60th Annual DSS Case 2019-11

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NO DISCLOSURES

LEARNING OBJECTIVES

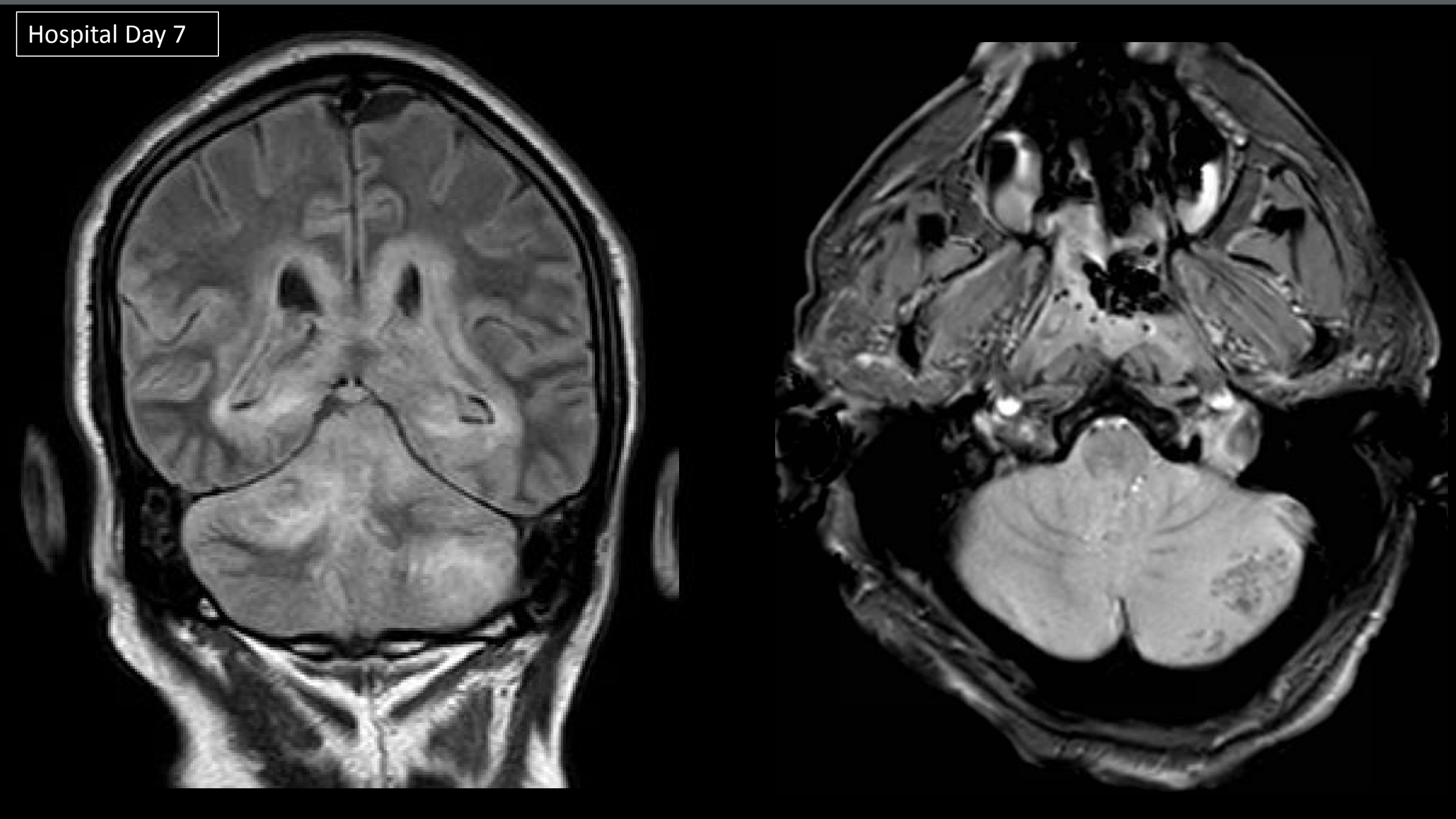
- Discuss differential diagnosis
- Analyze results of ancillary diagnostic studies
- Final diagnosis

CLINICAL HISTORY

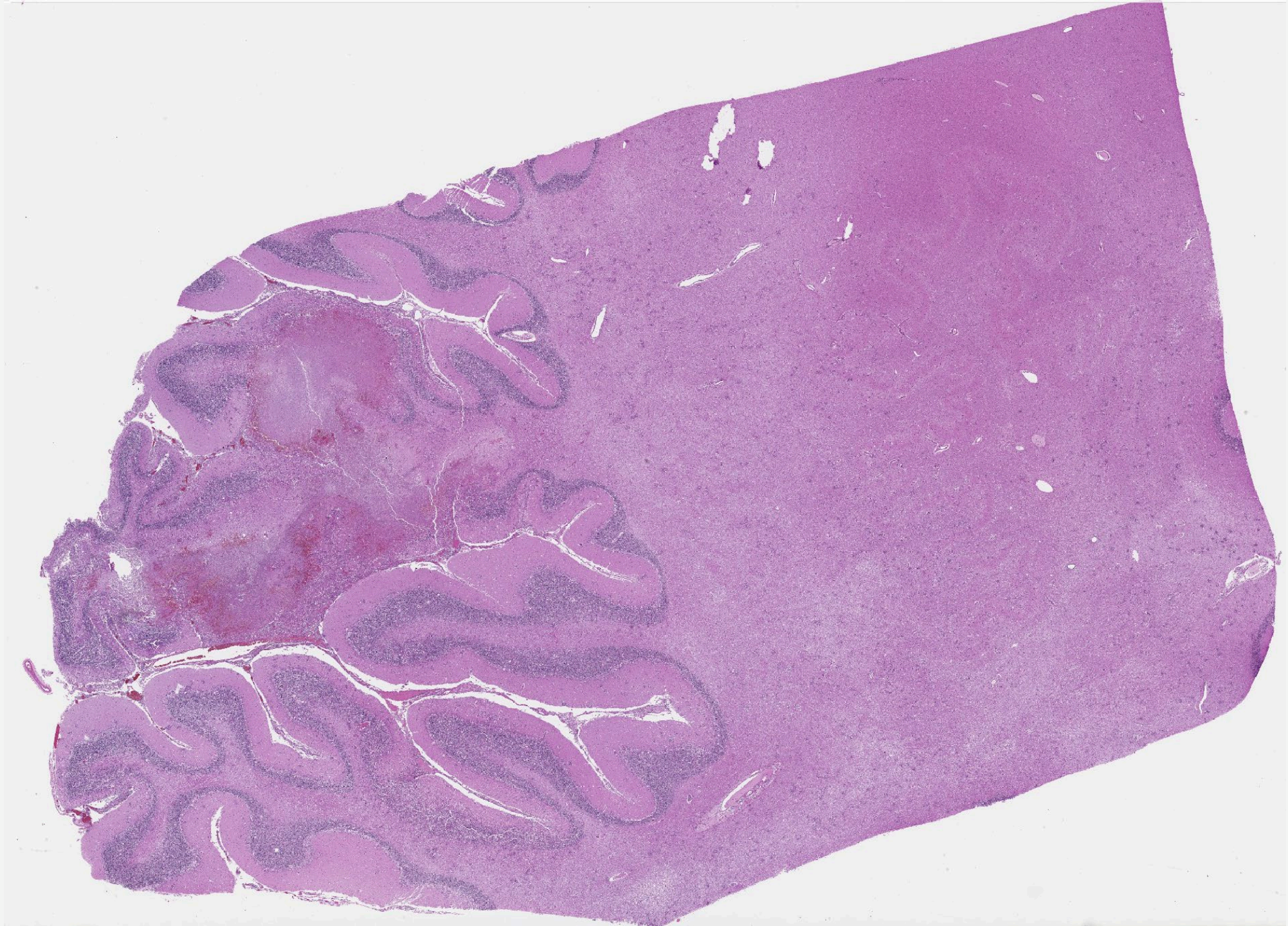
- 66-year-old male found collapsed
  - Presumed bacterial meningitis
  - CSF showed leukocytosis, elevated protein, and low glucose
  - Bronchoalveolar lavage culture grew *Aspergillus*
  - Multiple CSF cultures and PCR studies negative
  - Treated with antibiotics and steroids with no improvement, remained intubated with GCS of 3, died 10 days after admission

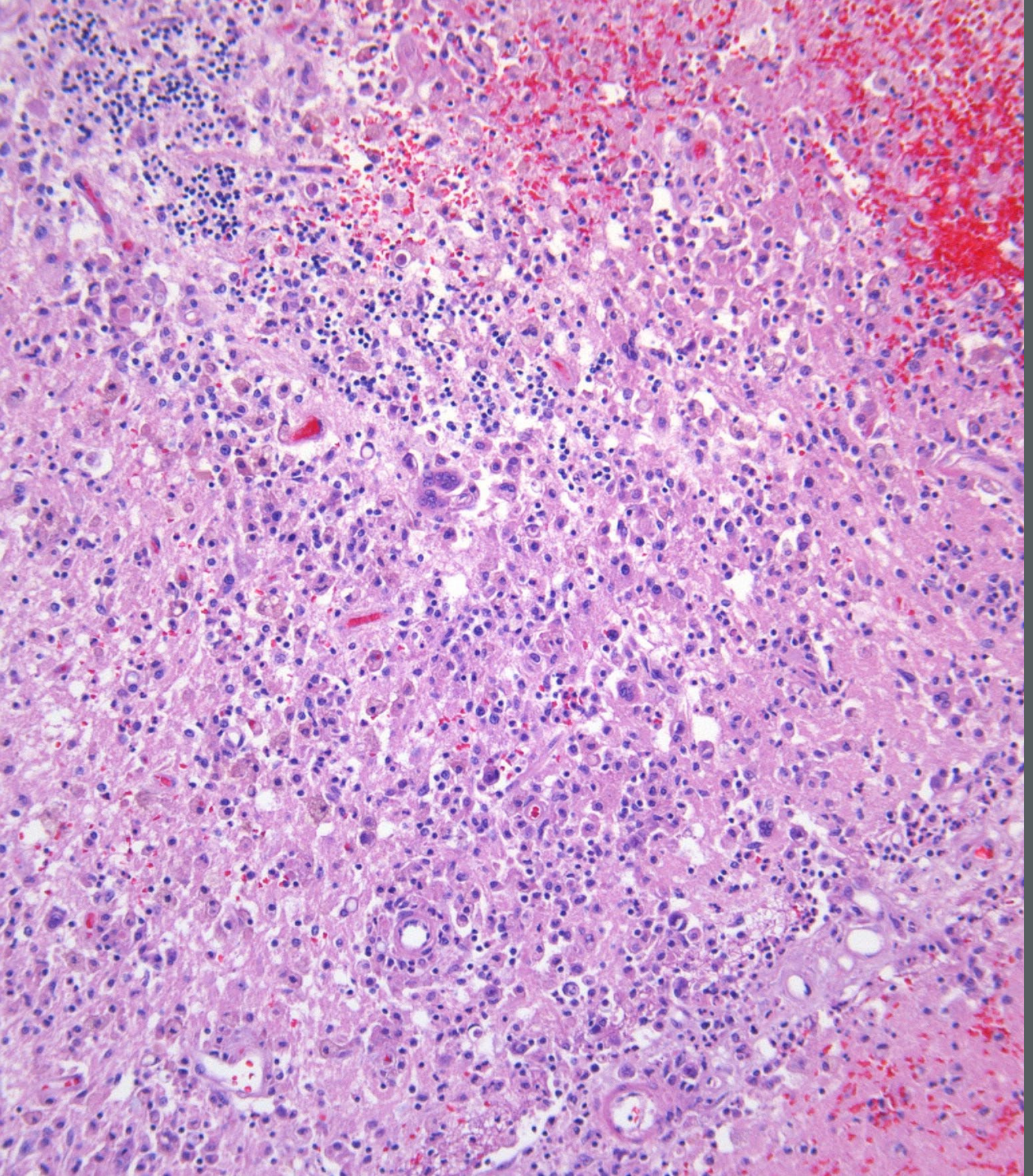
- Social History
  - Houseless
  - Emigrated from Mexico in 1990s
  - Worked in restaurants and landscaping
  - Only known travel outside Pacific Northwest was to California

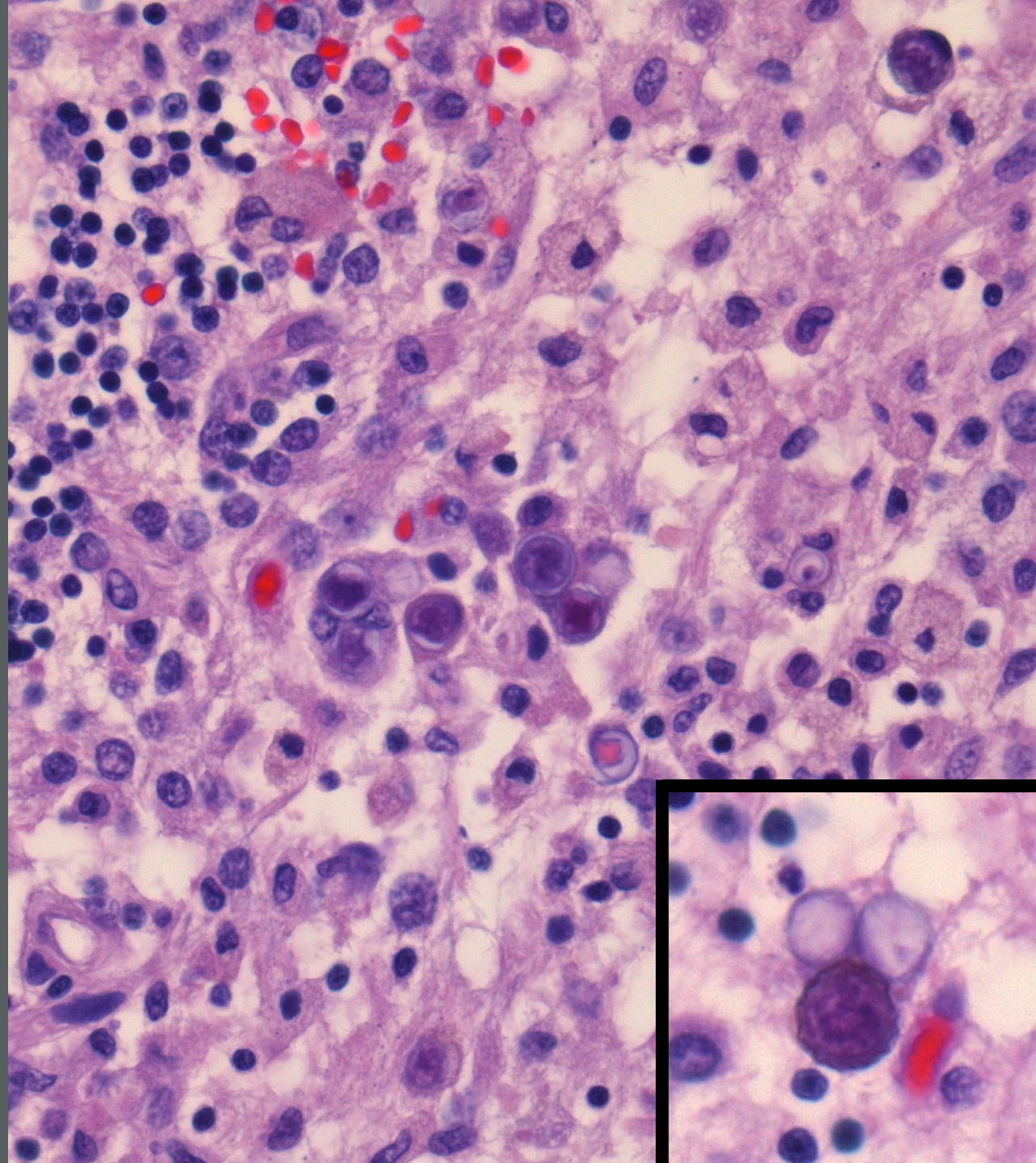
- Past Medical History
  - T-cell prolymphocytic leukemia
    - In remission since July 2017
  - Type 2 Diabetes mellitus
    - Poorly controlled
  - *Nocardia* pneumonia
    - 2017, partially treated

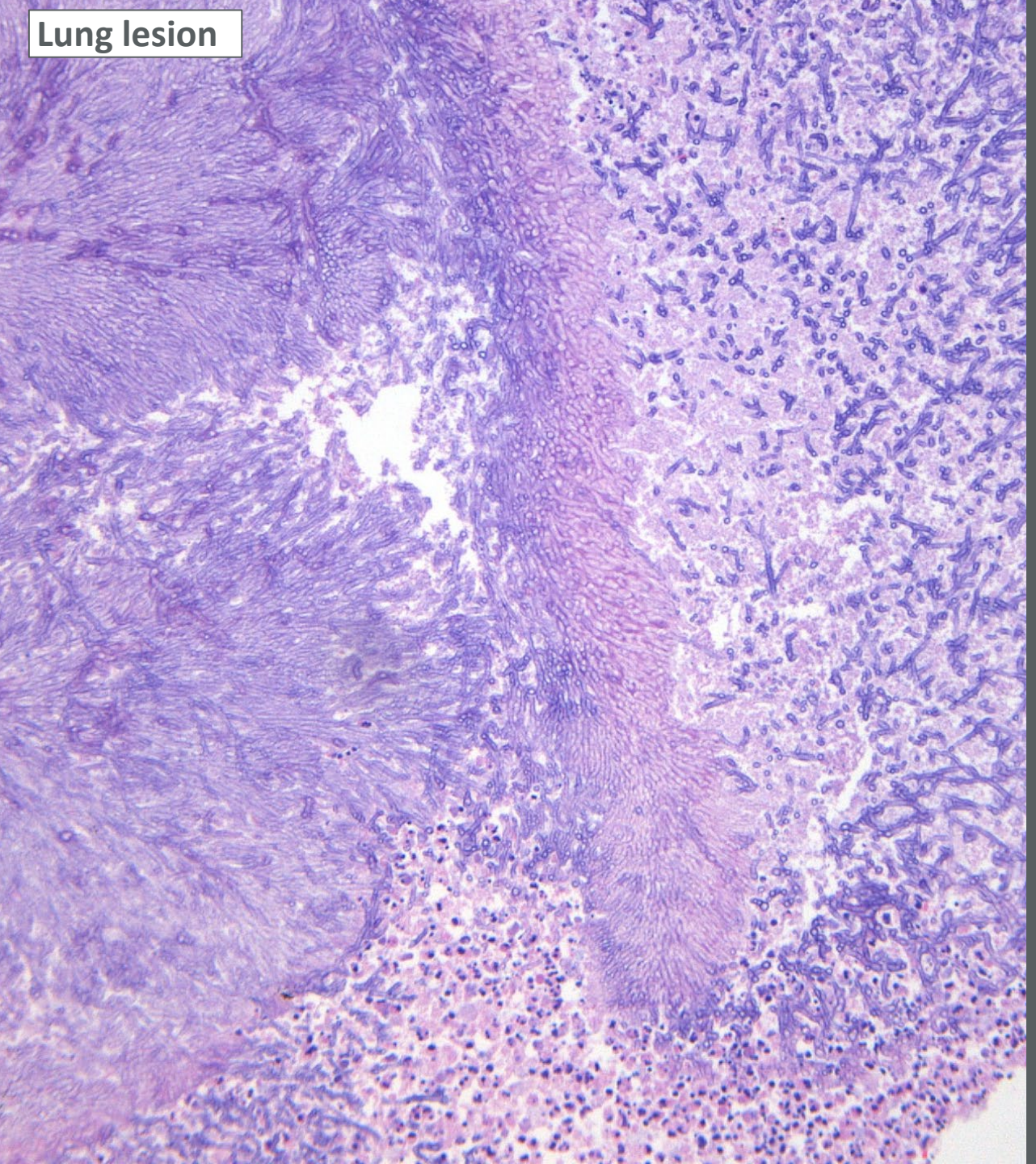

Hospital Day 7

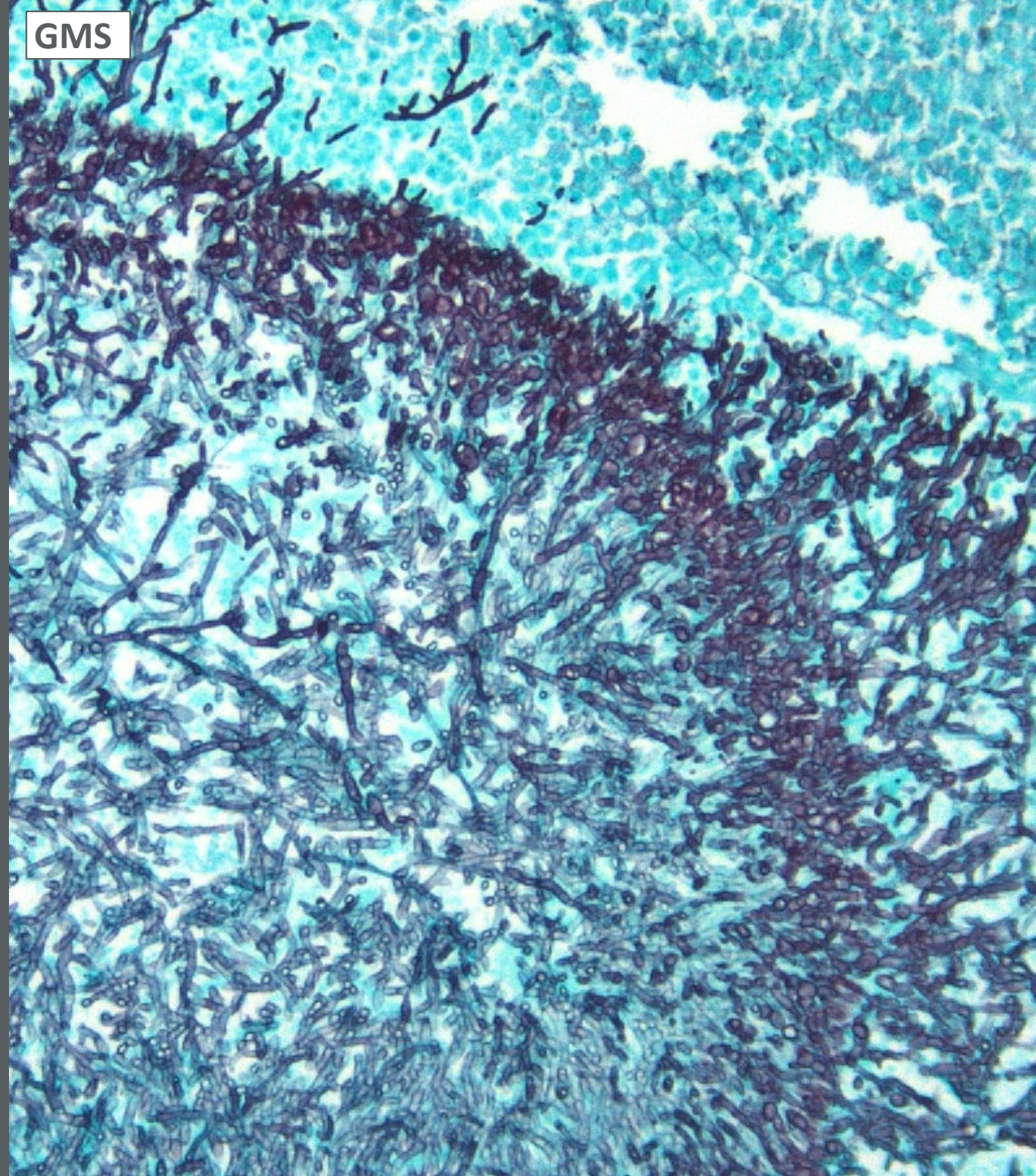
Cerebellum







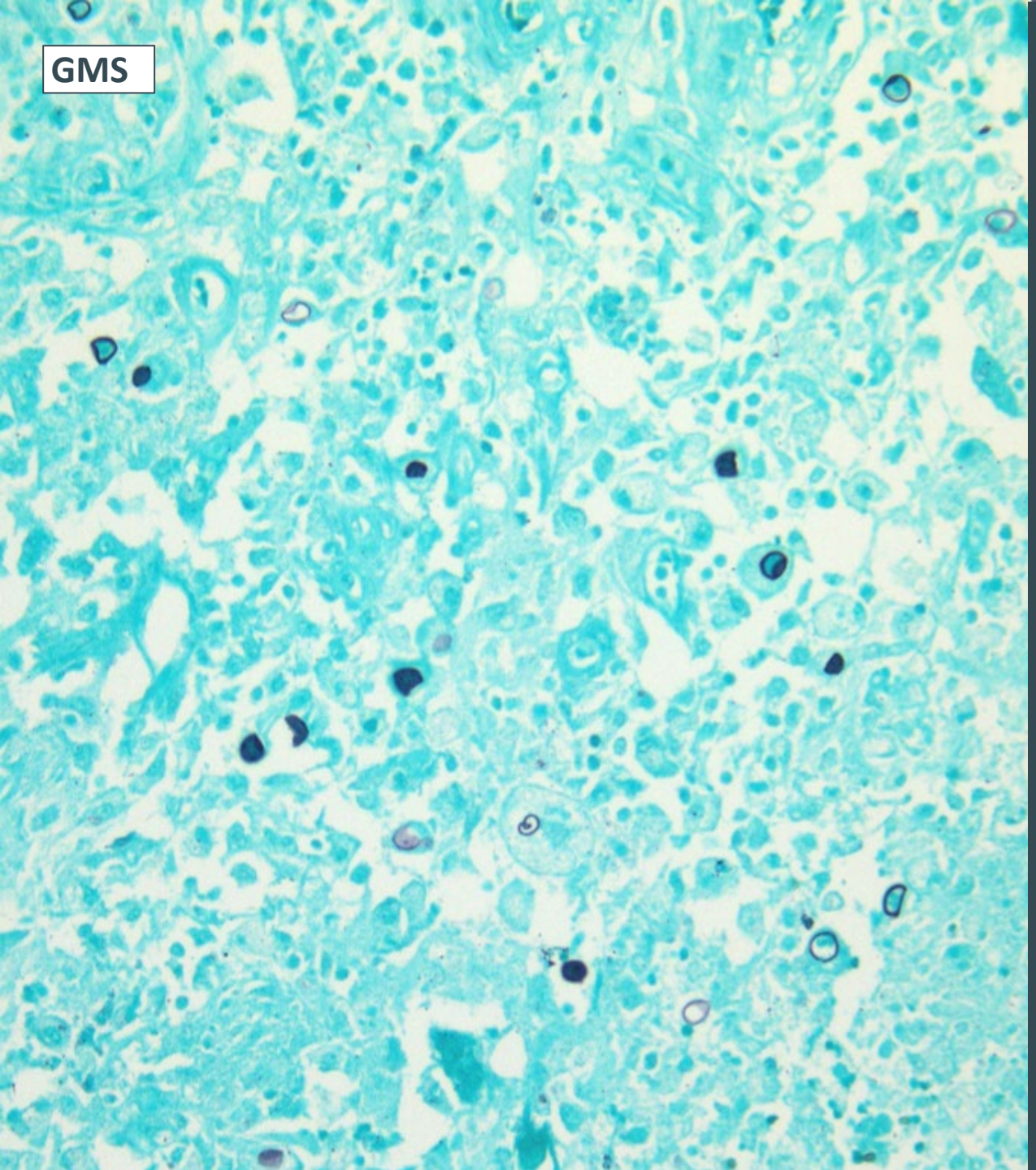

Lung lesion

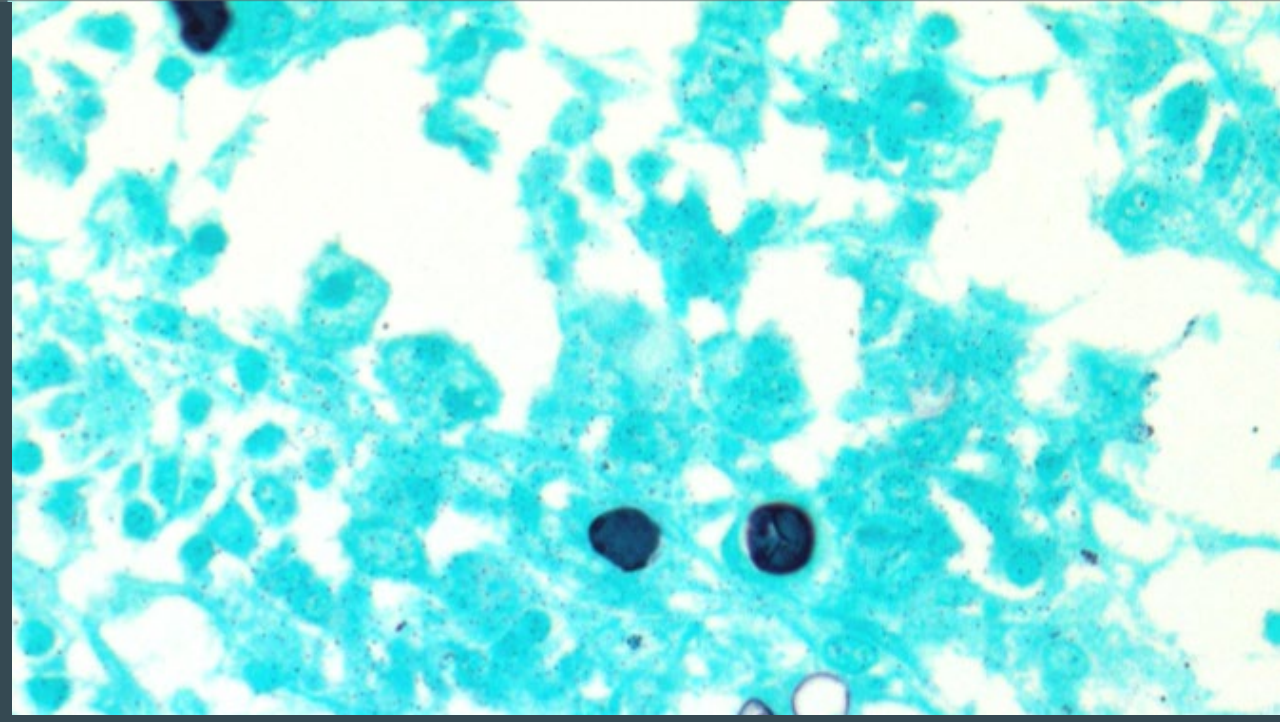

GMS

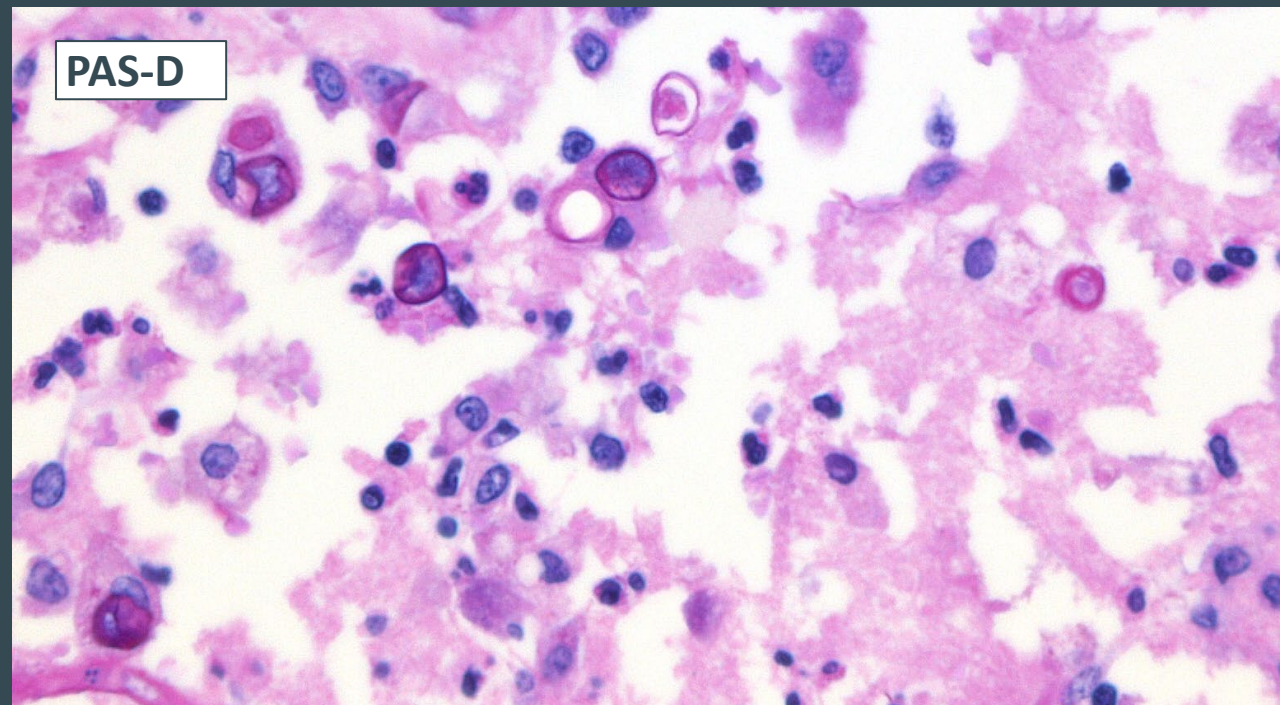
AUDIENCE DISCUSSION

DIFFERENTIAL DIAGNOSIS

- Amoebic encephalitis
  - *Acanthamoeba castellanii, Balamuthia mandrillaris, Naegleria fowleri*
- Brain involvement by disseminated fungal infection
  - *Aspergillus, Mucor, Blastomyces, Coccidioides, Cryptococcus*
- Algal infection
  - *Prototheca wickerhamii*
- Polymicrobial infection

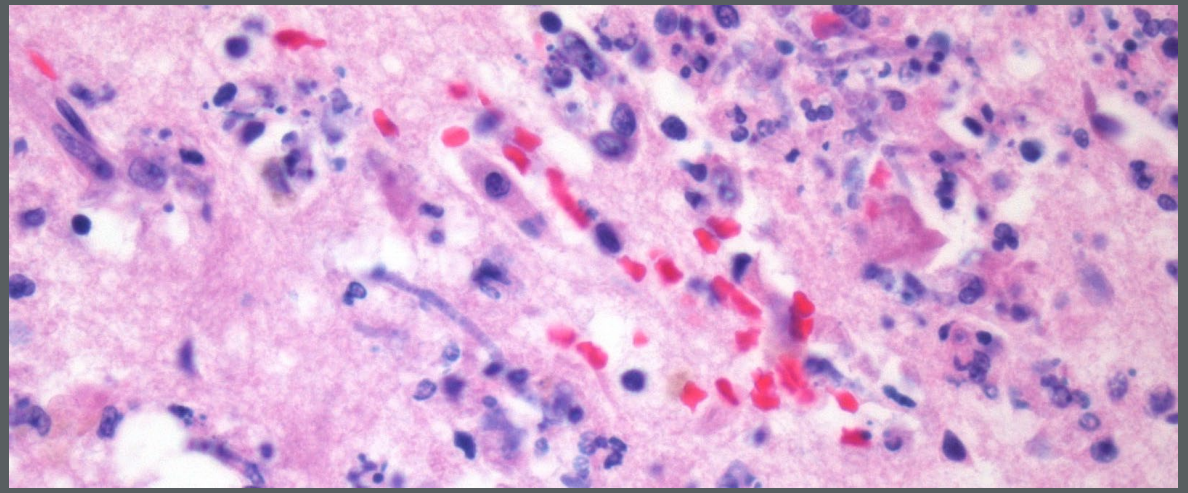

GMS

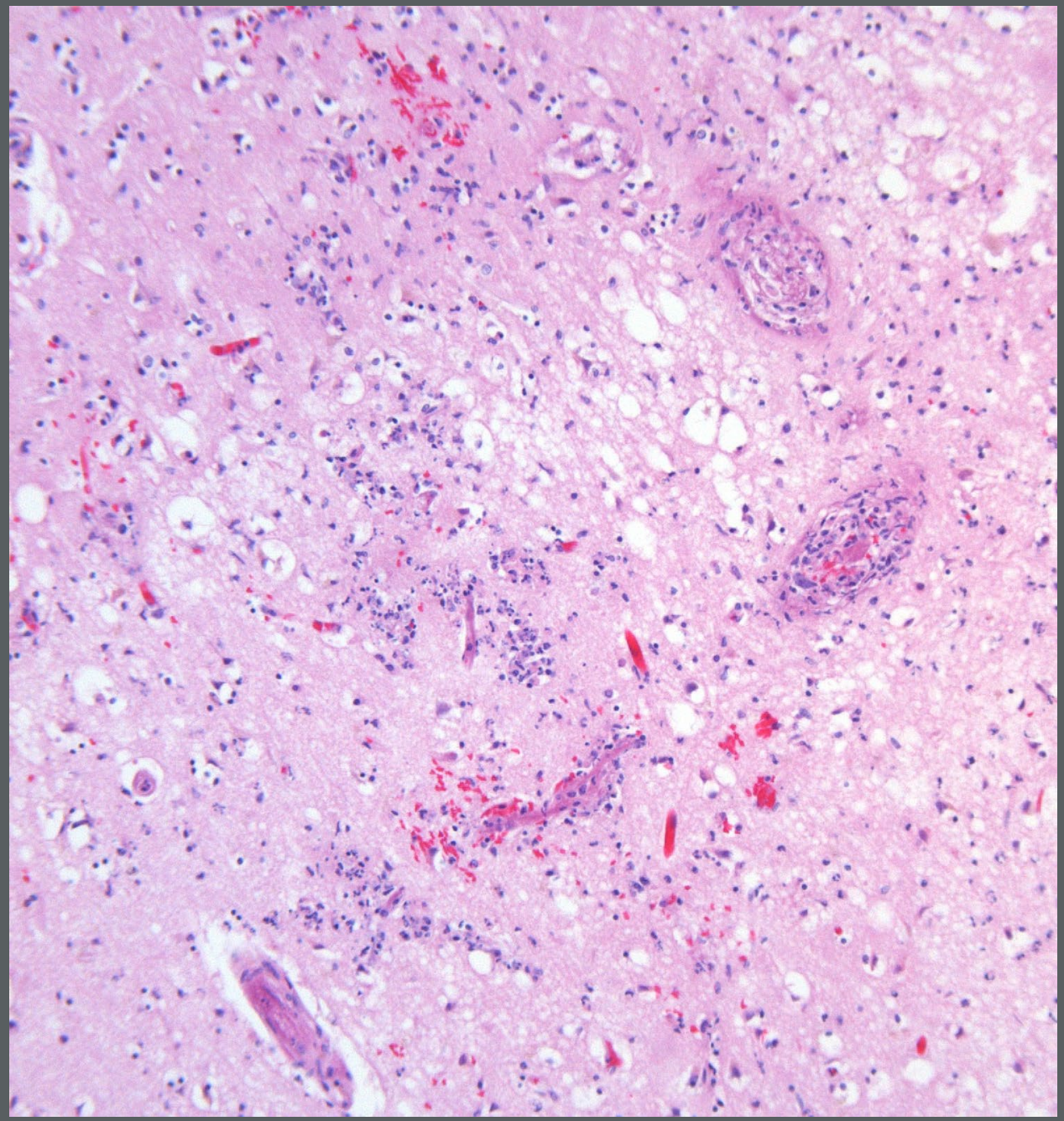



PAS-D

Aspergillus fumigatus

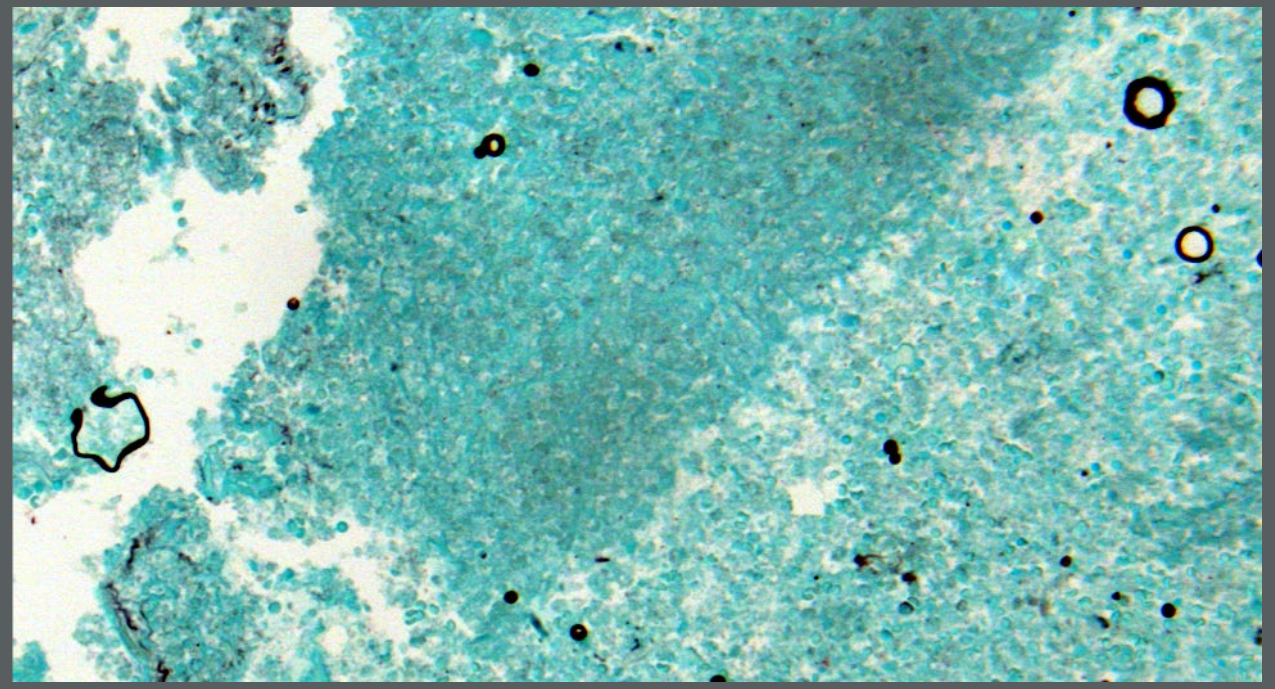
- Septate, acute branching, GMS-positive hyphae
- Hematogenous spread after pneumonia
- Necrotizing perivascular inflammation

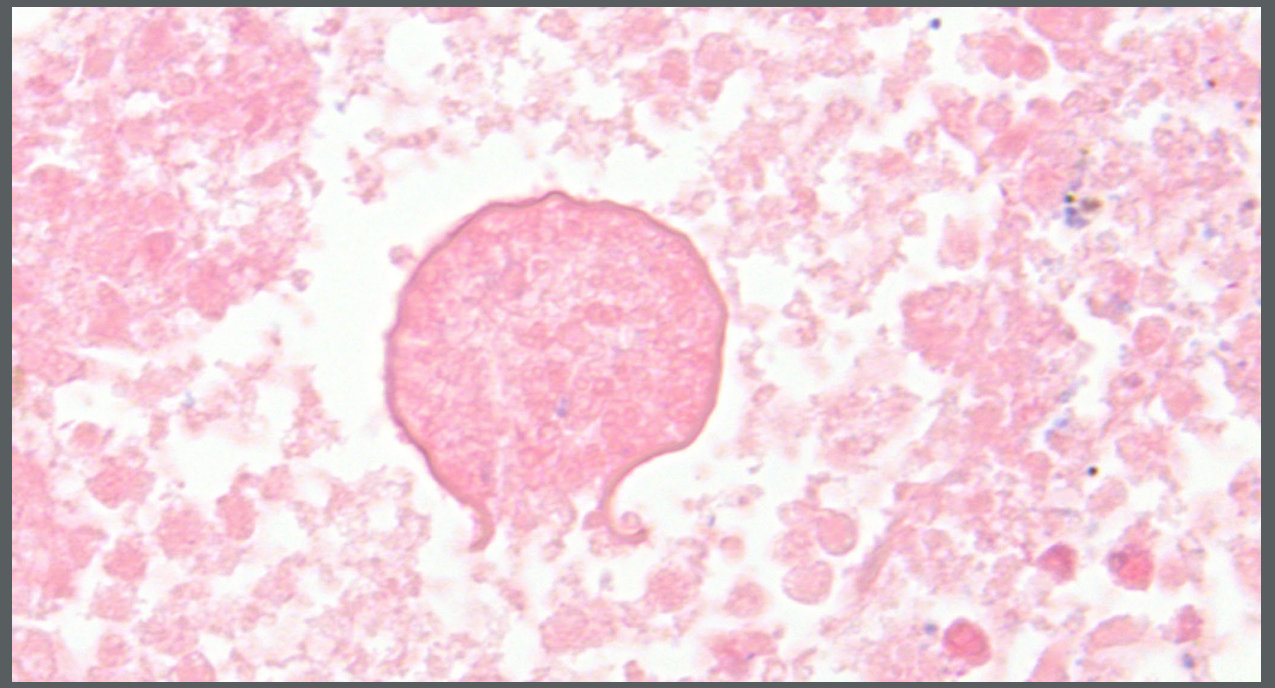




Coccidioides immitis

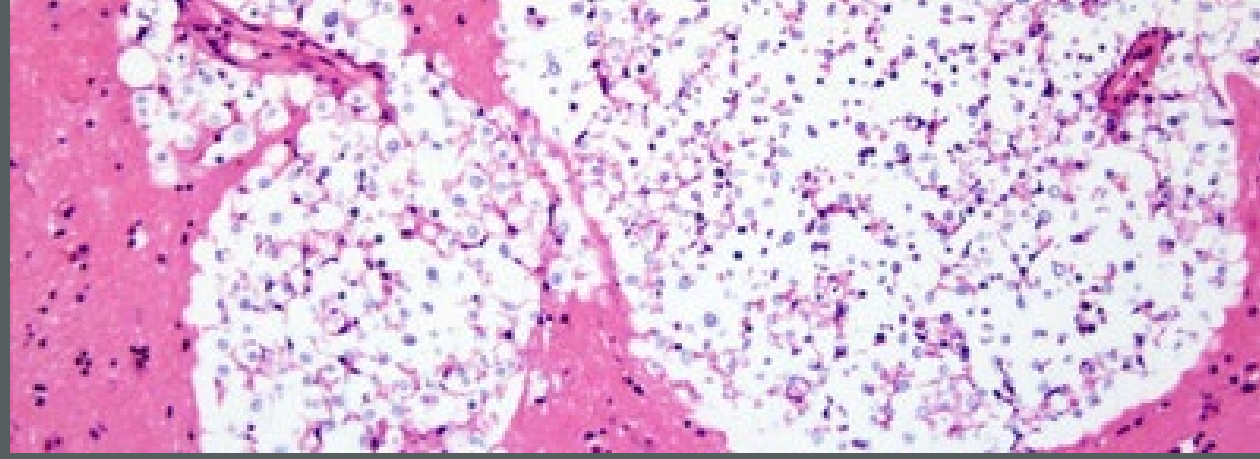
- Southwestern United States, Mexico, and South America
- Risk factors include immunocompromise and diabetes mellitus
- Chronic meningitis
- Numerous spherules with endospores on H&E





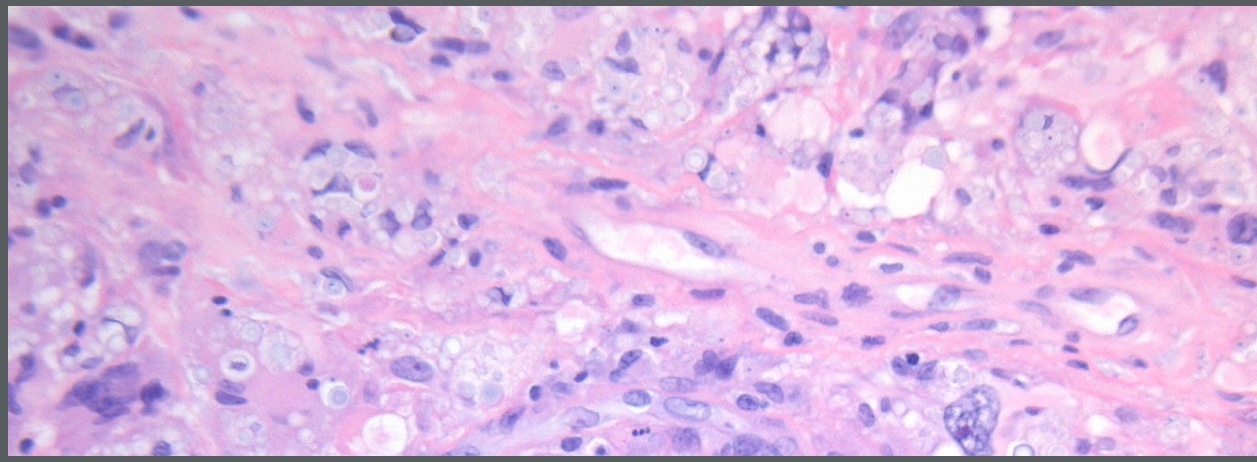
Cryptococcus spp.

- *C. gattii* in Pacific Northwest
- Cause of meningoencephalitis in immunocompromised patients



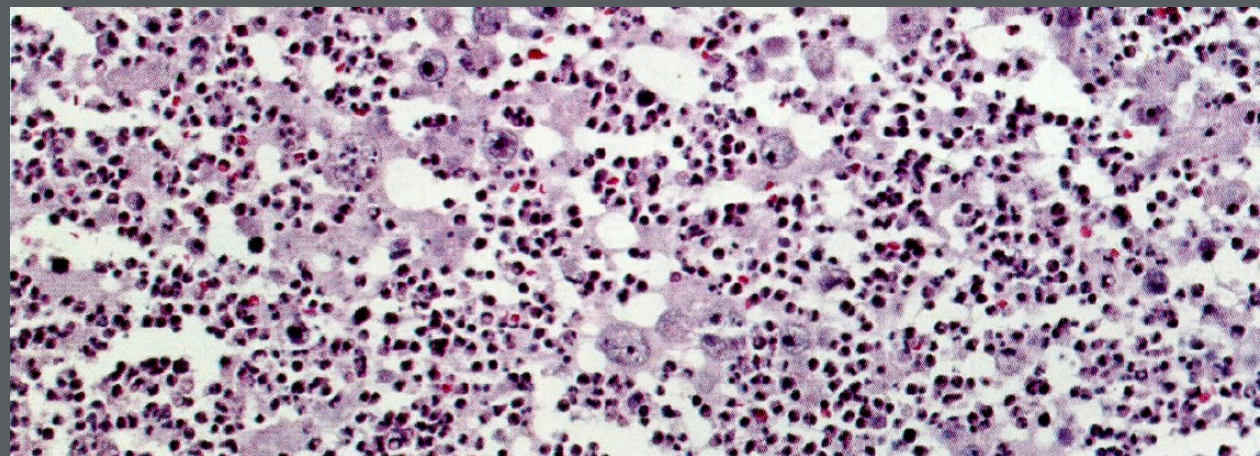
Blastomyces dermatitidis

- Ohio and Mississippi River Valleys
- Broad-based budding pathognomonic



Nocardia spp.

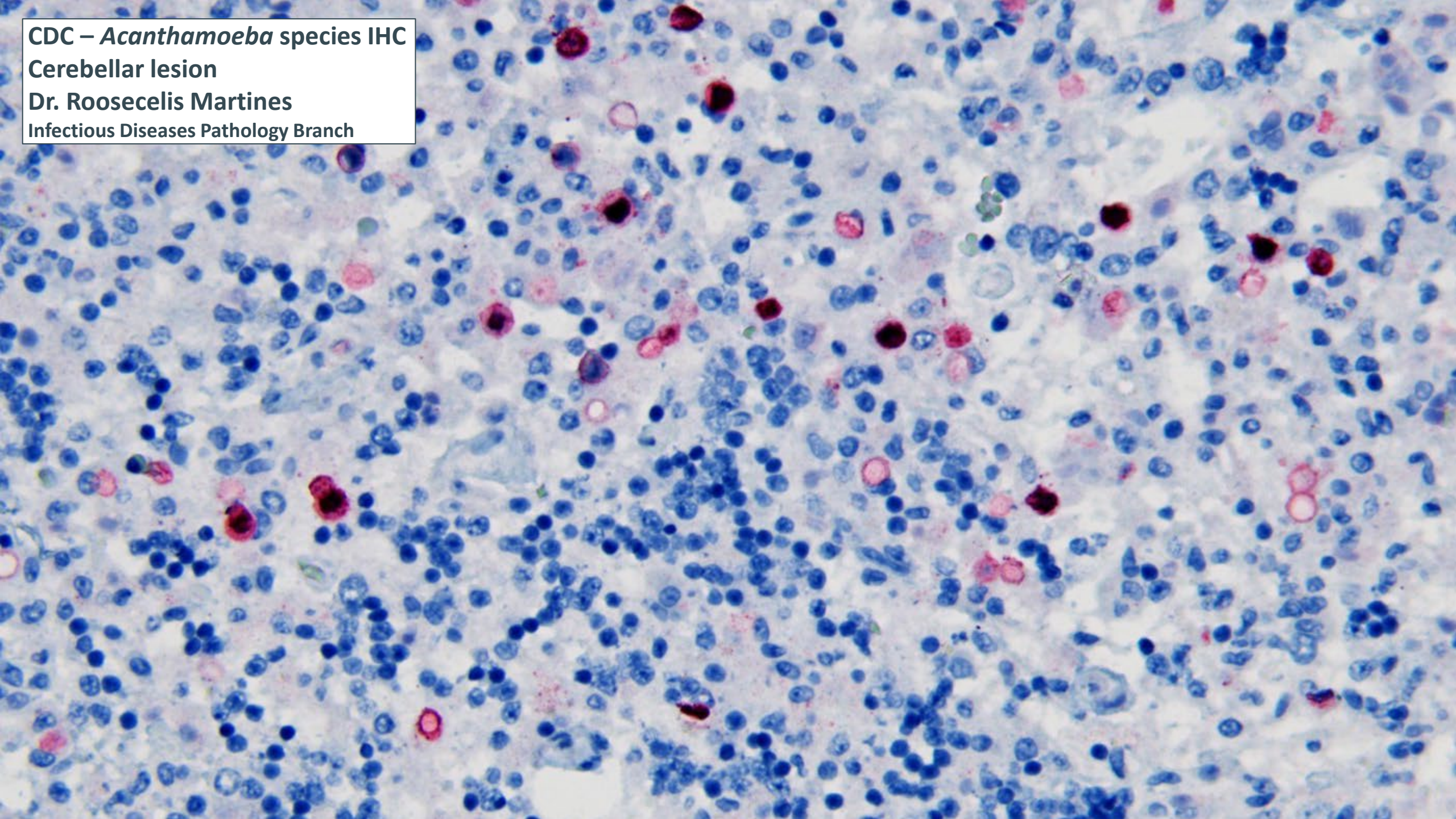
- Filamentous bacteria
- Rare cause of brain abscess



PLOS ONE 6(12): e28625. https://doi.org/10.1371/journal.pone.0028625
Louis et al. AFIP Atlas of Non-Tumor Pathology, 8 (2009).

ADDITIONAL STUDIES

- Immunohistochemical stains by Centers for Disease Control on fixed brain tissue were positive for
  - free-living amoebas (*Naegleria*, *Balamuthia*, and *Acanthamoeba*)
  - *Acanthamoeba* spp.


CDC – *Acanthamoeba* species IHC
Cerebellar lesion
Dr. Roosecelis Martines
Infectious Diseases Pathology Branch

MOLECULAR CONFIRMATION

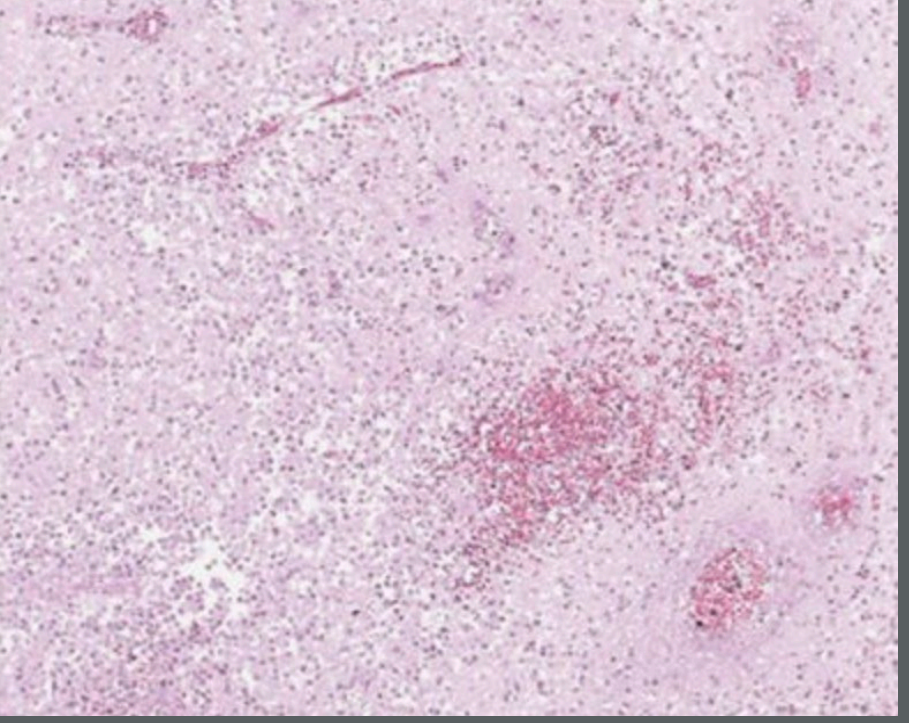
- CDC Sanger sequencing assay (461 bp in 18s small subunit rRNA)
  - Suggestive of *Acanthamoeba castellanii* species (>99%), T1 genotype
- Non-directed PCR for infectious organisms UC San Francisco (Wilson Lab)
  - Independently identified *Acanthamoeba castellanii* nucleic acid from cerebellar FFPE samples
  - No other infectious agents were identified
  - First identification of *Acanthamoeba* using this molecular testing platform

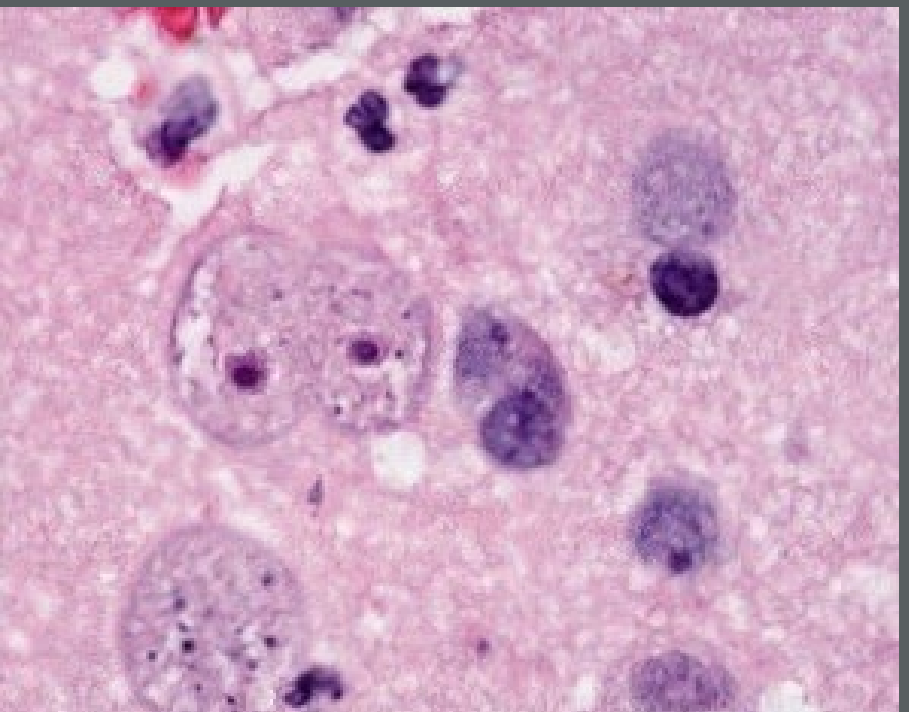
FINAL DIAGNOSIS

Amebic meningoencephalitis due to *Acanthamoeba castellanii*

AMOEBIC MENINGOENCEPHALITIS

- Caused by free-living amebae that exist ubiquitously.
- The three main types are:
  Acanthamoeba spp.
  Balamuthia mandrillaris
  Naegleria fowleri
- Infections classically classified as:
  Primary Amebic Meningoencephalitis (PAM)
  Granulomatous Amebic Encephalitis (GAE)





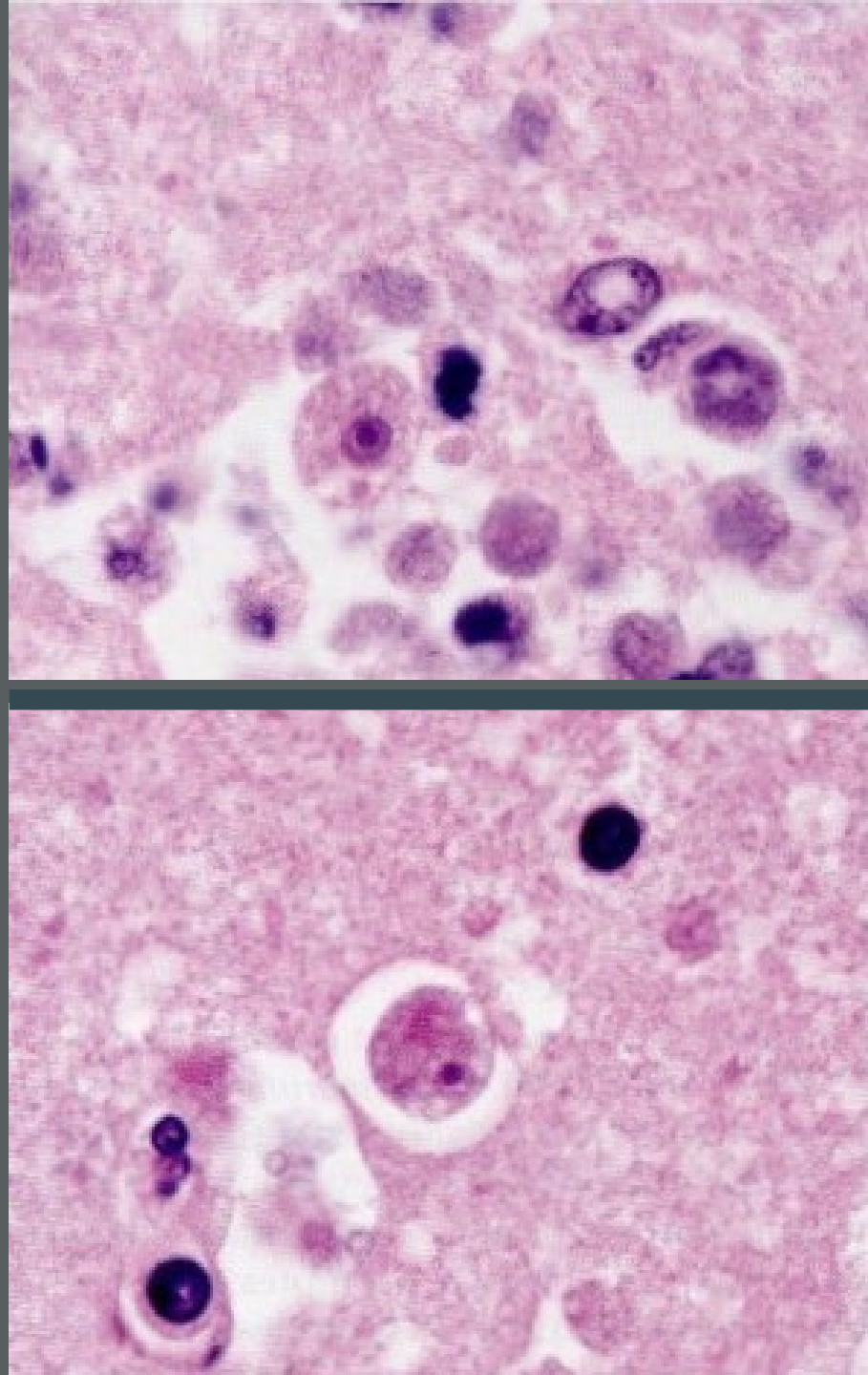
Primary Amebic Meningoencephalitis

- Due to *Naegleria fowleri*
- Young healthy patients
- Swimming and nasal irrigation
- Through cribriform plate into CNS
- Acute infection often rapidly fatal
- Neutrophils and hemorrhagic necrosis
- Trophozoites only

Mod Pathol. 2007 Dec;20(12):1230-7. Epub 2007 Oct 12.
Louis et al. AFIP Atlas of Non-Tumor Pathology, 8 (2009).

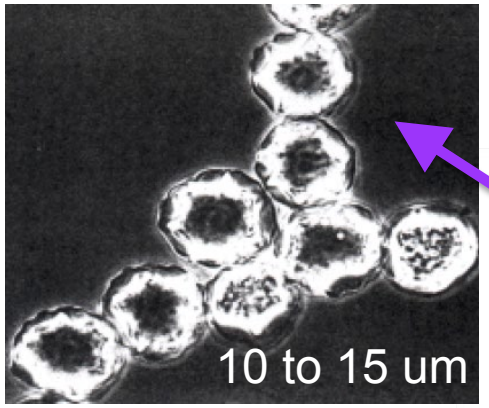
Granulomatous Amebic Encephalitis

- Due to *Acanthamoeba* spp. (top) or *Balamuthia mandrillaris* (bottom)
- Immunocompromised patients
- Hematogenous spread to CNS from lungs or skin infection
- More indolent than PAM
- Granulomatous infiltrate with focal necrosis
- Both trophozoites and cysts seen



Louis et al. AFIP Atlas of Non-Tumor Pathology, 8 (2009).

Acanthamoeba Life Cycle



Cysts

Amebae (cysts and trophozoites) can enter humans in various ways

Through the eye

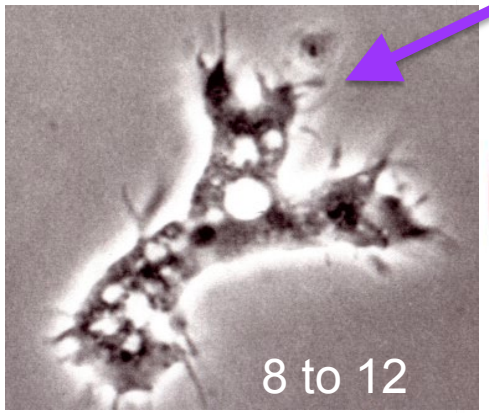
Through nasal passages to the lower respiratory tract

Through ulcerated or broken skin

Cysts and trophozoites in tissue

Trophozoite

Mitosis



EPA

CDC
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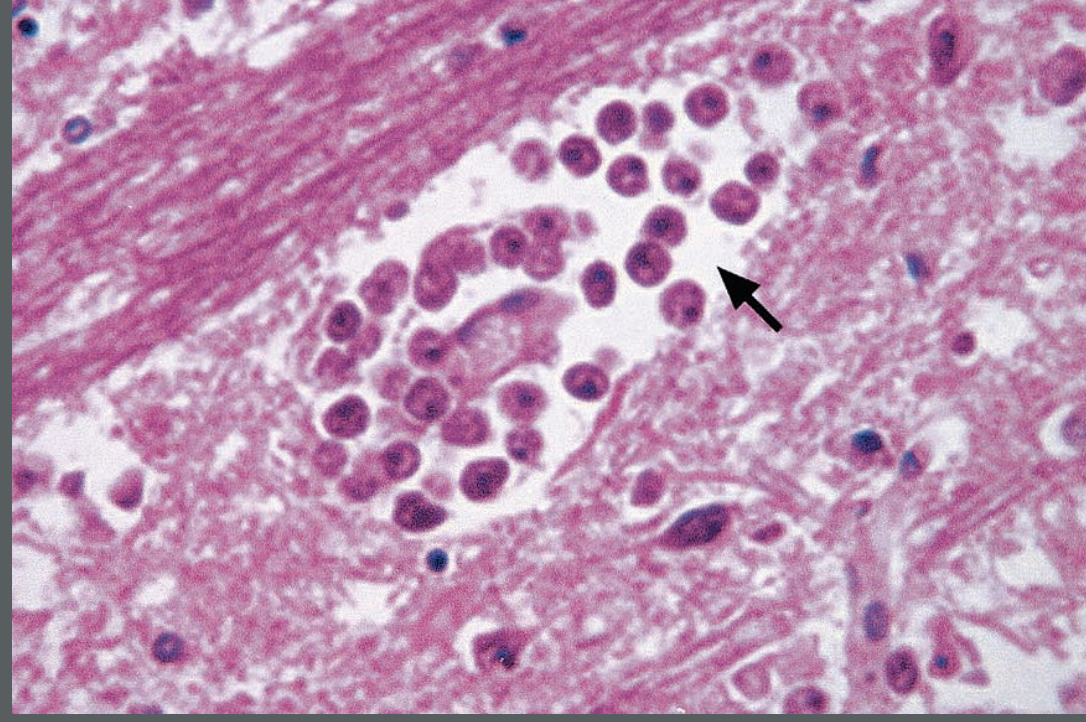
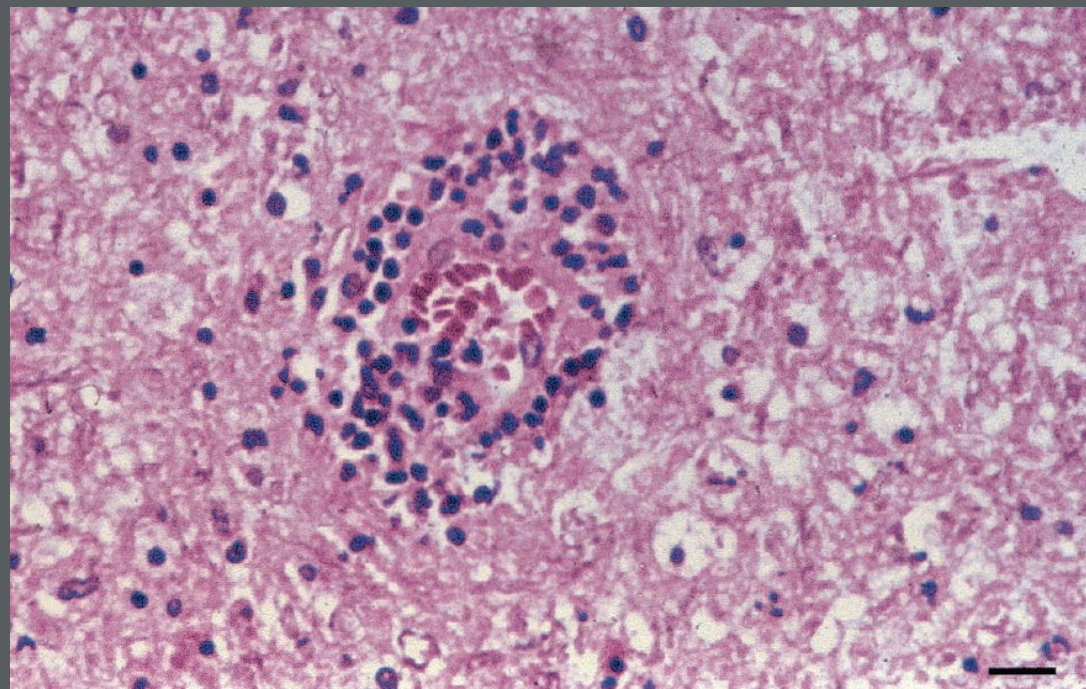
Acanthamoeba castellanii,

T1 genotype

- One of a few *Acanthamoeba* spp. to infect the CNS
- 12 genotypes
- Granulomatous infiltrate on H & E
- Amebic trophozoites resemble macrophages





Clin Micro Rev Apr 2003, 16 (2) 273 307; **DOI:** 10.1128/CMR.16.2.273-307.2003

SUMMARY

- Diagnosis: Amoebic meningoencephalitis, due to *Acanthamoeba castellanii,* T1 genotype
- Suspect ameba when cultures and PCR studies are negative
- First case of *Acanthamoeba* identified using metagenomic next-generation sequencing
- Two cases of *Acanthamoeba* meningoencephalitis reported in 2018 in Portland

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OHSU

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