



An En-lyte-ening case of osmotic injury

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DISCLOSURES

- No conflicts of interest to disclose
- Consent was received from the patient for this presentation

CASE

- 58 year old female seen in the ED

- Past History

- Diabetes Type II
- Hypertension
- GERD

- Home Medications

- Metformin
- Ramipril
- Amlodipine
- On eprazole

- Social History

- Originally from Philippines
- Travel to Philippines: duration 1 month, returned 2 months prior to presentation, acute diarrheal illness while away – now resolved
- Lives with daughter
- Non-smoker, No alcohol

Compliance?

TIMELINE – DAY 1

- Confusion, slurred speech, and gait instability noted by family – prompting ED visit
- Complains of lightheadedness, paresthesias of hands and feet, generalized weakness
- Physical Exam
 - Vitals: **MAP 40 BP 70/30 mmHg, HR 30-40**, RR 16, SaO₂ 96% RA, T36.0, appears unwell “drowsy”
 - **GCS 12-13 (E₂₋₃V₄M₆)**, Dysarthria, Power 3/5 bilateral upper extremity, Power 4+/5 bilateral lower extremity (Reflexes, cranial nerves, sensation, gait and coordination not documented)
 - CVS: Junctional escape rhythm, grade II/VI systolic ejection murmur at the LUSB, Bilateral lower extremity pitting edema
 - Resp: crackles auscultated at bases bilaterally
 - Abdomen: normal
 - MSK: normal

TIMELINE – DAY 1

- Bloodwork



Glucose 9.9

Lactate 4.3

Troponin 40

AG = 19 (corrected for albumin 21)

pH 7.25 pCO₂ 30

Serum Ketones: negative

Urinalysis: glucose and albumin

Microscopy: Coarse granular casts
ACR 500

Urine Na < 20 K 35 Cl < 20

CT Brain: moderate atrophy for age,
no acute intracranial abnormality

TIMELINE – DAY 1

- Management
 - Admission to ICU
 - 5L IV crystalloid
 - D50 and IV insulin to shift potassium (repeated several times)
 - IV dopamine to support HR
 - Bicarbonate Infusion
 - ...
 - IV lasix
 - Dialysis Catheter Insertion
- Vital signs improve but hyperkalemia not improving...

TIMELINE – DAY 2

- Off pressors
- Ongoing hyperkalemia and oliguria
- Hemodialysis

TIMELINE – DAY 3

- Urine output improves, potassium remains in normal range, no further dialysis
- Diagnosis of chronic kidney disease secondary to diabetic nephropathy
- Hyperglycemia: cap glucose **20-30**, A1c returns at **17.8**, managed with MDI insulin regimen
- Mental Status Improved, GCS 15, prior neurologic symptoms have improved
- Transfer to GIM ward

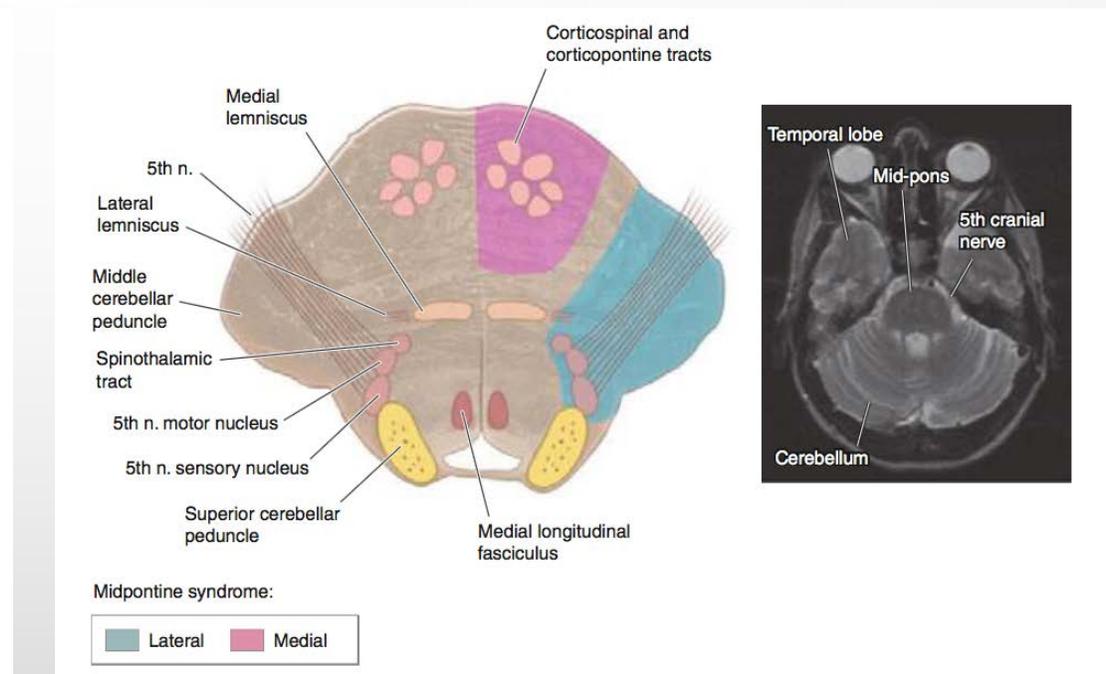
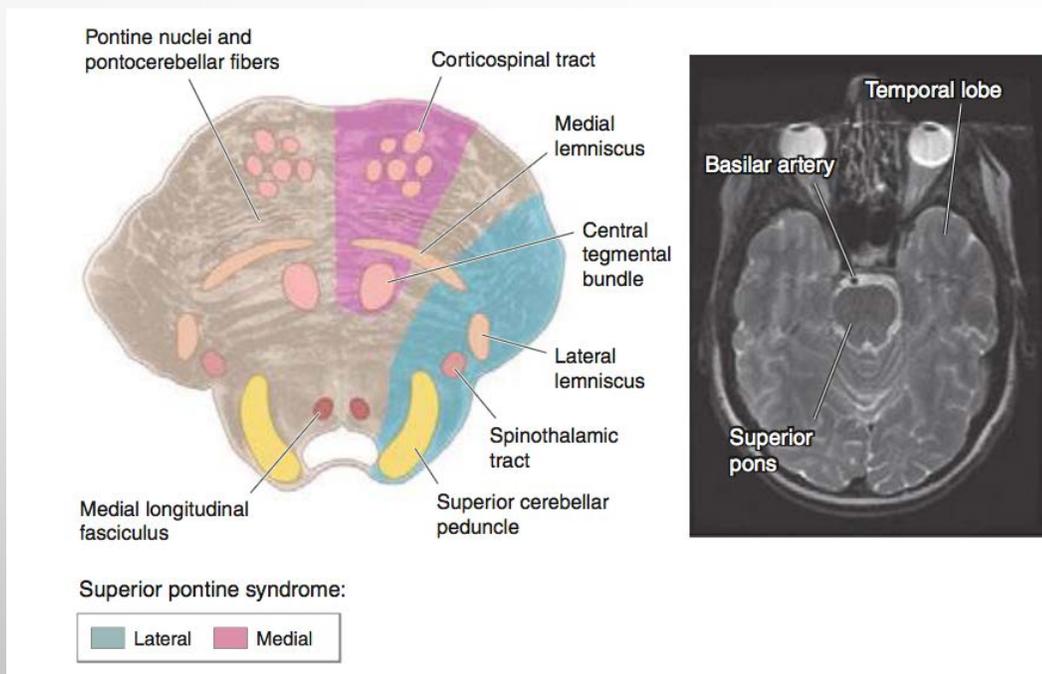
TIMELINE – DAY 8

- Complains of dizziness, slow speech, and unsteady gait
- Examination reveals:
 - Marked dysarthria
 - Bilateral dysmetria
 - Hypermetric saccades
 - Left upper and lower extremity pyramidal distribution weakness
 - Diffuse hyperreflexia

137	92	531	Glucose 26
3.9	28		Alb 33
			Ca 2.18
			PO4 2.36

Where is the lesion?

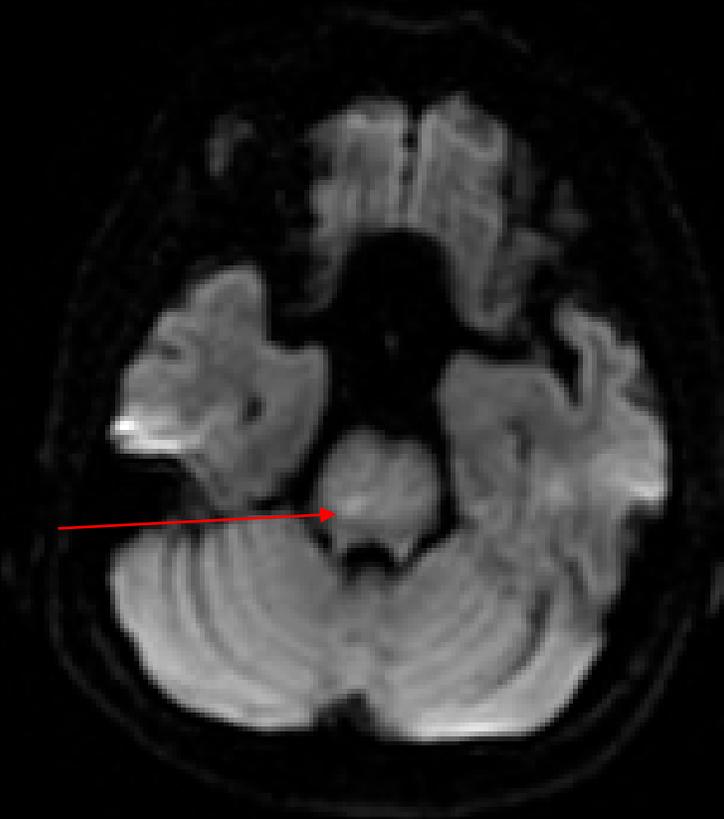
PONTINE SYNDROME?



Vascular Supply: Branches of the basilar artery

- Paramedian branches: wedge of pons on either side of midline
- Short circumferential: lateral 2/3 of pons and cerebellar peduncles

DW

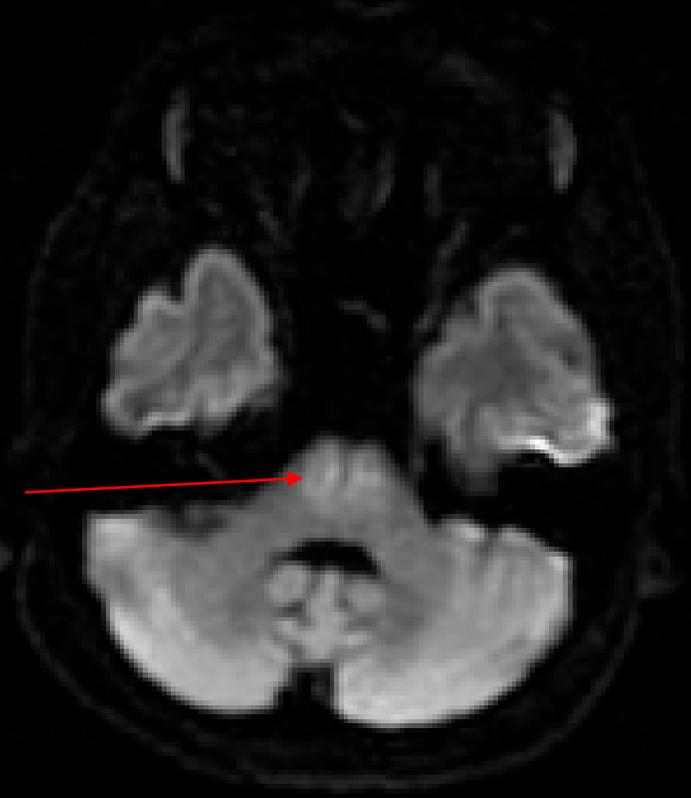


ADC



“There is diffusion restriction which has a somewhat atypical patchy appearance, involving nearly the complete superior basal pons, extending inferiorly in the anterior pons towards the pyramids.”

DW

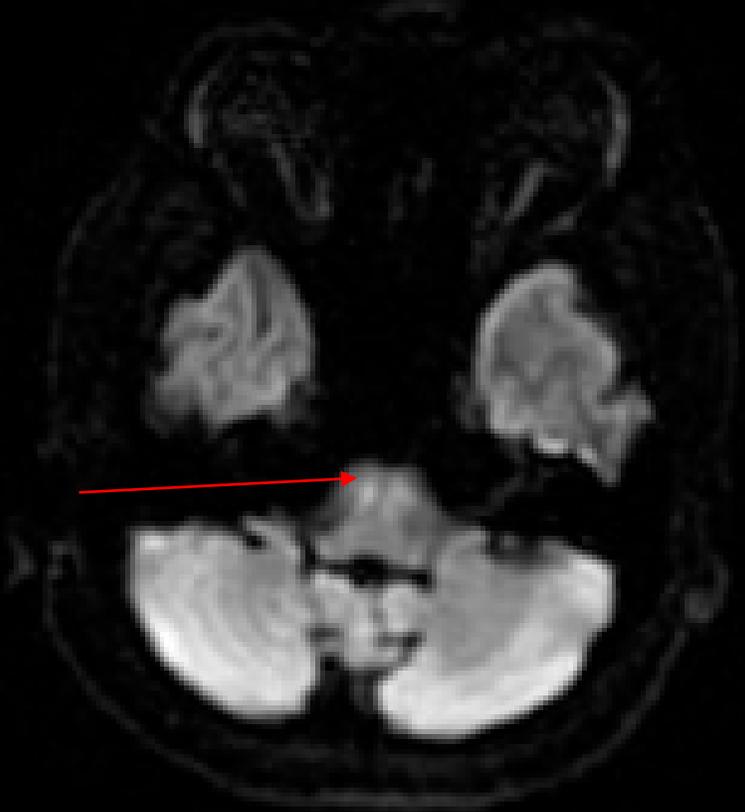


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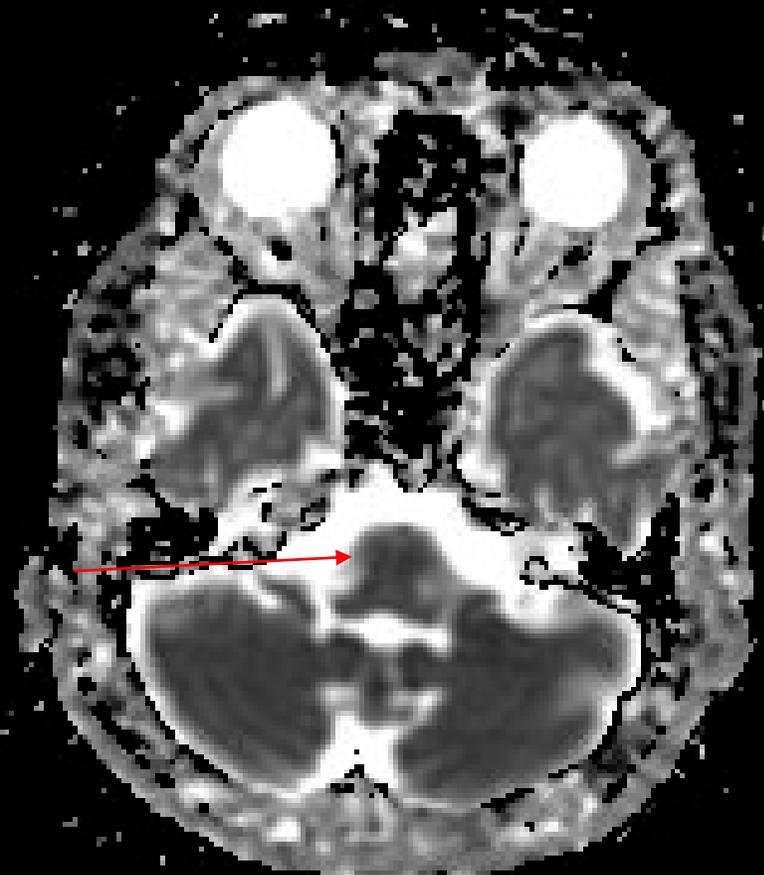


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DW



ADC



“There is diffusion restriction which has a somewhat atypical patchy appearance; involving nearly the complete superior basal pons, extending inferiorly in the anterior pons towards the pyramids.”

DIFFUSION RESTRICTION – CYTOTOXIC EDEMA

- INFECTIOUS
 - CEREBRAL ABSCESS
 - HSV ENCEPHALITIS
 - CJD
- NEOPLASTIC
 - PRIMARY TUMOR
 - LYMPHOMA
- ENCEPHALOPATHIES
 - HYPOXIC-ISCHEMIC
 - PRES
 - METABOLIC (PHENYLKETONURIA, TYROSINEMIA, WERNICKE)
- LEUKODYSTROPHIES
- DEMYELINATING DISEASES
 - MULTIPLE SCLEROSIS
 - **OSMOTIC MYELINOLYSIS**
- TRAUMA
 - DIFFUSE AXONAL INJURY
- NEUROVASCULAR
 - ACUTE ISCHEMIC STROKE

DIAGNOSIS: CENTRAL PONTINE MYELINOLYSIS

- CT is relatively insensitive
- MRI Findings Suggestive of CPM
 - Diffusion restriction within central pons can occur within 24 hours of symptoms and can improve within 1 week
 - T2 and T2-FLAIR signal abnormalities in the central pons follow DWI changes in 7-10 days
 - Classically described trident distribution
- Prototypical initial biphasic course:
 - encephalopathy
 - followed 8-10 days later by corticobulbar symptoms (dysarthria, dysphagia), quadriparesis, oculomotor and pupil dysfunction, locked in syndrome
- CPM has frequently been associated with rapid correction of hyponatremia
 - ...But...in our case there were no abnormal sodium values throughout the 7 day admission
- CPM itself has a differential diagnosis

CENTRAL PONTINE MYELINOLYSIS

- First described by Adams *et al.* in 1959 based on similar autopsy findings in four patients with alcoholism and malnutrition
 - Non-inflammatory, selective destruction myelin sheath and loss of oligodendrocytes in central pons
- Identified association with hyponatremia in 1970's
- Central Pontine Myelinolysis (CPM) and Extrapontine Myelinolysis (EPM) make up the osmotic demyelination syndrome
- A retrospective study of autopsy findings in severe burn patients by McKee *et al.* identified **association between CPM and serum hyperosmolarity**
 - A prolonged but non-terminal episode of extreme hyperosmolarity: hypernatremia, hyperglycemia, and azotemia, alone or combined

PREDISPOSING FACTORS

- CHRONIC ALCOHOLISM
- CORRECTION HYPONATREMIA
- POST LIVER-TRANSPLANT
- BURNS
- HYPERNATREMIA
- **HYPERGLYCEMIA**/HHS/DKA
- HYPOGLYCEMIA
- HYPOKALEMIA
- HYPOPHOSPHATEMIA
- REFEEDING SYNDROME
- **RENAL FAILURE/DIALYSIS**
- WILSON'S DISEASE
- HYPEREMESIS GRAVIDARUM
- ACUTE LEUKEMIA
- EATING DISORDERS

HYPEROSMOLAR STATE AND HYPERGLYCEMIA

- In order to explain the development of CPM in the absence of overly rapid correction of hyponatremia in their series of burn patients, McKee et al. hypothesized that CPM develops as a result of a “relatively hypertonic insult”
- Any situation in which the serum and extracellular space becomes hypertonic faster than the rate at which brain cells can compensate by accumulating organic osmoles can result in CPM
- The patient in our case had evidence of severe prolonged hyperglycemia with an A1c of 17.8 and blood glucose raging from 15-25 mmol/L on escalating doses of sc insulin during admission

HYPEROSMOLARITY AND AZOTEMIA

- Theory that uremic patients have some protection against developing CPM in hyponatremia with rapid correction during dialysis since the increase in osmolality from increased serum sodium is offset by decrease in serum urea
- However, in an autopsy series of patients with ESRD on hemodialysis there was a reported incidence of CPM of 14%.
- In a study using MRI to diagnose 17 cases of CPM onset within 24 hours of dialysis, CPM was associated with low BUN:Cr following dialysis
 - However, lesions showed faster resolution of MRI findings than in other cases of CPM, suggesting that the T2 FLAIR hyperintensity could have represented edema rather than demyelination
- In our case, symptoms were present before first treatment with hemodialysis and the BUN:Cr ratio was unchanged after dialysis

FINAL DIAGNOSIS: CENTRAL PONTINE MYELINOLYSIS SECONDARY TO CHRONIC UNCONTROLLED HYPERGLYCEMIA

- Glycemic control achieved on MDI insulin
 - A1c improved to 9.0% at 3 months and 7.8% at 6 months after presentation
- Initiated intermittent hemodialysis for ESRD
- Neurologic Improvement
 - Ongoing problems with fine motor, dysarthria
 - MRI repeated 1 week later showed stable appearance of pons

LEARNING POINTS

- Identify the radiologic finding of central pontine myelinolysis as a syndrome for which there is a differential diagnosis that includes hyponatremia and non-hyponatremic metabolic abnormalities.
- Recognize that CPM can present atypically in diabetic patients and a high index of clinical suspicion is required to make the diagnosis.
- Include CPM in a differential diagnosis for neurologic dysfunction in a patient with a history of rapid osmotic fluctuations

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- DR. JULIE LOVSHIN, ENDOCRINOLOGY
- DR. SARA MITCHELL, NEUROLOGY



QUESTIONS

The image features a light gray background with a subtle gradient. The word "QUESTIONS" is centered in a bold, black, sans-serif font. The corners of the image are decorated with several realistic water droplets of varying sizes, each with a soft shadow and a highlight, giving them a three-dimensional appearance.

REFERENCES

- Smith WS, Johnston SC, and Hemphill III, JC (2015). Cerebrovascular Diseases. In Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, and Loscalzo J (Eds). *Harrison's Principles of Internal Medicine 19e*. (pp. 2577-2579). New York City, NY: McGraw-Hill Education.
- O'Connor KM, Barest G, Moritani T, Sakai O, and Mian A. "Dazed and diffused": making sense of diffusion abnormalities in neurologic pathologies. *Br J Radiol* 2013;86:20130599.
- Karaarslan E and Arslan A. Diffusion weighted MR imaging in non-infarct lesions of the brain. *Eur J Radiol* 2008;65:402–416.
- McKee AC, Winkelman MD, Banker BQ. Central pontine myelinolysis in severely burned patients: relationship to serum hyperosmolality. *Neurology*. 1988;38:1211–7.

REFERENCES

Lampl C and Yazdi K. Central pontine myelinolysis. *Eur Neurol*. 2002;47(1):3-10.

Singh TD, Fugate Je, Rabinstein AA. Central pontine and extrapontine myelinolysis: a systematic review. *Eu J Neurol*. 2014;21(12):1443-1450.

Rodríguez-Velver KV, Soto-García AJ, Zapata-Rivera MA, Montes-Villarreal J, Villarreal-Pérez JZ, Rodríguez-Gutiérrez R. Osmotic demyelination syndrome as the initial manifestation of a hyperosmolar hyperglycemic state. *Case Rep Neurol Med*. 2014;65:23–5.

J. D. Burns, S. C. Kosa, and E. F. M. Wijdicks, Central pontine myelinolysis in a patient with hyperosmolar hyperglycemia and consistently normal serum sodium. *Neurocritical Care*; 2009;11:2:251–254.

REFERENCES

Herráiz L, Cuesta M, Runkle I. Osmotic demyelination syndrome in a patient with uncontrolled hyperglycemia. *Med Clin (Barc)*. 2017;149:370–37.

Saini M, Mamauag MJ, Singh R. Central pontine myelinolysis: a rare presentation secondary to hyperglycaemia. *Sing. Medical Journal*; 2015;56:71-73.

Swapna T, Charumathi R, Khan M, Kissell K. Atypical presentation of central pontine myelinolysis in hyperglycemia. *Endo. Diabetes Metab. Case Rep*. 2017;17:4-6.

Hirosawa T, Shimizu T. Osmotic demyelination syndrome due to hyperosmolar hyperglycemia. *Cleav. Clinic Journ. Med*. 2018; 85(7):511-513.

REFERENCES

Tarhan NC, Agildere AM, Benli US, Ozdemir FN, Aytekin C, and Can U. Osmotic demyelination syndrome in end-stage renal disease after recent hemodialysis: MRI of the brain. *AJR Am J Roentgenol* 2004;182(3):809-16.