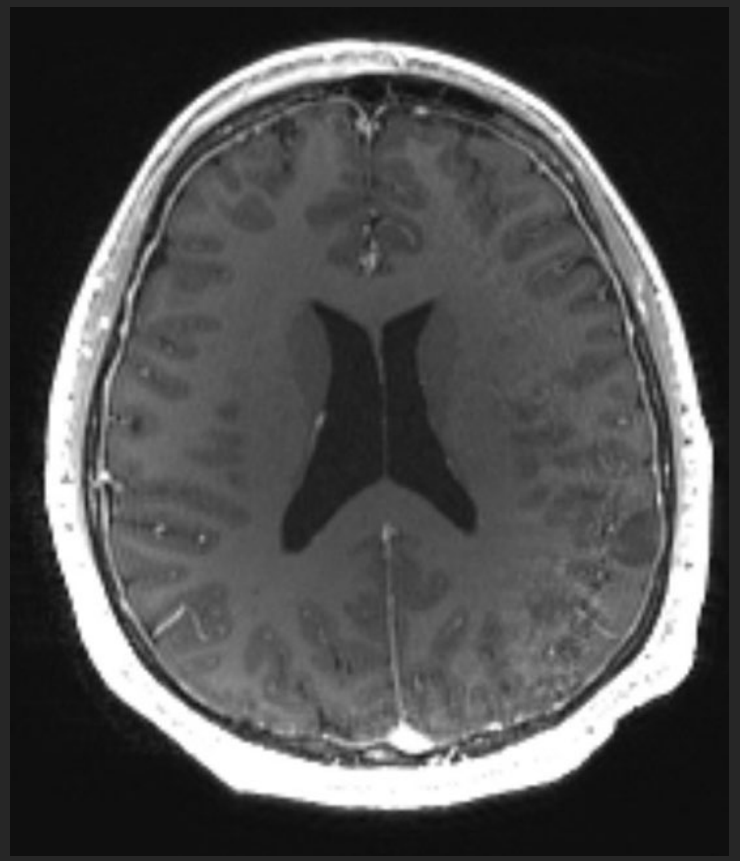
American Association of Neuropathologists (AANP)
2023 ANNUAL DIAGNOSTIC SLIDE SESSION

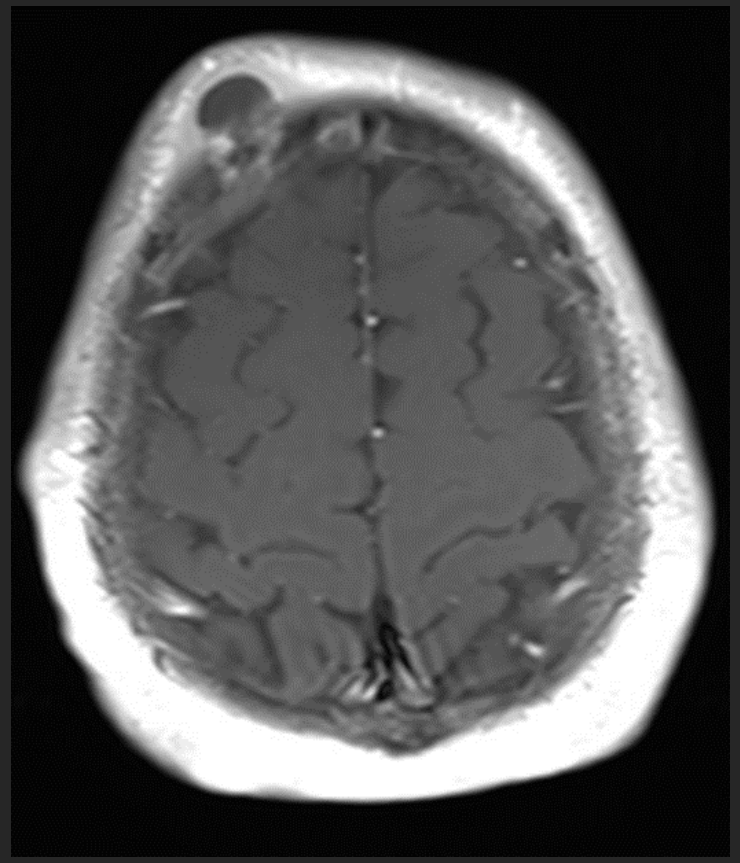
Cassie B. MacRae, M.D. & Isaac Solomon, M.D., Ph.D.

Department of Pathology
Brigham and Women's Hospital & Harvard Medical School
Boston, MA

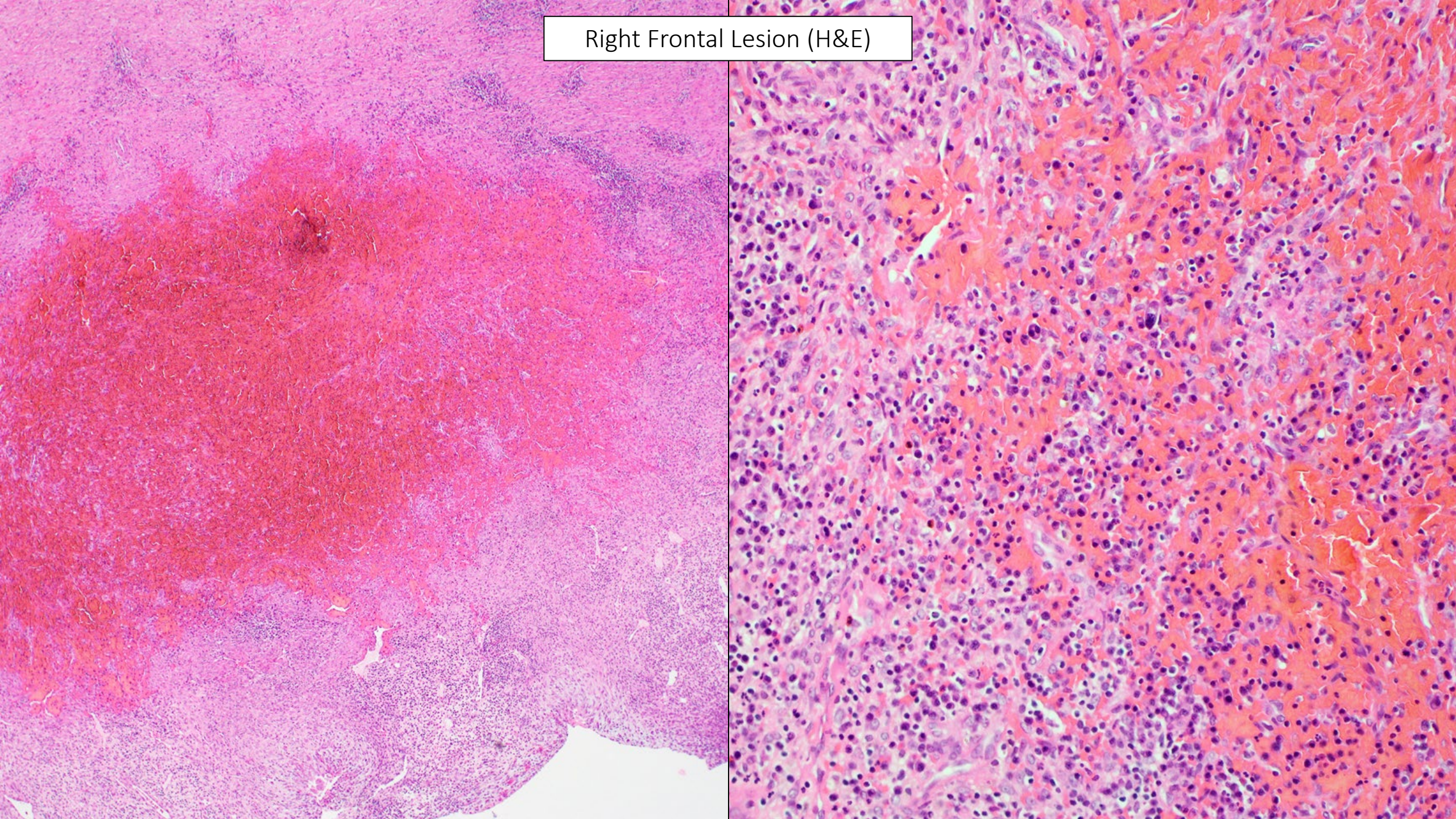
Clinical History

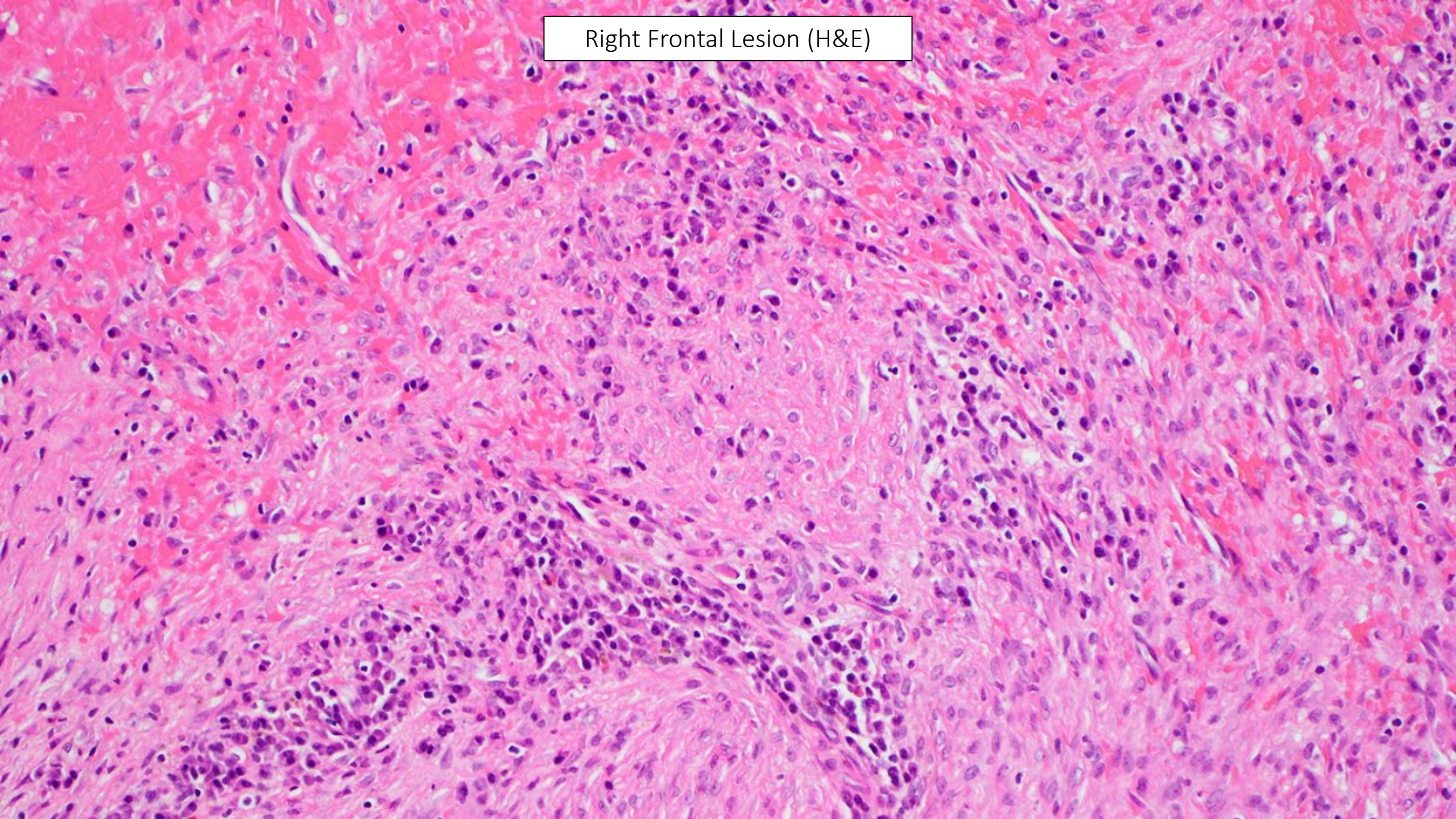
- 25-year-old previously healthy male, suffered a seizure while playing video games at home
- Head MRI: Left inferior parietal lesion, 1.6 cm cystic intraparenchymal lesion, low-grade glioma vs DNET
- He was started on levetiracetam, followed with serial imaging and scheduled for surgical resection
- Five months later, the patient presented with a new scalp lesion (initially tender, without erythema or discharge)
- MRI showed a 1.2 x 1.6 cm right frontal lesion with enhancement of the adjacent scalp, loss of the subjacent right frontal calvarial cortex, and thickening and enhancement of the underlying right frontal dura.
- His previously demonstrated cystic intraparenchymal lesion in the inferior left parietal lobe was unchanged/stable in appearance.

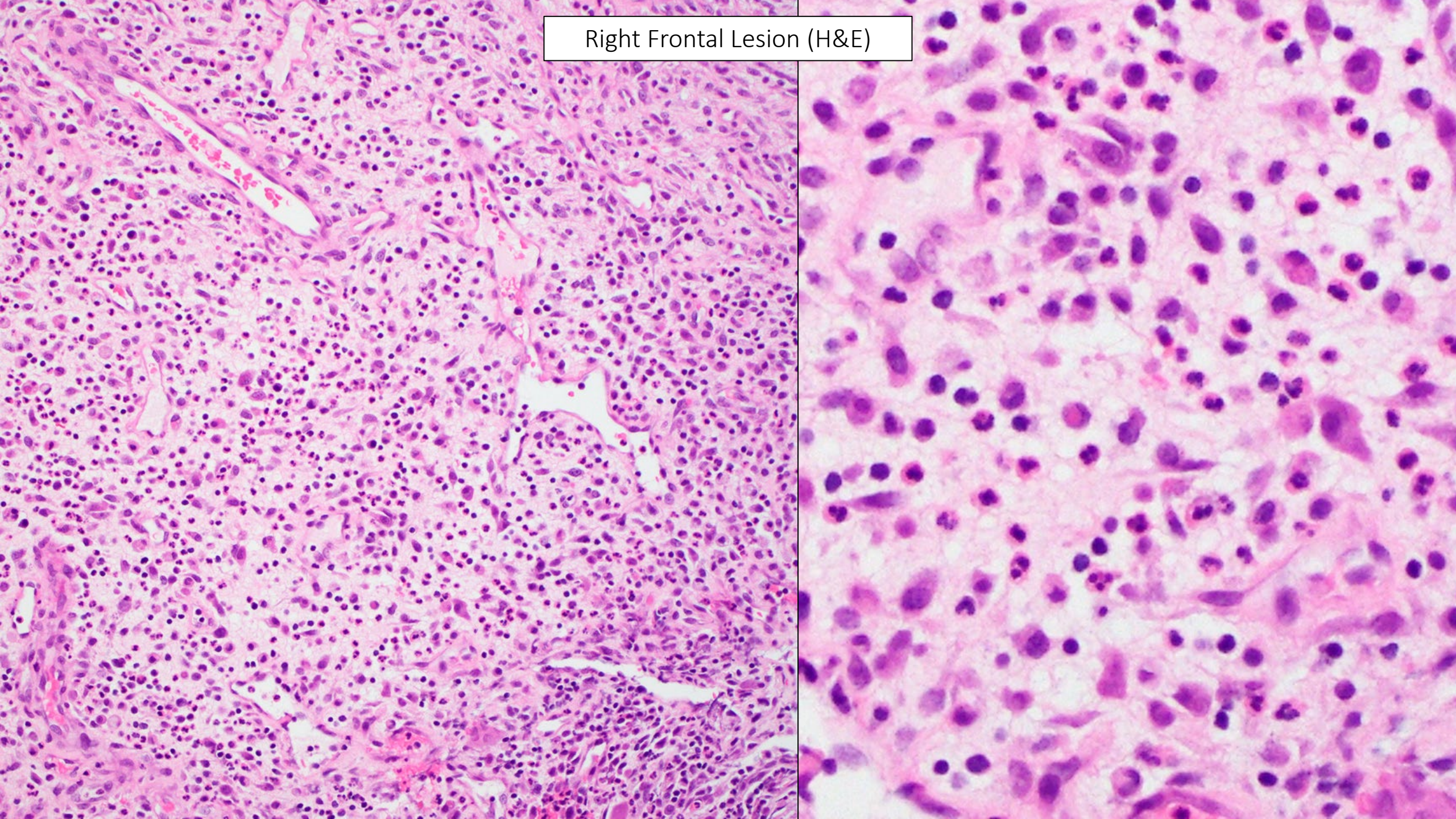




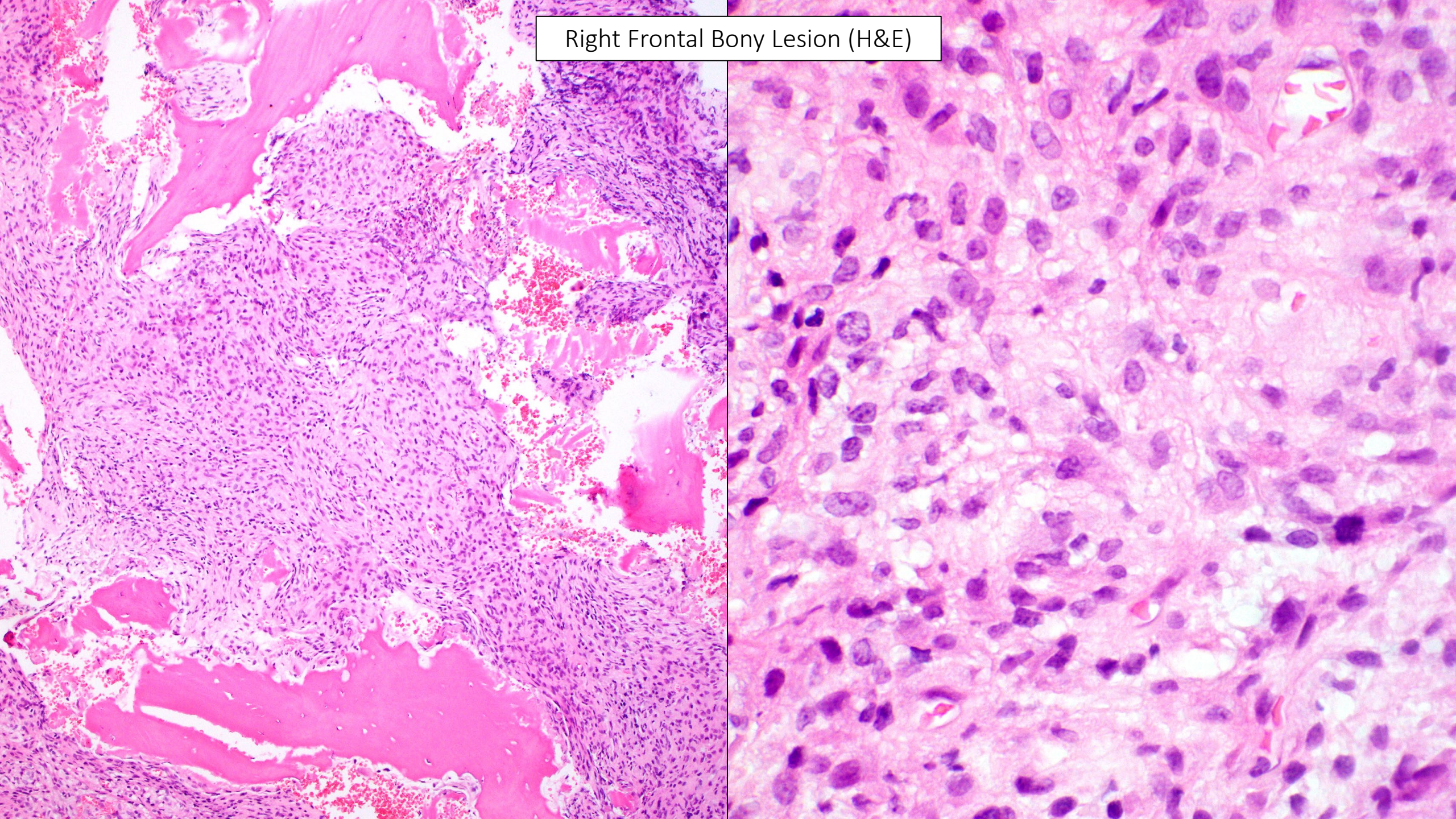

F


Right Frontal Lesion (H&E)

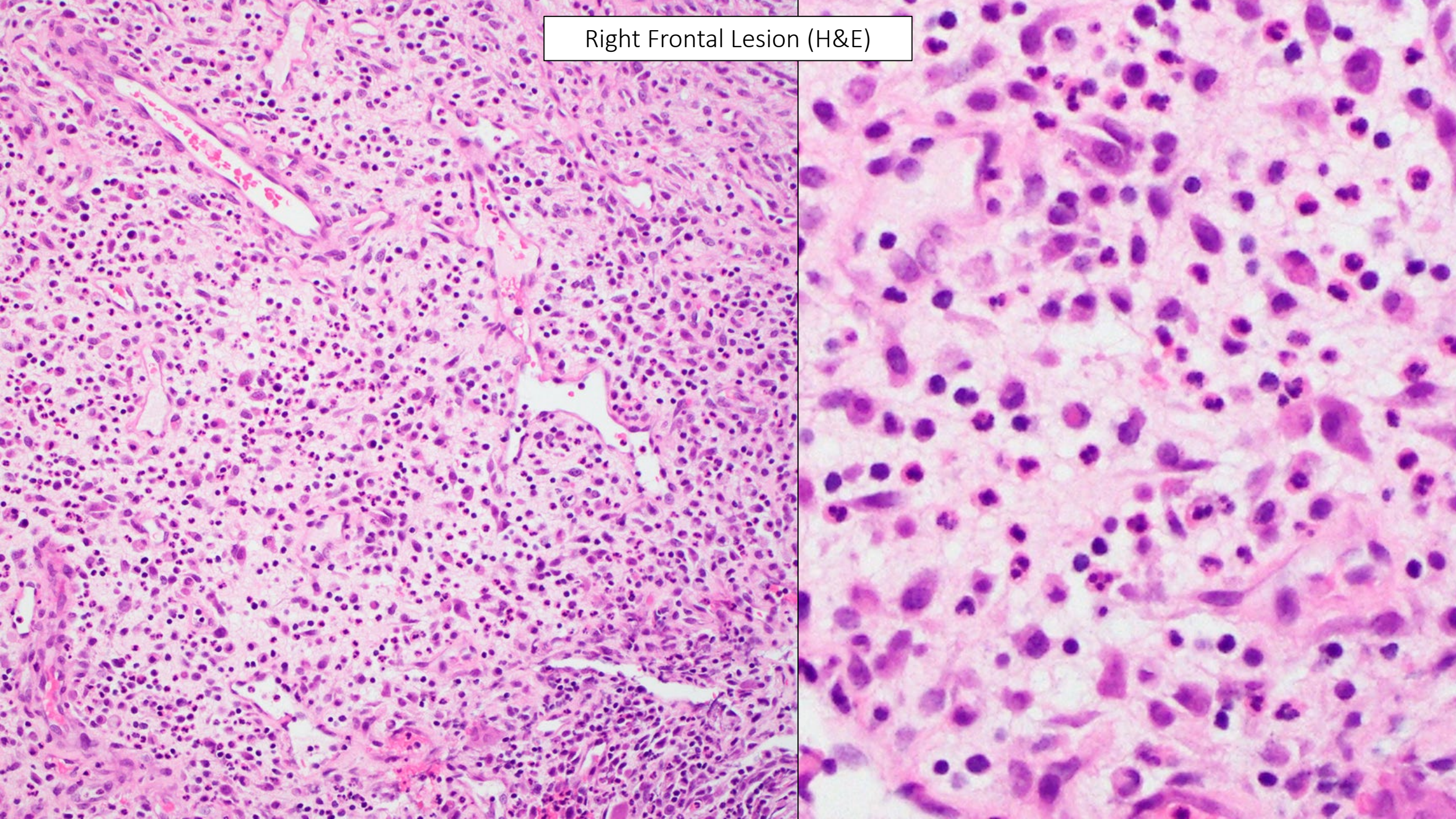

Right Frontal Lesion (H&E)

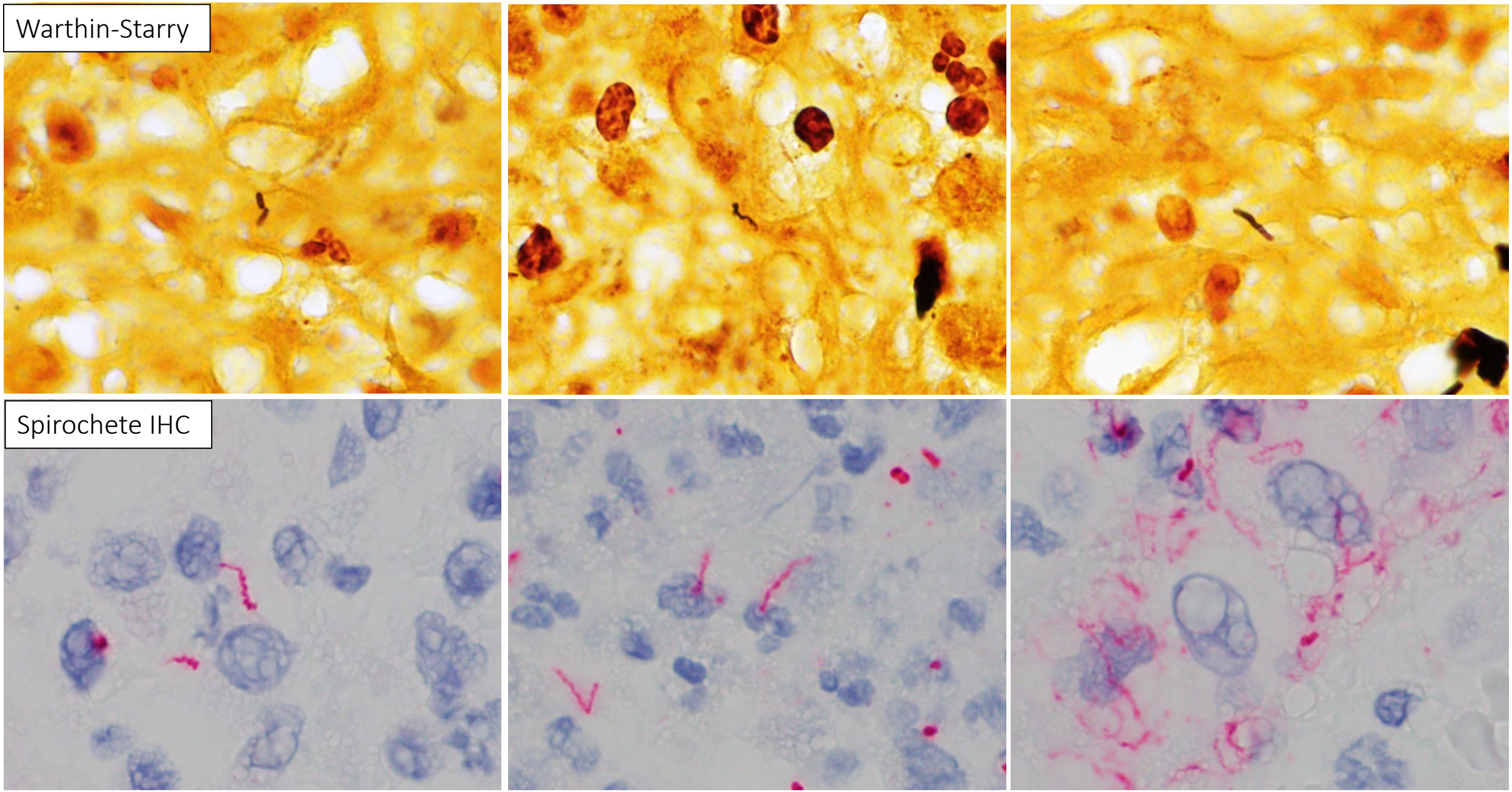

Right Frontal Lesion (H&E)

Right Frontal Bony Lesion (H&E)



Diagnosis?


Right Frontal Lesion (H&E)


Warthin-Starry
Spirochete IHC

A. RIGHT FRONTAL LESION:

Dura with dense infiltration of acute and chronic inflammatory cells and granulation tissue.
Spirochetes identified in immunostain and Warthin-Starry stain morphologically compatible with *Treponema pallidum*.

B. RIGHT FRONTAL BONY LESION:

Bone with reactive changes and acute and chronic inflammation

C. RIGHT FRONTAL LESION:

Fibrous tissue with acute and chronic inflammation.

Gram, MSS, AFB and CD1a stains are negative.

Laboratory Testing

- *Treponema pallidum* particle agglutination (TP-PA) positive
- Rapid plasma reagin (RPR) positive (1:64)
- HIV-1 negative (antigen, antibody, viral load)
- *Chlamydia trachomatis* and *Neisseria gonorrhoeae* nucleic acid detection negative

Treatment & Follow-Up

- Prior to developing scalp mass - patient reported experiencing diffuse, red, flat, non-pruritic rash on his chest, arms, and extremities
  - He attributed rash to allergic reaction, which resolved shortly after treatment with diphenhydramine HCl
- Admitted for initiation of high-dose intravenous penicillin therapy for syphilitic osteomyelitis of the skull.
  - Given proximity to dura, he was treated with penicillin G 6,000,000 units IV every 4 hours or 24,000,000 units / 24 hours by continuous infusion for 14 days followed by a dose of benzathine PCN in clinic.
- Patient doing well since last follow-up with infectious disease clinic
  - Urine and rectal gonorrhea swabs were positive, treated with ceftriaxone.
  - Doing well on HIV PrEP without side effects.
  - RPR trending down to 1:8 after 3 months and 1:4 after 4 months (initially at 1:64)
- Subsequent resection of left parietal lobe lesion
  - Dx: Low-grade glial/glioneuronal tumor

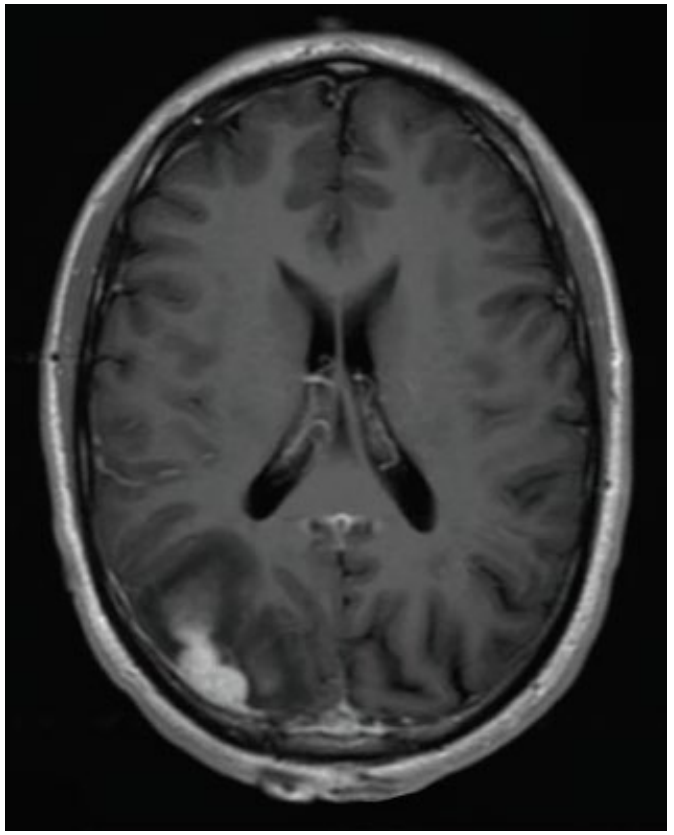
Syphilis

- Epidemiology (US)
  - ~130,000 reported cases in 2019
  - 47% of primary/secondary cases in MSM
  - >2,000 congenital cases in 2020
- Stages
  - Primary: firm, round, painless chancre near site of entry lasting 3-6 weeks
  - Secondary: while primary chancre healing or several weeks after; skin rashes on palms/soles and/or mucous membrane sores; condyloma lata
  - Latent: no visible signs or symptoms
  - Tertiary:10-30 years after infection; gummas can involve multiple body sites including bone

https://www.cdc.gov/std/syphilis/

- Secondary and early neurosyphilis with uveititis and four osseous lesions of skull in a 50 year old woman

- Syphilitc gumma in a 56 year old man with a history of treated syphilis who presented with seizures and confusion



- Meningovascular syphilis presenting as a mass forming brain lesion in HIV-negative 25 year old man with no prior history of syphilis

Kusler and Arthurs. Case Rep Infect Dis. 2018 May 8;2018:3148758.
Fargen et al. Neurosurgery. 2009 Mar;64(3):568-75
Pham et al. Open Forum Infect Dis. 2021 Aug 31;8(9):ofab455.

Take Home Points

- Bone involvement in syphilis is rare, usually occurring in tertiary or congenital cases
- Broad differential diagnosis for osteolytic lesions of skull:
  - metastases, pyogenic osteomyelitis, multiple myeloma, lymphoma, tuberculosis, leukemia, and Langerhans cell histiocytosis
- Diagnosis typically requires:
  - high degree of clinical suspicion
  - serological testing
  - biopsy with demonstration of organisms or positive molecular testing
- Treatment consists of high dose penicillin to prevent neurosyphilis and other severe manifestations

Thank you!