemic Encephalopathy & AHE



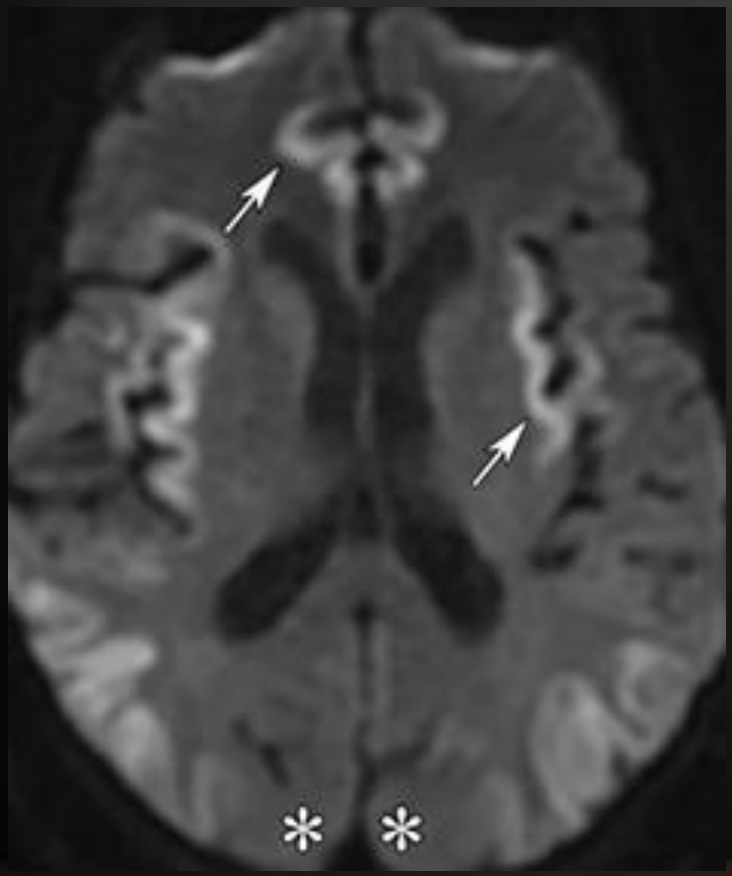
Pattern 3: Prominent Cortical Involvement

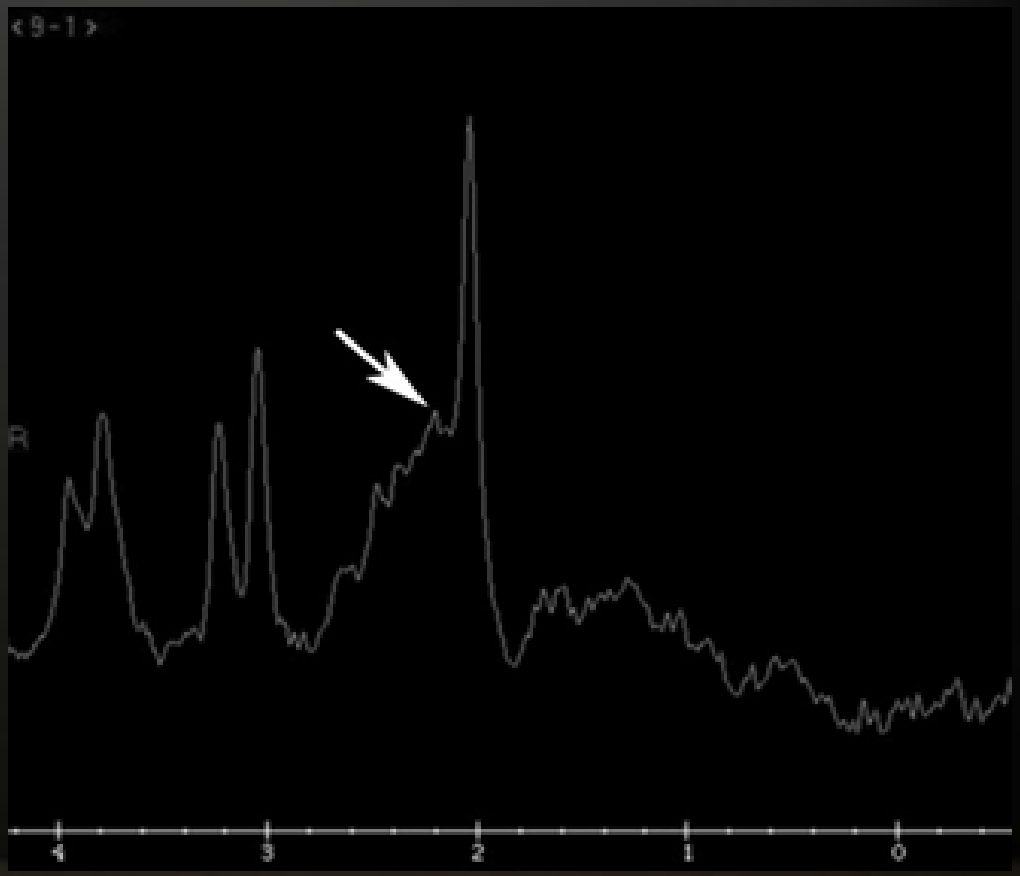
Hyperammonemic Encephalopathy & AHE

- **Imaging finding:**
  - Hyperintensity on T2WI & T2 FLAIR and restricted diffusion on DWI-ADC in the insular and cingulate gyri.
  - Relative sparing of occipital lobes and perirolandic region.
  - Less severe cases: periventricular white matter involvement without affecting the cortex, posterior limb of the internal capsule, dorsal brainstem.
  - MR spectroscopy: increased glutamate-glutamine peak between 2.1 – 2.4 ppm. (glutamine is used to metabolize ammonia).

Pattern 3: Prominent Cortical Involvement

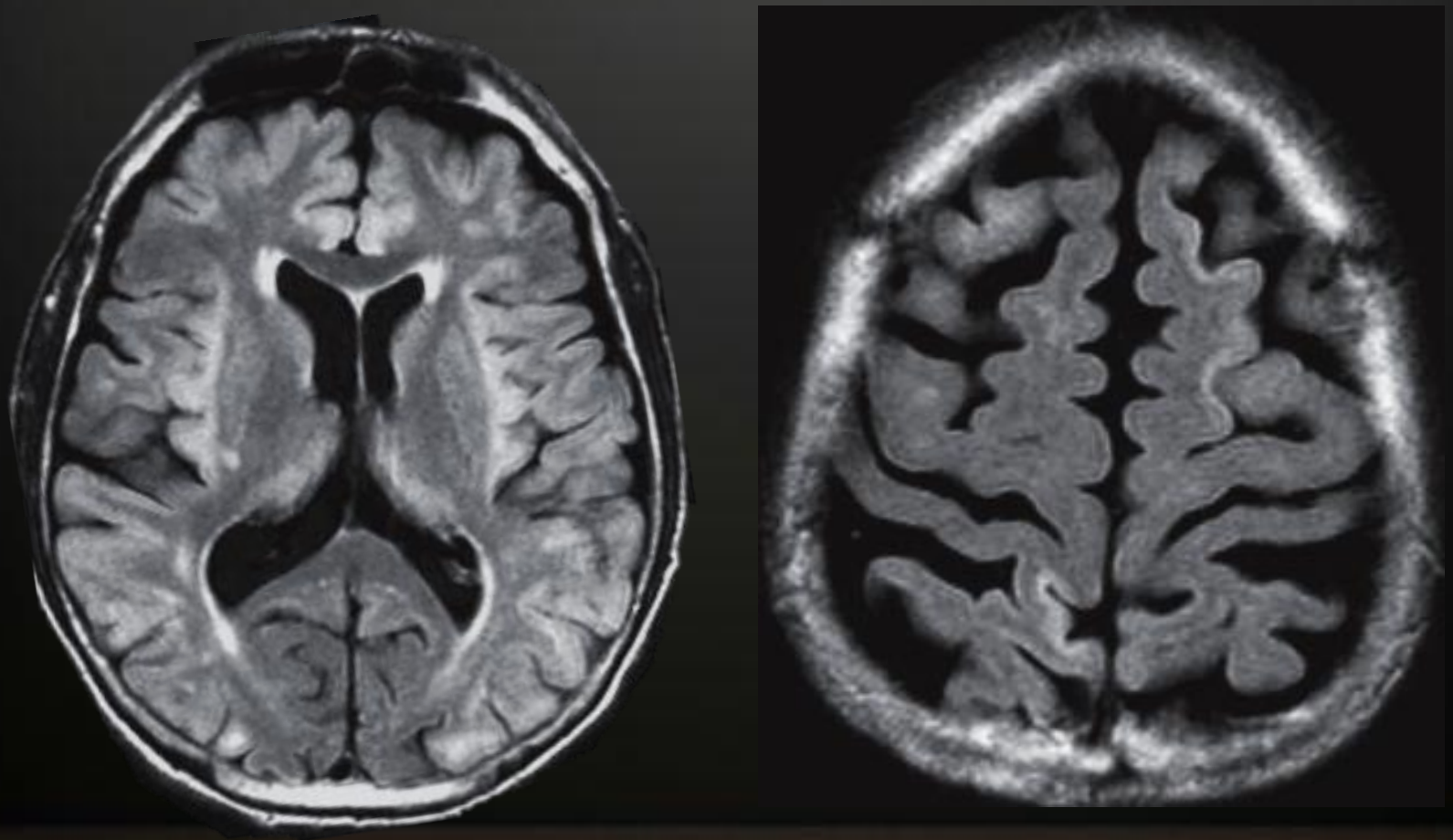
Hyperammonemic Encephalopathy & AHE





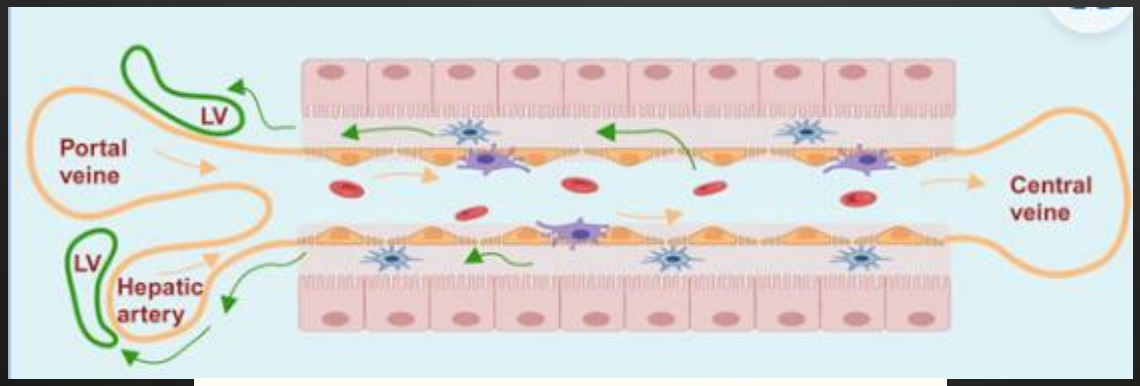
Pattern 3: Prominent Cortical Involvement

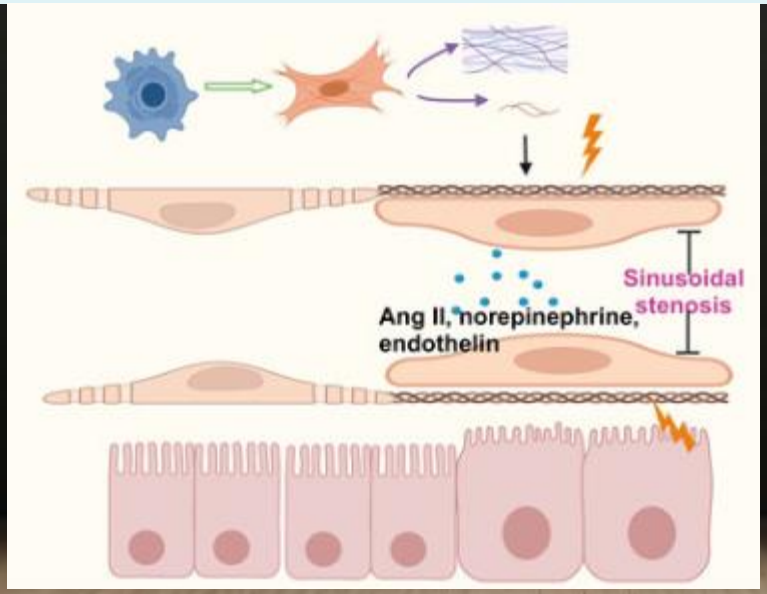
Hyperammonemic Encephalopathy & AHE



Pattern 3: Prominent Cortical Involvement

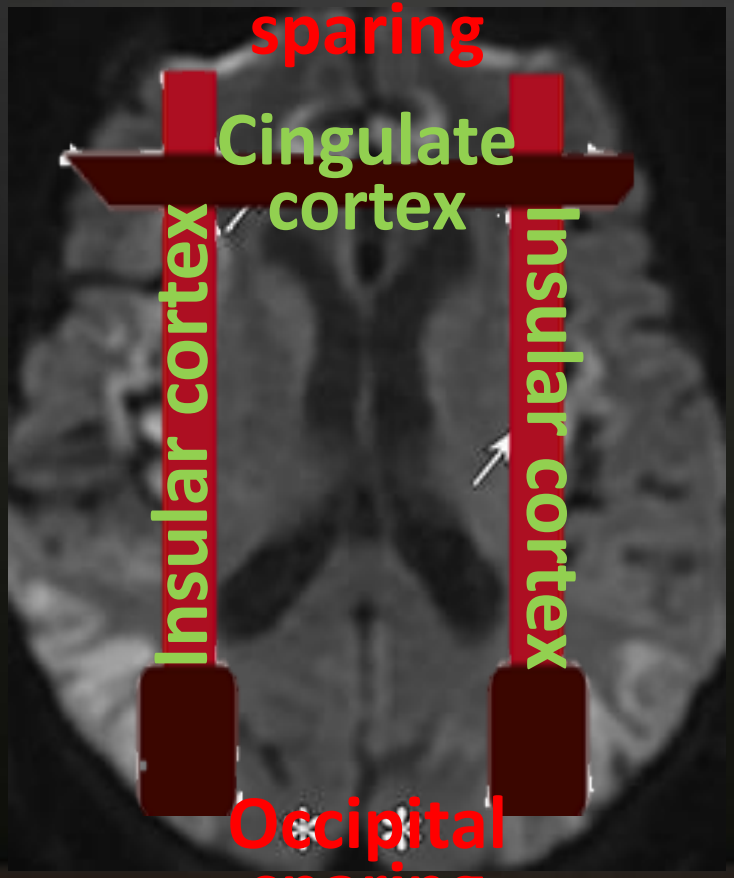
Hyperammonemic Encephalopathy & AHE





Pattern 3: Prominent Cortical Involvement

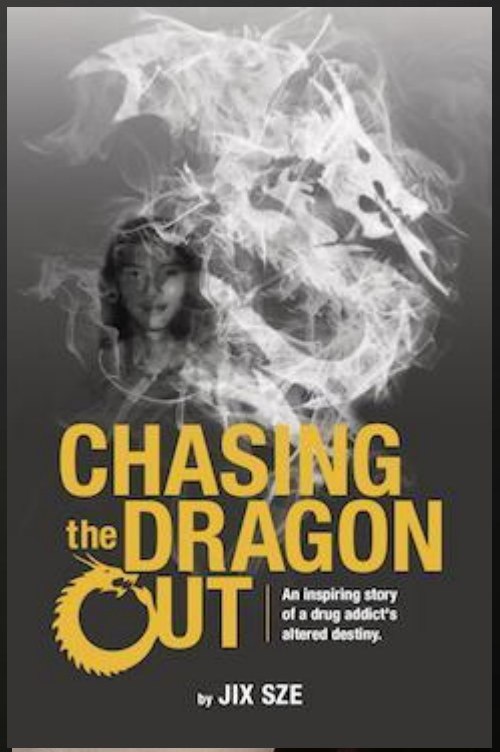
Hyperammonemic Encephalopathy & AHE



Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy

- Heroin is the most commonly used recreational drug (euphoric).
- Can be injected intravenously or inhaled.
- The most dramatic acute effects occurred with inhaled heroin.
- The freebase form is heated on alumunium foil, and the vapor are inhaled (chasing the dragon)



Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy

- Toxic leukoencephalopathy related to inhalation heroin has a nonlinear progression and can have a latent period before onset.
- The disease continues to progress for up to 6 months after cessation of heroin use.

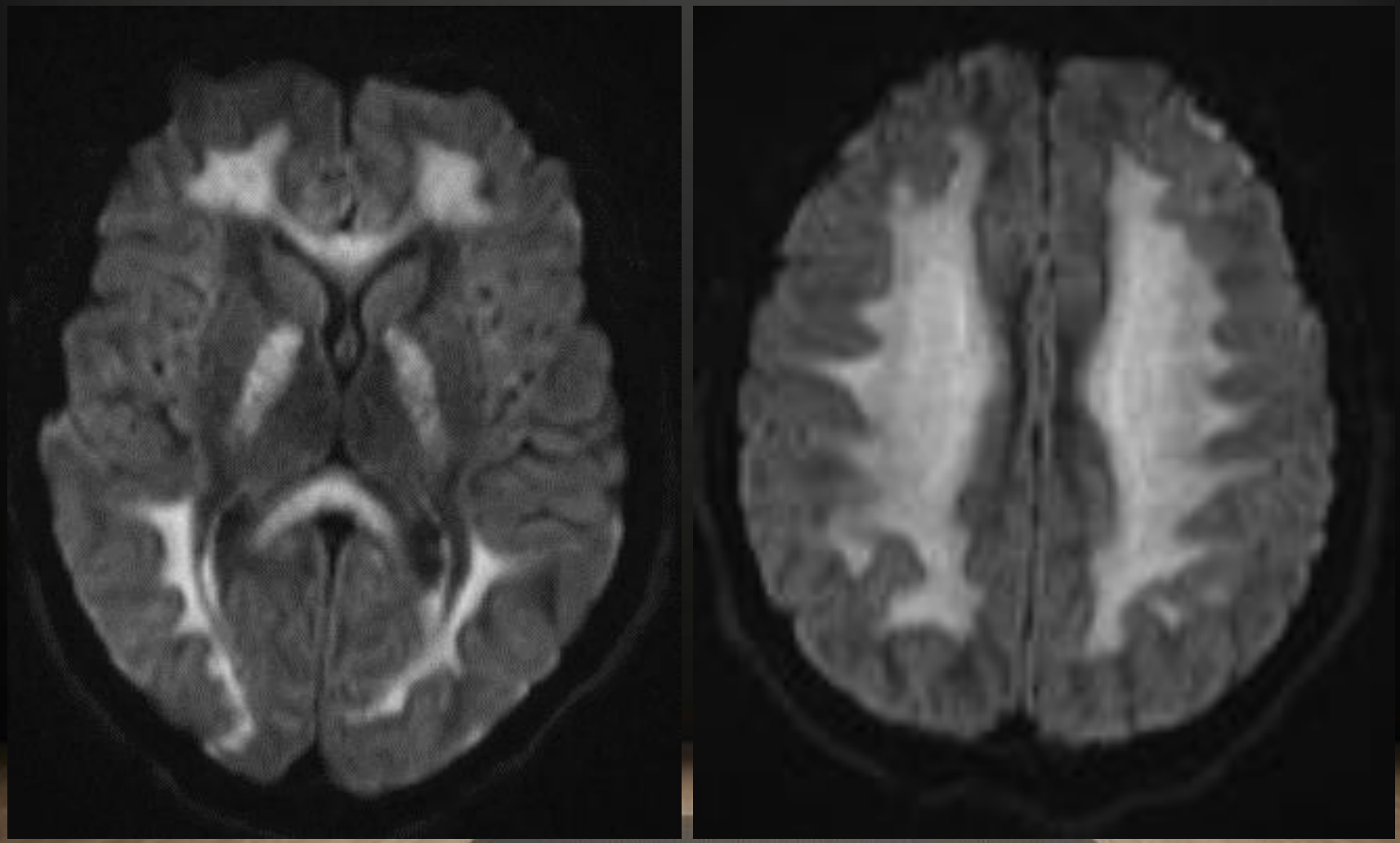
Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy

- **Imaging findings:**
  - Confluent, widespread, bilateral, symmetric white matter T2WI & T2 FLAIR hyperintensities.
  - Involving both supra & infratentorial
  - Selectively involved the posterior limb of the internal capsule & periventricular WM.
  - Sparing the anterior limb of internal capsule and subcortical U fibers.
  - Basal ganglia are rarely involved.
  - Cerebellar involvement manifest as symmetric WM hyperintensities with dentate nuclei sparing (butterfly wing pattern)
  - Restricted diffusion on DWI-ADC during the acute phase

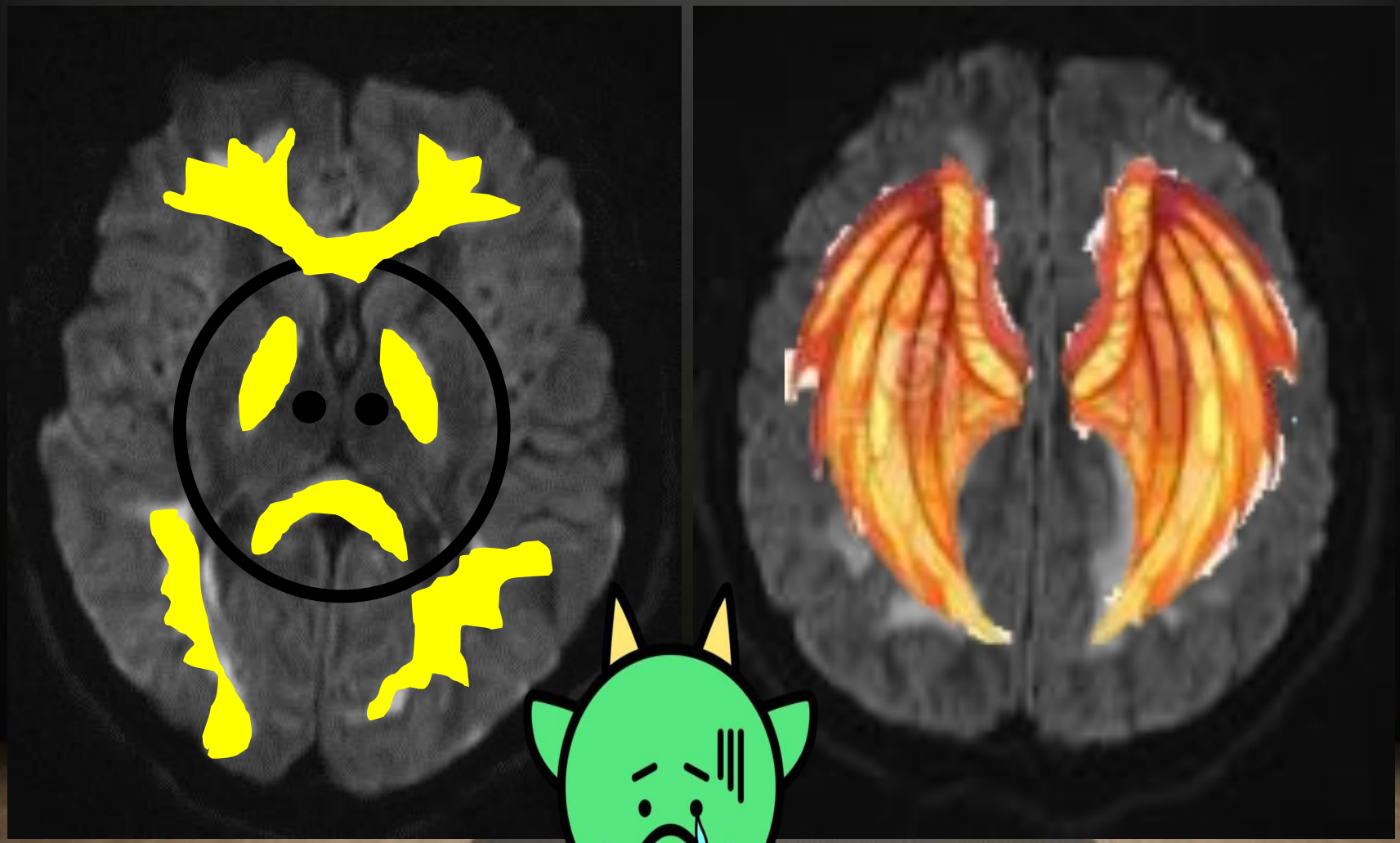
Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy



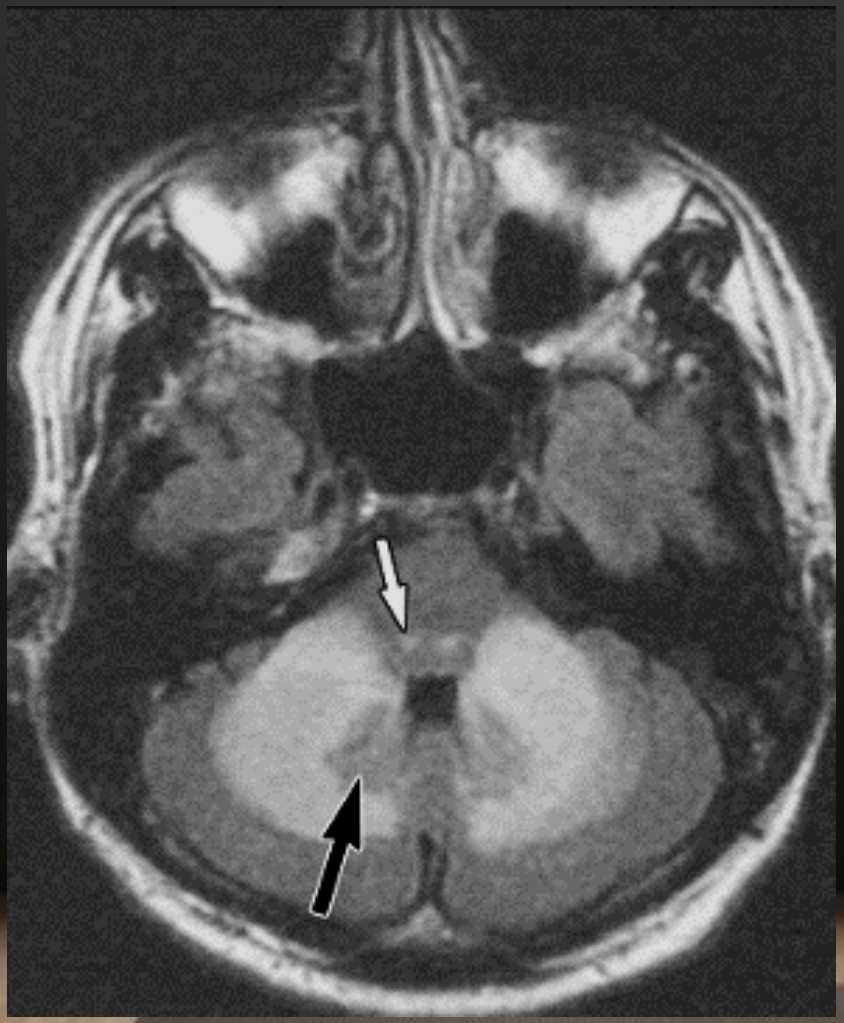
Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy



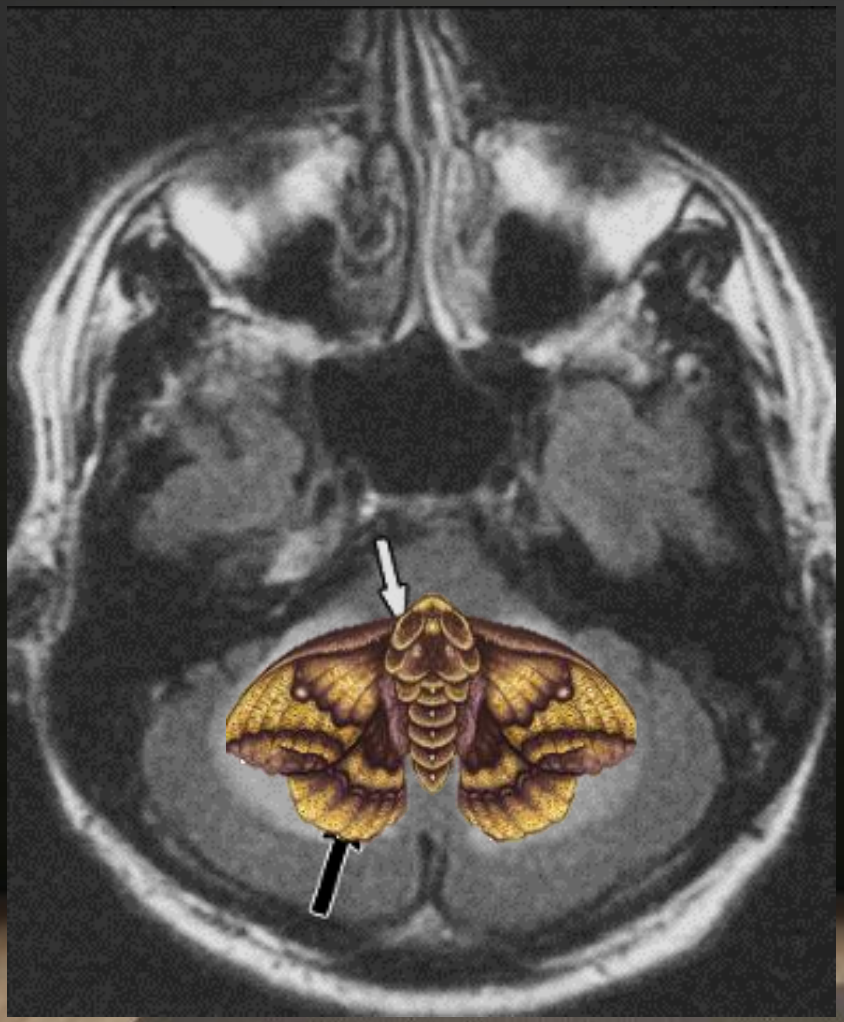
Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy



Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy

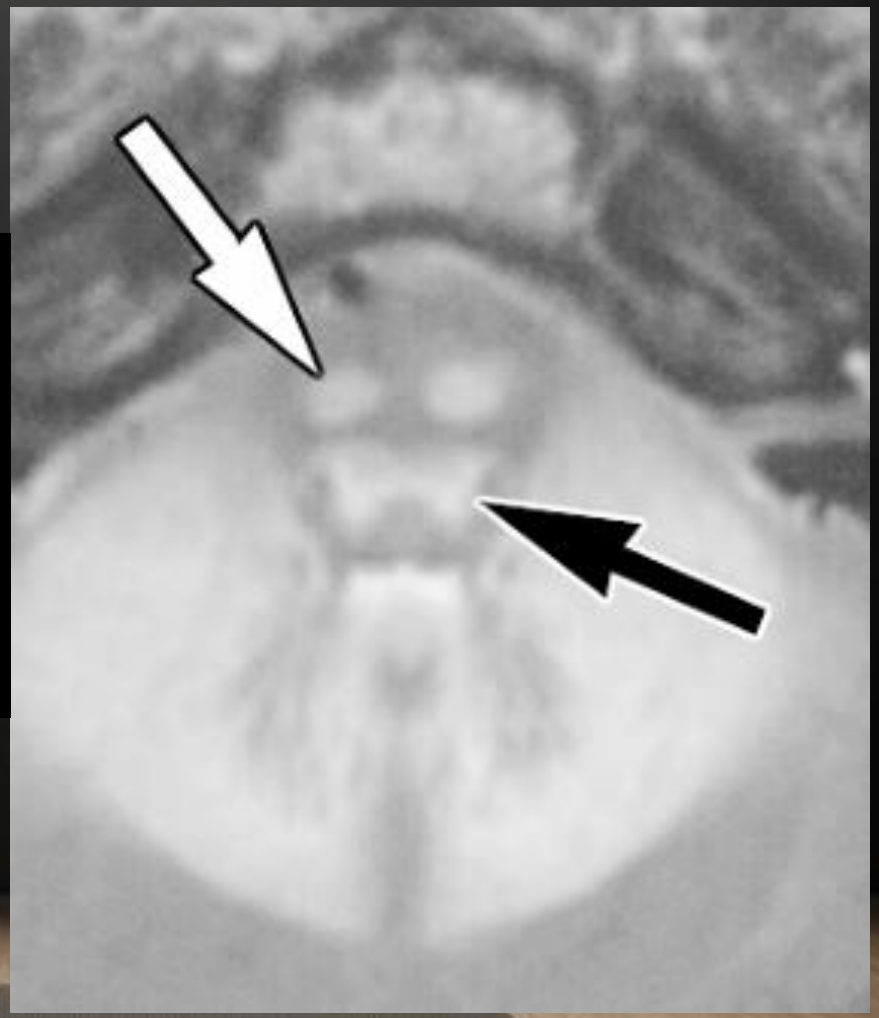


Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy

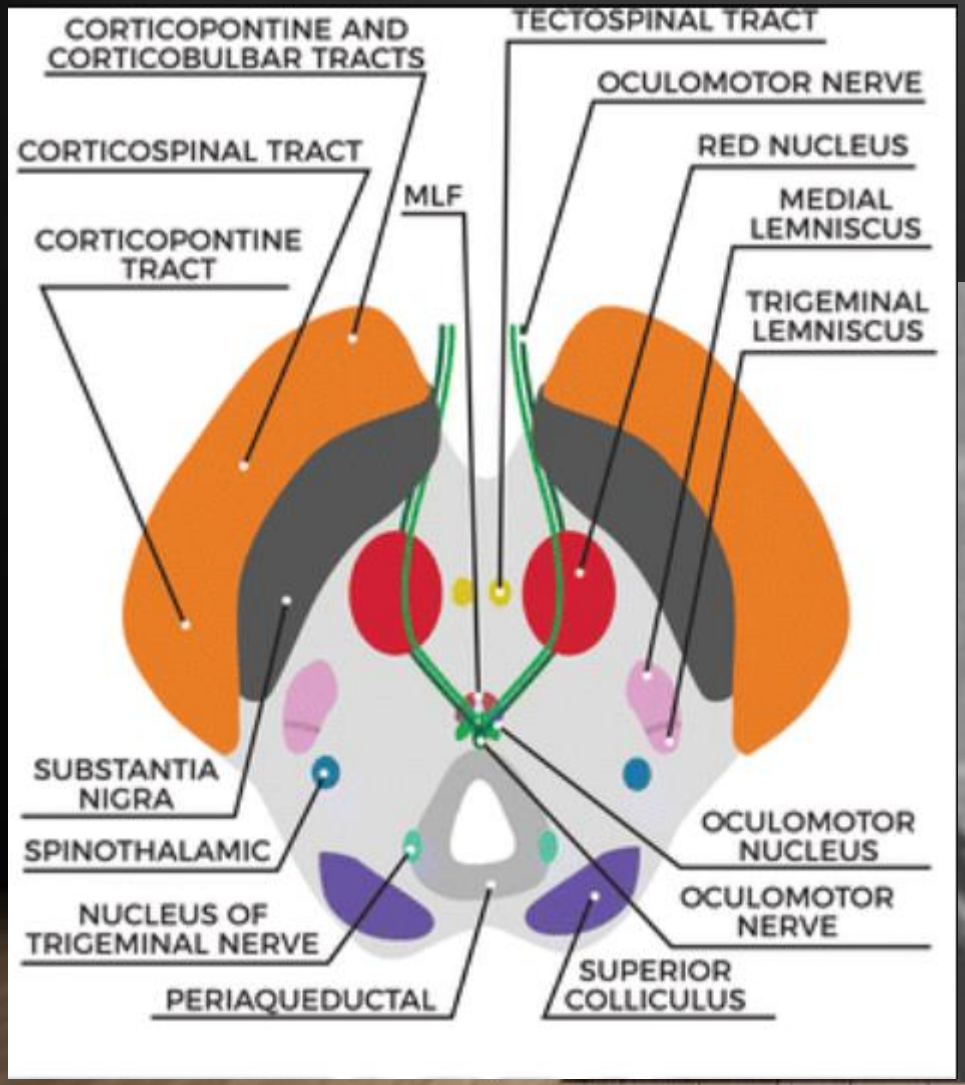
Bearded Skull Sign

Hyperintensity in cerebellar WM, sparing cortex & dentate nuclei. Abnormal signal in pons involving corticospinal tracts (white arrow), medial lemnisci & central tegmental tracts (black arrow)

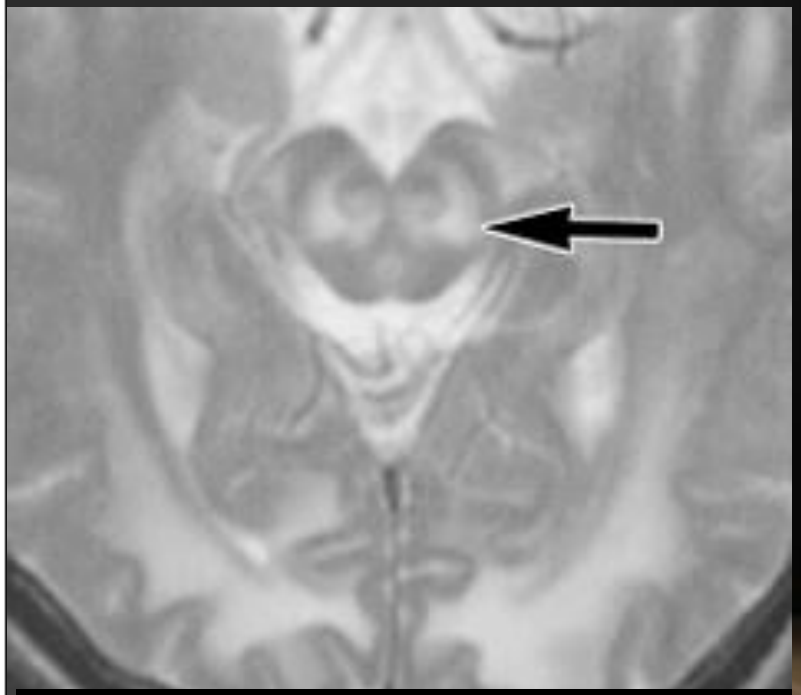


Pattern 4: Symmetric Periventricular WM Involvement

Heroin Toxic Leukoencephalopathy



Hyperintensity in medial lemnisci & spinothalamic tracts (arrow), with sparing of adjacent substantia nigra & red nuclei



Bat staring at viewer

Supplementary Pattern

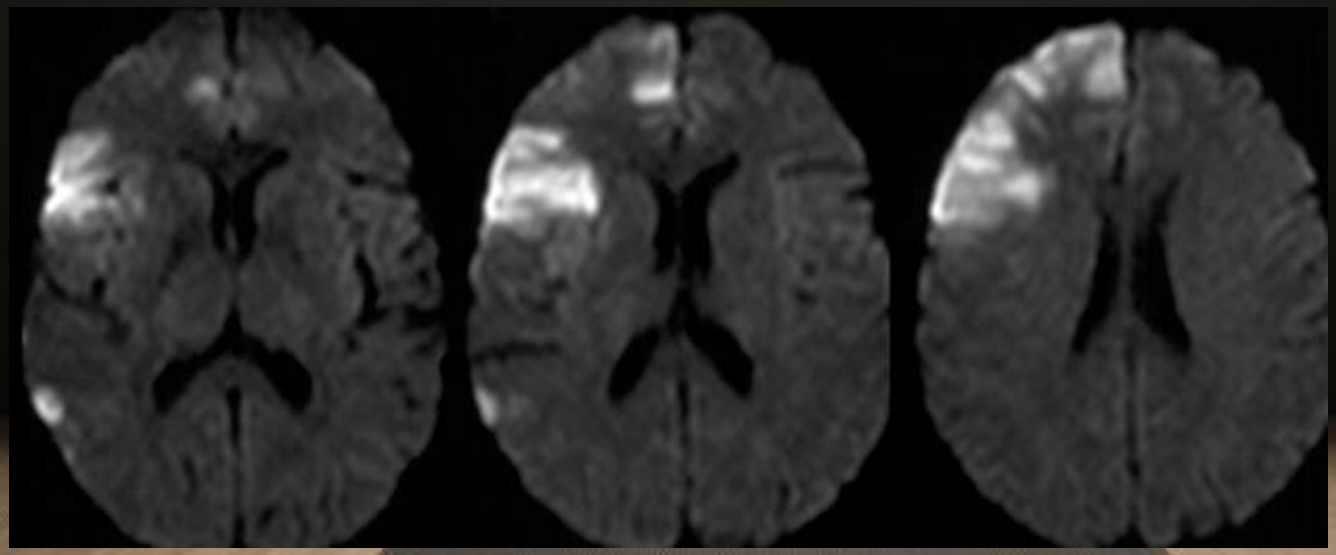
Acute Complication of Injected Heroin

- Most common acute complication of injected heroin is ischemic stroke.
- **Pathomechanism:**
  - Direct effects of the heroin with reversible vasospasm from stimulation of the vascular smooth muscle by the μ opioid receptor.
  - Vasculitis from immune-mediated responses
  - Embolic from crystalline impure additives

Supplementary Pattern

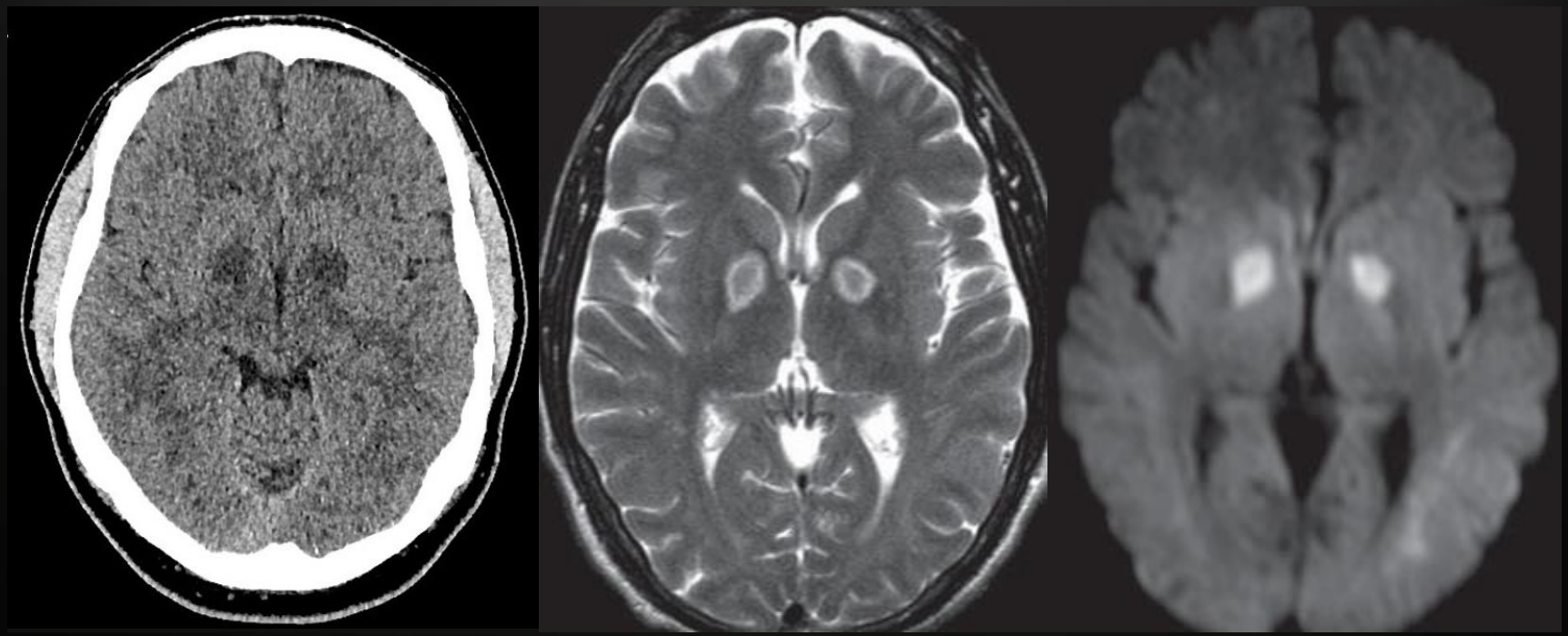
Acute Complication of Injected Heroin

- **Imaging:**
  - Ischemic stroke and hemorrhagic infarction.
  - Globus pallidus can also be involved (mimick CO poisoning).
  - White matter changes can be seen in chronic heroin abusers (diffuse symmetric bilateral T2 hyperintensities)



Supplementary Pattern

Acute Complication of Injected Heroin



Pattern 4: Symmetric Periventricular WM Involvement

Methotrexate and Other Chemotherapeutic Agents

- 3 main patterns for methotrexate-related CNS toxicity:
  - Toxic Leukoencephalopathy (most common manifestation)
  - Disseminated necrotizing encephalopathy
  - Subacute combined degeneration (related to Vit B12 deficiency → Pattern 5: Corticospinal Tract Involvement)

Pattern 4: Symmetric Periventricular WM Involvement

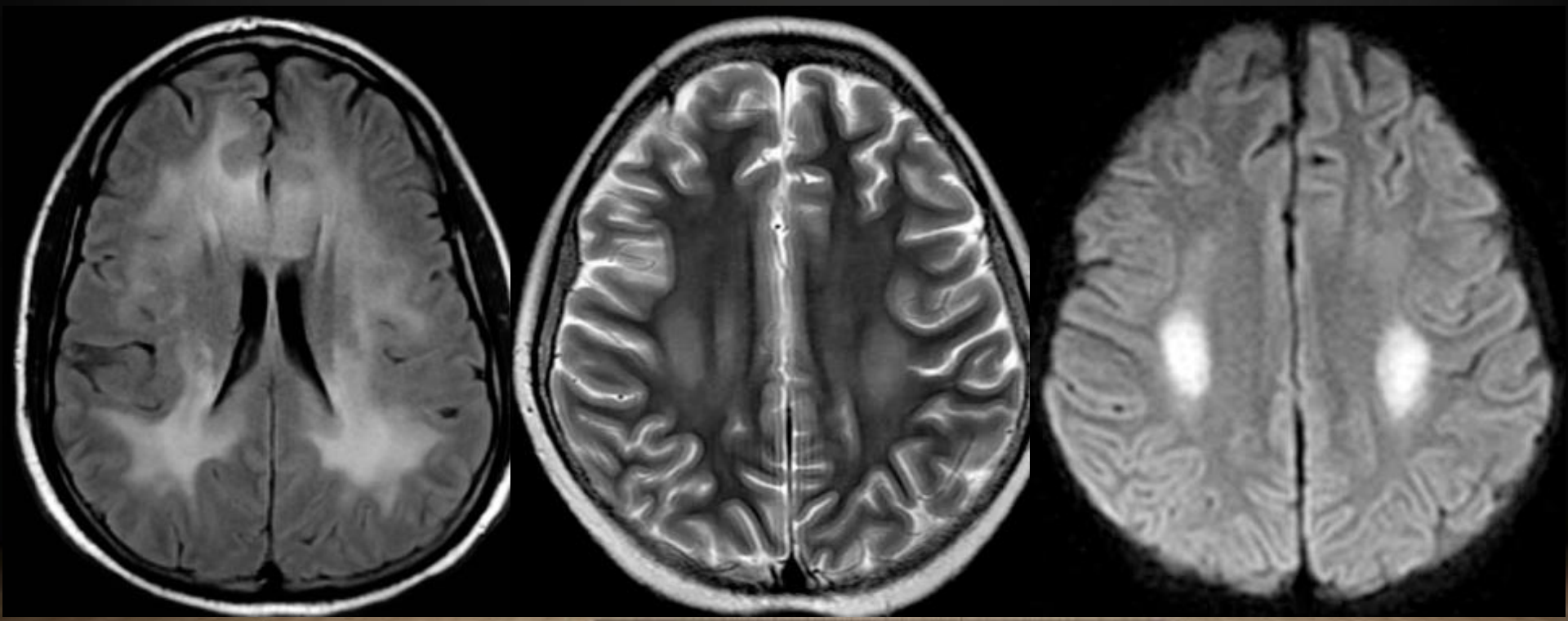
Methotrexate and Other Chemotherapeutic Agents

- **Toxic Leukoencephalopathy** (most common manifestation)
  - Manifest acutely between 2-14 days after administration
  - Imaging findings:
    - Hyperintensity on T2WI & T2 FLAIR
    - Restricted diffusion on DWI-ADC
    - Bilaterally symmetric/asymmetric across multiple vascular territories
    - Affecting centrum semiovale and sparing the subcortical U fibers

Pattern 4: Symmetric Periventricular WM Involvement

Methotrexate and Other Chemotherapeutic Agents

- **Toxic Leukoencephalopathy** (most common manifestation)



Pattern 4: Symmetric Periventricular WM Involvement

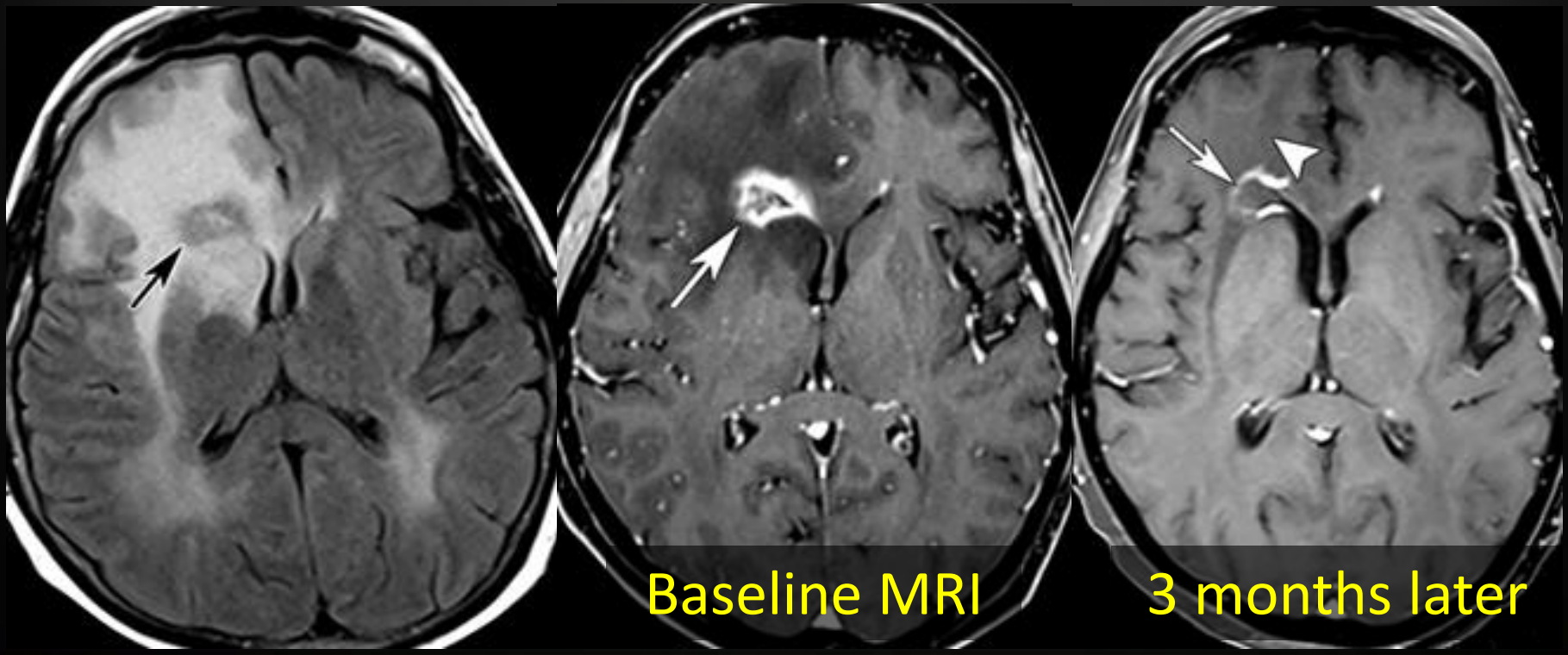
Methotrexate and Other Chemotherapeutic Agents

- **Disseminated necrotizing encephalopathy**
  - Rare manifestation.
  - Usually complication of intrathecal administration combined with whole brain radiation therapy.
  - **Imaging findings:**
    - Extensive white matter involvement, with multiple low-signal-intensity foci within the disseminated areas of T2 hyperintensity (pointing to hemorrhage).
    - The low-signal-intensity foci have peripheral or solid enhancement, as they are associated with mass effect (tumorlike pattern)

Pattern 4: Symmetric Periventricular WM Involvement

Methotrexate and Other Chemotherapeutic Agents

- Disseminated necrotizing encephalopathy



*de Oliveira AM, Paulino MV, Vieira APF, McKinney AM, da Rocha AJ, Dos Santos GT, Leite CDC, Godoy LFS, Lucato LT. Imaging Patterns of Toxic and Metabolic Brain Disorders. Radiographics. 2019 Oct;39(6):1672-1695. doi: 10.1148/rg.2019190016. PMID: 31589567.

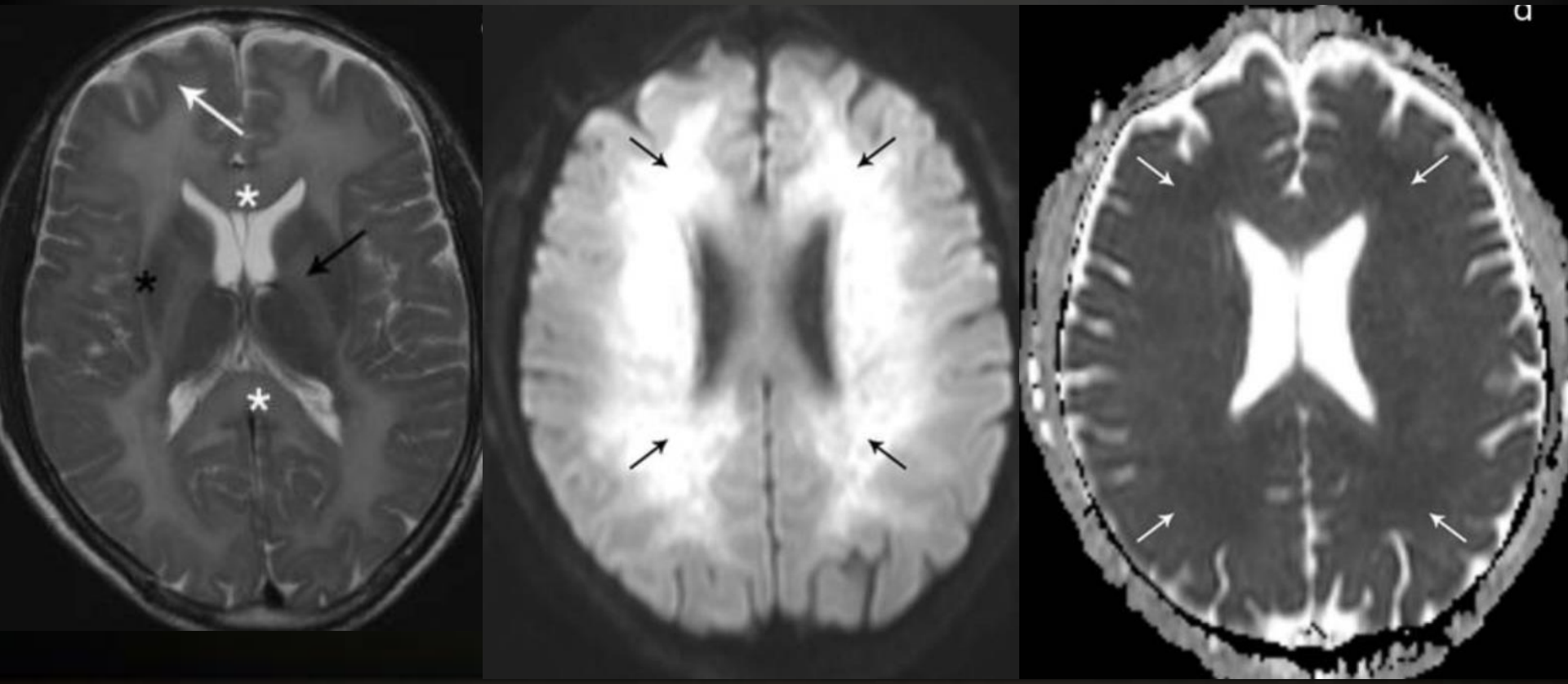
Pattern 4: Symmetric Periventricular WM Involvement

Carbon Monoxide Poisoning

- 2nd most commonly affected site of CO poisoning: cerebral white matter (1/3 of cases → Pattern 4: Symmetric Periventricular WM).
- Delayed leukoencephalopathy in the subacute phase (weeks after the initial insult)
- Important to correlate with the history of past CO poisoning.

Pattern 4: Symmetric Periventricular WM Involvement

Carbon Monoxide Poisoning



*Geraldo AF, Silva C, Neutel D, Neto LL, Albuquerque L. Delayed leukoencephalopathy after acute carbon monoxide intoxication. J Radiol Case Rep. 2014 May 31;8(5):1-8. doi: 10.3941/jrcr.v8i5.1721. PMID: 25426224; PMCID: PMC4242060.

Pattern 4: Symmetric Periventricular WM Involvement

Uremic Encephalopathy

- 10% of uremic encephalopathy can manifest as acute toxic leukoencephalopathy.
- Imaging findings: confluent bilateral & symmetrical periventricular white matter involvement.

Previously on Pattern 1a: Basal Ganglia and/or Thalamic Involvement (T2WI & T2 FLAIR Hyperintensity)

- Metabolic disorder in acute or chronic renal failure.
- Endogenous uremic toxin
- **Imaging finding (unspecific):**
  - Basal ganglia involvement (lentiform fork sign).
  - Cortical subcortical involvement (PRES-like).
  - White matter involvement.

Pattern 4: Symmetric Periventricular WM Involvement

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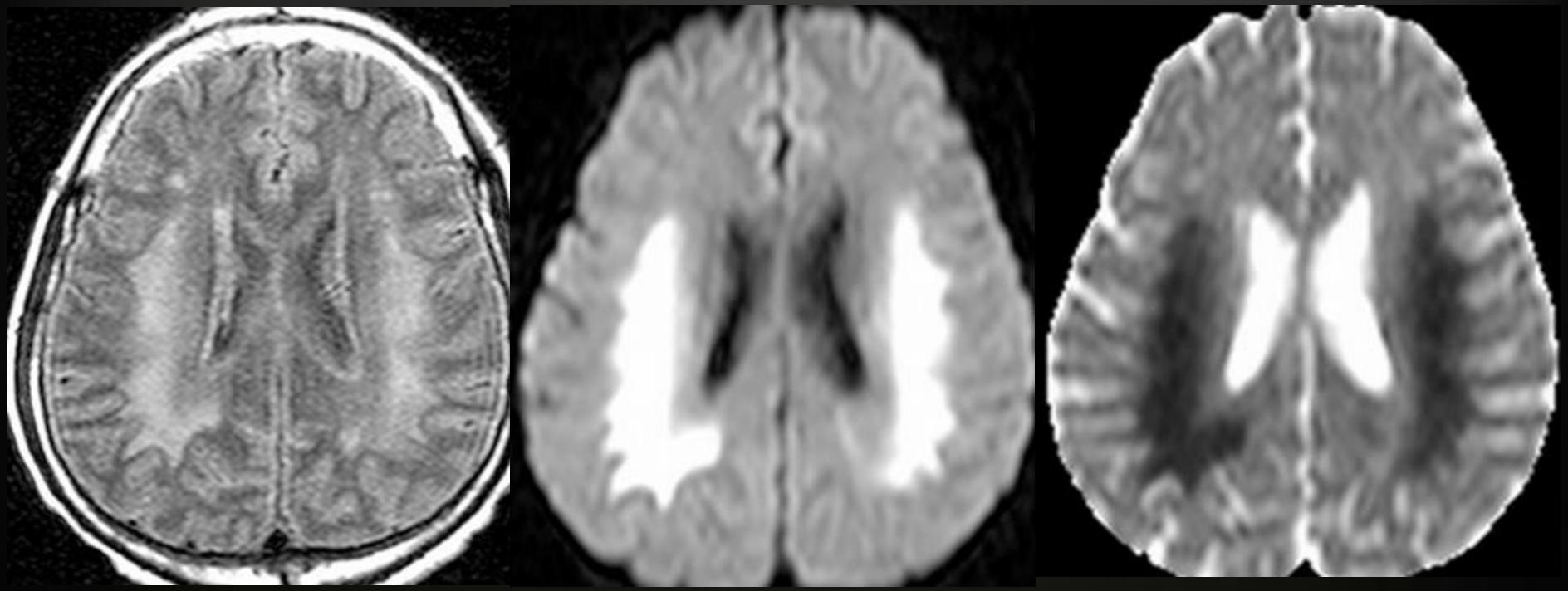
Pattern 4: Symmetric Periventricular WM Involvement

Uremic Encephalopathy



Kang E, Jeon SJ, Choi SS. Uremic encephalopathy with atypical magnetic resonance features on diffusion-weighted images. Korean J Radiol. 2012 Nov-Dec;13(6):808-11. doi: 10.3348/kjr.2012.13.6.808. Epub 2012 Oct 12. PMID: 23118581; PMCID: PMC3484303.

Pattern 4: Symmetric Periventricular WM Involvement

Acute Hepatic Encephalopathy

- Acute hepatic encephalopathy is a cause of acute toxic leukoencephalopathy in 15% of cases.
- Third most common cause of acute toxic leukoencephalopathy.

Previously on Pattern 3: Prominent cortical involvement

- **Imaging finding:**
  - Hyperintensity on T2WI & T2 FLAIR and restricted diffusion on DWI-ADC in the insular and cingulate gyri.
  - Relative sparing of occipital lobes and perirolandic region.
  - Less severe cases: periventricular white matter involvement without affecting the cortex, posterior limb of the internal capsule, dorsal brainstem.
  - MR spectroscopy: increased glutamate-glutamine peak between 2.1 – 2.4 ppm. (glutamine is used to metabolize ammonia).

Pattern 4: Symmetric Periventricular WM Involvement

Acute Hepatic Encephalopathy

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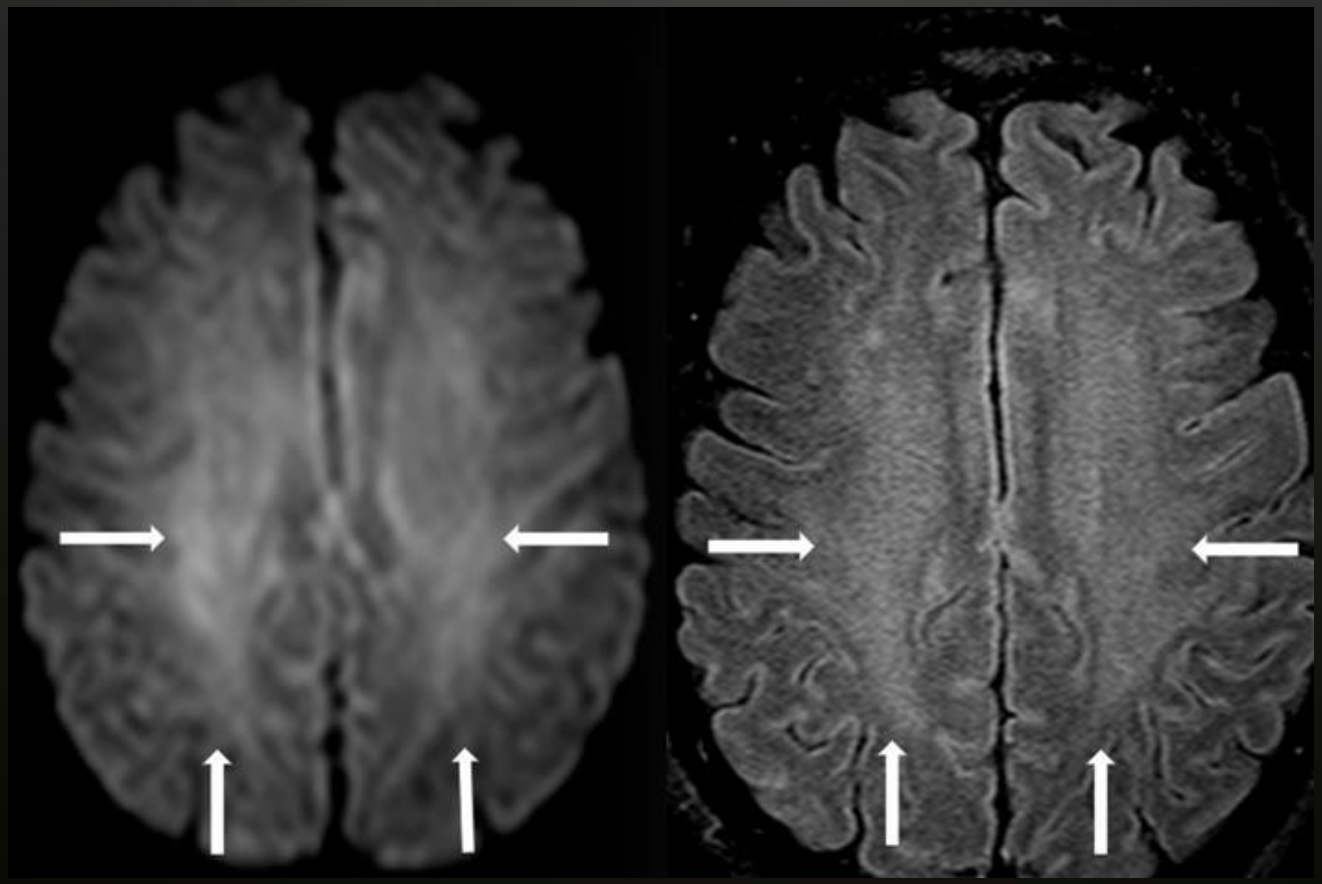
Pattern 4: Symmetric Periventricular WM Involvement

Acute Hepatic Encephalopathy



Koksel Y, Ozutemiz C, Rykken J, Ott F, Cayci Z, Oswood M, McKinney AM. "CHOICES": An acronym to aid in delineating potential causes of non-metabolic, non-infectious acute toxic leukoencephalopathy. Eur J Radiol Open. 2019 Jun 28;6:243-257.

Pattern 4: Symmetric Periventricular WM Involvement

Table 1: Summary of variables with respect to groups of cause of ATL

Variable	Statistic	All ATL (*n* = 101)	CTX (*n* = 35)	O/H (*n* = 19)	AHE (*n* = 14)	ID (*n* = 11)	Unknown (*n* = 7)	Other (*n* = 6)	PM[a] (*n* = 4)	CO (*n* = 3)	Alcohol (*n* = 2)
Sex	Male	50	17	11	7	2	2	4	2	3	2
	Female	51	18	8	7	9	5	2	2	0	0
Age (years)	Mean (SD)	40.72 (17.6)	41.3 (18.9)	34.6 (14.7)	44.6 (14.2)	52.1 (19.7)	33.6 (13.0)	36.4 (21.2)	49.0 (20–68)[b]	31.3 (20–44)[b]	31.0 (25–37)[b]
mRS score	Mean (SD)	1.97 (2.1)	2.71 (2.2)	2.33 (2.0)	2.07 (2.2)	0.40 (0.5)	1.50 (1.6)	1.80 (2.5)	0.25 (0–1)[b]	1.67 (0–5)[b]	0.50 (0–1)[b]
ATLOS score	Mean (SD)	1.60 (1.6)	2.29 (1.7)	1.67 (1.4)	1.57 (1.7)	0.60 (0.97)	1.17 (1.2)	1.40 (2.0)	0.25 (0–1)[b]	1.33 (0–4)[b]	0.50 (0–1)[b]
DWI severity	Mean (SD)	2.59 (1.1)	2.63 (1.0)	3.26 (1.1)	2.07 (0.9)	2.00 (0.77)	2.14 (1.2)	3.20 (1.3)	2.75 (2–4)[b]	2.67 (1–4)[b]	2.00 (1–3)[b]
FLAIR severity	Mean (SD)	2.52 (1.2)	2.34 (1.3)	3.32 (0.9)	2.15 (1.0)	2.55 (0.5)	2.00 (1.3)	3.40 (1.3)	1.67 (1–3)[b]	2.33 (0–4)[b]	1.50 (1–2)[b]
ADC % loss	Mean (SD)	35.6% (17.9)	34.0% (20.1)	41.3% (16.2)	30.5% (14.2)	28.2% (13.7)	32.4% (20.0)	34.3% (13.7)	44.4% (20.8–62.1)[b]	63.8% (58.9–71.6)[b]	38.9% (29.5–48)[b]

Note:—CTX indicates Chemotherapeutics; O/H, Opiates/Heroin; AHE, Acute Hepatic Encephalopathy; ID, Immunosuppressive drugs; PM, Prescribed medications; CO, Carbon Monoxide.

[a] Including metronidazole (*n* = 2), lorazepam (*n* = 1), and cefepime (*n* = 1).

[b] Minimum-Maximum.

Özütemiz C, Roshan SK, Kroll NJ, Benson JC, Rykken JB, Oswood MC, Zhang L, McKinney AM. Acute Toxic Leukoencephalopathy: Etiologies, Imaging Findings, and Outcomes in 101 Patients. AJNR Am J Neuroradiol. 2019 Feb;40(2):267-275. doi: 10.3174/ajnr.A5947. Epub 2019 Jan 24. PMID: 30679224; PMCID: PMC7028629.

Pattern 5: Corticospinal Tract Involvement

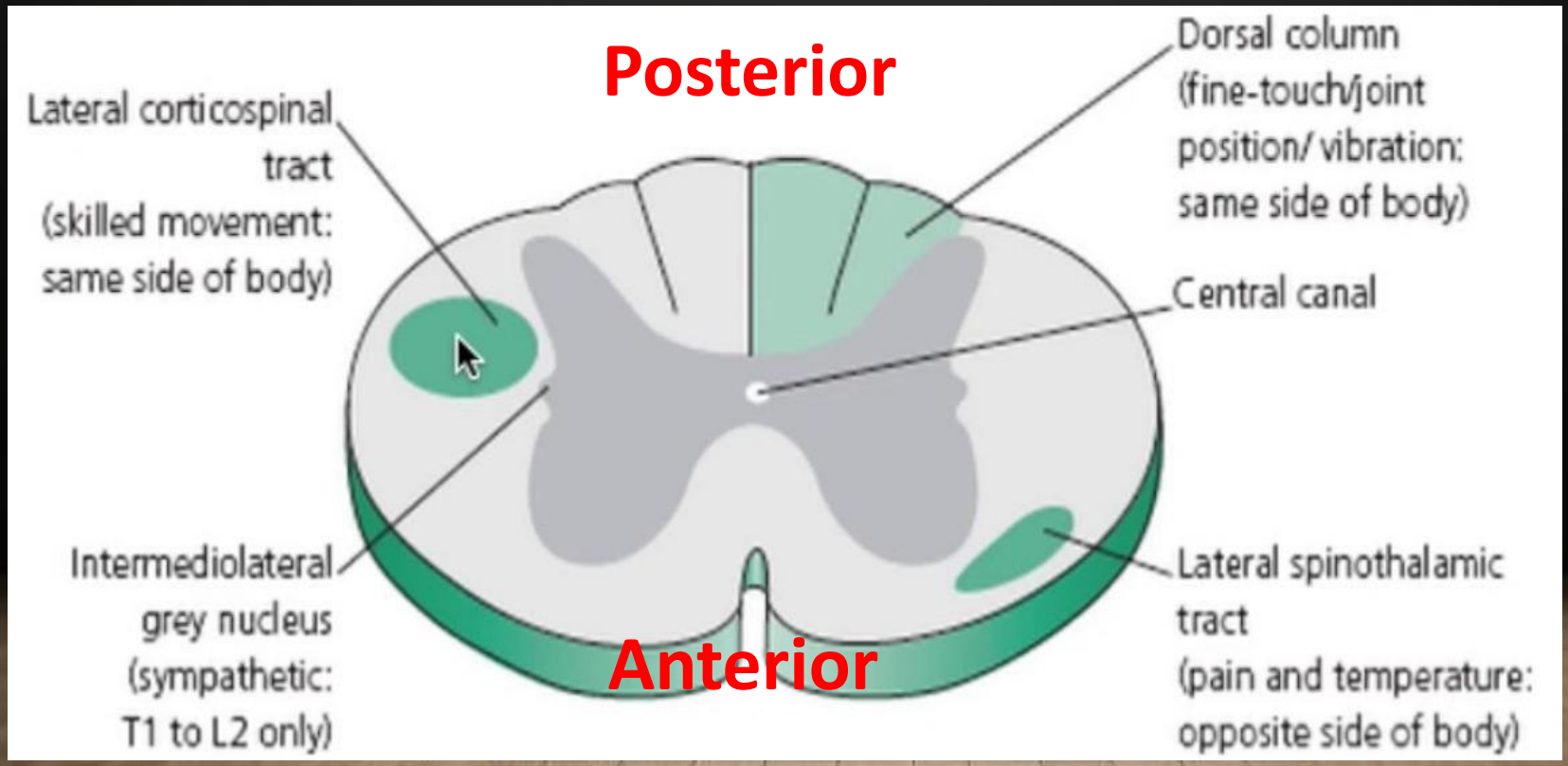
Cobalamine Deficiency

- Cobalamine (Vit B12) deficiency etiology:
  - Insufficiensy intrinsic factor
    - Pernicious anemia
    - Atrophic gastritis
    - Gastrectomy
  - Ileal malabsorption
    - Crohn disease
    - Resection of ileum
    - Infective ileitis
  - Malnutrition
    - Alcohol excess
    - Veganism
  - Prolonged use of some medication
    - H2 receptor histamint antagonist
    - Metformin
    - Proton pump inhibitor
    - Methotrexate

Pattern 5: Corticospinal Tract Involvement

Cobalamine Deficiency

- Cobalamine deficiency cause subacute combined degeneration that affect:
  - Dorsal/posterior spinal cord column
  - Lateral spinal cord column



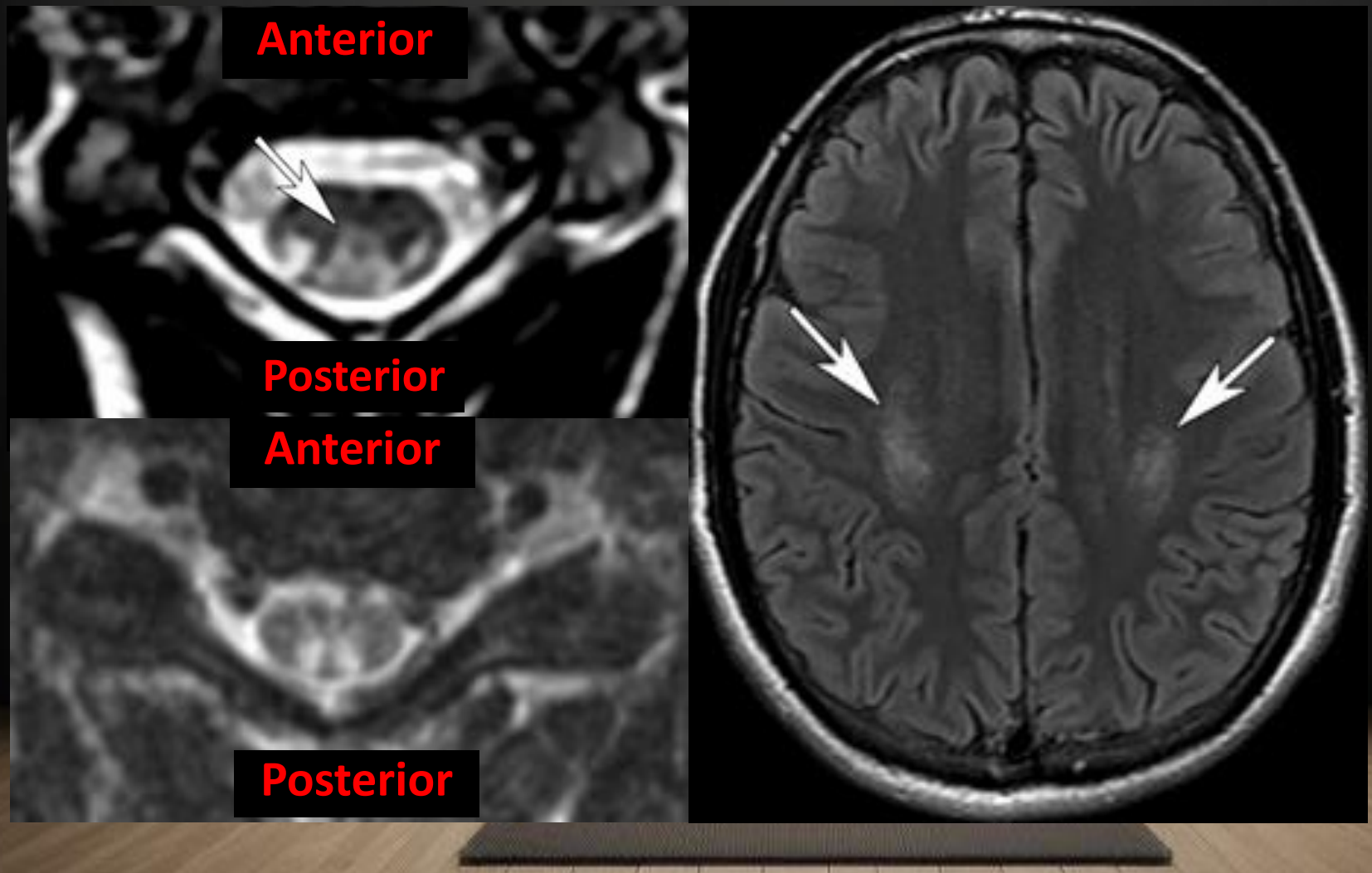
Pattern 5: Corticospinal Tract Involvement

Cobalamine Deficiency

- **MRI findings:**
  - Brain: Bilateral hyperintensities on T2WI & T2 FLAIR following the path of corticospinal tract.
  - Spinal cord: Hyperintensities symmetrically affecting the dorsal columns at T2WI with a characteristic inverted V shape
  - Usually there is complete resolution within 3 months after treatment.

Pattern 5: Corticospinal Tract Involvement

Cobalamine Deficiency



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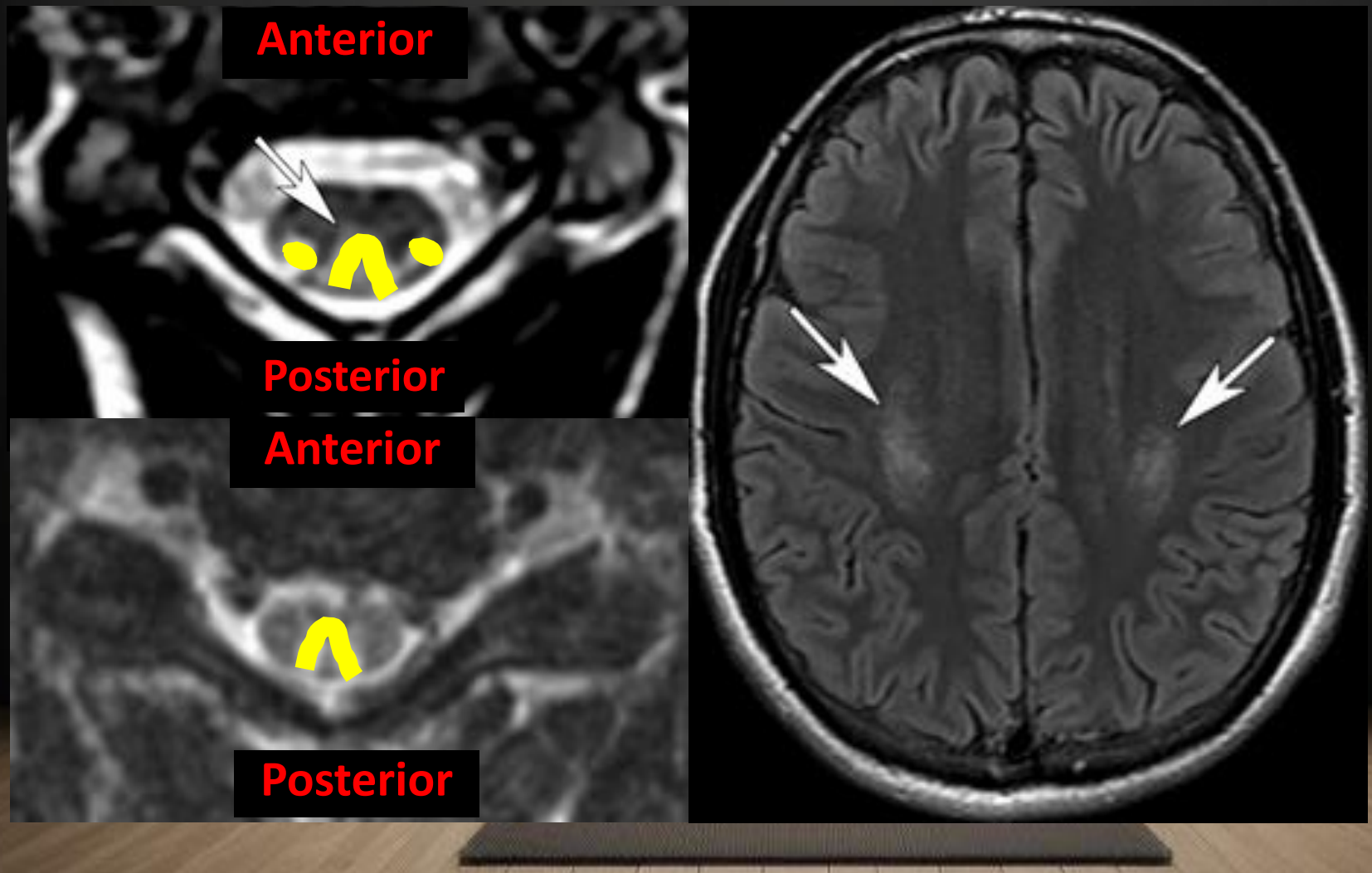

Pattern 5: Corticospinal Tract Involvement

Chronic Hepatic Encephalopathy

- Other than manganese accumulation in the globi pallidi & substantiae nigrae, chronic hepatic encephalopathy can cause vasogenic brain edema from glutamine accumulation within the brain tissue
- Mainly involving the corticospinal tract

Previously on Pattern 1c: Basal Ganglia and/or Thalami Involvement - T1 Hyperintensity

- **Imaging findings:**
  - Bilateral & symmetric T1 hyperintensity involving the globi pallidi & substantiae nigrae.
  - After liver transplant, changes can decrease or even disappear, typically normalizing after 1 year.
  - Glutamine-glutamate peak at MR spectroscopy with short echo times, resonating at 2.1–2.4 ppm
  - FLAIR → bilateral vasogenic edema (without restriction at DWI) in cerebral white matter, mainly involving the corticospinal tract.

Pattern 5: Corticospinal Tract Involvement

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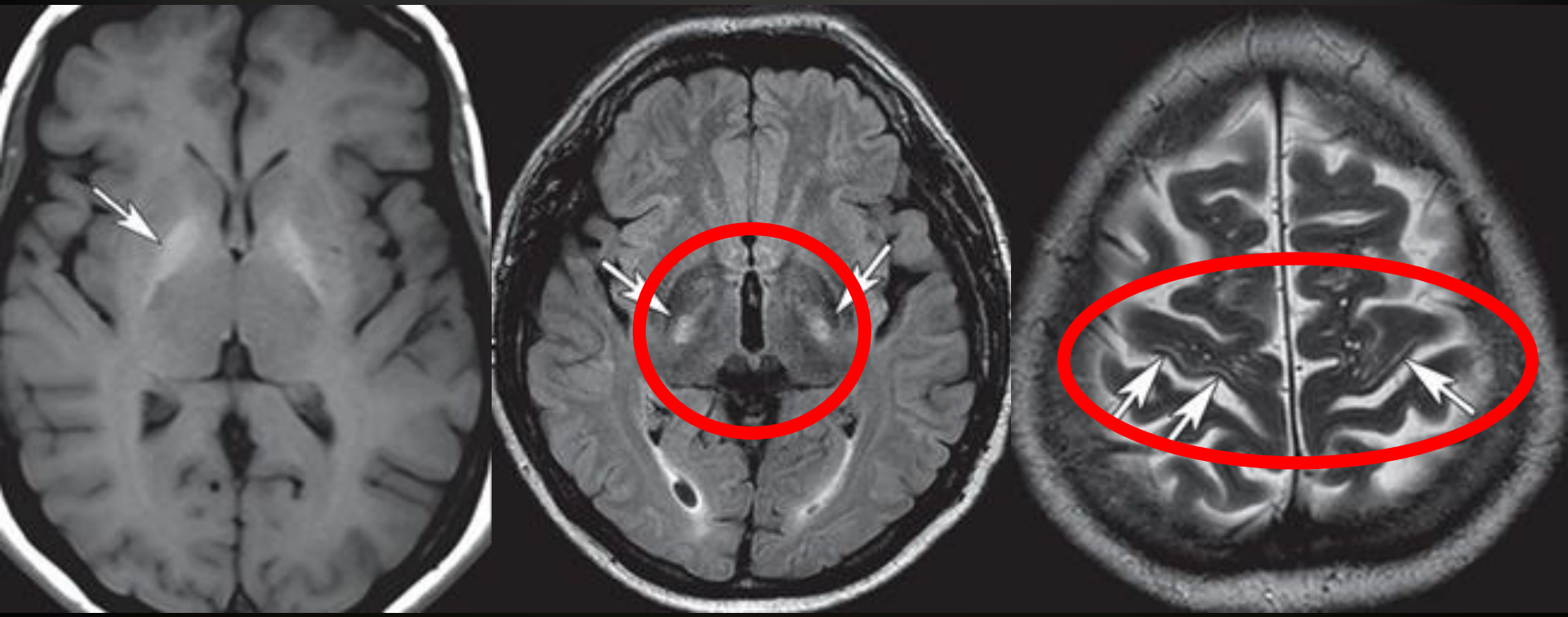
Pattern 5: Corticospinal Tract Involvement

Chronic Hepatic Encephalopathy



Pattern 6: Corpus Callosum Involvement

Marchiafava-Bignami Disease

- Marchiafava-Bignami Disease (MBD) is characterized by osmotic demyelination & subsequent necrosis of the corpus callosum
- Associated with chronic ethanol (alcohol) use and vit B complex deficiency (not exclusively vit B1 deficiency as in cases of Wernicke Encephalopathy)

Ettore Marchiafava 1847-1935

Amico Bignami 1862- 1929

Italy for me

Wines of Tuscany – All You Need to Know

Pattern 6: Corpus Callosum Involvement

Marchiafava-Bignami Disease

- **Two clinical form:**
  - Type A (acute):
    - Present with seizure and/or coma with involvement of the entire corpus callosum
    - Usually progresses to death within several days
  - Type B (chronic):
    - Mild encephalopathy with focal lesions in the corpus callosum (usually in the genu).
- MBD is usually accompanied by other alcohol-related pathologic conditions (MBD + WE)

Pattern 6: Corpus Callosum Involvement

Marchiafava-Bignami Disease

- **Imaging findings:**
  - Corpus callosum involvement.
  - Selective middle layers of the corpus callosum (Sandwich sign).
  - Hyperintensity on T2WI & T2 FLAIR
  - Acute phase: restricted diffusion on DWI-ADC and contrast enhancement on acute phase.
  - Chronic phase: thinning of the corpus callosum with central linear on T1WI

Pattern 6: Corpus Callosum Involvement

Marchiafava-Bignami Disease

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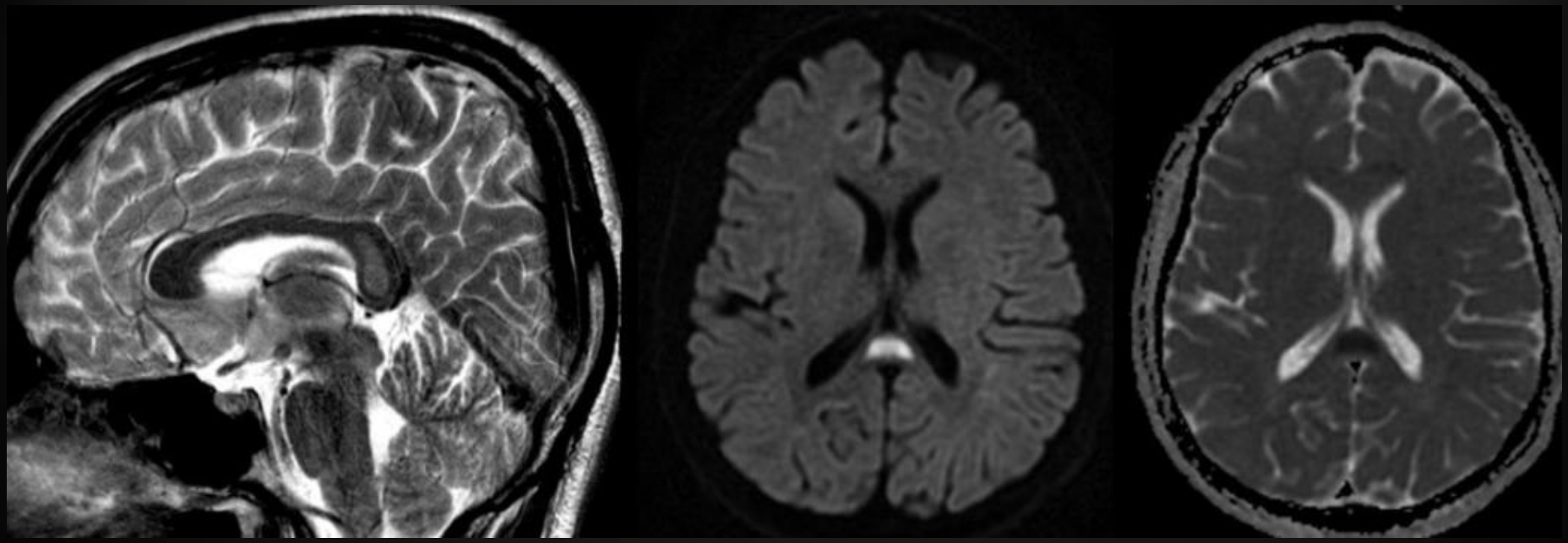
Pattern 6: Corpus Callosum Involvement

Marchiafava-Bignami Disease



Pattern 6: Corpus Callosum Involvement

Reversible Splenial Lesion

- Reversible splenial lesion (RSL) or cytotoxic lesion of the corpus callosum (CLOCC).
- RSL is usually reversible and involve the splenium of the corpus callosum but not always, hence the name CLOCC is currently preferred.
- **Pathophysiology:** probable due to excitotoxic intracellular and/or intramyelinic edema as the splenium has a high density of excitatory receptors that render it vulnerable to cytotoxic edema.

Pattern 6: Corpus Callosum Involvement

Reversible Splenial Lesion

- Etiology of RSL/CLOCC:
  - Use and subsequent withdrawal of antiepileptic drugs
  - Viral infection
  - Metabolic abnormalities (hypoglycemia, hypernatremia, acute alcohol poisoning)
- Patients are often asymptomatic (different clinical presentation from MBD)

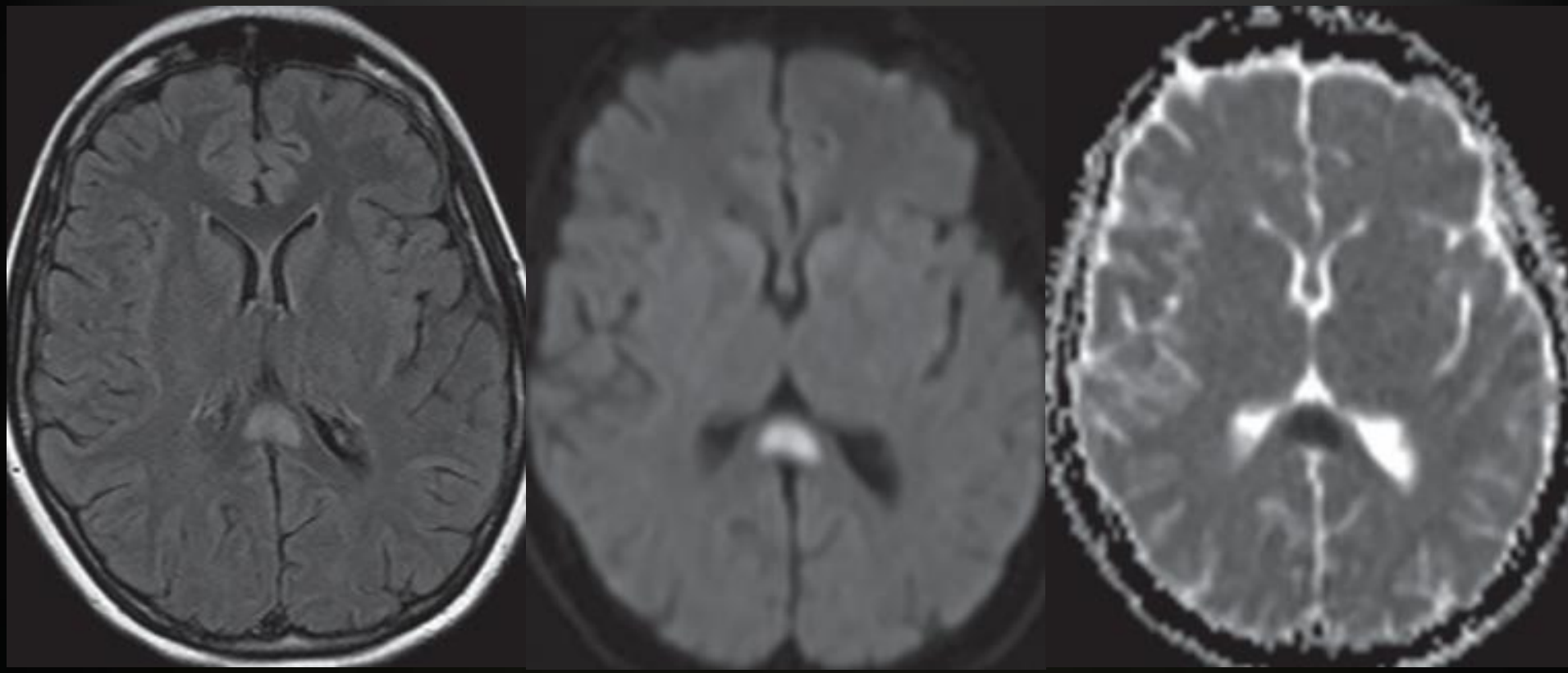
Pattern 6: Corpus Callosum Involvement

Reversible Splenial Lesion

- **Imaging findings:**
  - Ovoid lesion involving the central splenium.
  - Hyperintense on T2WI & T2 FLAIR.
  - Hypointense on T1WI.
  - Restricted diffusion on DWI-ADC.
  - No enhancement on T1WI+C
- Can also be considered subtype of ATL (overlap causes).
- RSL appears to be the mildest severity of ATL (only involving the splenium and with resolution)

Pattern 6: Corpus Callosum Involvement

Reversible Splenial Lesion



Starkey, Jay; Kobayashi, Nobuo; Numaguchi, Yuji; Moritani, Toshio . (2017). Cytotoxic Lesions of the Corpus Callosum That Show Restricted Diffusion: Mechanisms, Causes, and Manifestations. RadioGraphics, 37(2), 562–576. doi:10.1148/rg.2017160085

Pattern 6: Corpus Callosum Involvement

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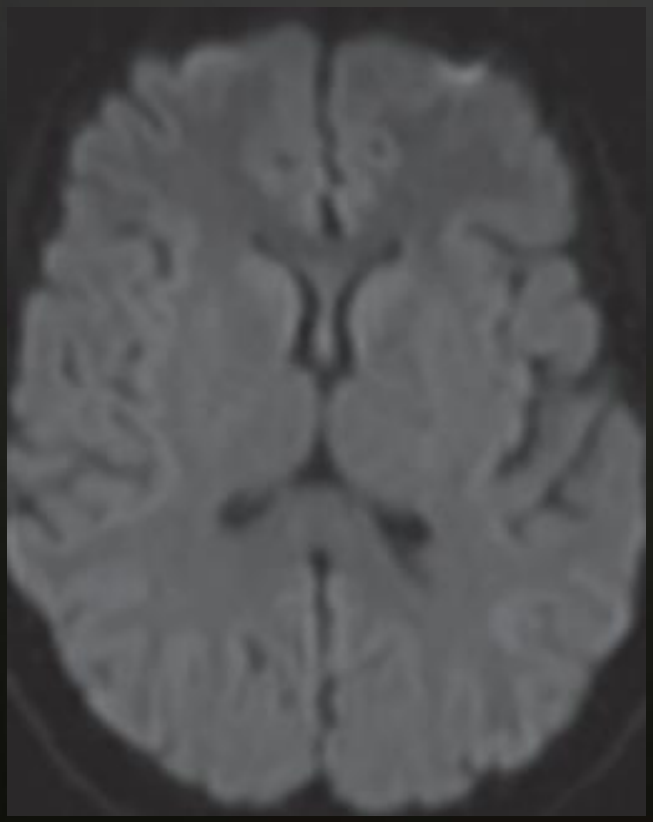

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Entities Associated with CLOCCs and Helpful Imaging and Clinical Features

Type of CLOCC	Helpful Imaging Features	Helpful Clinical Features	Reported Causes
Drug-associated CLOCCs	Abnormality of the dentate nuclei with metronidazole therapy	History of seizure, antiseizure therapy (eg, carbamazepine), chemotherapy, or other recent drug therapy	Carbamazepine, cyclosporine, diet pills with a sympathomimetic stimulant, fluorouracil, glufosinate ammonium, intravenous immunoglobulin therapy, lamotrigine, methyl bromide, metronidazole, neuroleptic malignant syndrome (amitriptyline, clozapine), phenytoin, corticosteroids, withdrawal of antiseizure therapy
Malignancy-associated CLOCCs	Evidence of CNS malignancy, including mass lesions and leptomeningeal enhancement	History of malignancy or chemotherapy	Acute lymphocytic leukemia, esophageal cancer, leptomeningeal glioblastomatosis, spinal meningeal melanocytoma
Infection-associated CLOCCs	Abscess formation or leptomeningeal enhancement, imaging findings that vary widely with the infectious agent and localization	Fever, leukocytosis, nuchal rigidity, altered mental status, history of travel to endemic areas (malaria)	Adenovirus, aseptic meningitis or encephalitis, Epstein-Barr virus (EBV), *Escherichia coli*, herpes, influenza virus A (H1N1), influenza, *Legionella*, malaria, measles, *Mycoplasma*, mumps, rotavirus, *Salmonella*, *Staphylococcus*, *Streptococcus*, tick-borne encephalitis, varicella-zoster virus
SAH-associated CLOCCs	Extensive hemorrhage within the subarachnoid space, lack of vessel irregularity on angiograms	Thunderclap headache, "worst headache of life," loss of consciousness, seizures in a patient with hypertension	Aneurysm, arteriovenous malformation
Metabolic disorder–associated CLOCCs	Classic central lesion in central pontine myelinolysis; symmetric lesions in the medial thalami and the mammillary bodies and surrounding the third ventricle and cerebral aqueduct in Wernicke encephalopathy; "eye of the panda" sign in Wilson disease	Fluid-electrolyte imbalances; history of cirrhosis or hepatic dysfunction, liver transplantation, malnutrition, or AIDS that may predispose to osmotic demyelination; history of alcoholism or malnutrition in Marchiafava-Bignami disease or Wernicke encephalopathy; Kayser-Fleischer rings in Wilson disease	Acute renal failure, alcoholism, extrapontine myelinolysis, central pontine myelinolysis, hepatic encephalopathy, hyperammonemia, hypernatremia, hypoglycemia, hyponatremia, malnutrition, Marchiafava-Bignami disease, Wernicke encephalopathy, Wilson disease
Trauma-associated CLOCCs	Brain contusions; multifocal punctate lesions on FLAIR, diffusion-weighted, or susceptibility-weighted MR images at the gray matter–white matter junction or in the corpus callosum or brainstem	Trauma with immediate loss of consciousness and persistent coma, altered mental status, or seizures	Trauma of various causes
CLOCCs associated with other entities	Varies with the cause	Varies with the cause	Acute high-altitude sickness, anti–glutamate receptor antibody, anti–voltage-gated potassium channel antibody, eclampsia, hemolytic uremic syndrome, vaccination, Kawasaki disease, posterior reversible encephalopathy syndrome, postpartum cerebral angiopathy, seizure without drug therapy, status epilepticus

Pattern 7: Asymmetric WM Involvement

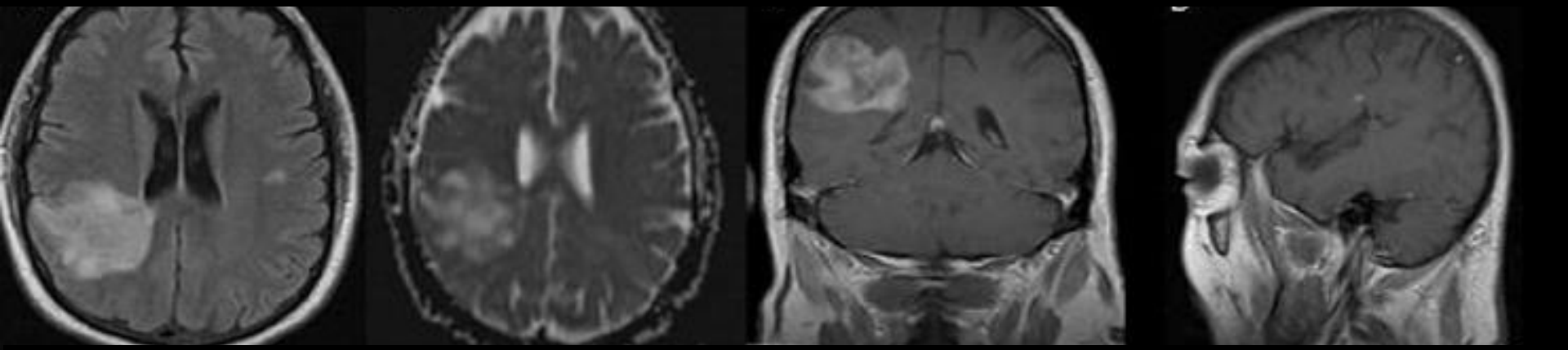
Chemotherapeutic & Immunomodulator Agents

- Asymmetric WM involvement→ mimicking demyelinating leukoencephalopathy pattern with multiple ovoid asymmetric WM hyperintensities in a perivenular distribution.
- Some chemotherapeutic & immunomodulator agents are related to this pattern:
  - TNF-α blockers (infliximab, adalimumab)
  - Vincristine

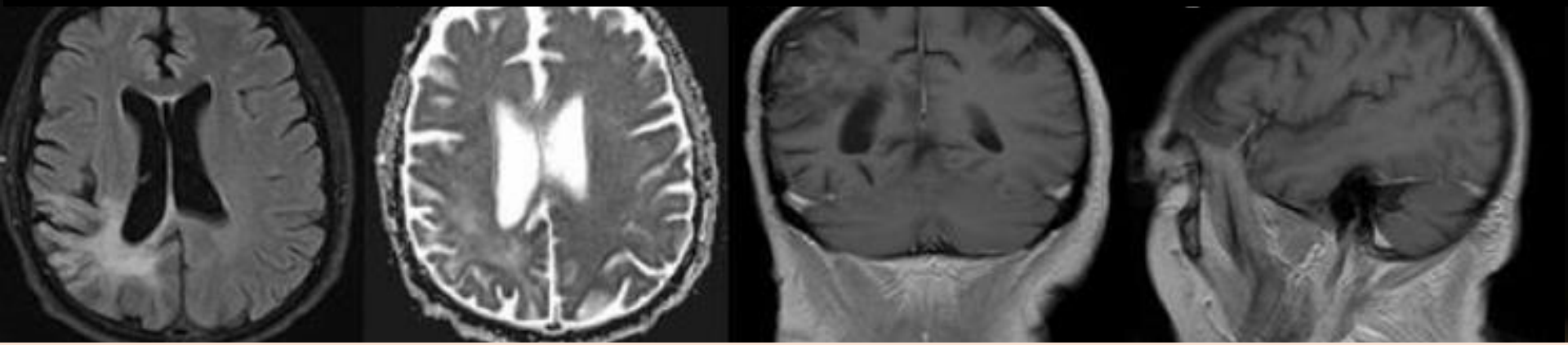
Pattern 7: Asymmetric WM Involvement

Chemotherapeutic & Immunomodulator Agents

Infliximab induced CNS demyelination (first MRI)



Infliximab induced CNS demyelination (2 years later)



Kalinowska-Lyszczarz A, Fereidan-Esfahani M, Guo Y, Lucchinetti CF, Tobin WO. Pathological findings in central nervous system demyelination associated with infliximab. Mult Scler. 2020 Aug;26(9):1124-1129. doi: 10.1177/1352458519894710. Epub 2019 Dec 17. PMID: 31845616

Pattern 8: Parieto-occipital Subcortical Vasogenic Edema

Posterior Reversible Encephalopathy Syndrome

- Clinical manifestation: seizure, altered mental function, headache & visual disturbance
- Predisposing factor:
  - Hypertension
  - Preeclampsia
  - Renal failure (uremic encephalopathy)
  - Sepsis
  - Thrombocytopenia
  - Cytotoxic/immunosuppressive medications (cyclosporin, tacrolismus)

Pattern 8: Parieto-occipital Subcortical Vasogenic Edema

Posterior Reversible Encephalopathy Syndrome

- Pathophysiology:
  - Inability of the posterior circulation to autoregulate in response to acute changes in blood pressure.
  - Usually caused by hypertension (but 20-30% normotensive)
  - Endothelial injury & dysfunction secondary to different causes (cytotoxic, immunogenic)
  - Hyperperfusion → disruption of the blood-brain barrier → vasogenic oedema, usually without infarction
  - Despite its name, PRES is not always reversible and not always posterior.

Pattern 8: Parieto-occipital Subcortical Vasogenic Edema

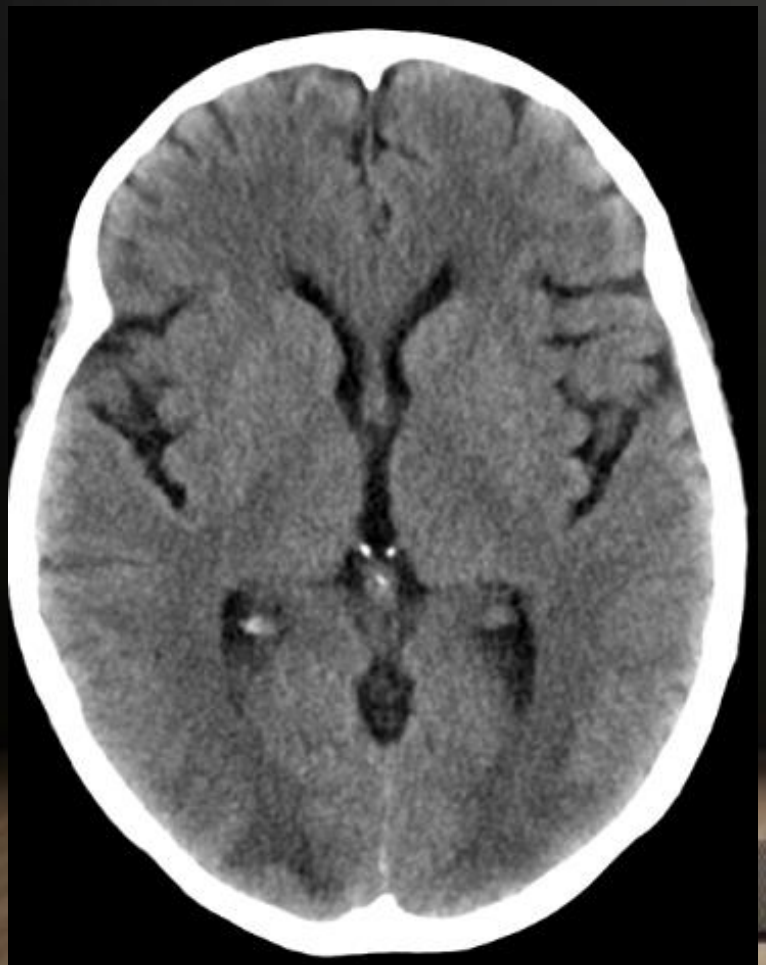
Posterior Reversible Encephalopathy Syndrome

- Imaging findings:
  - Vasogenic edema (commonly bilateral)
  - Hypodense on CT scan
  - Hyperintensity on T2WI & T2 FLAIR
  - Not giving restricted diffusion on DWI-ADC.
  - Location:
    - Parieto-occipital involvement (up to 90 %) classic PRES
    - Superior frontal sulcus pattern (70%)
    - Holohemispheric watershed pattern (50%)
    - Less common sites: cerebellum, basal ganglia & brain stem.
  - Ischaemic stroke (11%), intracerebral haemorrhage (10%) & subarachnoid haemorrhage (7%).

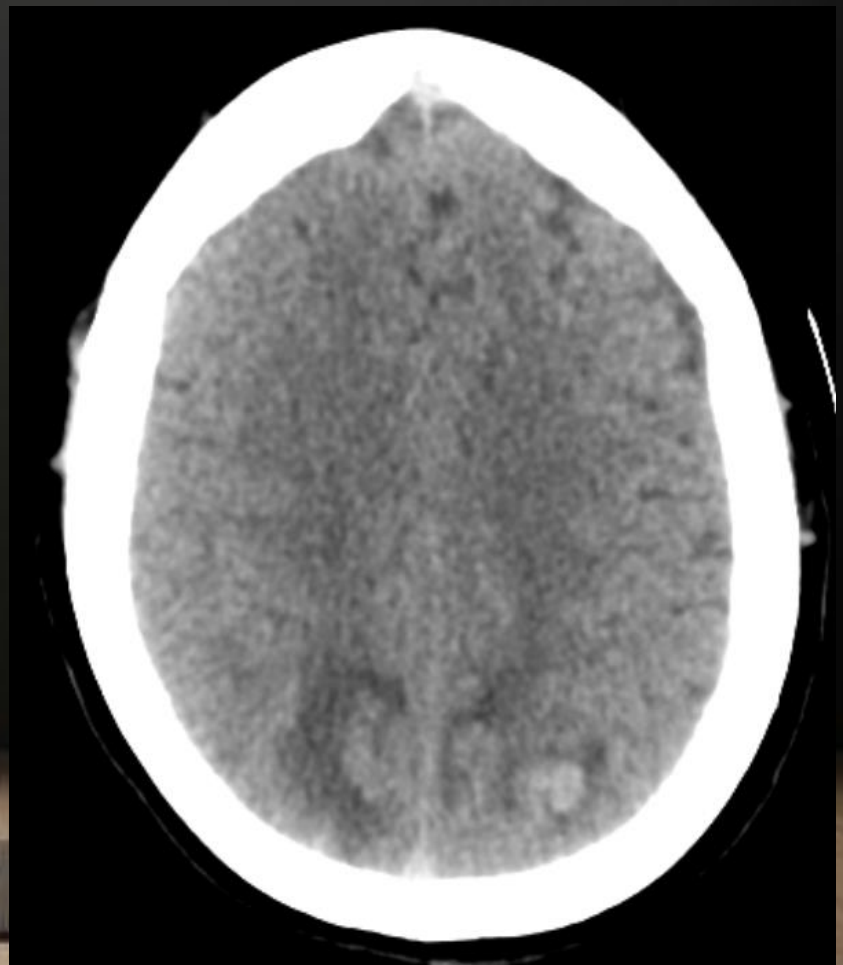
Pattern 8: Parieto-occipital Subcortical Vasogenic Edema

Posterior Reversible Encephalopathy Syndrome

Vasogenic edema only

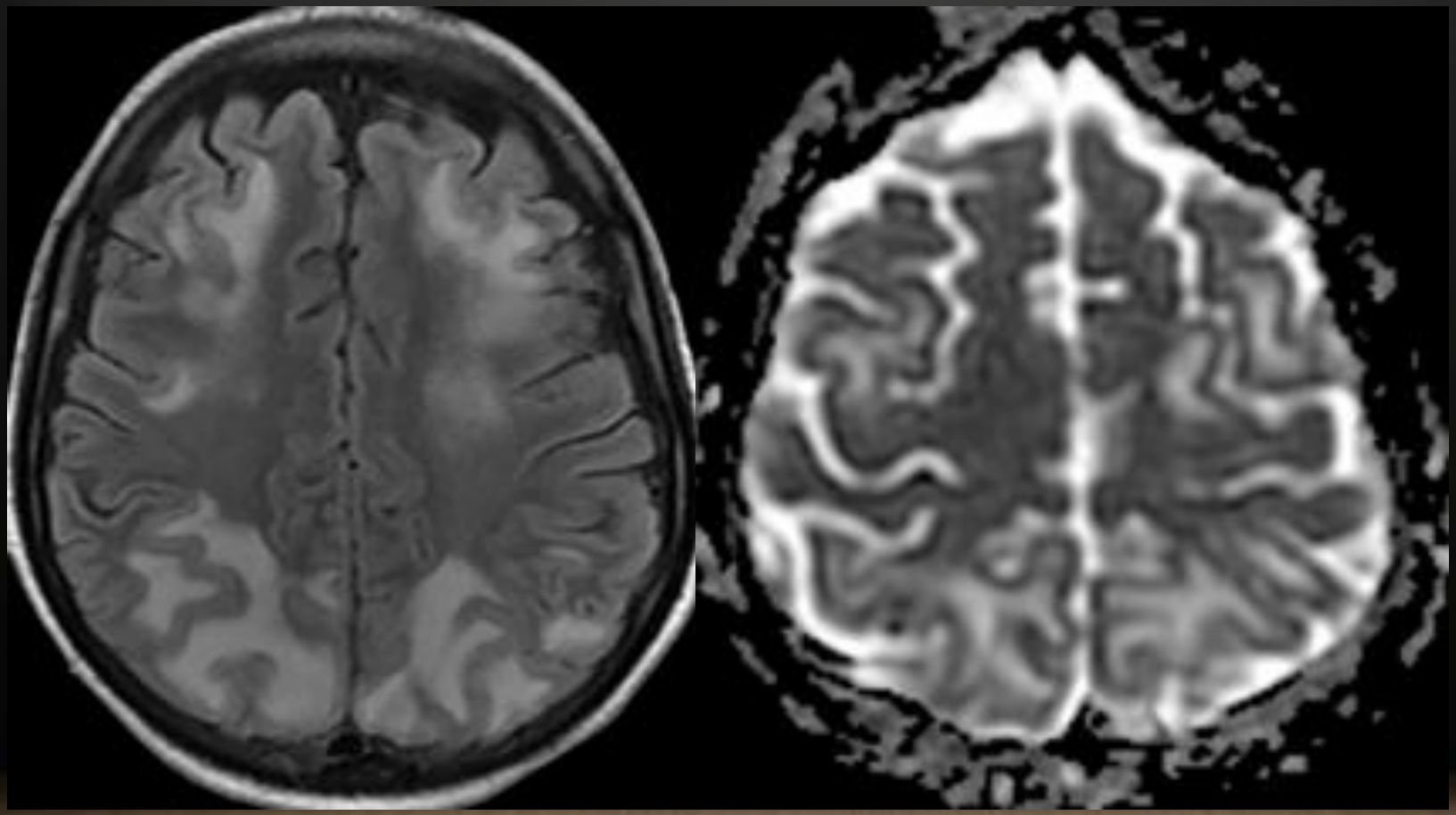


Vasogenic edema with hemorrhage



Pattern 8: Parieto-occipital Subcortical Vasogenic Edema

Posterior Reversible Encephalopathy Syndrome



Pattern 9: Symmetric Central Pontine Involvement

Osmotic Demyelination Syndrome

- ODS : acute form of demyelination caused by rapid shift in serum osmolality
- Most common cause is a rapid correction of hyponatremia (usually sodium level <115mmol/L and correction >12mmol/L per day)
- But ODS may occur in patient with normonatremic.
- Clinical manifestation:
  - Seizures
  - Altered mental status (often biphasic)

Pattern 9: Symmetric Central Pontine Involvement

Osmotic Demyelination Syndrome

Causes:

- Rapid hyponatremia correction
- Alcoholism
- Liver transplant (hyperammonemia)
- Malnutrition
- Hyper- or hypoglycemia
- Azotemia & hemodyalisis

Predisposing conditions:

- Renal, adrenal & pituitary disease
- Hyperemesis
- History of transplantation
- Severe burns
- Prolonged use of diuretics
- Paraneoplastic disease

Pattern 9: Symmetric Central Pontine Involvement

Osmotic Demyelination Syndrome

- Olygodendrocytes are especially vulnerable to osmotic changes (particularly at the pons).
- Was classically called central pontine myelinolysis.
- Nevertheless, any brain cells can be affected by osmotic imbalance.
- **Location:**
  - Isolated pontine lesions (50%)
  - Pontine & extrapontine (30%)
  - Extrapontine only (20%)

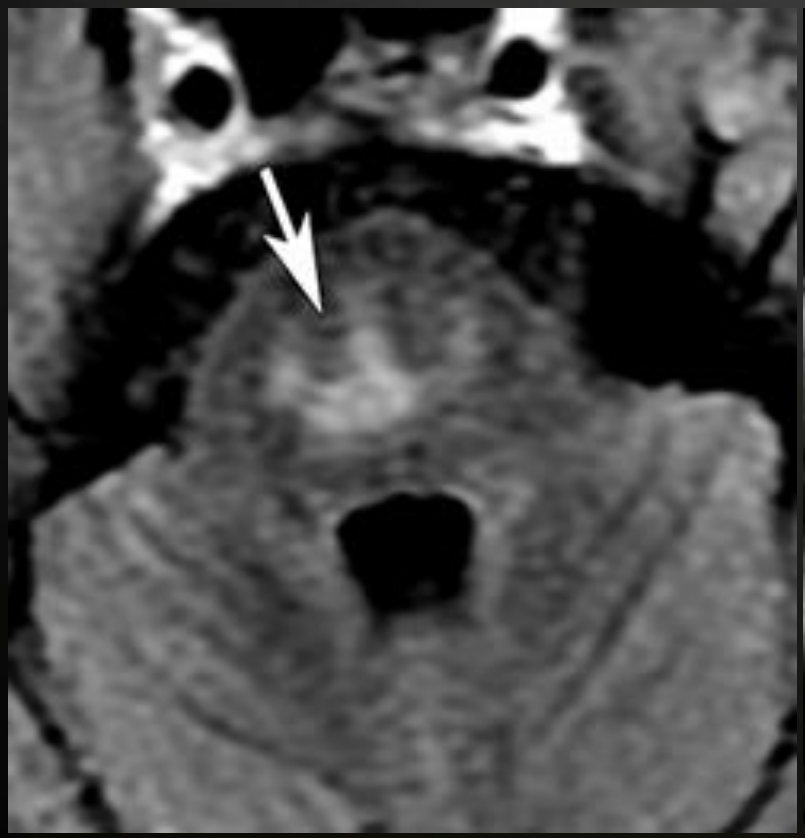
Pattern 9: Symmetric Central Pontine Involvement

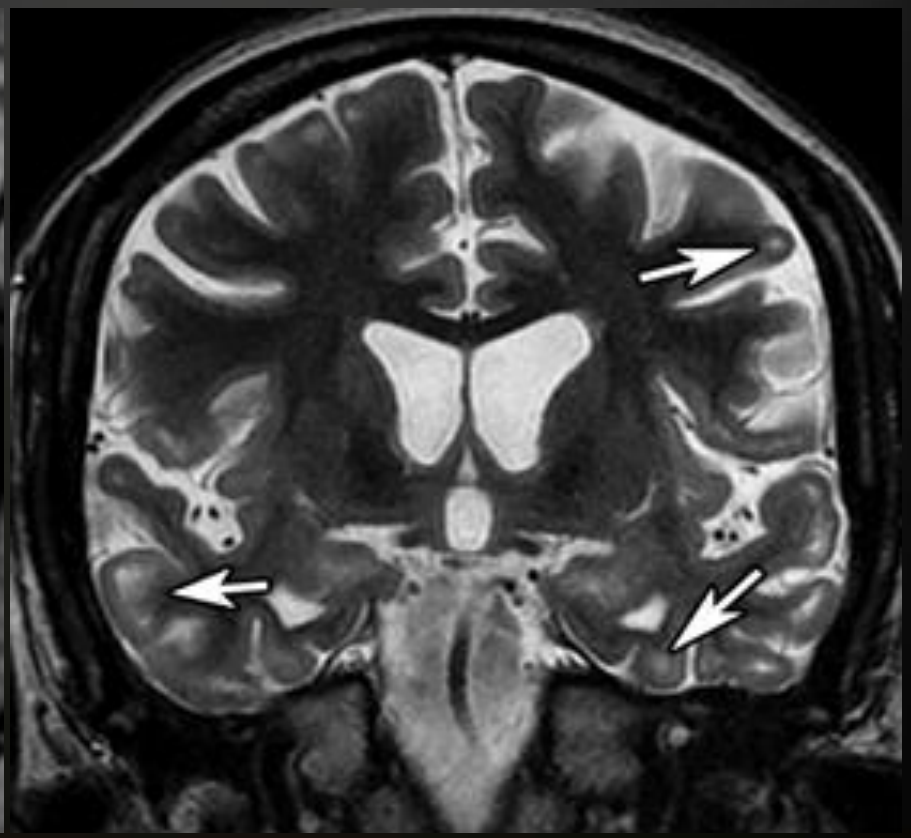
Osmotic Demyelination Syndrome

- **Imaging findings:**
  - Well demarcated & symmetric, rounded or trident shaped lesions on the central pons that classically spare the peripheral pons and corticospinal tract regions.
  - Sparing of the transverse pontine fibers
  - Hypodense on CT
  - Hyperintense on T2WI & T2 FLAIR
  - Restricted diffusion on DWI-ADC (acute phase)
  - Extrapontine sites: basal ganglia, thalami and hemispheric white matter often symmetrically (juxtacortical).

Pattern 9: Symmetric Central Pontine Involvement

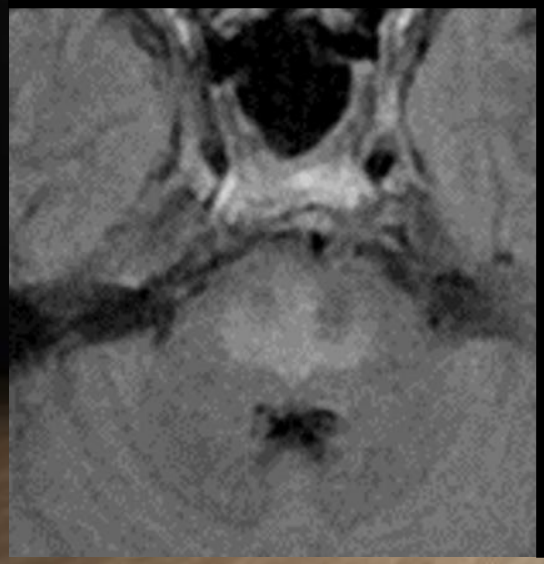
Osmotic Demyelination Syndrome

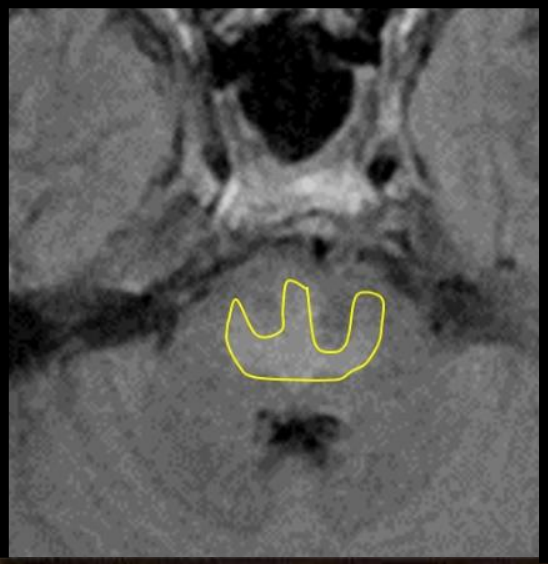


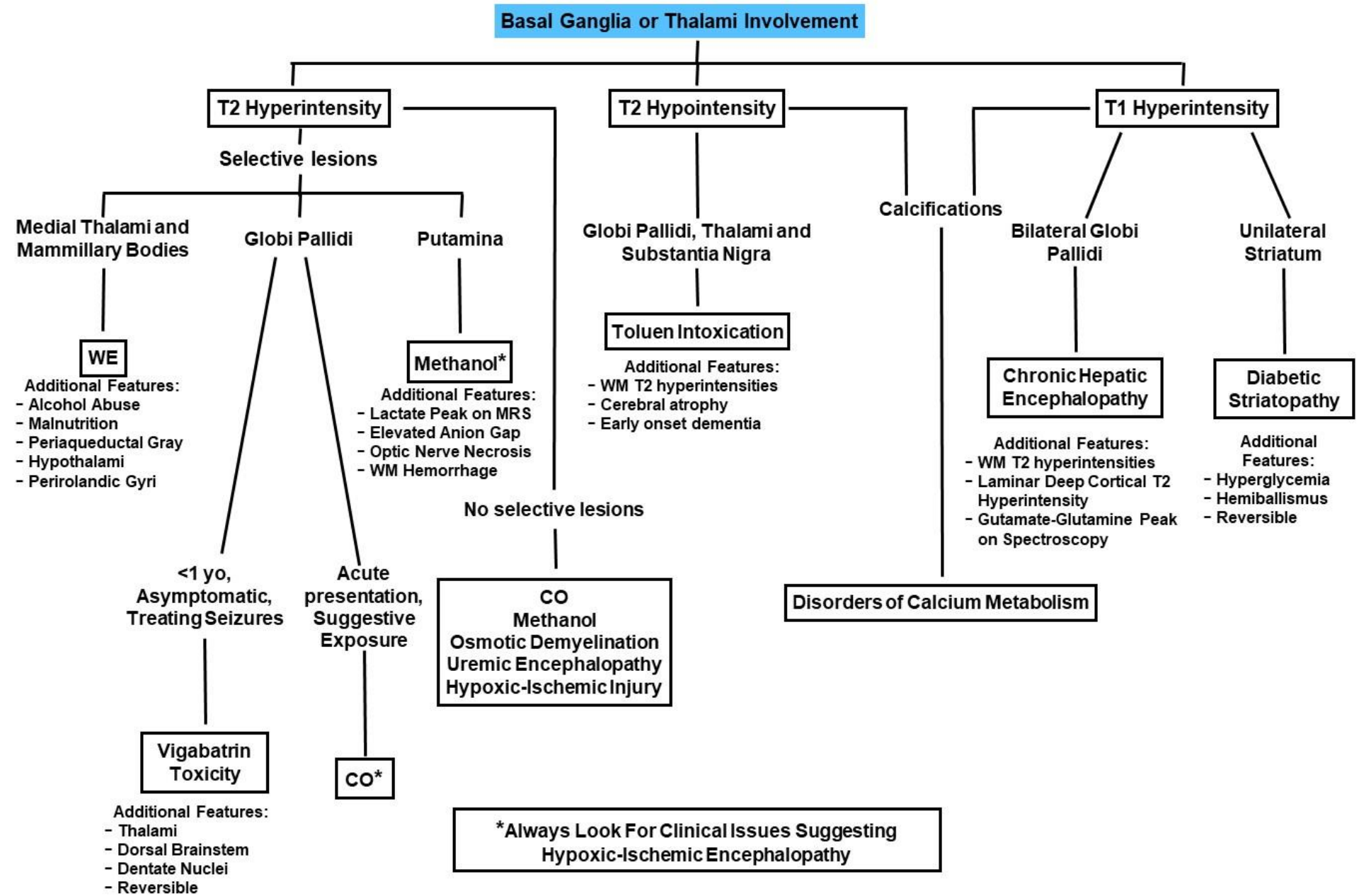


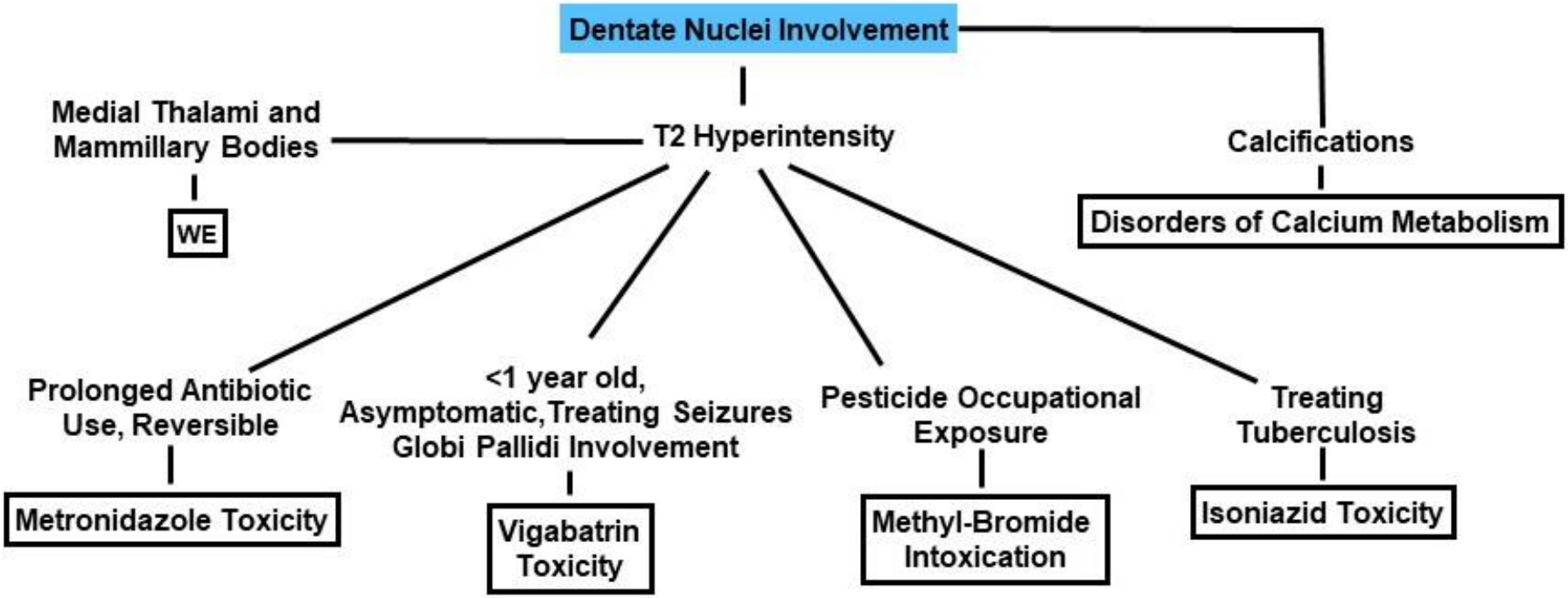
Pattern 9: Symmetric Central Pontine Involvement

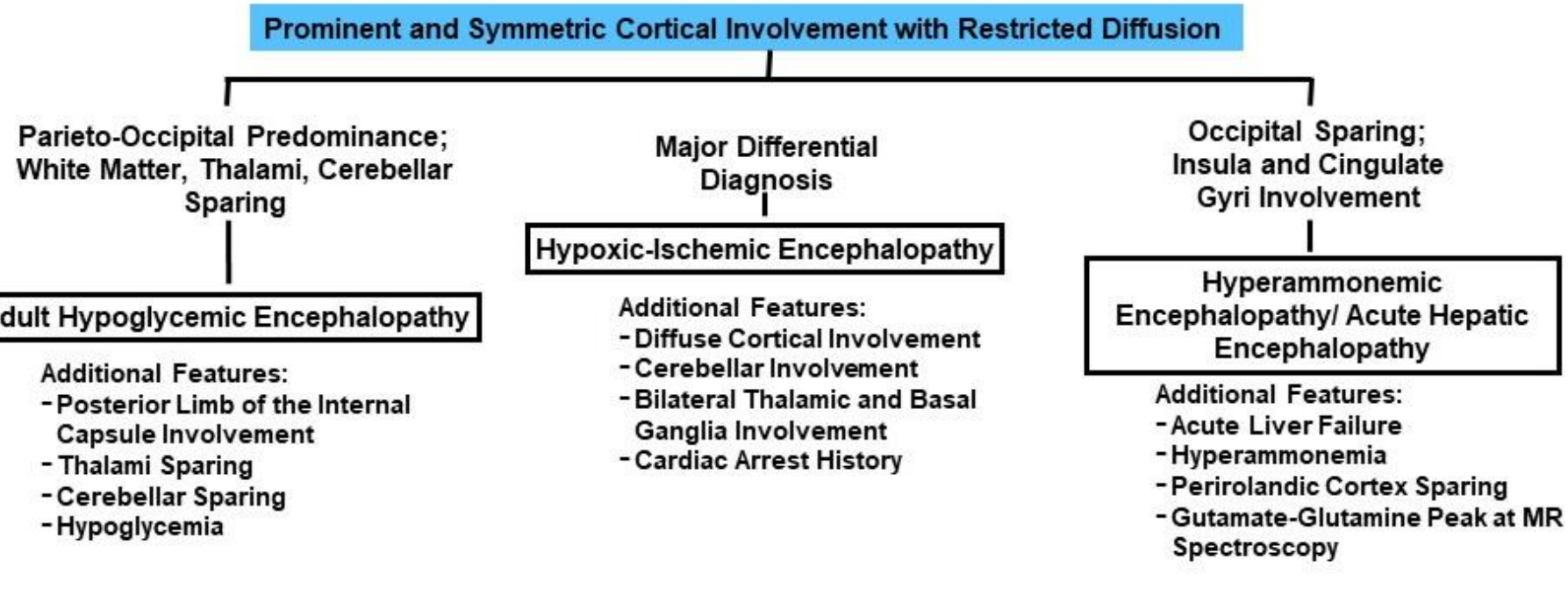
Osmotic Demyelination Syndrome

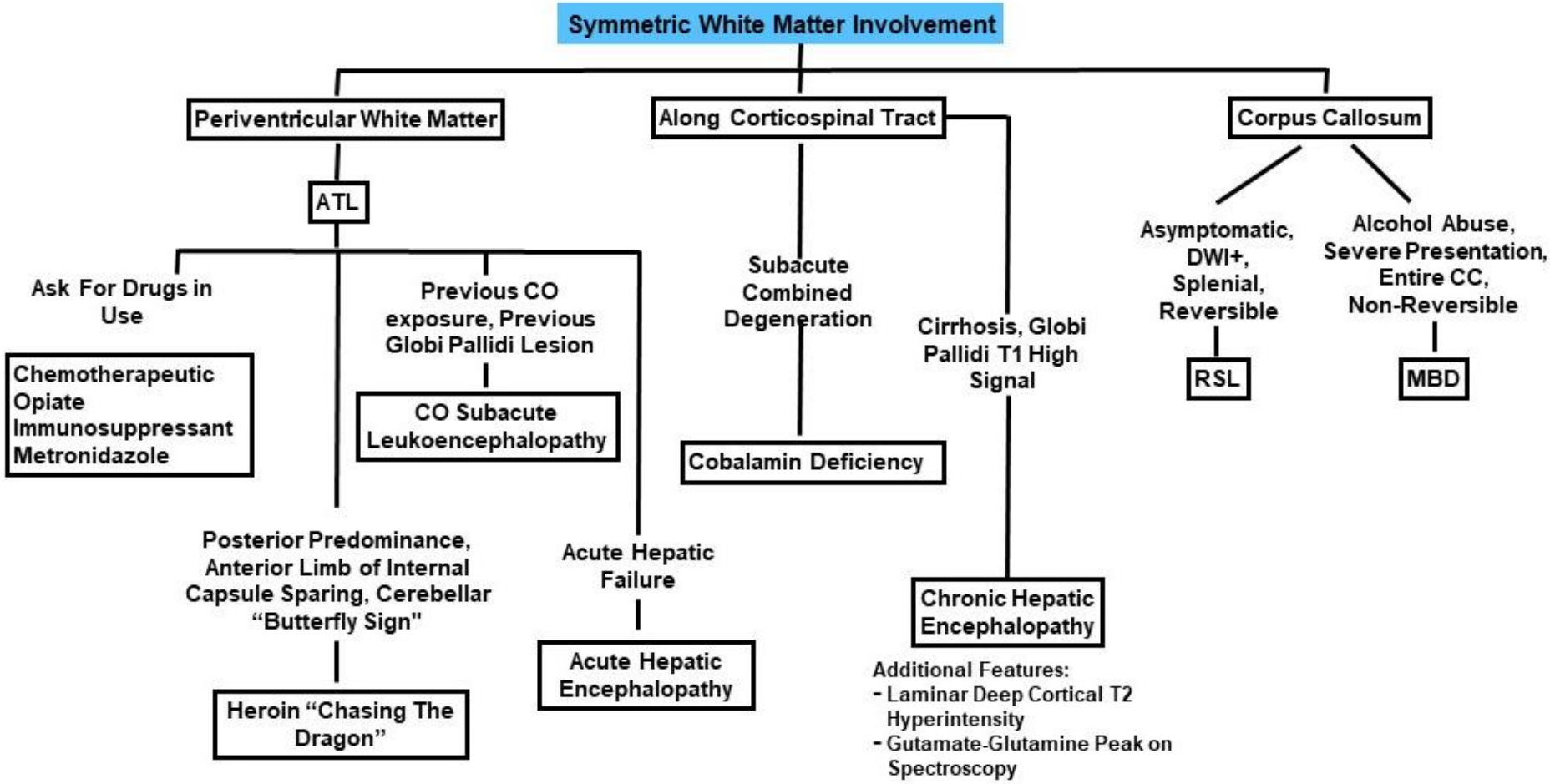




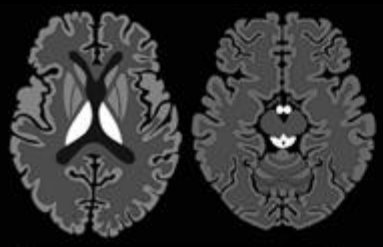

Basal Ganglia or Thalami Involvement
T2 Hyperintensity
T2 Hypointensity
T1 Hyperintensity
Selective lesions
Medial Thalami and Mammillary Bodies
Globi Pallidi
Putamina
Globi Pallidi, Thalami and Substantia Nigra
Calcifications
Bilateral Globi Pallidi
Unilateral Striatum
WE
Additional Features:
- Alcohol Abuse
- Malnutrition
- Periaqueductal Gray
- Hypothalami
- Perirolandic Gyri
Methanol*
Additional Features:
- Lactate Peak on MRS
- Elevated Anion Gap
- Optic Nerve Necrosis
- WM Hemorrhage
Toluen Intoxication
Additional Features:
- WM T2 hyperintensities
- Cerebral atrophy
- Early onset dementia
Chronic Hepatic Encephalopathy
Additional Features:
- WM T2 hyperintensities
- Laminar Deep Cortical T2 Hyperintensity
- Gutamate-Glutamine Peak on Spectroscopy
Diabetic Striatopathy
Additional Features:
- Hyperglycemia
- Hemiballismus
- Reversible
No selective lesions
<1 yo, Asymptomatic, Treating Seizures
Acute presentation, Suggestive Exposure
CO
Methanol
Osmotic Demyelination
Uremic Encephalopathy
Hypoxic-Ischemic Injury
Disorders of Calcium Metabolism
Vigabatrin Toxicity
Additional Features:
- Thalami
- Dorsal Brainstem
- Dentate Nuclei
- Reversible
CO*
*Always Look For Clinical Issues Suggesting Hypoxic-Ischemic Encephalopathy


Dentate Nuclei Involvement
Medial Thalami and Mammillary Bodies
T2 Hyperintensity
Calcifications
WE
Disorders of Calcium Metabolism
Prolonged Antibiotic Use, Reversible
<1 year old, Asymptomatic, Treating Seizures Globi Pallidi Involvement
Pesticide Occupational Exposure
Treating Tuberculosis
Metronidazole Toxicity
Vigabatrin Toxicity
Methyl-Bromide Intoxication
Isoniazid Toxicity

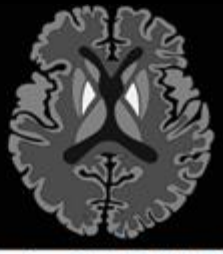

Prominent and Symmetric Cortical Involvement with Restricted Diffusion
Parieto-Occipital Predominance; White Matter, Thalami, Cerebellar Sparing
Adult Hypoglycemic Encephalopathy
Additional Features:
- Posterior Limb of the Internal Capsule Involvement
- Thalami Sparing
- Cerebellar Sparing
- Hypoglycemia
Major Differential Diagnosis
Hypoxic-Ischemic Encephalopathy
Additional Features:
- Diffuse Cortical Involvement
- Cerebellar Involvement
- Bilateral Thalamic and Basal Ganglia Involvement
- Cardiac Arrest History
Occipital Sparing; Insula and Cingulate Gyri Involvement
Hyperammonemic Encephalopathy/ Acute Hepatic Encephalopathy
Additional Features:
- Acute Liver Failure
- Hyperammonemia
- Perirolandic Cortex Sparing
- Gutamate-Glutamine Peak at MR Spectroscopy


Symmetric White Matter Involvement
Periventricular White Matter
Along Corticospinal Tract
Corpus Callosum
ATL
Ask For Drugs in Use
Chemotherapeutic
Opiate
Immunosuppressant
Metronidazole
Previous CO exposure, Previous Globi Pallidi Lesion
CO Subacute Leukoencephalopathy
Posterior Predominance, Anterior Limb of Internal Capsule Sparing, Cerebellar "Butterfly Sign"
Heroin "Chasing The Dragon"
Acute Hepatic Failure
Acute Hepatic Encephalopathy
Subacute Combined Degeneration
Cobalamin Deficiency
Cirrhosis, Globi Pallidi T1 High Signal
Chronic Hepatic Encephalopathy
Additional Features:
- Laminar Deep Cortical T2 Hyperintensity
- Gutamate-Glutamine Peak on Spectroscopy
Asymptomatic, DWI+, Splenial, Reversible
RSL
Alcohol Abuse, Severe Presentation, Entire CC, Non-Reversible
MBD

Suggestive Sites of Involvement



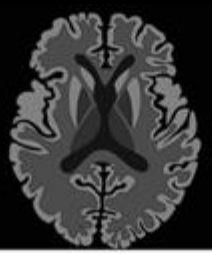
Thalami, Mammillary Bodies and Tectum:
Wernicke Encephalopathy



Selective Globi Pallidi T2 High Signal:
CO Poisoning

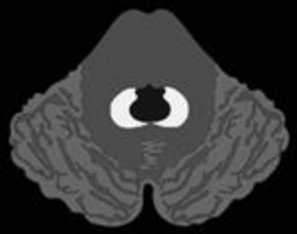
Globi Pallidi T1 High Signal:
Chronic Hepatic Encephalopathy

Selective Putamina T2 High Signal:
Methanol Poisoning

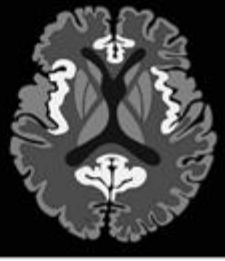


Thalami and Globi Pallidi T2 Low Signal:
Toluene Intoxication
Parathyroid Disorders

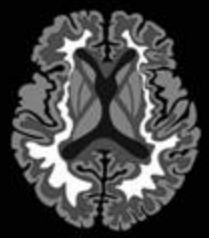
Unilateral Striatum T1 High Signal:
Diabetic Striatopathy



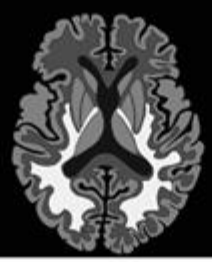
Dentate Nuclei:
Metronidazole
Isoniazid
Methyl-Bromide
Wernicke Encephalopathy



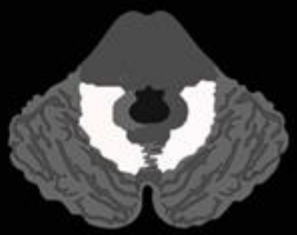
Insular and Cingulate Cortex:
Hyperammonemic Encephalopathy



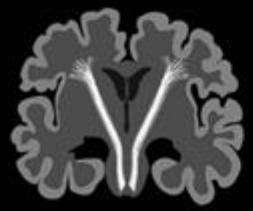
Periventricular White Matter Symmetric Restricted Diffusion:
ATL



ATL With Posterior Predominance:
Heroin Inhalation

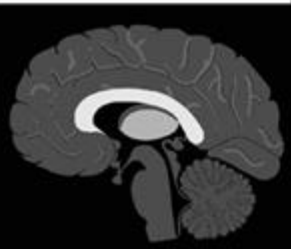


"Butterfly Wing":
Heroin Inhalation



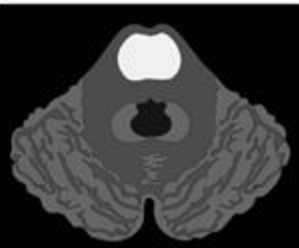
Corticospinal Tracts Involvement:
Chronic Hepatic Encephalopathy
Cobalamin Deficiency

Splenium:
CLOCCs



Corpus Callosum:
MBD
CLOCCs

Parieto-Occipital Vasogenic Edema:
PRES



Central Pons:
ODS

Conclusion

- Neuroimaging diagnosis of toxic & metabolic brain disorders remains **challenging**.
- Heterogenous groups & unspecific.
- But some condition can be quite specific and can help guide the diagnosis.
- **Pattern based approach can be used** to reduce the number of differential diagnosis.
- **Clinical history** should always be looked as it points to subjacent toxic and metabolic causes.

Thank you for your attention