



# CLINICAL NEUROIMAGING OF THIAMINE DEFICIENCY

JEROME J. GRABER, MD, MPH

ASSOCIATE PROFESSOR OF NEUROLOGY AND NEUROSURGERY

UNIVERSITY OF WASHINGTON, SEATTLE CANCER CARE  
ALLIANCE

SEATTLE, WA



# ASNI 2021 DISCLOSURE

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company in the past 24 months which could be considered a conflict of interest. I'd like to voluntarily disclose that I serve on the Social Media Board of the Journal of Neuroimaging



# 47 YEAR OLD WOMAN WITH MEMORY LOSS

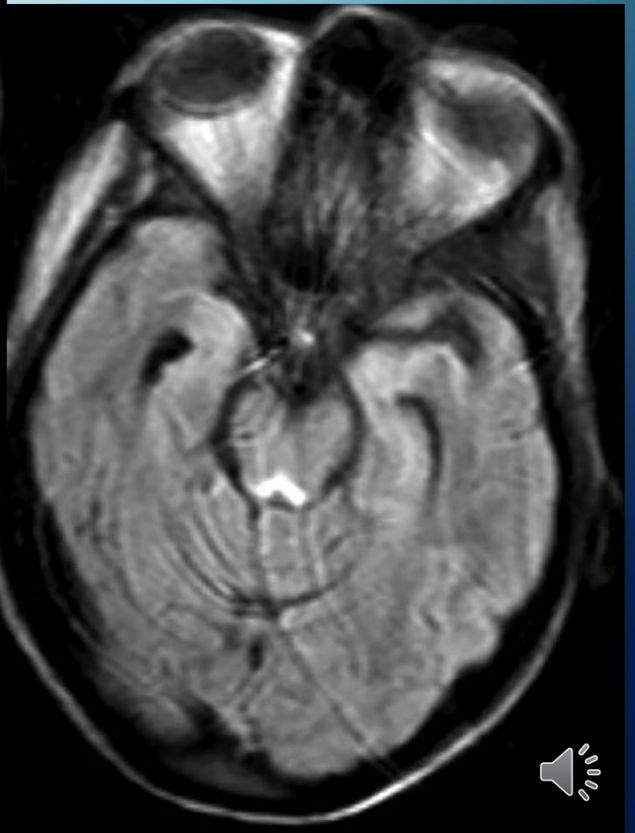
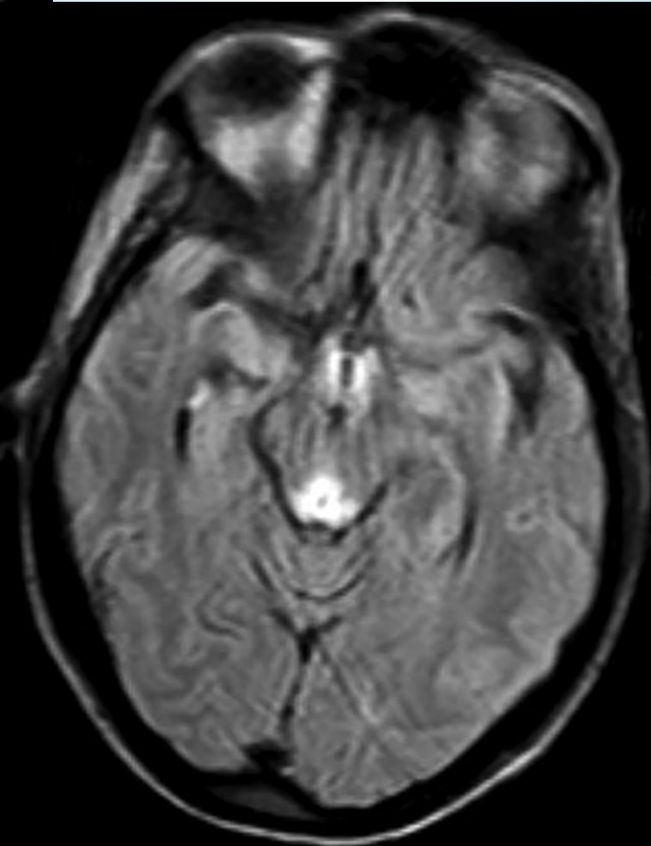
- Three years ago had laryngeal cancer treated with:
  - Radiation, docetaxel, 5-fluorouracil, cisplatin (which caused ESRD needing dialysis)
- Three months ago locoregional recurrence, refused feeding tube placement and has lost 43 kg in last 6 mo.
- Now admitted with nausea, bacteremic, given ampicillin
- Improved and tolerating PO, but then became confused, tremulous and impaired short term memory a few days later, with unstable gait and reporting blurry vision



# 47 YEAR OLD WOMAN WITH MEMORY LOSS

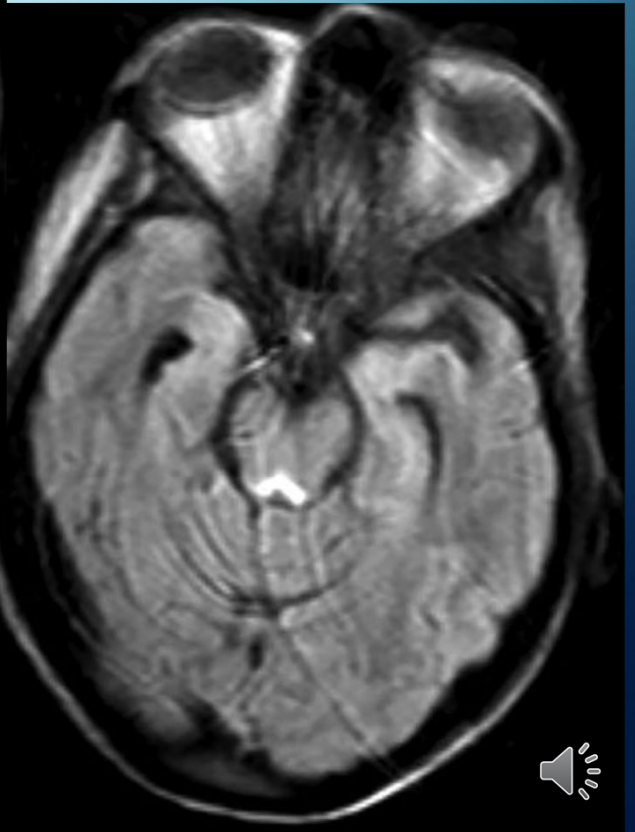
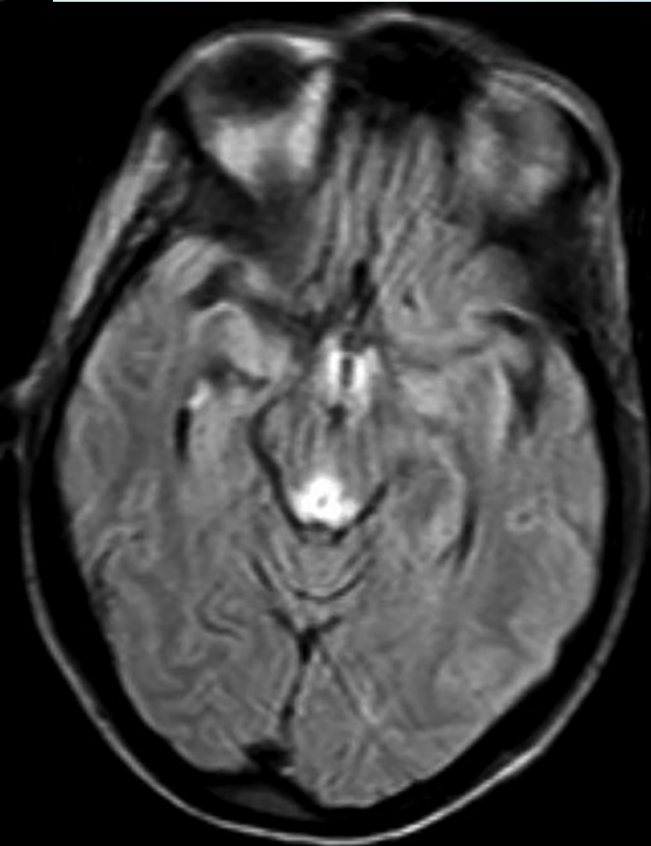
- Summary: Recurrent laryngeal cancer, lost 43 kg in last 6 mo, bacteremia treated with ampicillin, but then confused, tremulous, amnesic
- On exam: drowsy, inattentive, very impaired short term memory, horizontal rapid nystagmus, truncal ataxia (could not ambulate or even sit up in bed without using arms)
- CSF cytology, protein and cell counts normal.





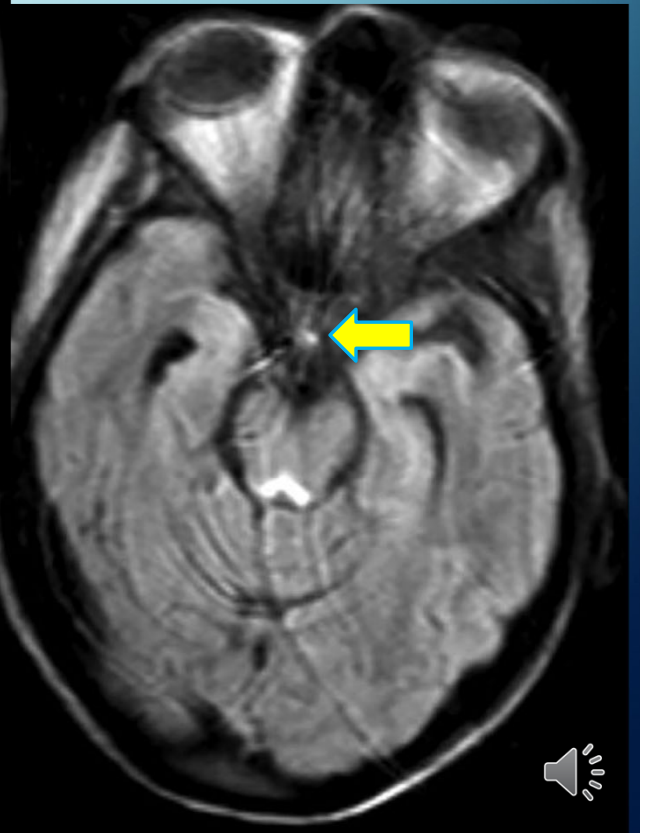
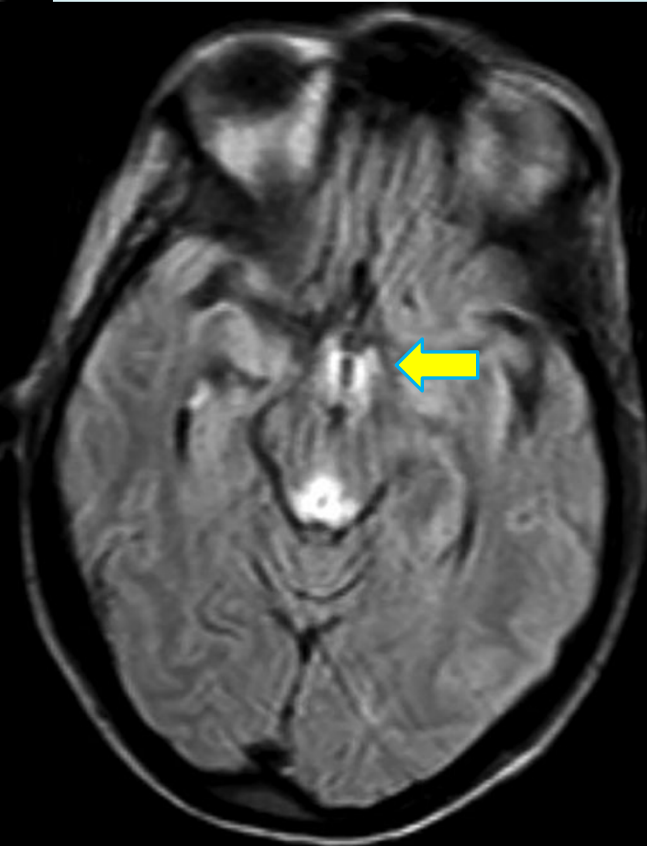
No enhancement or DWI changes





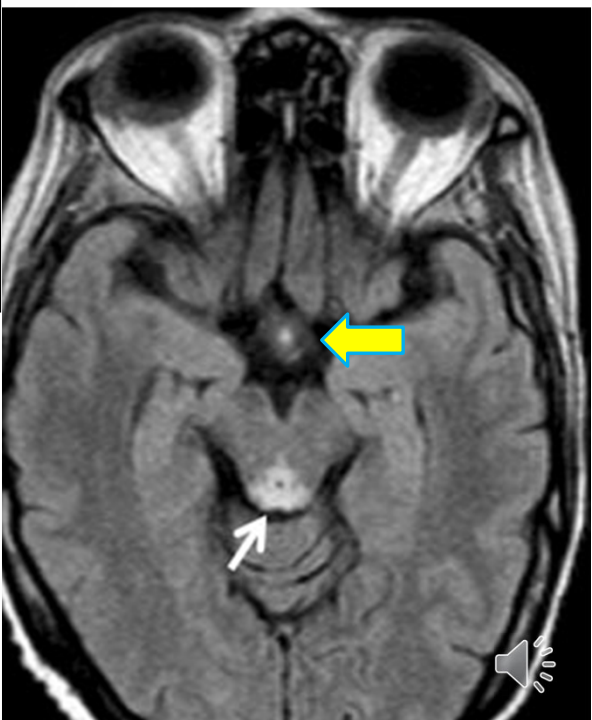
How many abnormal lesions do you see?



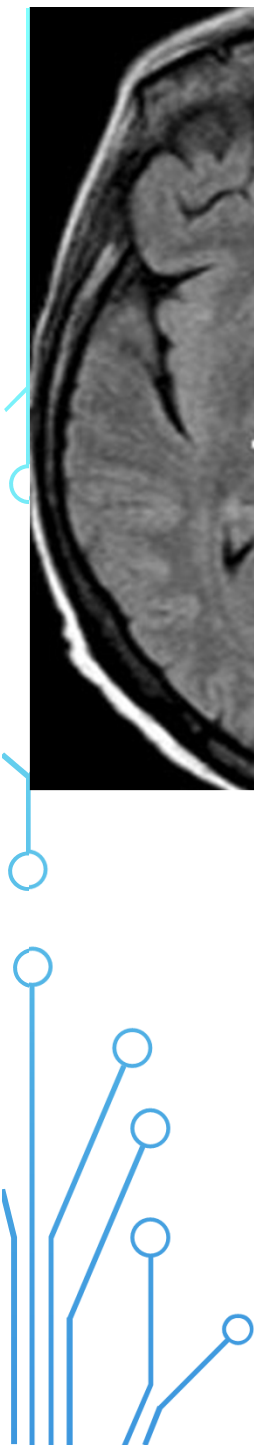


Medial thalami, tectal plate and periaqueductal region....AND mamillary bodies, 3<sup>rd</sup> ventricle periaqueductal grey and pituitary stalk (?)





This is another case (that held still!). Looks strikingly similar....

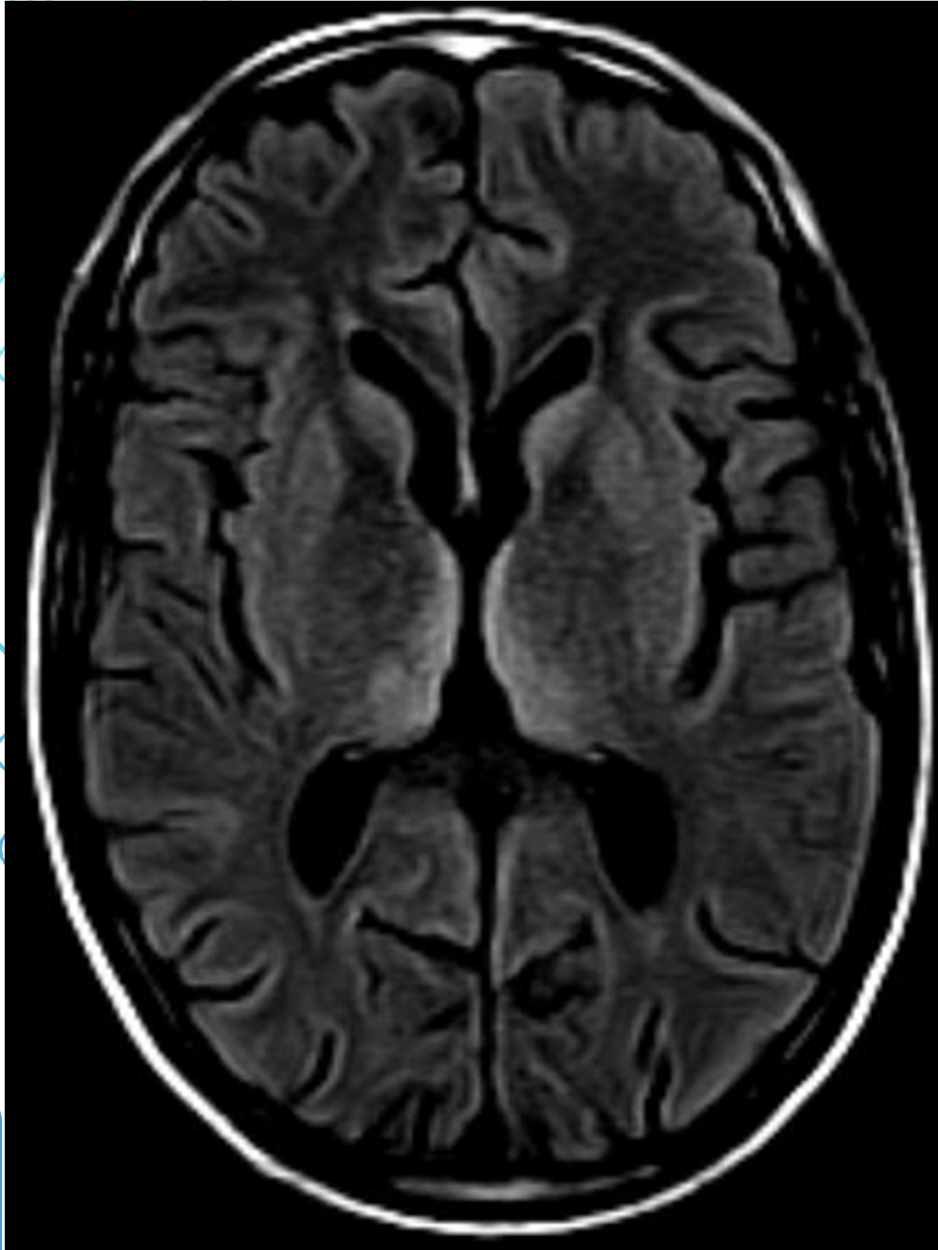


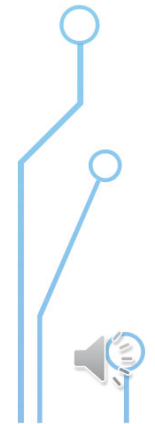
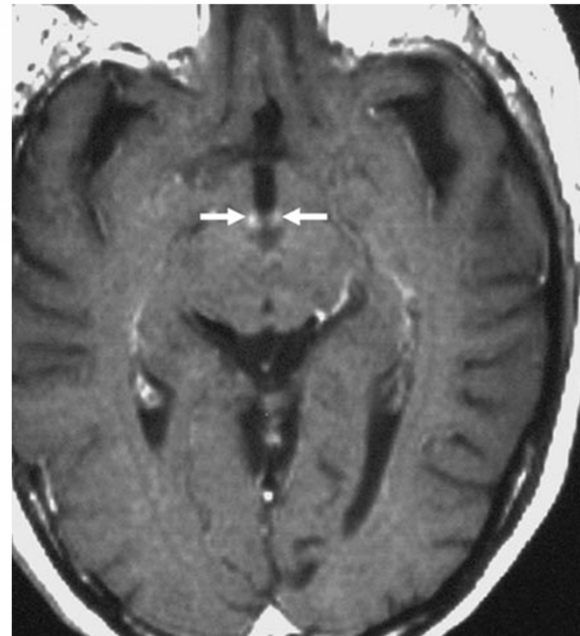
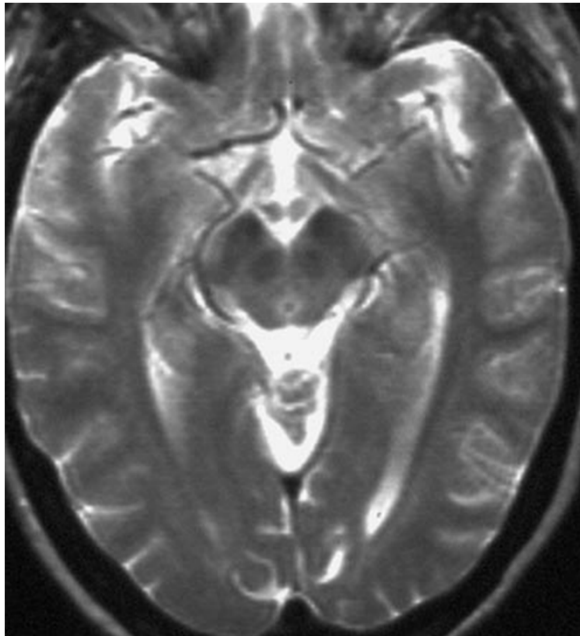
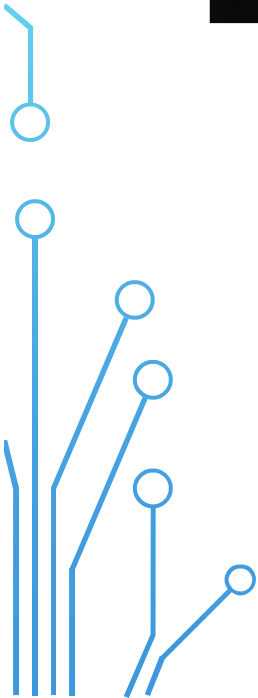
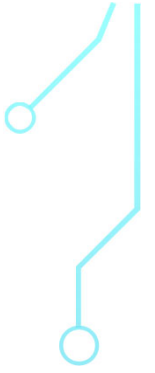
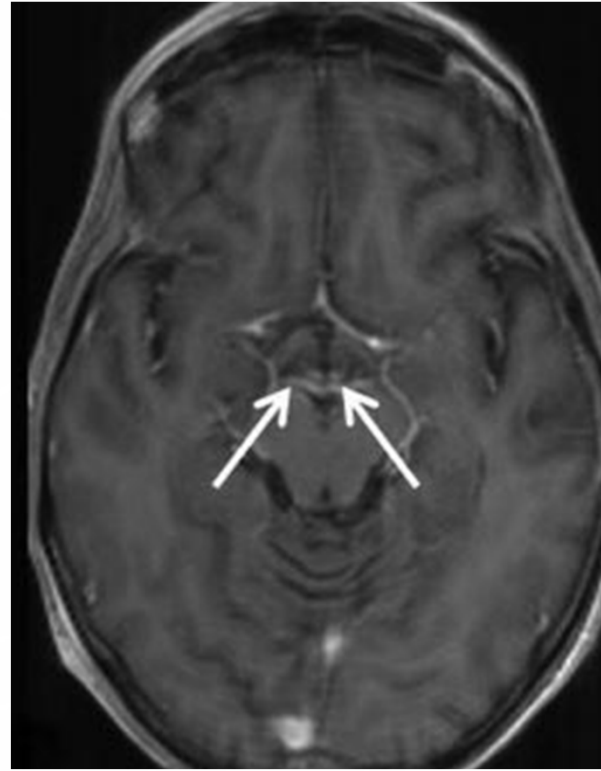
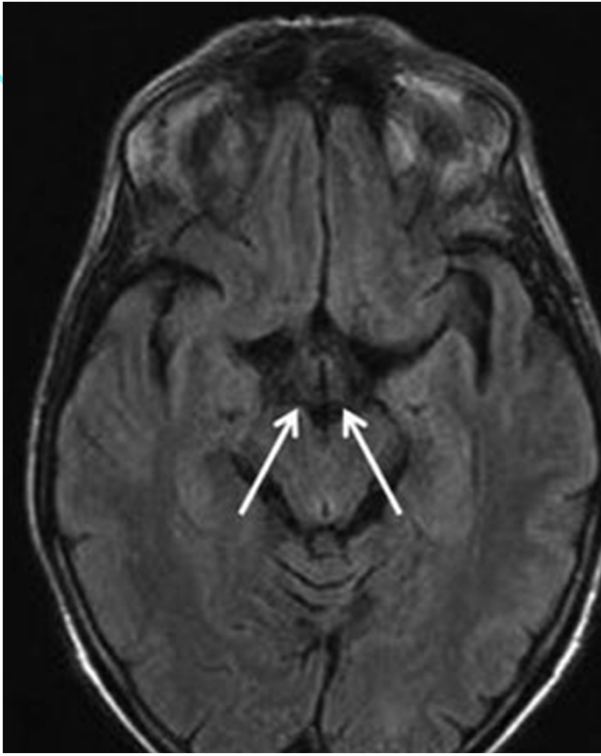
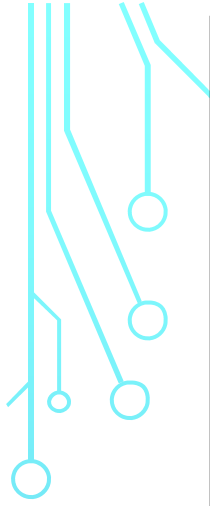


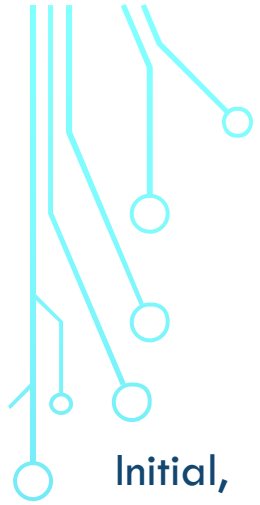
# 47 YEAR OLD WOMAN WITH MEMORY LOSS

- Summary: Recurrent laryngeal cancer, lost 43 kg in last 6 mo, bacteremia treated with ampicillin, but then confused, tremulous, amnesic
- On exam: drowsy, inattentive, severe short term memory impairment, horizontal rapid nystagmus, truncal ataxia
- Treated with IV thiamine 500mg q8hr x 5 days
- Rapid improvement in attention, nystagmus and gait, but persistent moderate residual short term memory loss

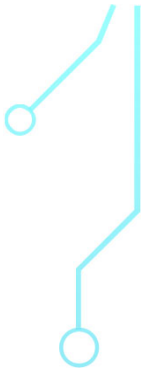
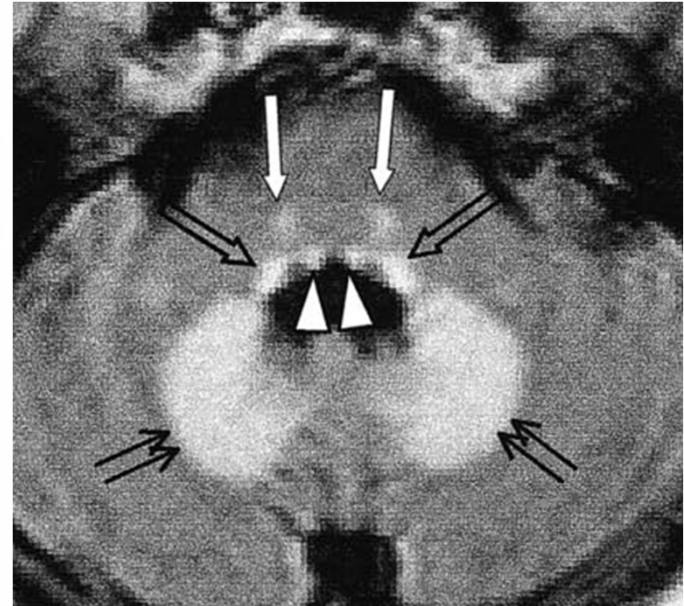
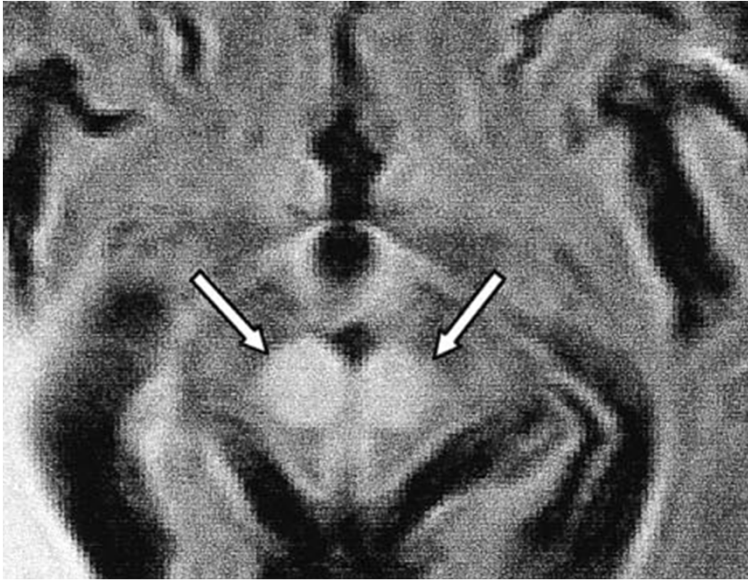




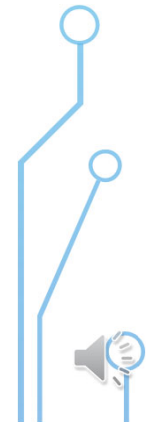
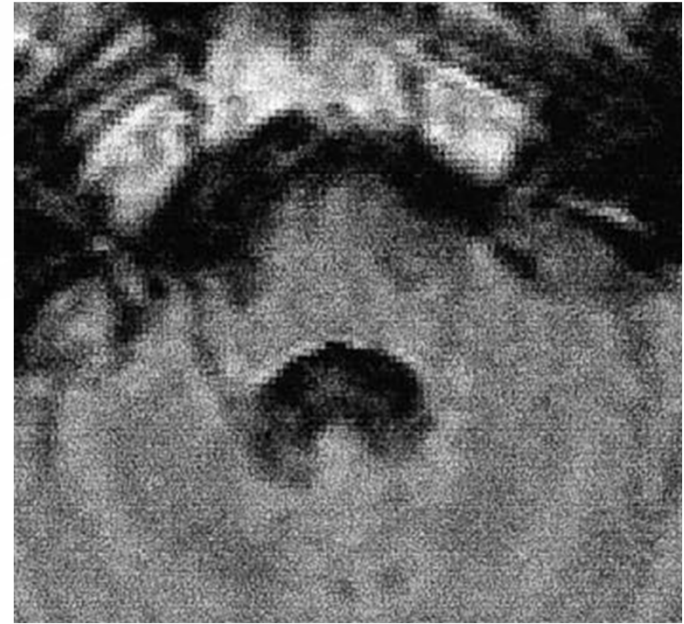
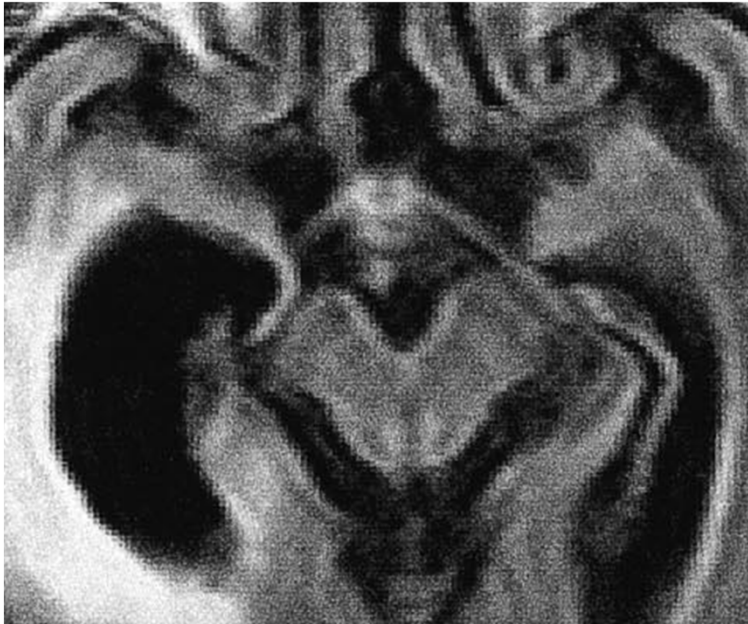




Initial,  
treated  
with IV  
thiamine



40  
days  
later



# DIFFERENTIAL DIAGNOSES- MRI

- Abnormal symmetric FLAIR hyperintense signal in the medial thalami can be due to:
  - deep cerebral venous thrombosis
  - top-of-the-basilar syndrome
  - artery of Percheron infarct
  - viral encephalitis
  - atypical CJD (both can have “hockey stick” pulvinar sign)
  - PCNSL (should not be as symmetric)
  - West Nile and other viral meningoencephalitis
  - Marchiafava-Bignami Disease (chronic toxic demyelination of corpus callosum & splenium, usually enhances with cystic degeneration (T1 hypointense) and has global atrophy)
  - Biotin-thiamine responsive Basal Ganglia Disease (SLC25A19 mutations)
- Differential diagnosis of abnormal FLAIR hyperintense signal in the dentate nuclei, cranial nerve nuclei, red nuclei, and splenium should include metronidazole-induced encephalopathy and other toxic exposures



# PREDISPOSING CONDITIONS:

- Cancer (esp. hematologic or GI)
- HIV
- Chronic Renal Insufficiency
- Diabetes
- Hyperemesis gravidarum
- Cannabis hyperemesis syndrome
- Chronic pancreatitis
- Sequelae of GI surgeries

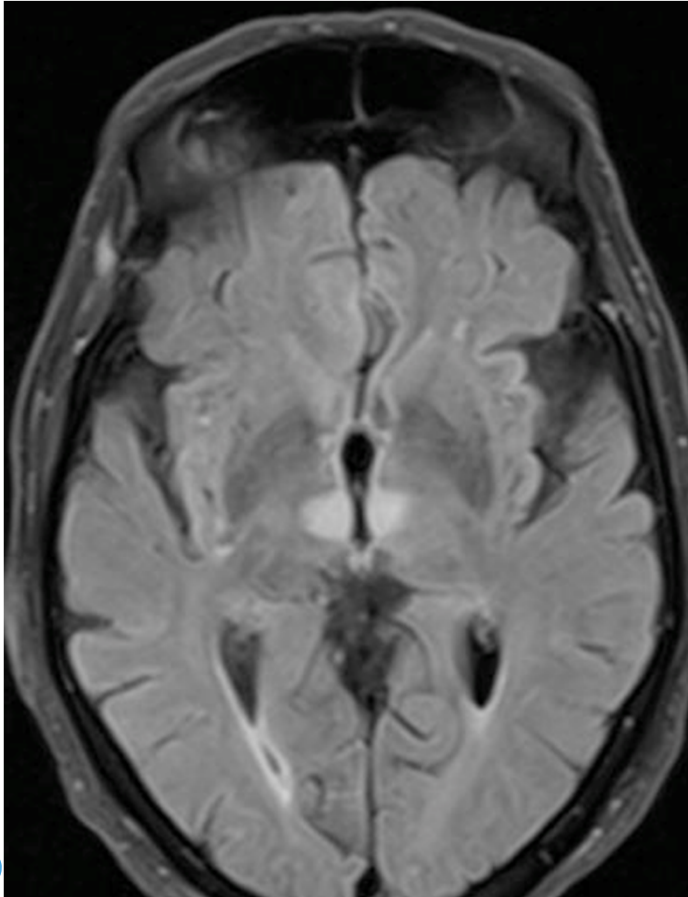
2020 Apr;74(4):663-665. doi: 10.1038/s41430-020-0592-9.

2019 Aug 22;19(4):154-156. doi: 10.1016/j.tjem.2019.08.001.

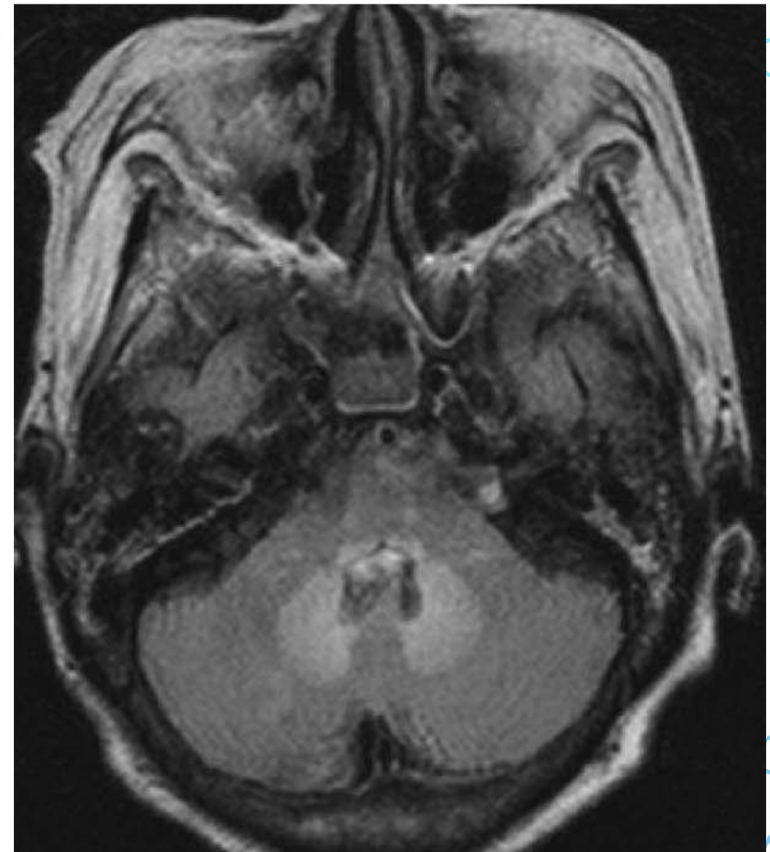
2019 Jul 9;11(7):e5109. doi: 10.7759/cureus.5109.



Artery of Percheron infarct



Metronidazole-induced encephalopathy



Courtesy of Dr. Vias Hatzoglou, Memorial Sloan Kettering, with permission



## OTHER IMAGING FINDINGS

- HALF of patients with clinical Wernicke's encephalopathy responsive to thiamine have NORMAL MRI
- Case reports have found hypometabolism of mamillary bodies and hippocampus on FDG-PET
- MRI has shown edema of affected muscles in thiamine deficient neuropathy

Antunez E, et al. Usefulness of CT and MR imaging in the diagnosis of acute Wernicke's encephalopathy. AJR Am J Roentgenol. 1998;171(4):1131.

2018 Dec 11;9:1083. doi: 10.3389/fneur.2018.01083.

2019 Jul;44(7):e456-e457. doi: 10.1097/RLU.0000000000002601





# BIOCHEMICAL, HISTOPATHOLOGIC AND IMAGING CORRELATION

- Thiamine is a water-soluble vitamin involved in the maintenance of cell membrane integrity and osmotic gradients across membranes
- Stored as thiamine diphosphate (TDP), especially in the liver
- Essential cofactor for the pyruvate dehydrogenase (converts pyruvate to acetyl-CoA) and alpha-ketoglutarate dehydrogenase complexes in the Krebs cycle
- TDP is also an important cofactor of the enzyme transketolase in the pentose phosphate pathway
- Reduced Krebs cycle and pentose phosphate pathway efficiency has negative downstream effects



# BIOCHEMICAL, HISTOPATHOLOGIC AND IMAGING CORRELATION

- Reduced passage of pyruvate into Krebs cycle produces cellular energy deficit and intracellular accumulation of toxic intermediates such as lactate; decreased pH and acidosis
- Intracellular accumulation of glutamate leads to impaired function of ATP-dependent cellular pumps which limits maintenance of cellular electrolyte homeostasis
- Discharge of glutamate into the extracellular space
- Excessive extracellular glutamate leads to excitatory damage of neurons



# BIOCHEMICAL, HISTOPATHOLOGIC AND IMAGING CORRELATION

- Glial cells and neurons cannot adequately control ionic gradients across cell membranes and cytotoxic edema ensues
- Thiamine deficiency can also induce BBB dysfunctions with development of vasogenic edema
- Acute WE pathologic findings: intra- and extracellular edema, increased microglial cells, variable degrees of necrosis, demyelination, vascular proliferation, petechial hemorrhage, and disruption of BBB
- Inferior colliculus seems particularly vulnerable in animal models, possibly due to its high metabolic rate related to constant gating of environmental monitoring

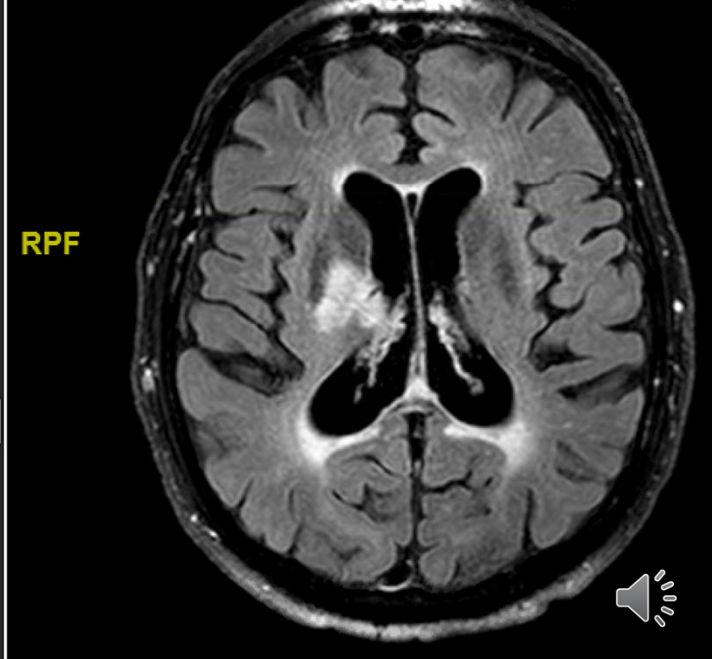
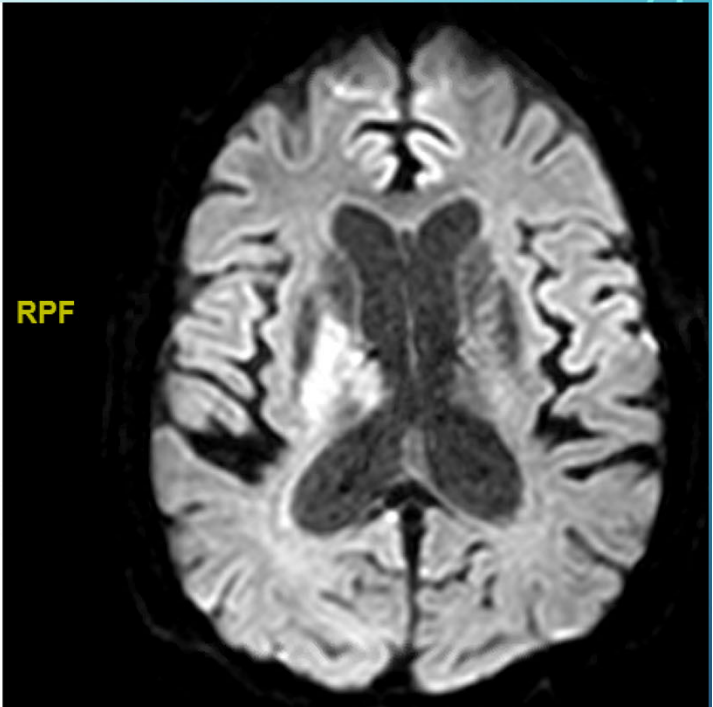
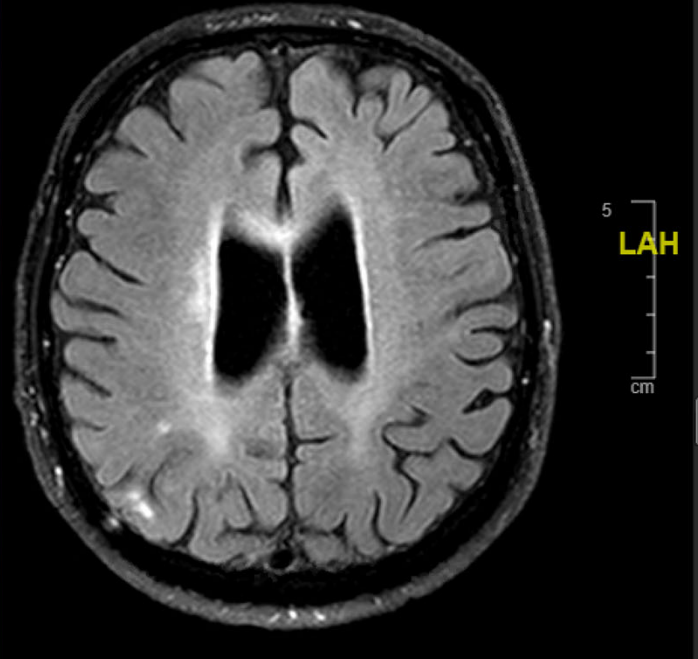
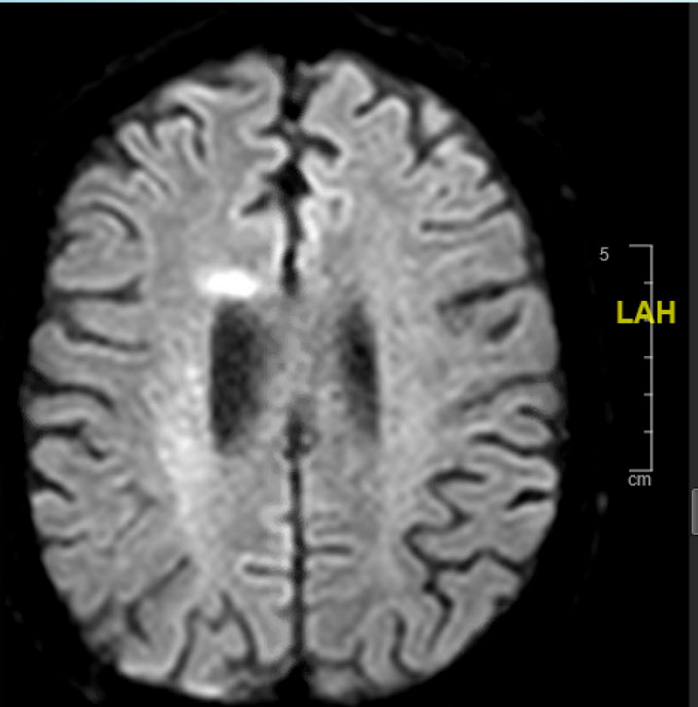


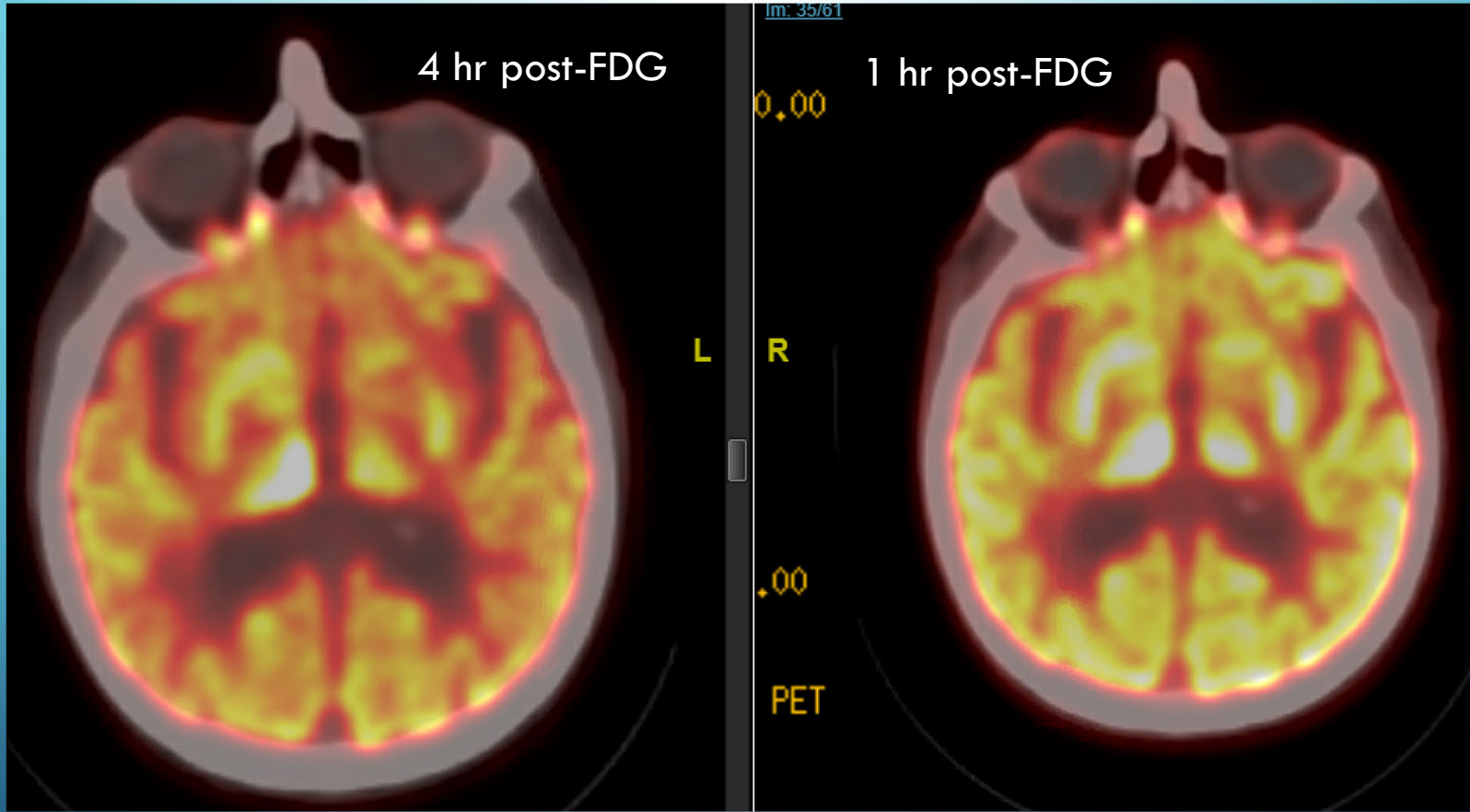
# 73 YEAR OLD MAN: MEMORY LOSS

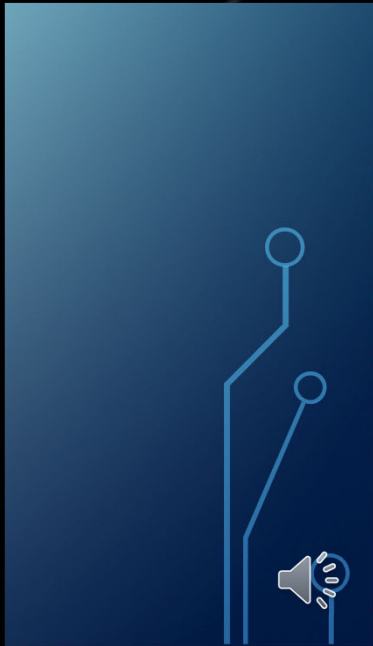
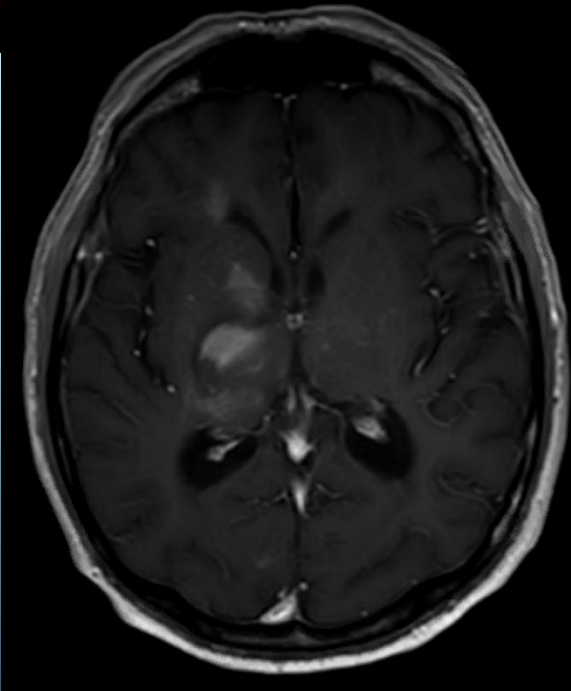
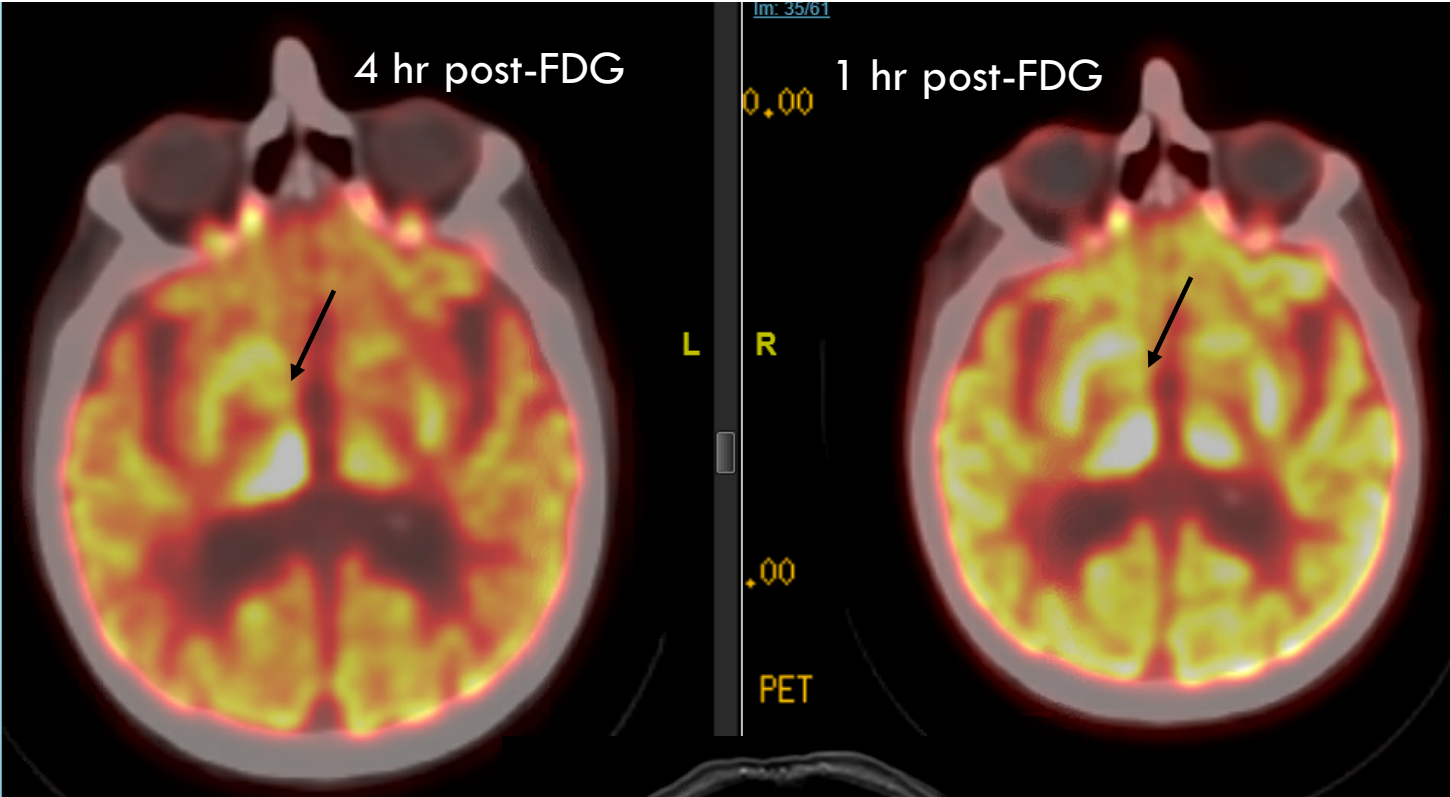
- Three years ago had PCNSL treated with:
  - Rituximab, methotrexate, temozolomide, cytarabine
- Achieved complete remission, mild residual memory loss
- Now had sudden onset severe memory impairment and behavioral changes
- Spouse reports poor appetite and 2-6 beers most days for last few months preceding this change
- On exam, severe memory loss, mild ataxia, eyes normal



DWI + ADC =  
No enhancement





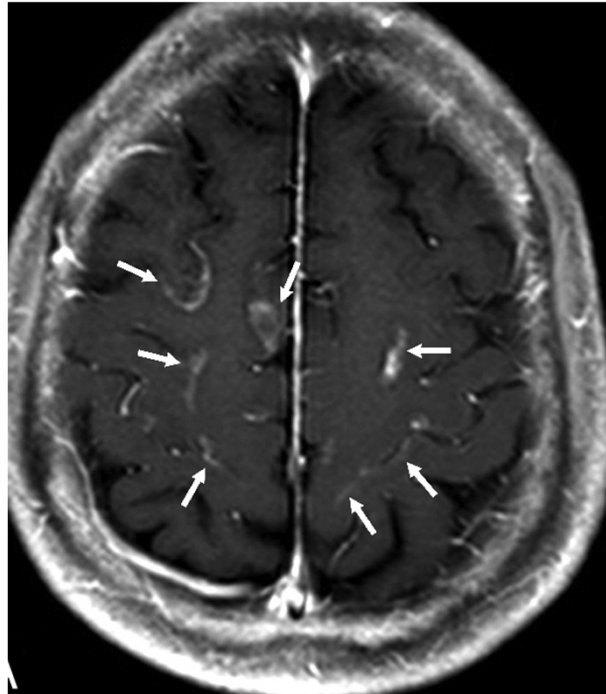
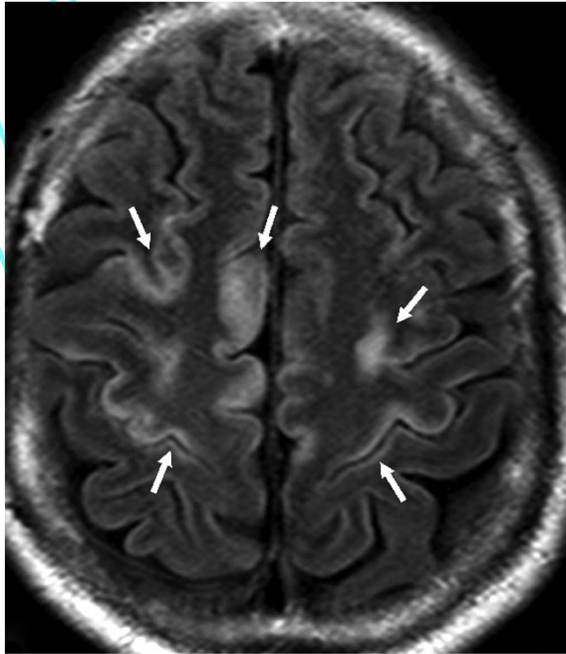


# WERNICKE VS METASTASES

- 10% of metastases do not enhance
  - More common on steroids or anti-angiogenic agents
- Usually asymmetrical
- PET imaging can differentiate from metastases or vascular lesions
  - Consider getting early vs delayed PET imaging

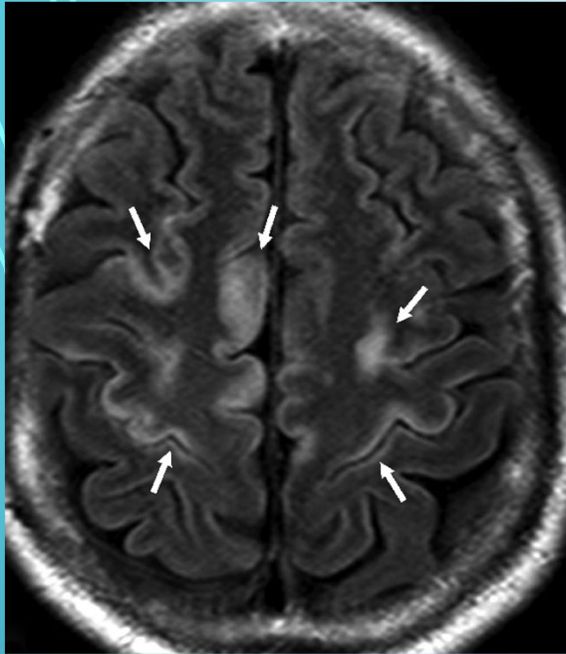




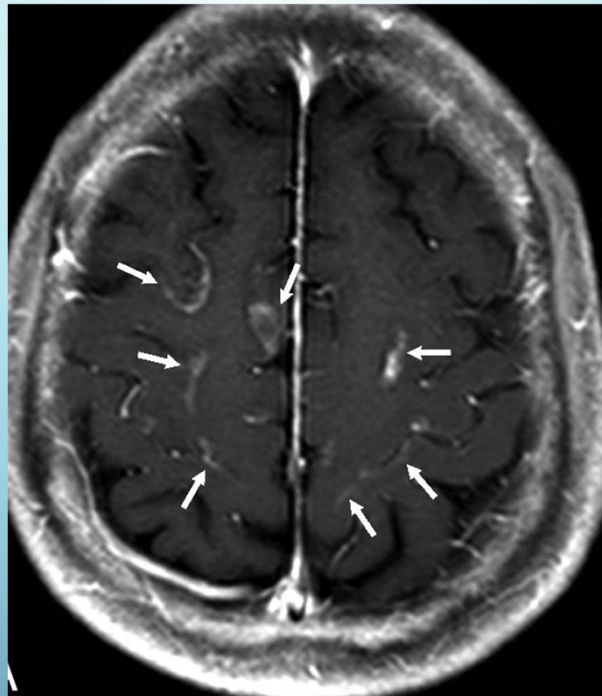


Courtesy of Dr. Vias Hatzoglou

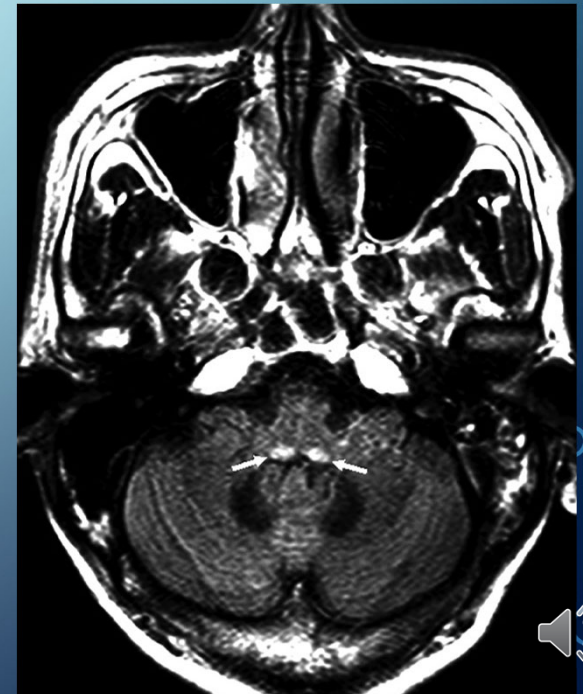




Leptomeningeal Metastases  
with Enhancement →



Non-enhancing FLAIR hyperintense ~  
thiamine deficiency (symmetric) →



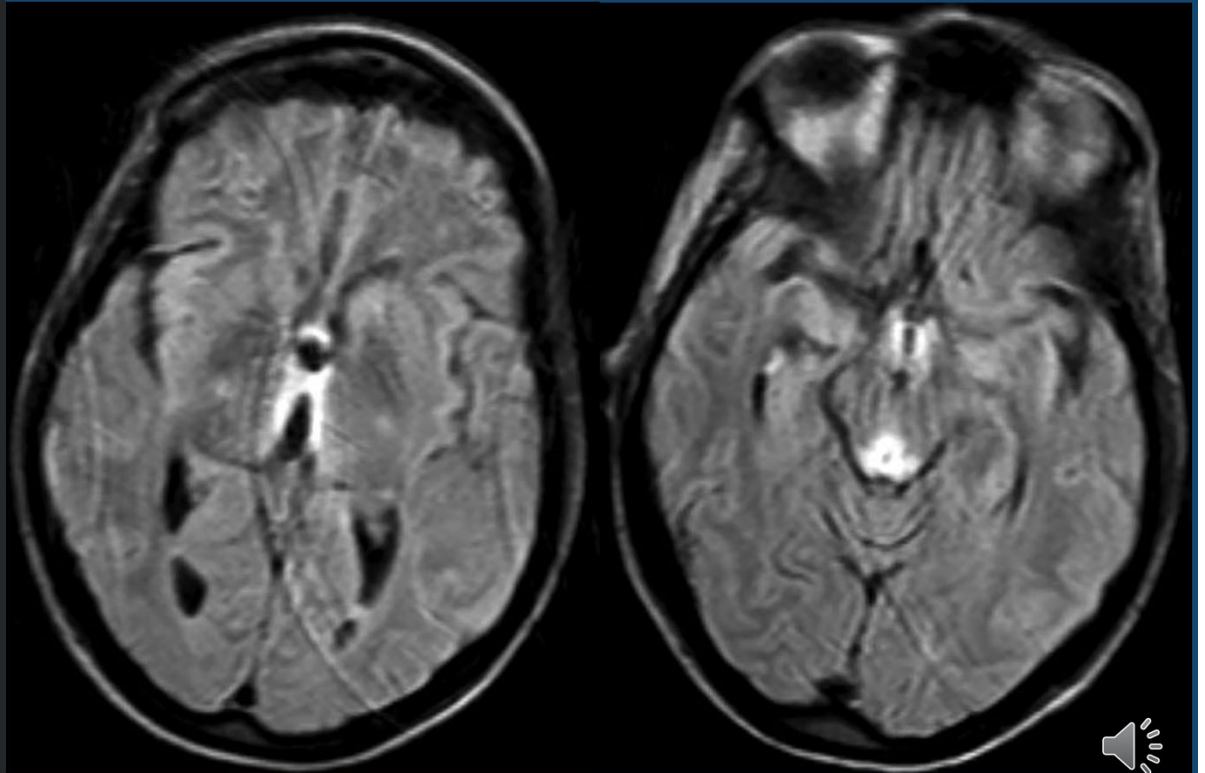
# SUMMARY

- Thiamine deficiency
  - Can occur in absence of alcohol (or known history)
  - Very typical imaging findings (mamillary bodies, thalami, 3<sup>rd</sup> and 4<sup>th</sup> ventricular walls)
  - 50% of clinical cases have normal MRI
  - Can be complicated and occur together with other findings
  - Easily TREATABLE
  - ALERT your clinical team IMMEDIATELY and prompt to start highly effective IV thiamine 400mg



## ACKNOWLEDGMENTS

- Dr. Vias Hatzoglou: Neuroradiology, Memorial Sloan Kettering Cancer Center, New York
- Dr. Elie Isenberg-Grzeda: Psychiatry, Sunnybrook Health Sciences Center, Odette Cancer Center, Toronto



## REFERENCES

2020 Dec 31;21:e928272. doi: 10.12659/AJCR.928272

2020 Dec 11;14:606345. doi: 10.3389/fnsys.2020.606345

2019 Jul;44(7):e456-e457. doi: 10.1097/RLU.0000000000002601

2018 Dec 11;9:1083. doi: 10.3389/fneur.2018.01083.

2016 Sep;3(3):196-207. doi: 10.1093/nop/npv036. Epub 2015 Sep 22

Antunez E, et al. Usefulness of CT and MR imaging in the diagnosis of acute Wernicke's encephalopathy. AJR Am J Roentgenol. 1998;171(4):1131.

