100th Annual Meeting

American Association of Neuropathologists

Diagnostic Slide Session: Case 11

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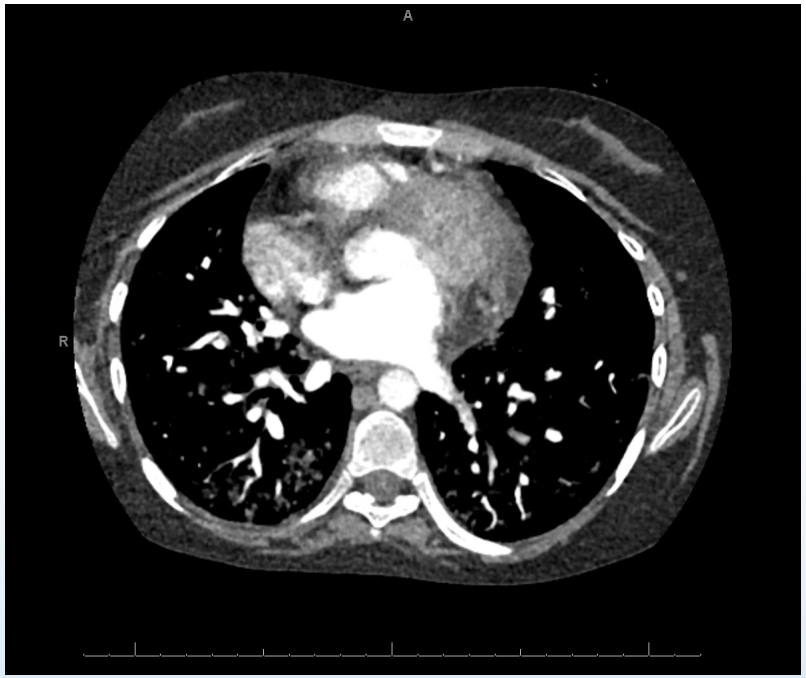
Clinical History

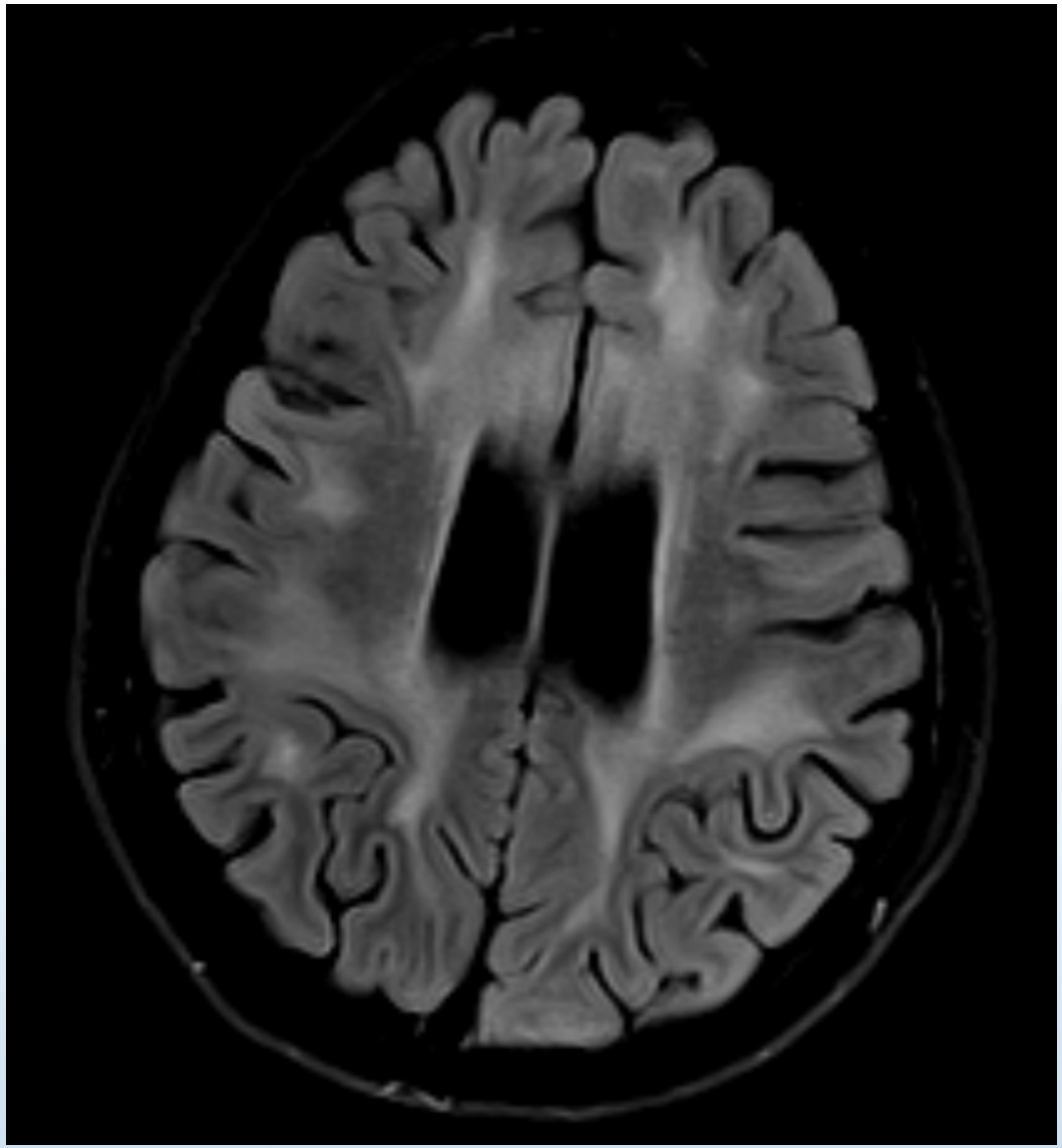
- 13-year-old female status post liver transplant at 3 years of age.
- Neurological history: focal epilepsy secondary to PRES and several recent hospitalizations for hepatic encephalopathy.
- Presented to the ED in acute respiratory distress with substernal chest pain and hemoptysis, found to have liver failure.



CT chest showed diffuse centrilobular pulmonary nodules with ground-glass opacities and consolidation

Brain MRI

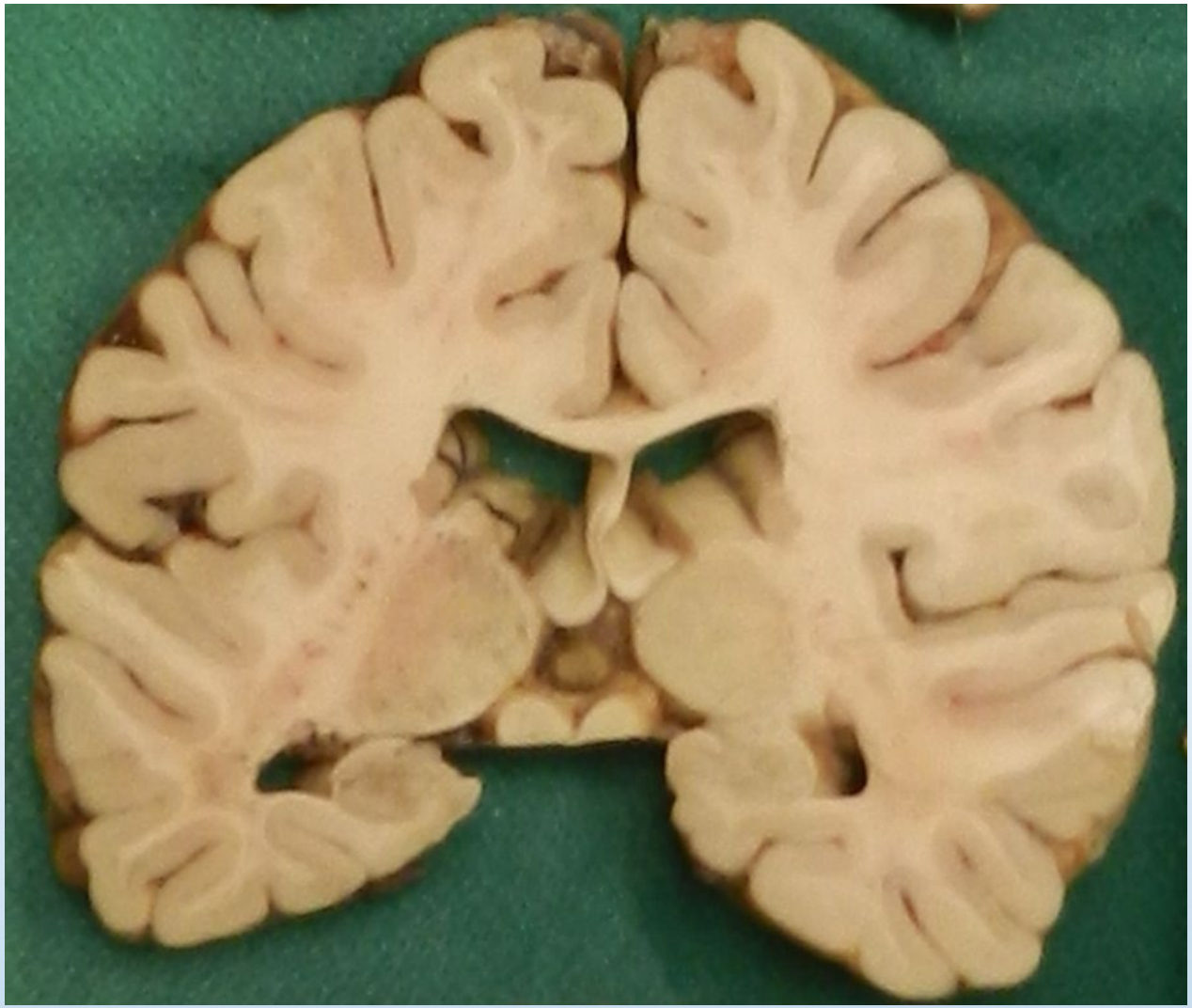
- Lateral ventricular enlargement
- Prominent sulci
- Non-specific patchy subcortical white matter hyperintensity



T2 Flair – transverse section

Autopsy Findings

- Brain weight
  - 1,052 grams



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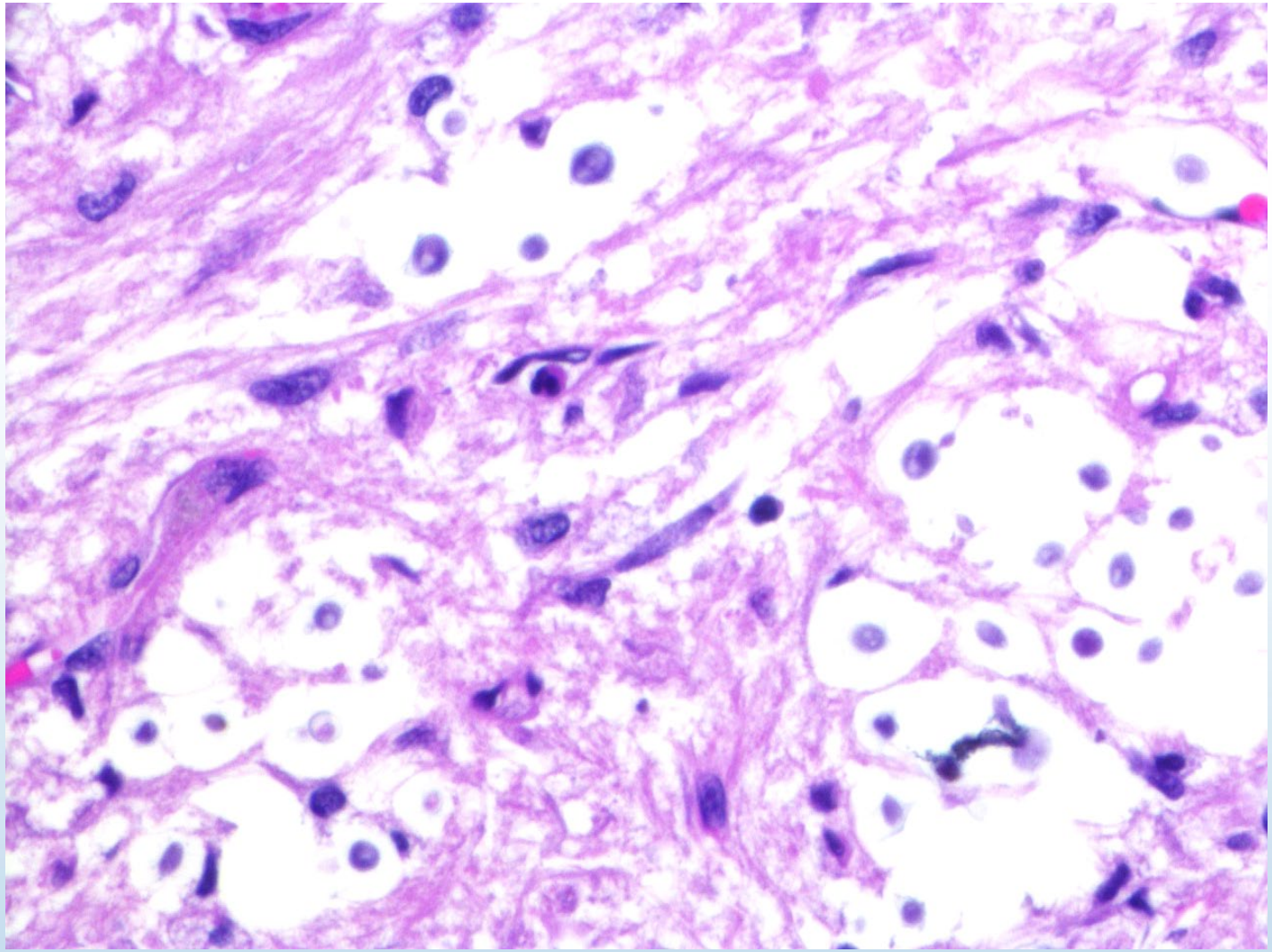
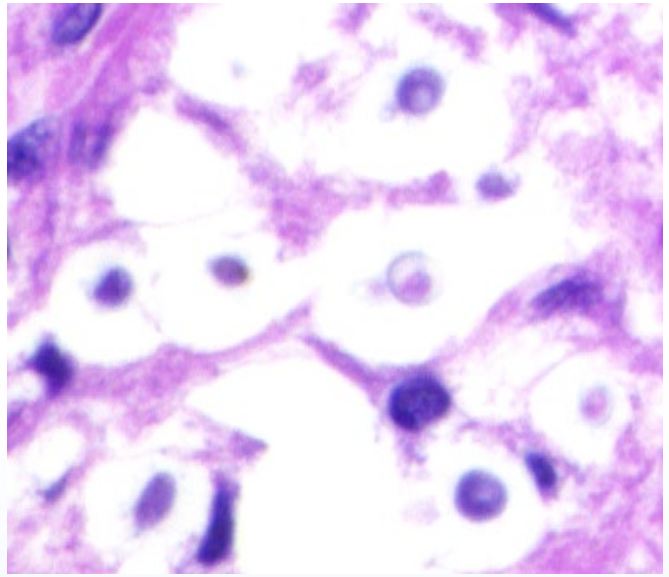
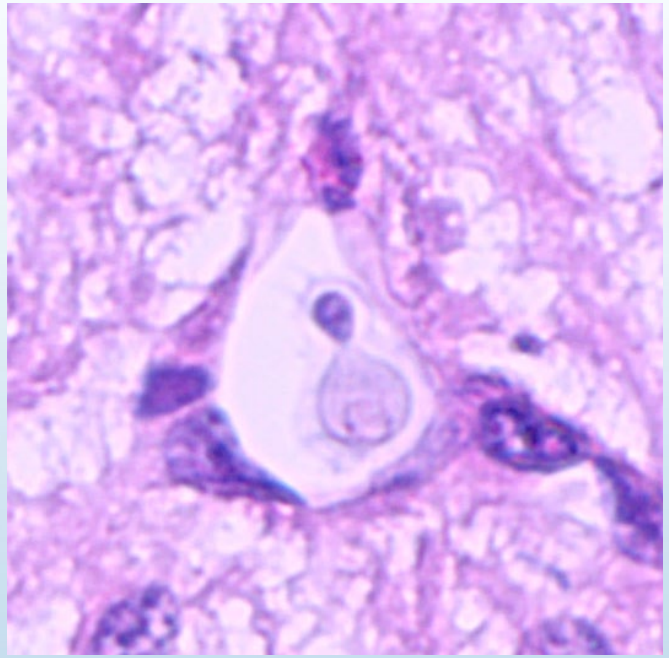
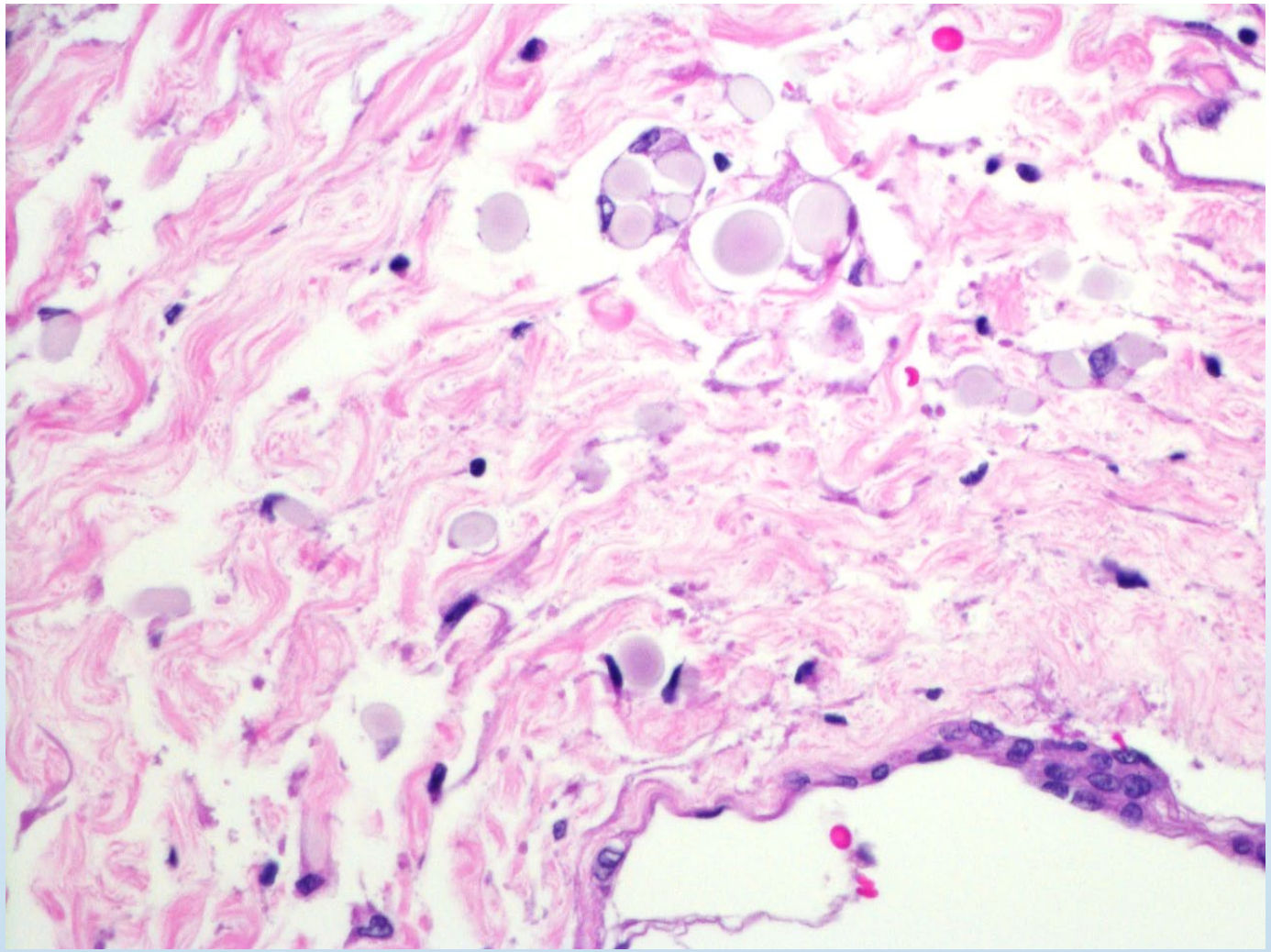
Microscopic Findings

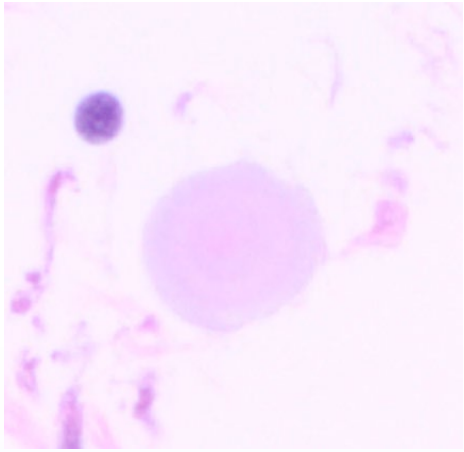


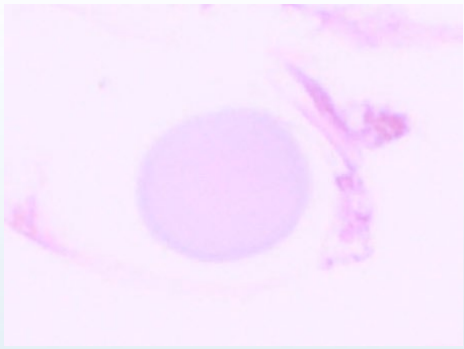




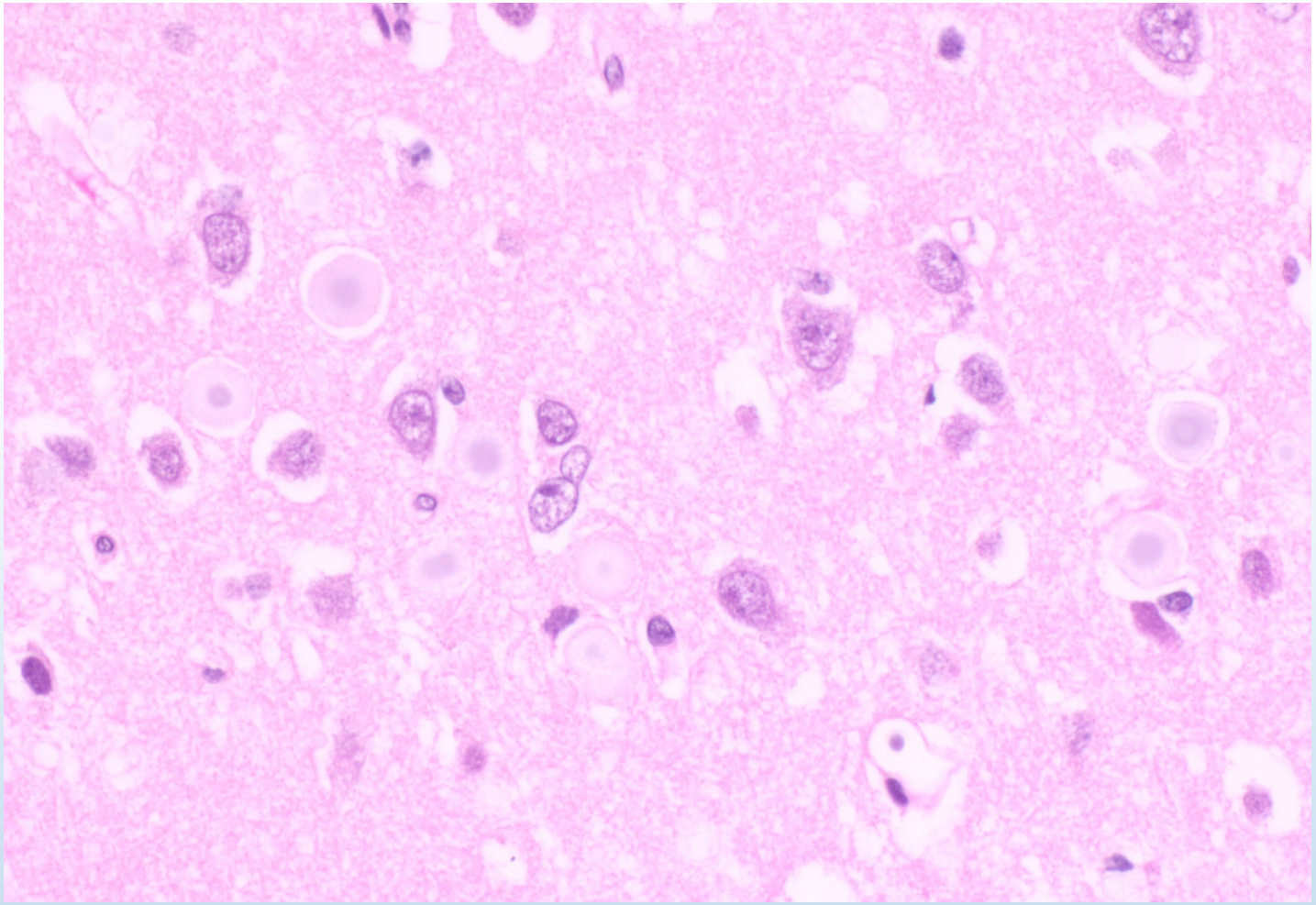
Microscopic Findings

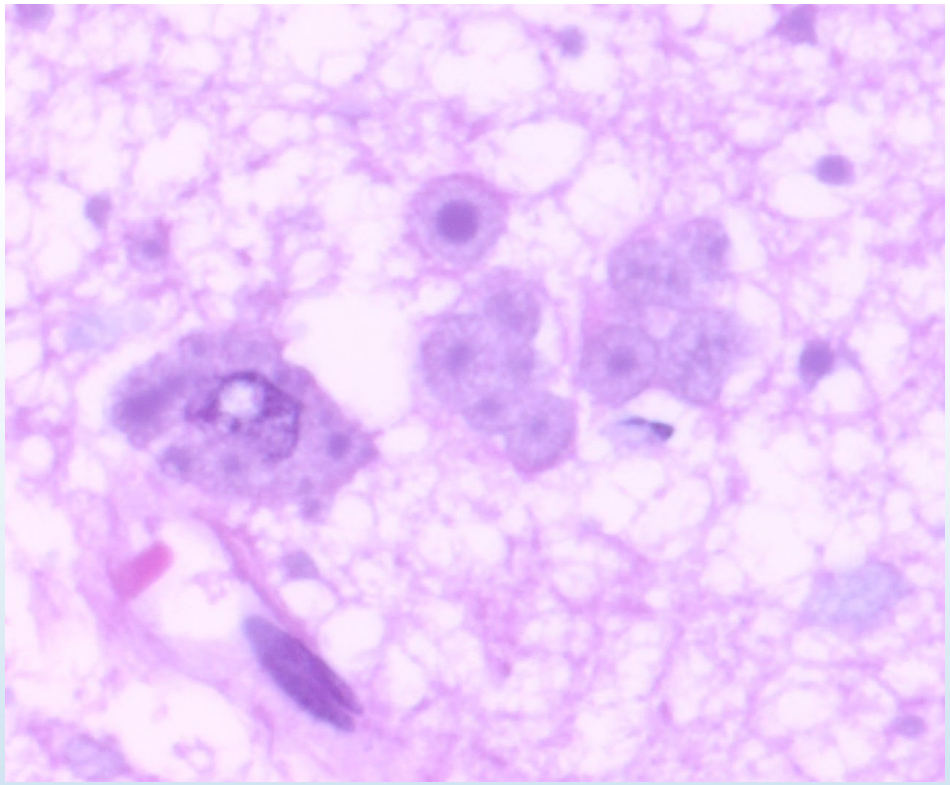






Microscopic Findings





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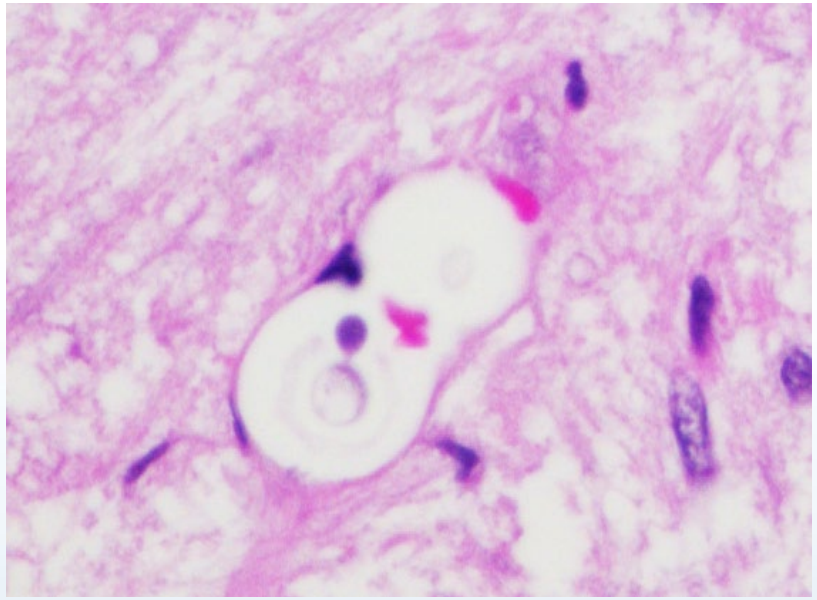
Discussion

Diagnosis

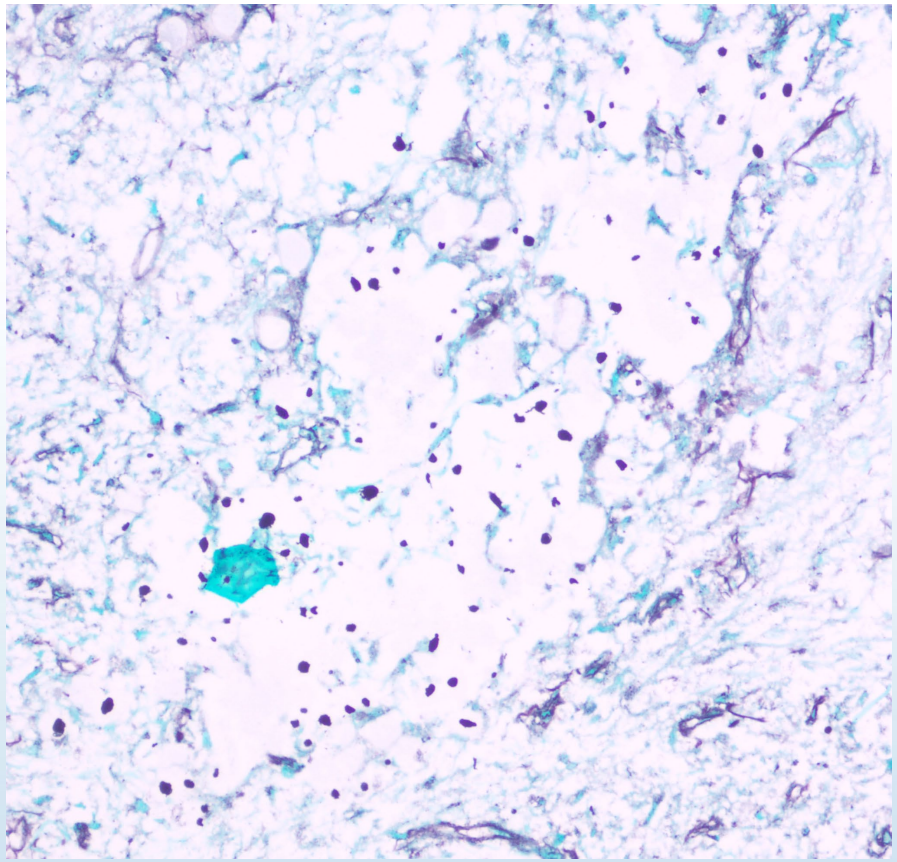
- Central nervous system involvement by disseminated *Cryptococcus neoformans*
- Polyglucosan bodies consistent with underlying Glycogen storage disease type IV

Cryptococcus neoformans

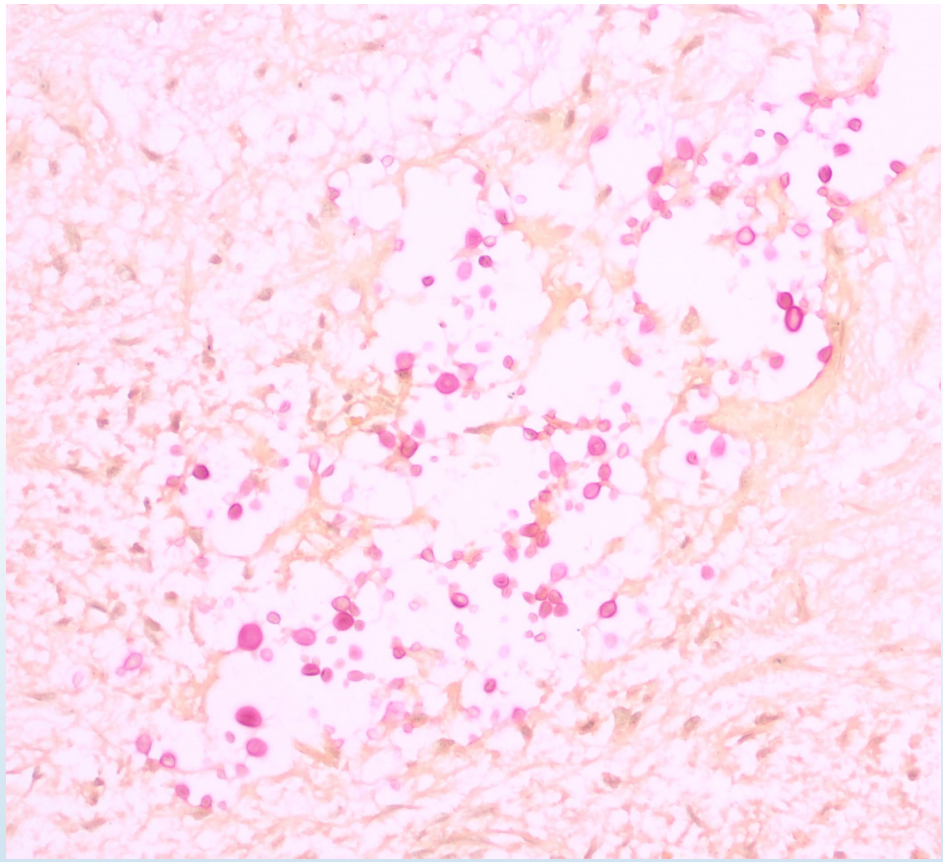


- 3.5-8.0 µm in diameter
- Variably sized, spherical to ovoid yeast
- Clear “halo” representing the capsule
- Narrow-based budding
- Pseudohyphae are absent
- PAS or GMS stains can be used to detect
- Alcian blue and mucicarmine stains will highlight capsule

Cryptococcus neoformans

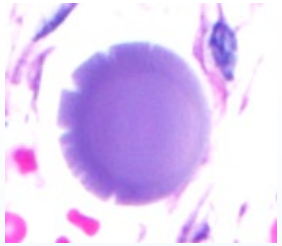


GMS

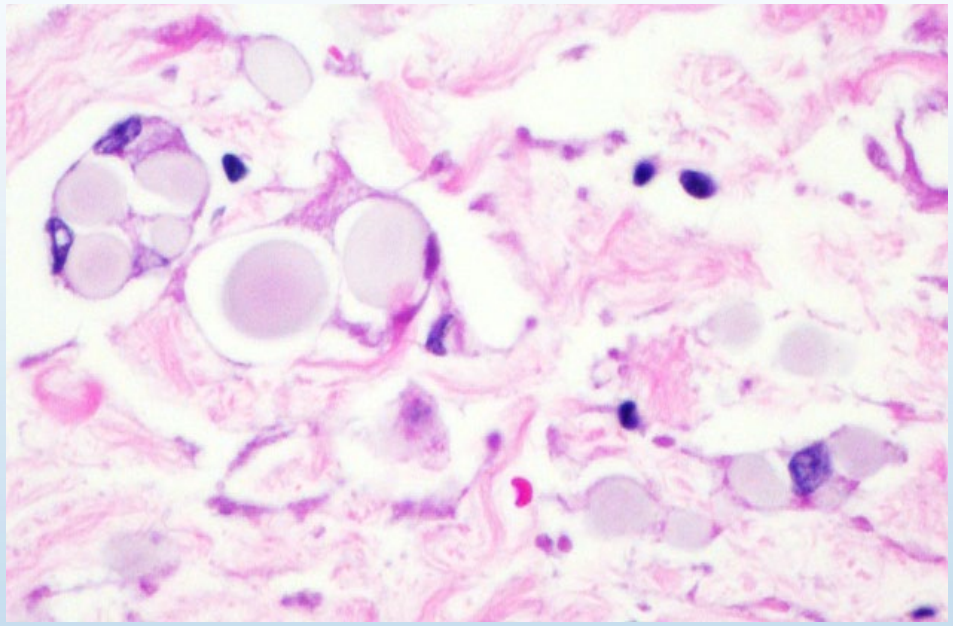


Mucicarmine

Polyglucosan Bodies (PGBs)



- Accumulation of abnormal structural form of glycogen
  - striated and smooth muscle, brain, nerve, liver, and skin
- Violet or hyaline intracytoplasmic vacuoles or extracellular structures within tissues
- Stain with PAS, GMS, and ubiquitin
- Pathologic features of different genetic diseases
- PGBs in the brain
  - Non-specific
  - Seen as part of aging (corpora amylacea)

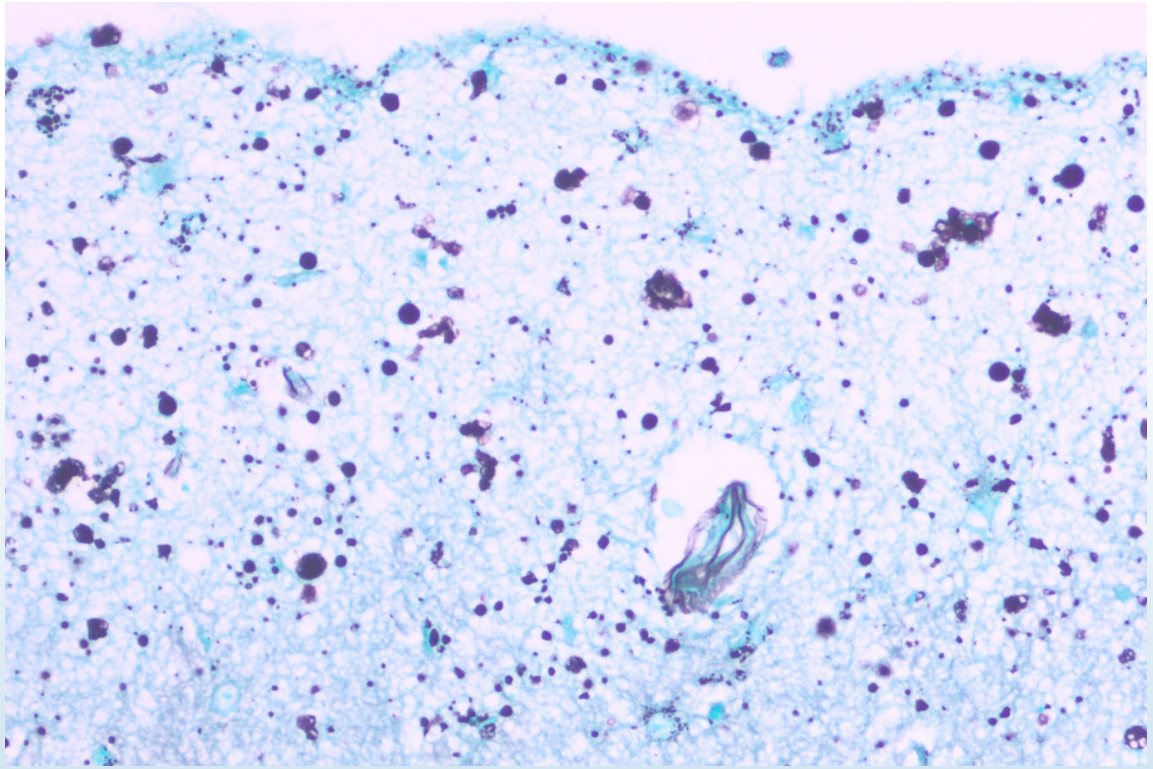


Update on polyglucosan storage diseases

Giovanna Cenacchi[1] · V. Papa[1] · R. Costa[1] · V. Pegoraro[2] · R. Marozzo[2] · M. Fanin[3] · C. Angelini[4]

PMID: 31363843 DOI: 10.1007/s00428-019-02633-6

Polyglucosan Bodies (PGBs)



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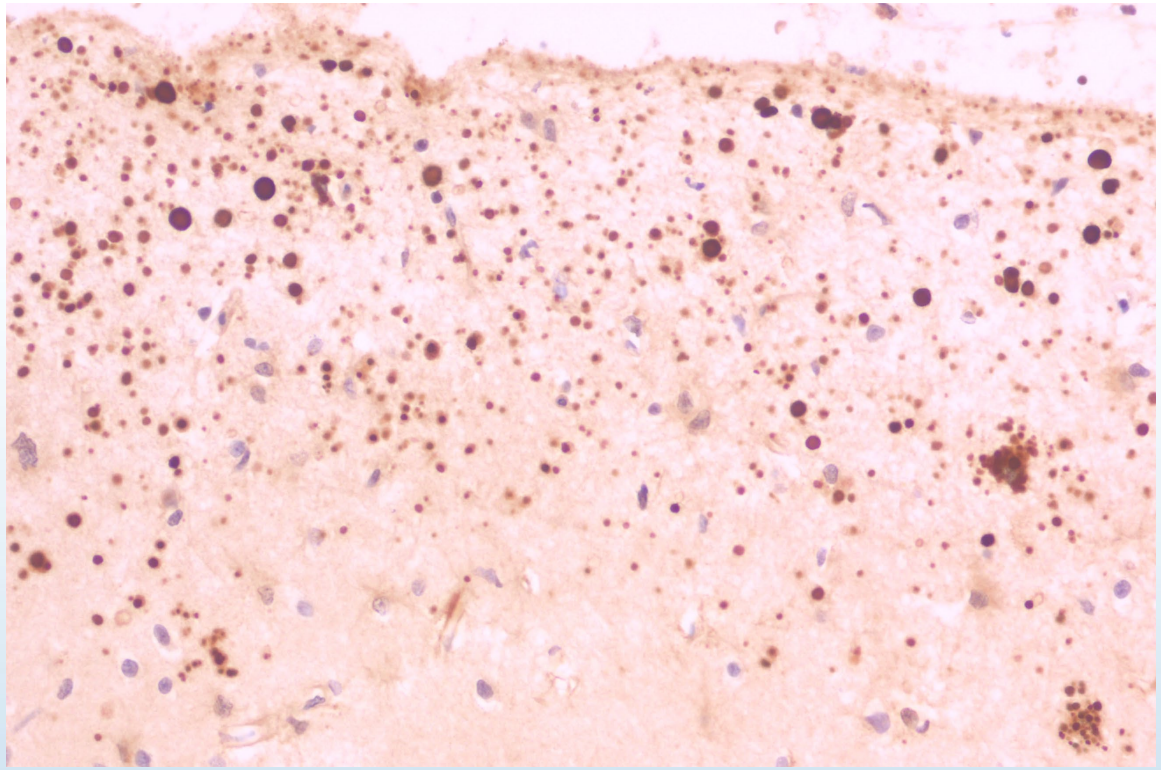
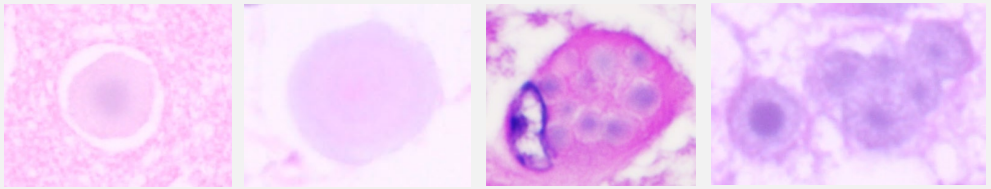
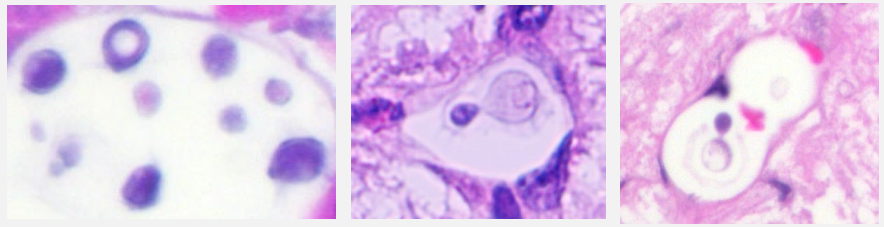
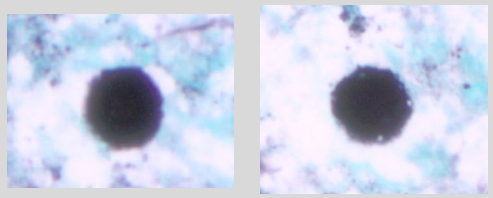
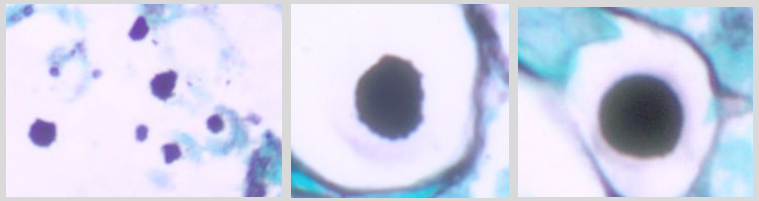
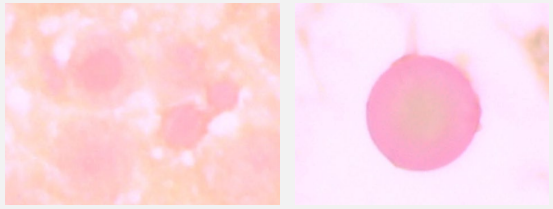
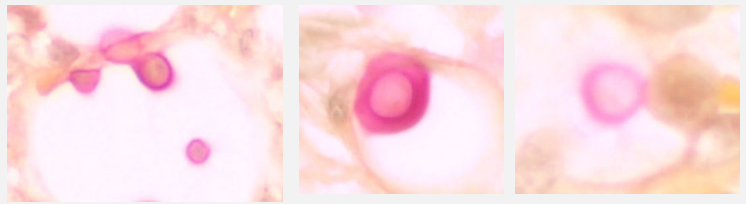
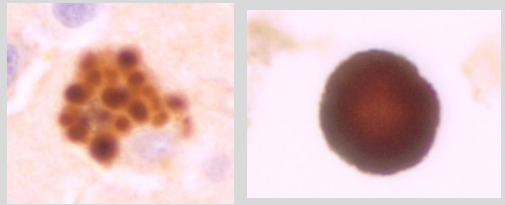


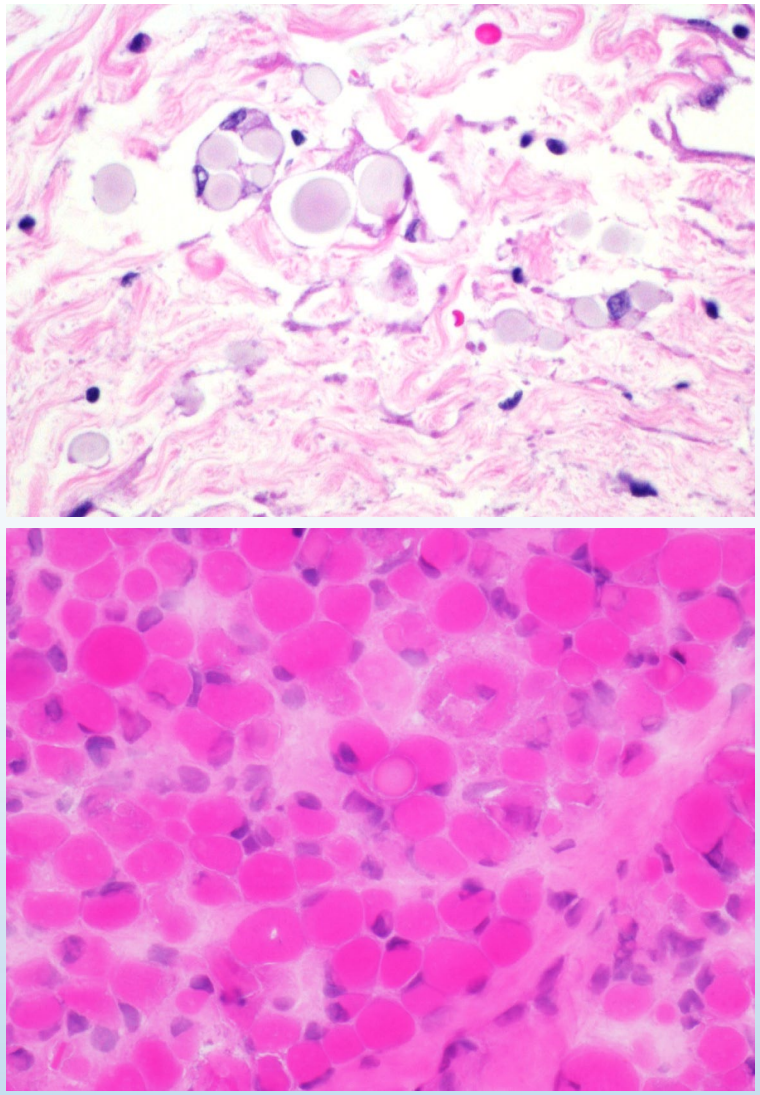
Ubiquitin

Polyglucosan Bodies vs *Cryptococcus*

	Polyglucosan Bodies	*Cryptococcus*
H&E		
GMS		
Mucicarmine		
Ubiquitin		

Glycogen Storage Disease Type IV (Andersen Disease)

- Autosomal recessive disorder
- Defect in amylo-1,4-1,6 transglucosidase
- *GBE1* gene mutations
- Skeletal muscle biopsy frequently shows PGB accumulation
- PGBs also observed in cardiac muscle, smooth muscle, liver, motor neurons, brain, amniocytes, fibroblasts, leukocytes, and sweat glands
- Clinical presentations divided into hepatic and neurologic/neuromuscular forms



Conclusions

- Several hepatic diseases have manifestations in the CNS
- Overlapping clinical presentations and affected tissues affected in many metabolic diseases (importance for genetic sequencing)
- High suspicion for infectious disease in immunosuppressed/immunocompromised patients
- Don’t write off extensive “corpora amylacea” – could be other PGBs (e.g. Adult polyglucosan body disease)
- Don’t miss an additional diagnosis when you have found one

Acknowledgements

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References

- Cenacchi G, Papa V, Costa R, et al. Update on polyglucosan storage diseases. Virchows Arch. 2019;475(6):671-686.
- Szymańska E, Szymańska S, Truszkowska G, et al. Variable clinical presentation of glycogen storage disease type IV: from severe hepatosplenomegaly to cardiac insufficiency. Some discrepancies in genetic and biochemical abnormalities. Arch Med Sci. 2018;14(1):237-247.
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