American Association of Neuropathologists

Diagnostic Slide Session 2023
Case 5

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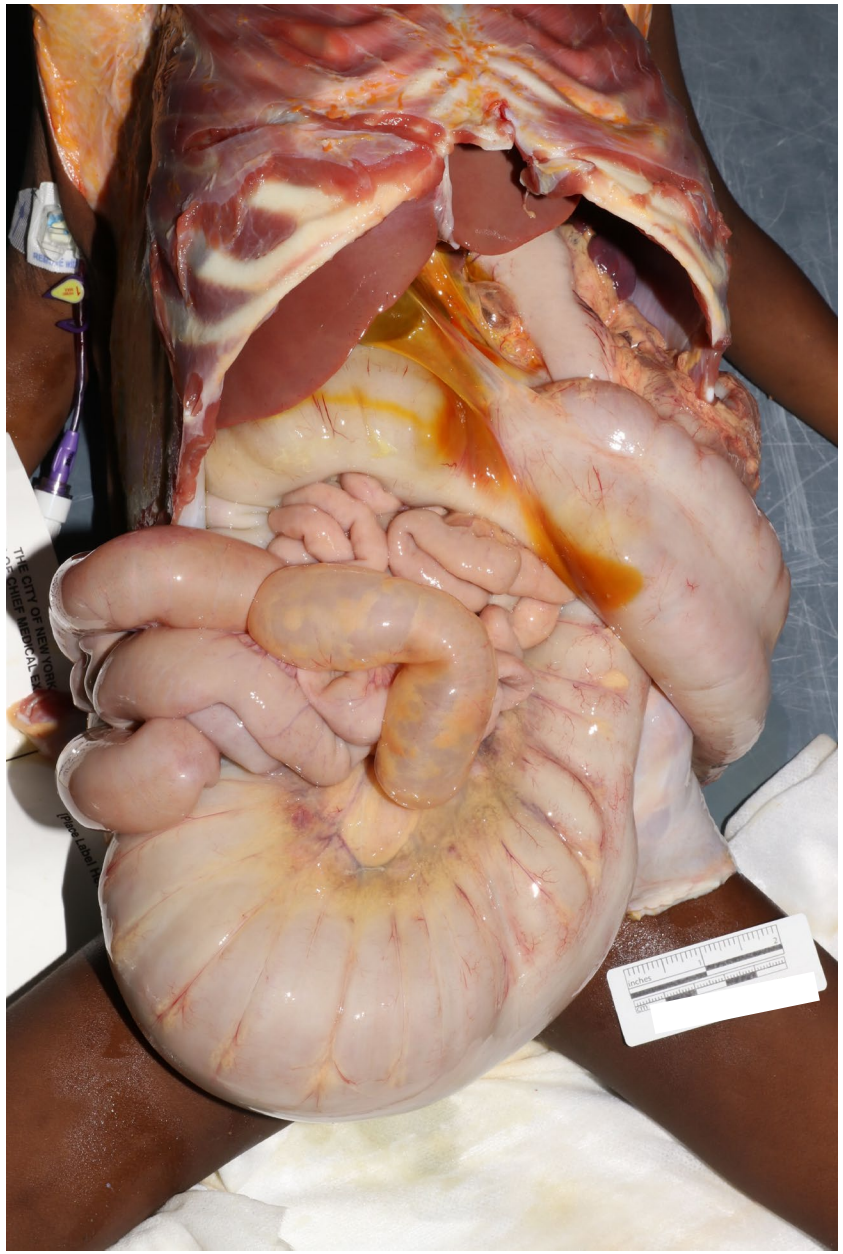
Clinical history:

- 3 1/2-year-old girl
- History of Hirschsprung Disease, diagnosed soon after birth (born preterm at 26 gestational weeks)
  - Repeated enterocolitis alternating with chronic constipation, treated by parents at home with over-the-counter enema preparations
  - Status post “pull-through” procedure, at age 3 years
  - Status post placement of intraosseus line for treatment of dehydration, 2 months prior to death
    - Complicated by osteomyelitis during the 2 weeks prior to death
  - Continued vomiting and poor fluid intake, 4 days prior to death
  - Saline enema, night prior to death
- Found unresponsive in the morning, could not be resuscitated

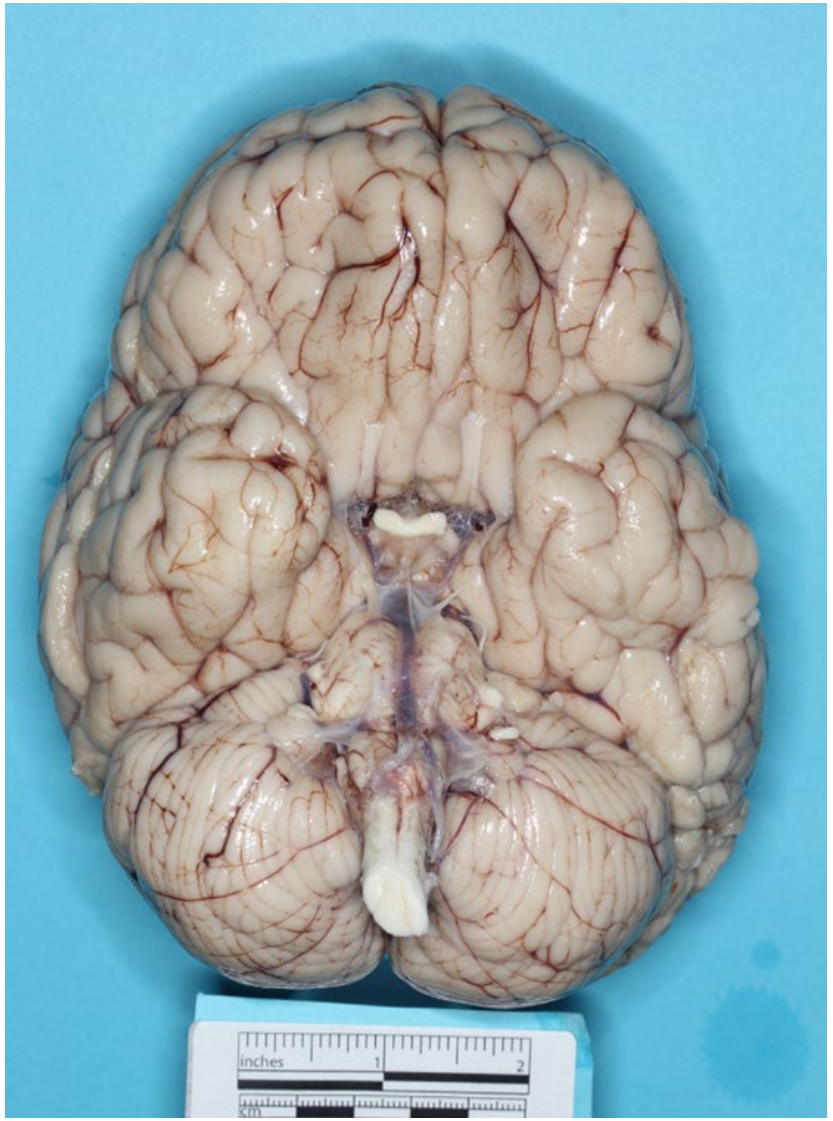
Findings at autopsy:

- Hirschsprung Disease:
  - Status post “pull-through” procedure (intact)
  - Dilated large colon filled with liquid stool
  - Full-length, full-thickness colitis
- Vitreous electrolyte panel:

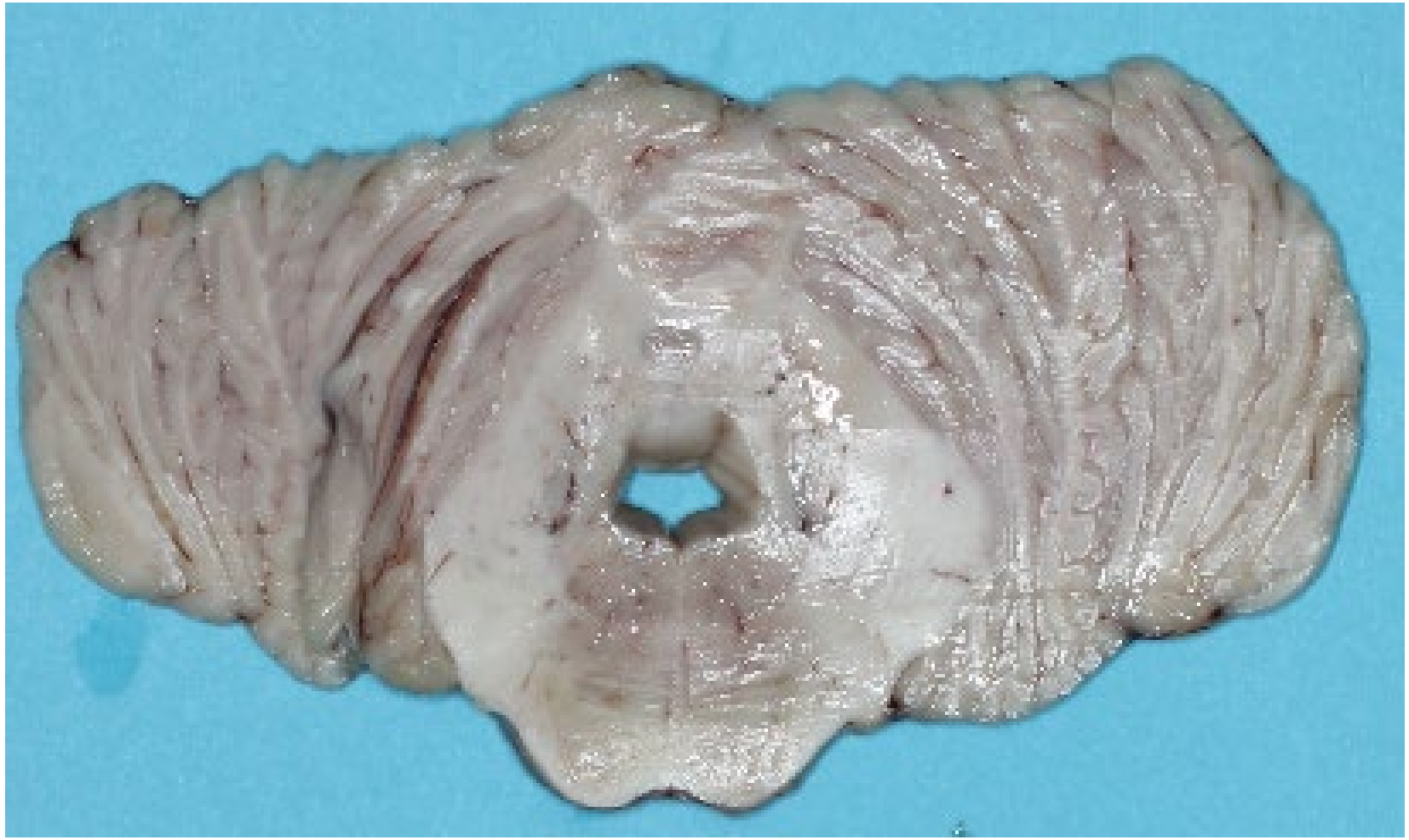
Glucose	13.0 mg/dL (Normal <200 mg/dL)
Urea Nitrogen	42.6 mg/dL (Normal 8-20 mg/dL)
Sodium	143 mmol/L (Normal 135-150 mmol/L)
Potassium	13.6 mmol/L (Normal <15 mmol/dL)
Chloride	123 mmol/L (Normal 105-135 mmol/L)
Creatinine	Not detected (Normal 0.6-1.3 mg/dL)



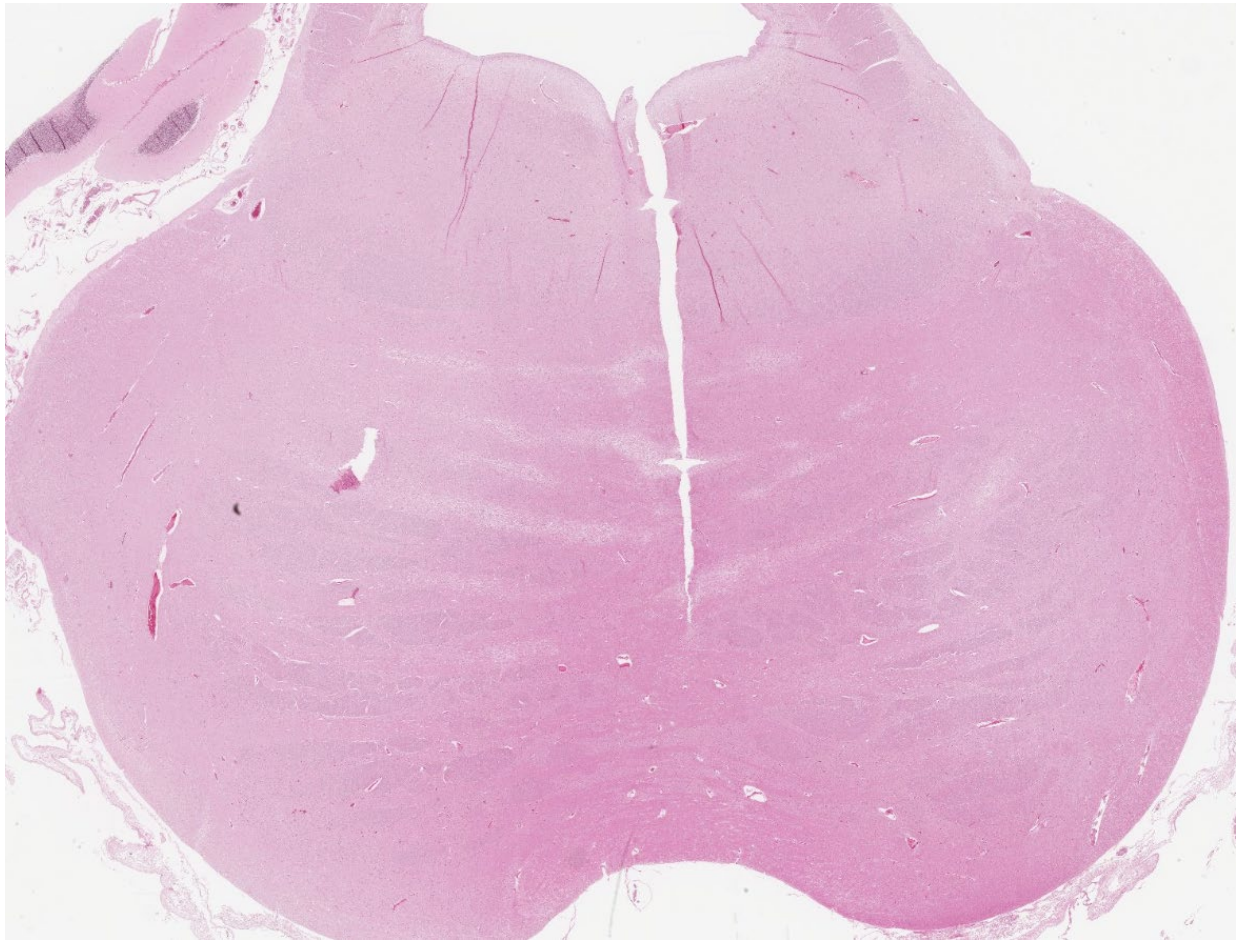
Macroscopic neuropathology:

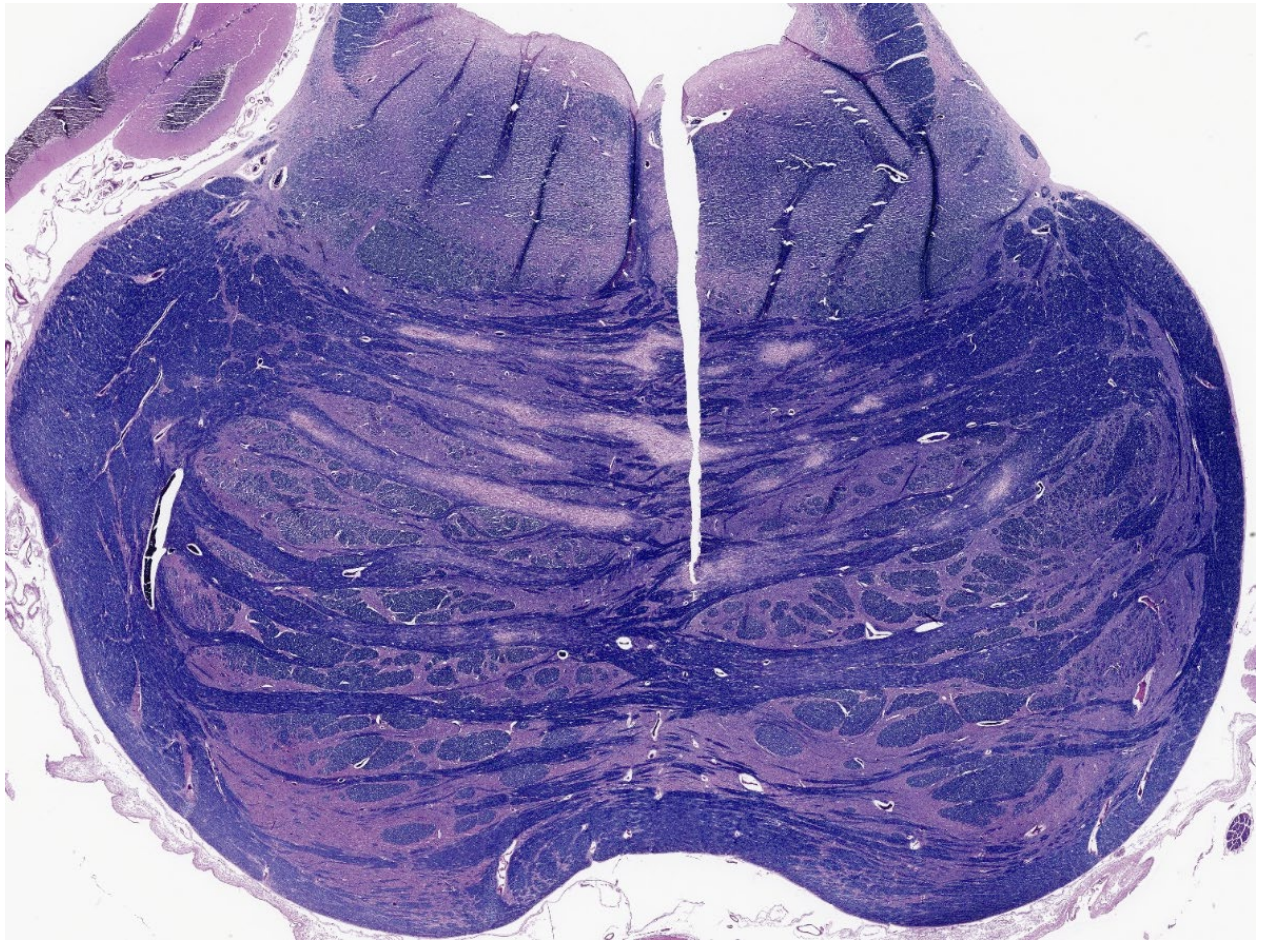


Weight, 1110g
(expected for age 3 years, 1100g)



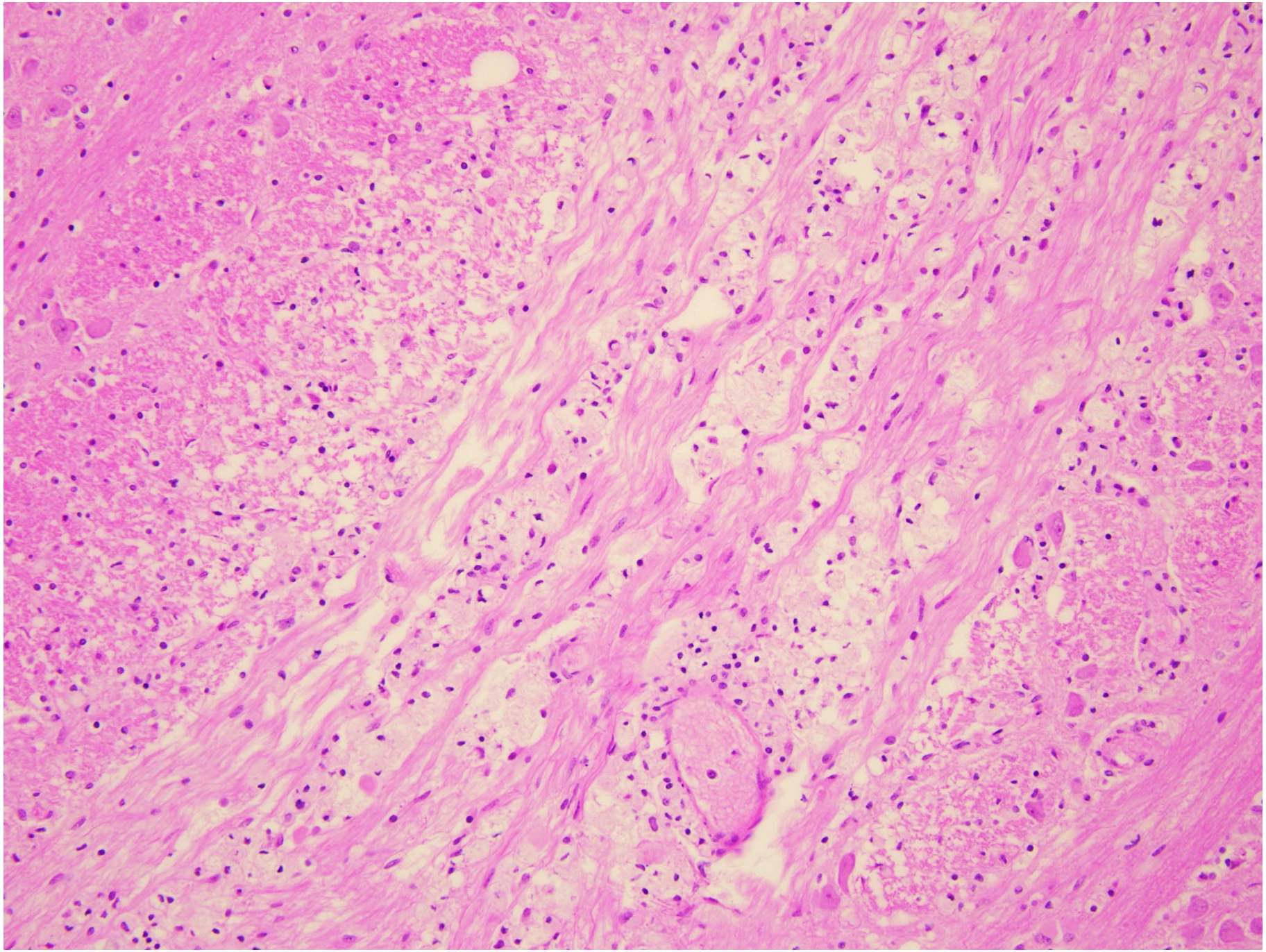
Slightly overall swollen appearance of brain
Slight grayish discoloration of basis pontis



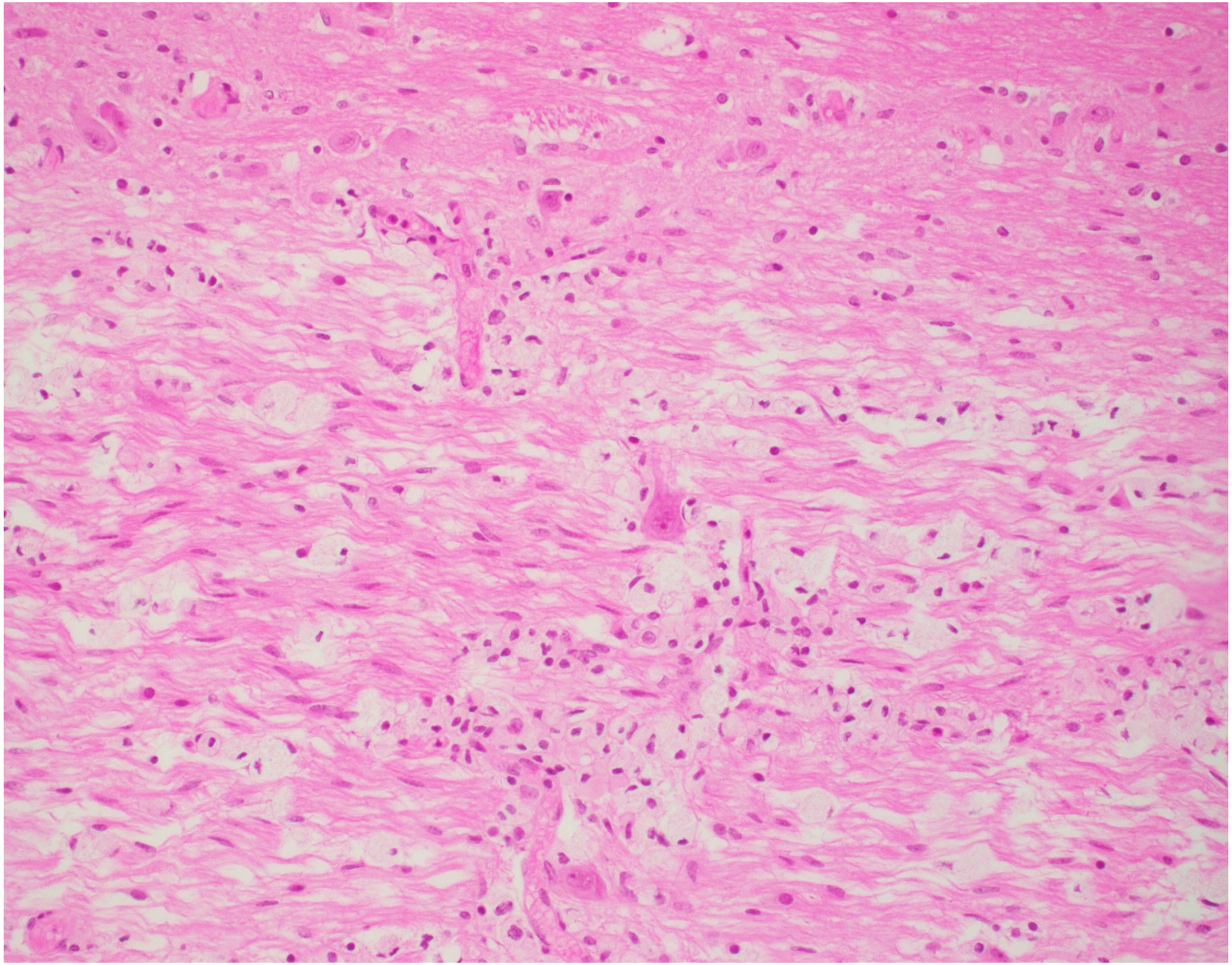


Pons
(H&E, LFB/PAS; 1x)

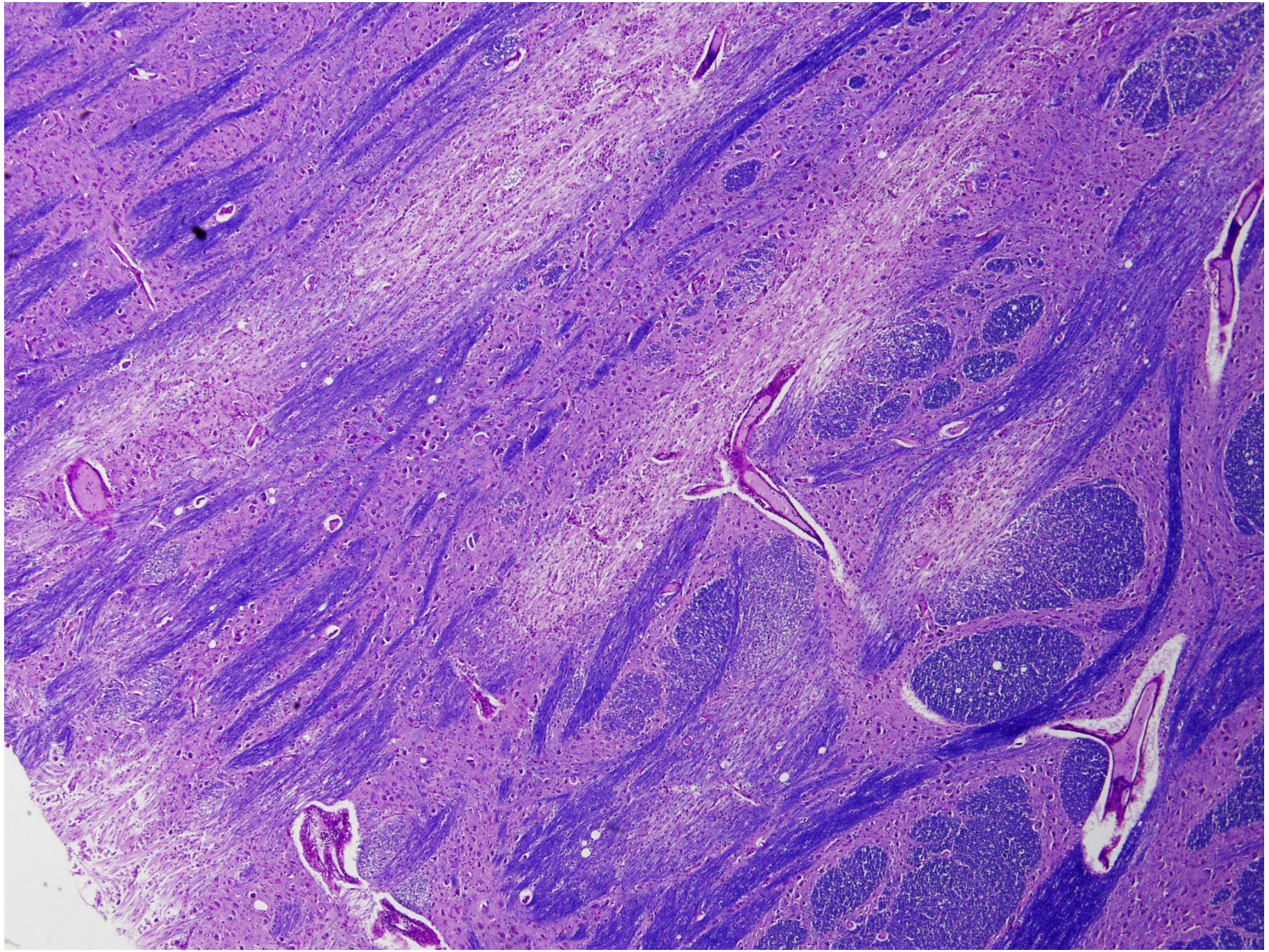
Diagnosis?



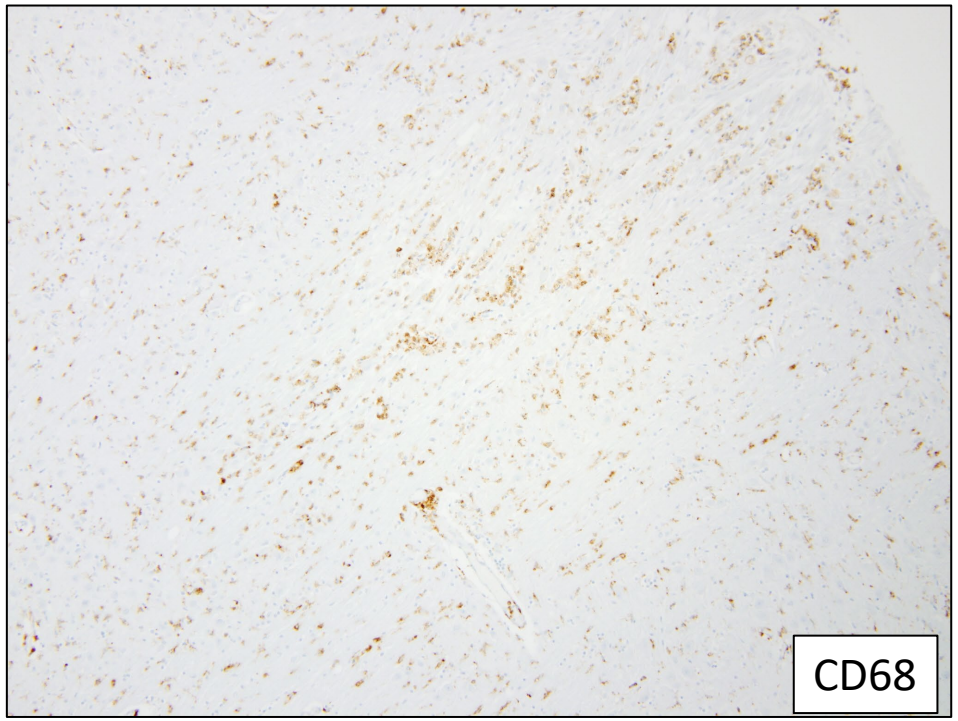
Midline basis pontis
(H&E, 200x)



Midline basis pontis
(H&E, 200x)



Midline basis pontis
(LFB/PAS, 40x)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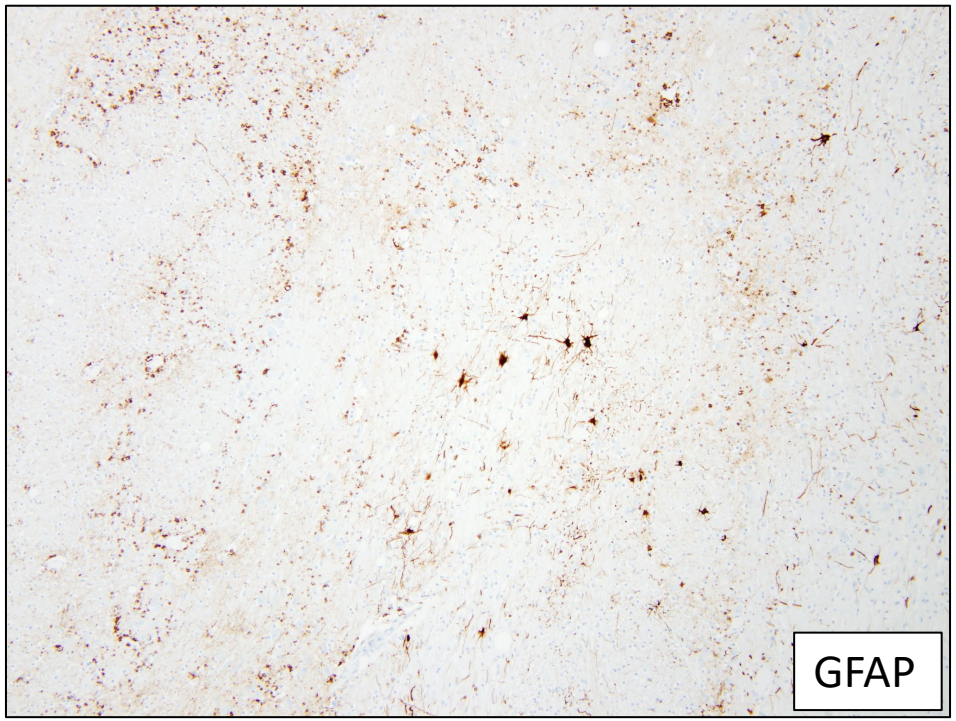
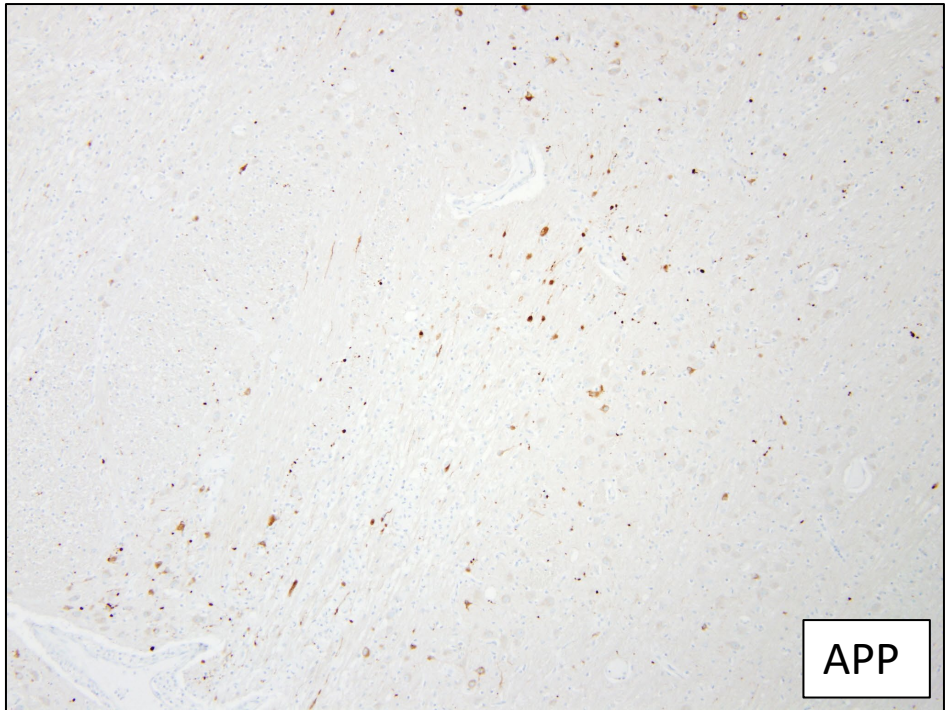

GFAP


APP

Neuropathologic diagnosis

- Central pontine myelinolysis, organizing, with focal axonal injury

- (History of Hirschsprung Disease with episodic fluid and electrolyte imbalance)

Discussion - Pathophysiology

- Effects of chronic hyponatremia and/or its rapid correction
  - Intracellular osmolyte imbalance
  - Decrease in cell volume with cell death
    - Oligodendrocytes have high level of vulnerability
  - Relative sparing of axons, unless severe
- Areas of predilection include oligodendrocyte- and myelin-rich regions
  - Pons, cerebellum, lateral geniculate body, external capsule, thalamus
- Occurrence in children rare, but known in Hirschsprung Disease
  - Also seen in DKA, Bartter syndrome, chronic renal failure

References

- Bansal LR, Zinkus T. Osmotic Demyelination Syndrome in Children. Pediatr Neurol. 2019 Aug;97:12-17. doi: 10.1016/j.pediatrneurol.2019.03.018. Epub 2019 Mar 28. PMID: 31128892.
- Chaudhary A, Chaudhary A, Yadav RS, Shrestha Y, Shah R. Pediatric osmotic demyelination syndrome in a case of type 1 diabetes mellitus with diabetic ketoacidosis. Clin Case Rep. 2022 Mar 19;10(3):e05584. doi: 10.1002/ccr3.5584. PMID: 35340640; PMCID: PMC8934147.
- Gargano G, Manfredi M, Pedori S, Di Dio F, Spagnoli C, Frattini D. A highly unusual case of osmotic demyelination syndrome and extrapontine myelinolysis in a 3-month-old infant with Bartter syndrome. J Int Med Res. 2020 Oct;48(10):300060520966494. doi: 10.1177/0300060520966494. PMID: 33107776; PMCID: PMC7645388.