DÉJÀ VU?

West Coast Transplant ID Meeting

Chris Pfeiffer, MD, MHS

VA Portland Health Care System

OHSU

CASE

[redacted] yo [redacted] s/p OHT seen for altered mental status (AMS)

- 2 months prior to admission (PTA): s/p OHT for longstanding NICM
  - CMV D+R+, toxo D-R-
  - MMF, CyA, PRED, Valgancyclovir, TMP-SMX, flucon (weekly) PPx
  - c/b B UE DVT
- 2 weeks PTA: 2-day admission w/ c/f new focal seizures at home
  - Keppra started
  - EEG - rare epileptiform activity in R frontal region
  - Head CT w/o contrast negative; no MRI performed d/t known retained pacemaker wires
  - Dx - ?PRESS / tac-related toxicity → changed to CyA, anticoagulation d/c'ed
- 3 days PTA: Clinic f/u – mild L hand/arm weakness noted
- 1 day PTA: Routine R heart catheterization – Bx w/o rejection

DAY OF ADMISSION

- His wife called to report sudden onset of strange behavior, including wandering around house opening doors for no clear reason, attempting to shower with clothes on, fumbling w/ belt.
  - Also noted headache that morning, resolved w/ acetaminophen
  - Patient was advised to present to ED

- In ED – T 37.8→ 38.3, BP 172/94, HR 107, R 20
  - Gen: comfortable, NAD, awake, alert
  - CV: RRR
  - Lungs: CTA B
  - Abd: S NT ND
  - Ext: No edema
  - Skin: No rash
  - Neuro: neurology consult exam summary:
    - Grossly intact neuro exam confounded by inattention but appears to show visual and tactile neglect on the left.

ADDITIONAL BACKGROUND

- Additional PMHx –
  - Longstanding NICM s/p ICD 2003,
  - Known cerebellar peduncle cavernous malformation

- Social Hx
  - From [redacted], NV, moved to Portland ~2000
    - h/o negative QFT Gold & Coccy ID pre-Tx
  - No smoking, no ETOH, no IDU
  - One dog
  - No ill contacts

- FHx – heart disease in father and mother, otherwise n/c

INITIAL LABS & TESTS

- WBC 2.34, HGB 11.2, HCT 34.3, PLT 203
- Na 131, K 4.0, CL 97, HCO3 24, Cr 1.44 (previously 1.18), GLUC 130
- LFTs all WNL
- ProBNP 2054 (previously 1006), TROP HS 210 (0hr) → 204 (2h)

- EKG – sinus tach, no ischemia
- POCUS – no obvious new heart function deficits
- LP unsuccessful x2

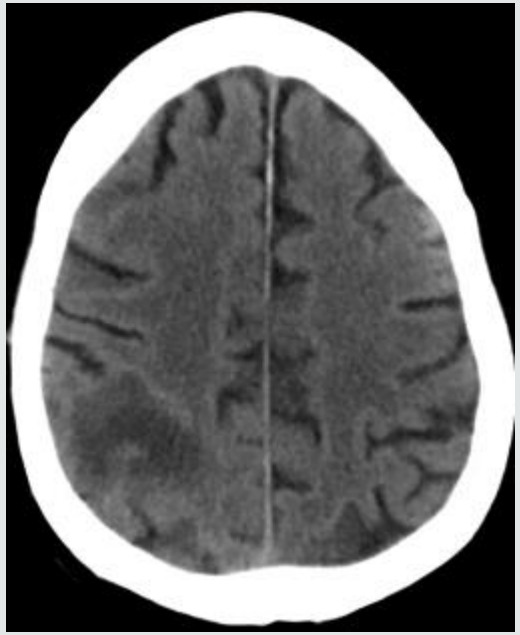
INITIAL IMAGING

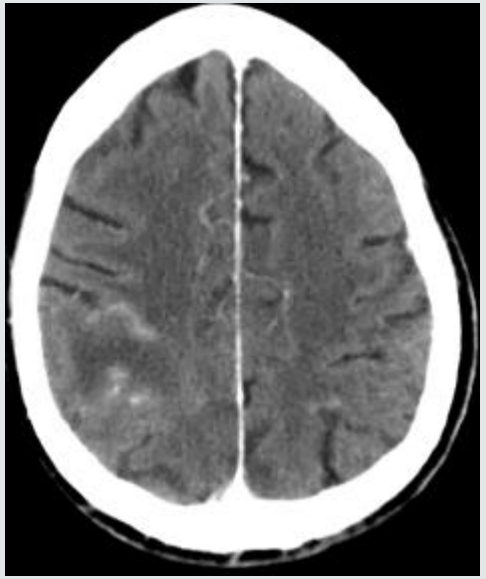
- CT Head w/o contrast:
  - New loss of gray-white differentiation with edema in the right occipital lobe is most concerning for ischemia/infarction however other intracranial processes such as encephalitis could look similar. Recommend further evaluation with CTA head and neck and MRI of the brain.

- CT Head w/ contrast
  - Right parietal cortical hypoattenuation and enhancement. Differential considerations include infectious/inflammatory process. Infarction is considered less likely given nonvascular distribution. Consider MRI.

- CTA Head/Neck – No hemorrhage, non-opacification of L transverse sinus extending into sigmoid sinus and L IJ incompletely evaluated. Recommend CTV or MRV.

- CTV Head – No dural venous sinus thrombosis.





WHAT IS YOUR LEADING DIAGNOSIS?

A. Listeria meningoencephalitis
B. West Nile Virus encephalitis
C. Coccy meningo-encephalitis
D. Fusarium meningo-encephalitis
E. Other?

INITIAL COURSE

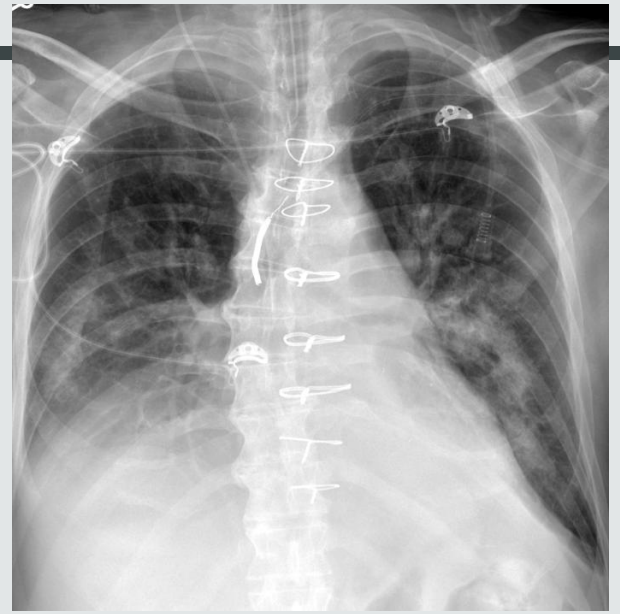
- Started on vanc, ceftriaxone, ampicillin, acyclovir
- UA neg
- Serum studies:
  - Blood Cx x3 pending
  - CRAG neg
  - CMV PCR neg
  - AdenoV PCR pending
  - Toxo PCR pending

~12h later – LP obtained – CSF studies:

- WBC 27
  - PMN 70, Lymph 12, Mono 16, Baso 2, Eo 0
- Prot 61
- Gluc 71

- Gram stain – WBC present, NOS
- Meningoencephalitis panel neg
- Crypto Ag
- JCV PCR pending
- Toxo IgG and PCR neg
- HSV1/2 pending

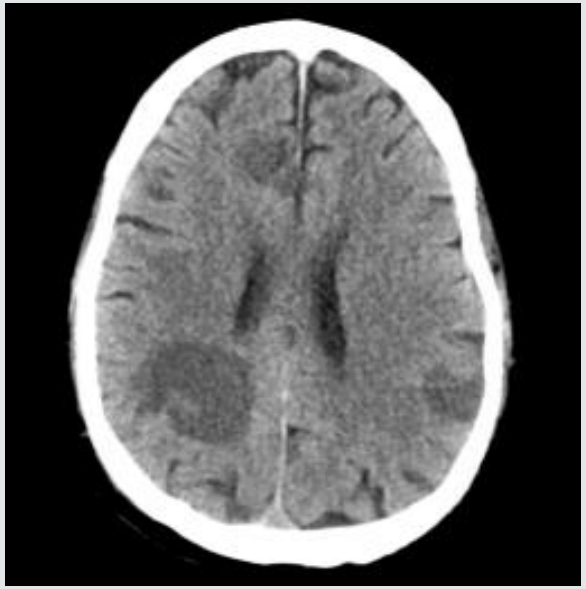
HOSPITAL DAYS (HD) 1-4



- Mental status worsened w/ further confusion, agitation

- Oxygenation acutely worsened → intubated
  - BP stable – not septic appearing
  - CXR: Increased bilateral perihilar and bibasilar groundglass and consolidative opacities

- CT Head w/ contrast (2-day interval scan)
  - Progressive enlargement of the right superior parietal hypoattenuating lesion and two new foci with similar characteristics in the left parietal lobe and right pericallosal frontal white matter. Given the time course and appearance of these lesions, multifocal infarction is likely, which could arise from a central source or secondary to underlying meningitis.



- TTE – technically difficult, EF 40-45%, no obvious vegetations
  - Culture-negative endocarditis workup initiated

- All pending tests returned negative including CSF HSV1/2, JCV, toxo

FURTHER WORKUP? TREATMENT?

What was done:

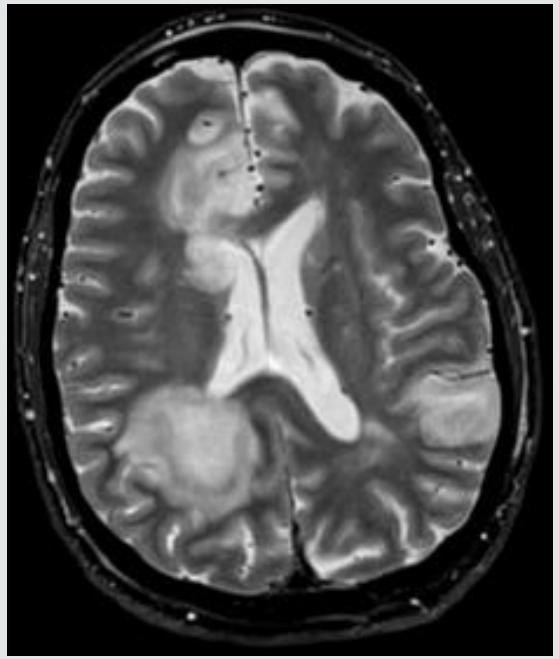
- Antibiotics broadened– meropenem, doxycycline, and Ambisome added; acyclovir & ceftriaxone stopped
- Discussion of MRI risk/benefit with cardiology and radiology – proceed to MRI
- TEE
- Plasma metagenomic sequencing (Karius Spectrum)
- Repeat LP – repeat CSF counts, CSF flow, CSF metagenomic sequencing (Mayo - MSCSF)
- Discussion with OPO – any other donors w/ similar concerns?

NEXT TESTS

- TEE – no vegetation

- MRI brain w/ and w/o contrast
  1. Extensive multifocal non-enhancing masslike T2/FLAIR hyperintense lesions with peripheral diffusion restriction and microhemorrhages. Multifocality of these lesions favors central embolic cause. Possible differentials are septic emboli with associated infarction and early cerebritis. Imaging appearance is atypical for uncomplicated multifocal acute infarction. Given patient's immunosuppressed status and microhemorrhages associated with these lesions, hematogenously spread angioinvasive fungal cerebral infection cannot be excluded.

  2. No significant intracranial mass effect - no midline shift or herniation.



CASE CONTINUED

- Repeat LP
  - WBC 611
    - PMN 87, Lymph 8, Mono 5
  - Prot 681
  - Gluc <10
  - Gram stain – WBC present, NOS
  - Wright stain for parasites - negative

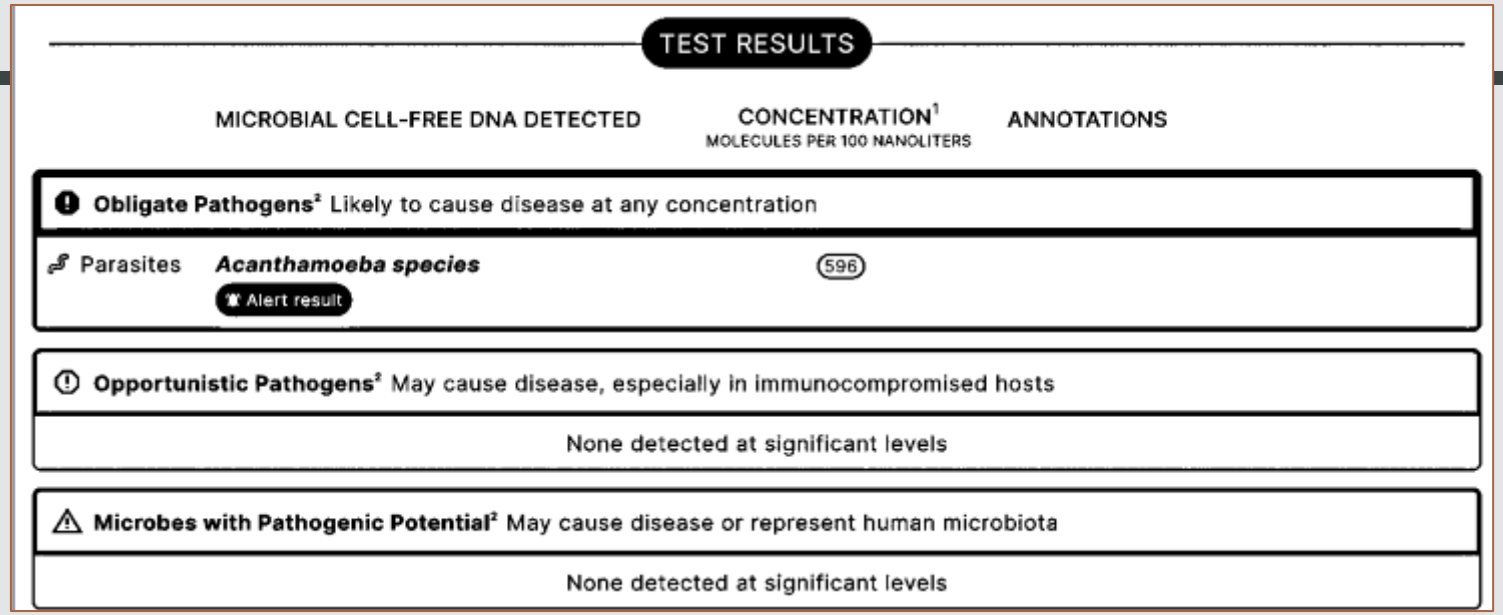
- Shortly after LP, patient became unresponsive with fixed dilated pupils. CT confirmed massive herniation, life-support was withdrawn, & patient died.

WHAT HAPPENED?

FOLLOW-UP

- 1 day later –

Karius Spectrum *+Acanthamoeba spp*

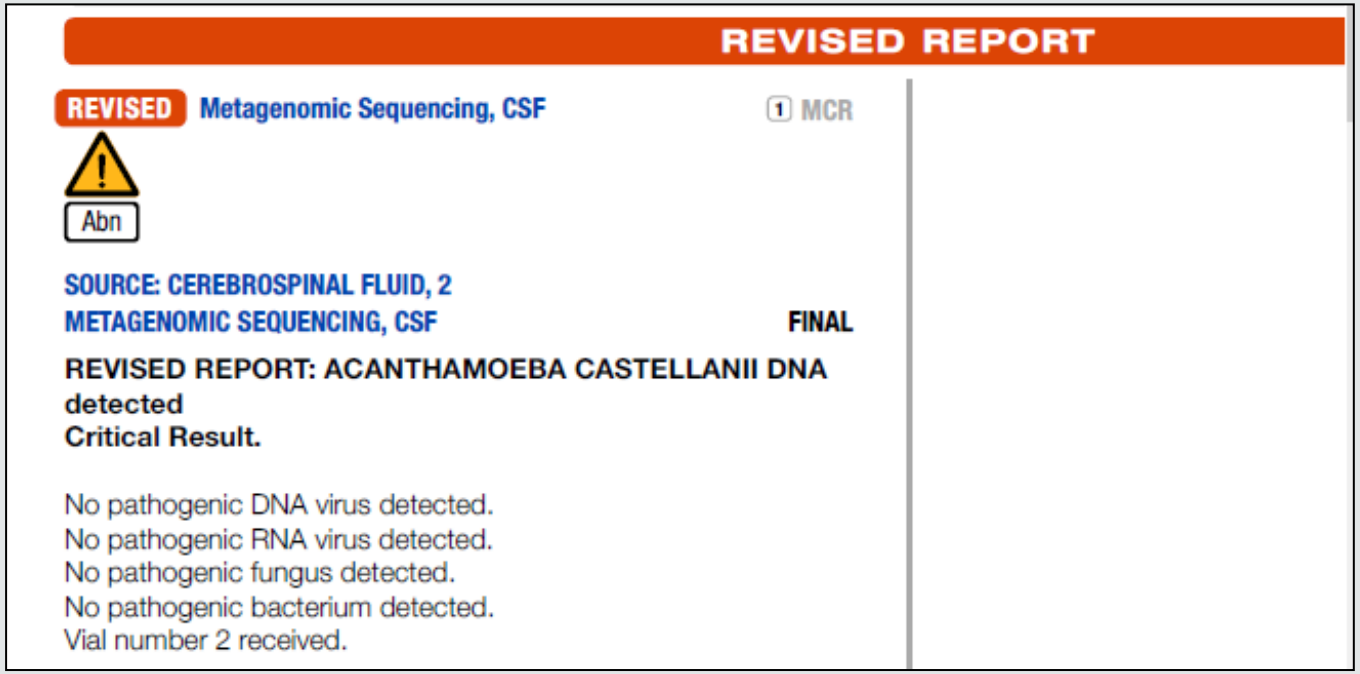


TEST RESULTS

MICROBIAL CELL-FREE DNA DETECTED		CONCENTRATION[1] MOLECULES PER 100 NANOLITERS	ANNOTATIONS
Obligate Pathogens[2] Likely to cause disease at any concentration			
Parasites	***Acanthamoeba species*** Alert result	596	
Opportunistic Pathogens[2] May cause disease, especially in immunocompromised hosts			
None detected at significant levels			
Microbes with Pathogenic Potential[2] May cause disease or represent human microbiota			
None detected at significant levels			

- ~2 wks later --

Mayo Clinic CSF NGS *+Acanthamoeba castellani*



REVISED REPORT

REVISED Metagenomic Sequencing, CSF 1 MCR

Abn

SOURCE: CEREBROSPINAL FLUID, 2
METAGENOMIC SEQUENCING, CSF FINAL

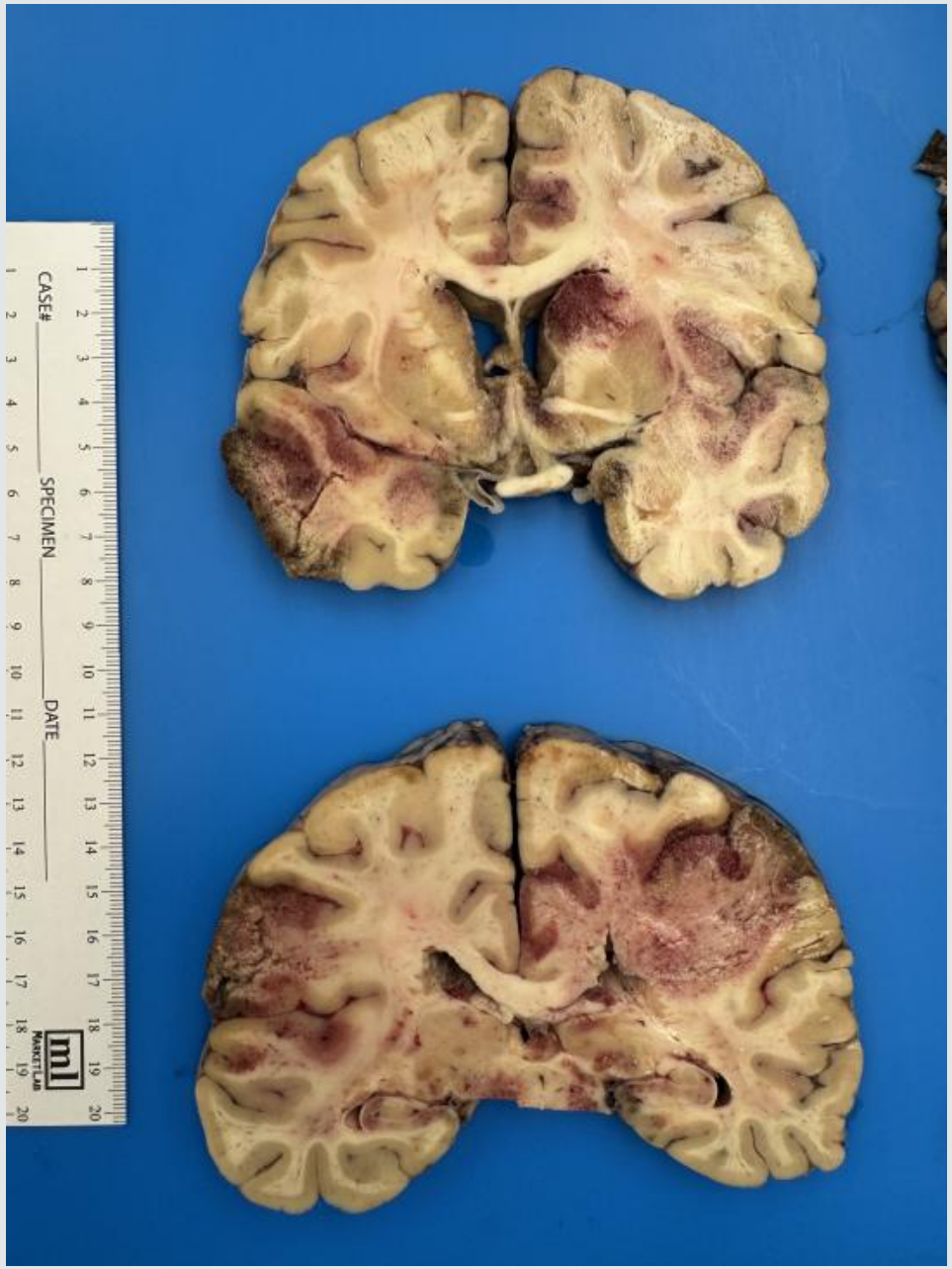
REVISED REPORT: ACANTHAMOEBA CASTELLANII DNA detected
Critical Result.

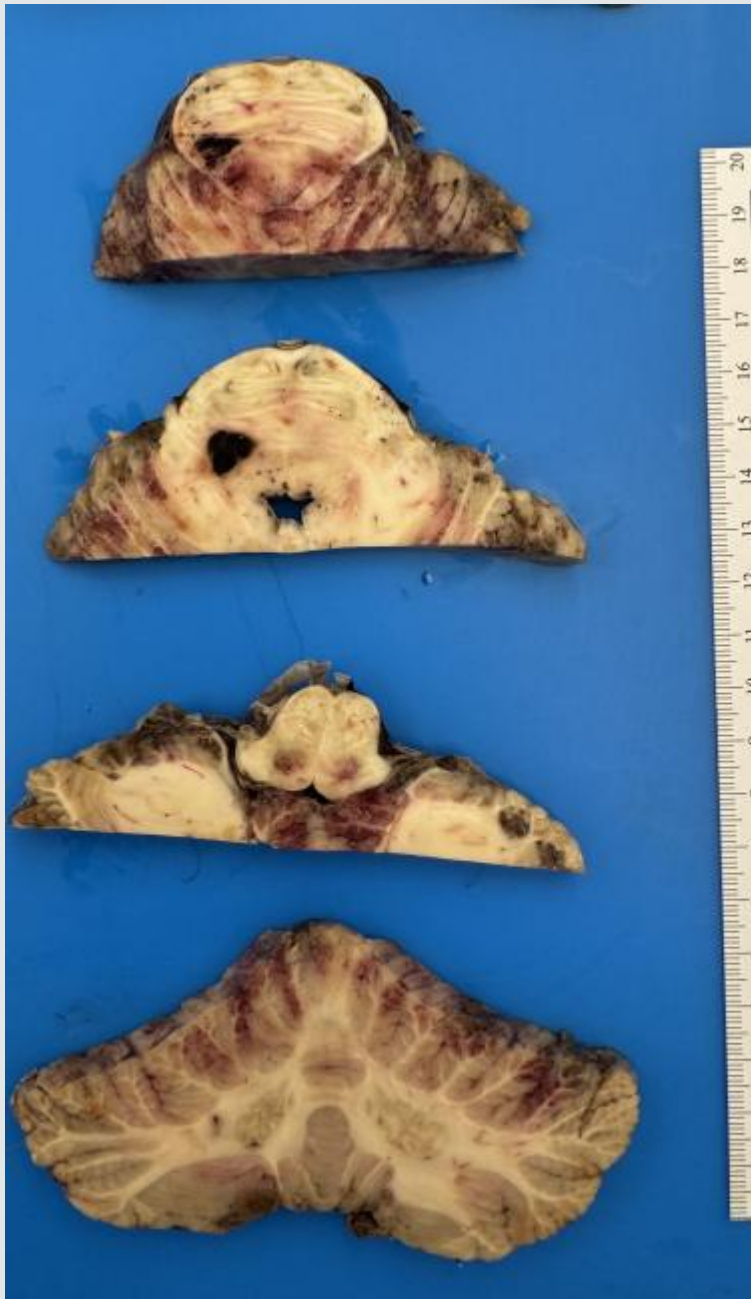
No pathogenic DNA virus detected.
No pathogenic RNA virus detected.
No pathogenic fungus detected.
No pathogenic bacterium detected.
Vial number 2 received.

- In background - Karius Spectrum of donor negative

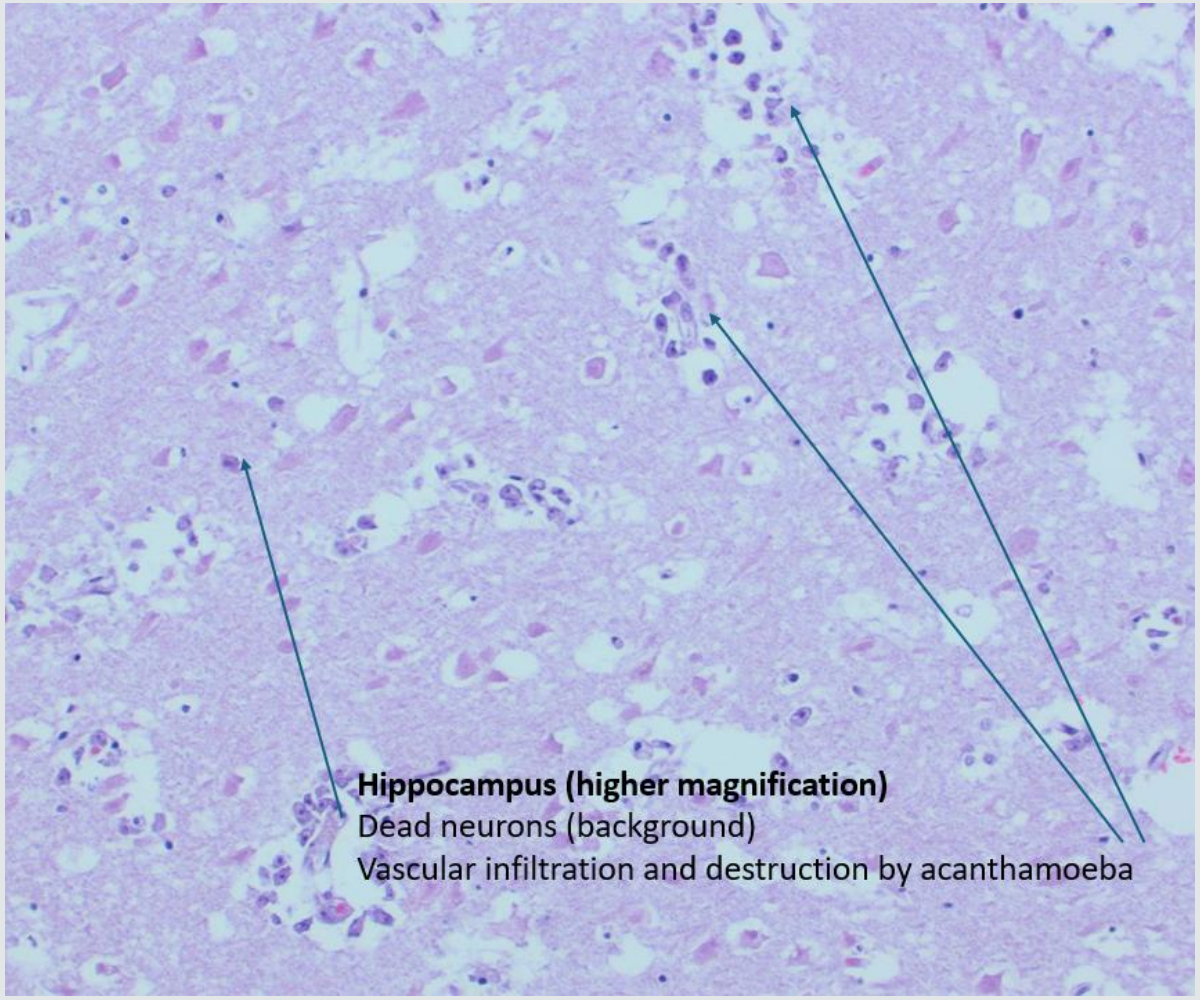
AUTOPSY





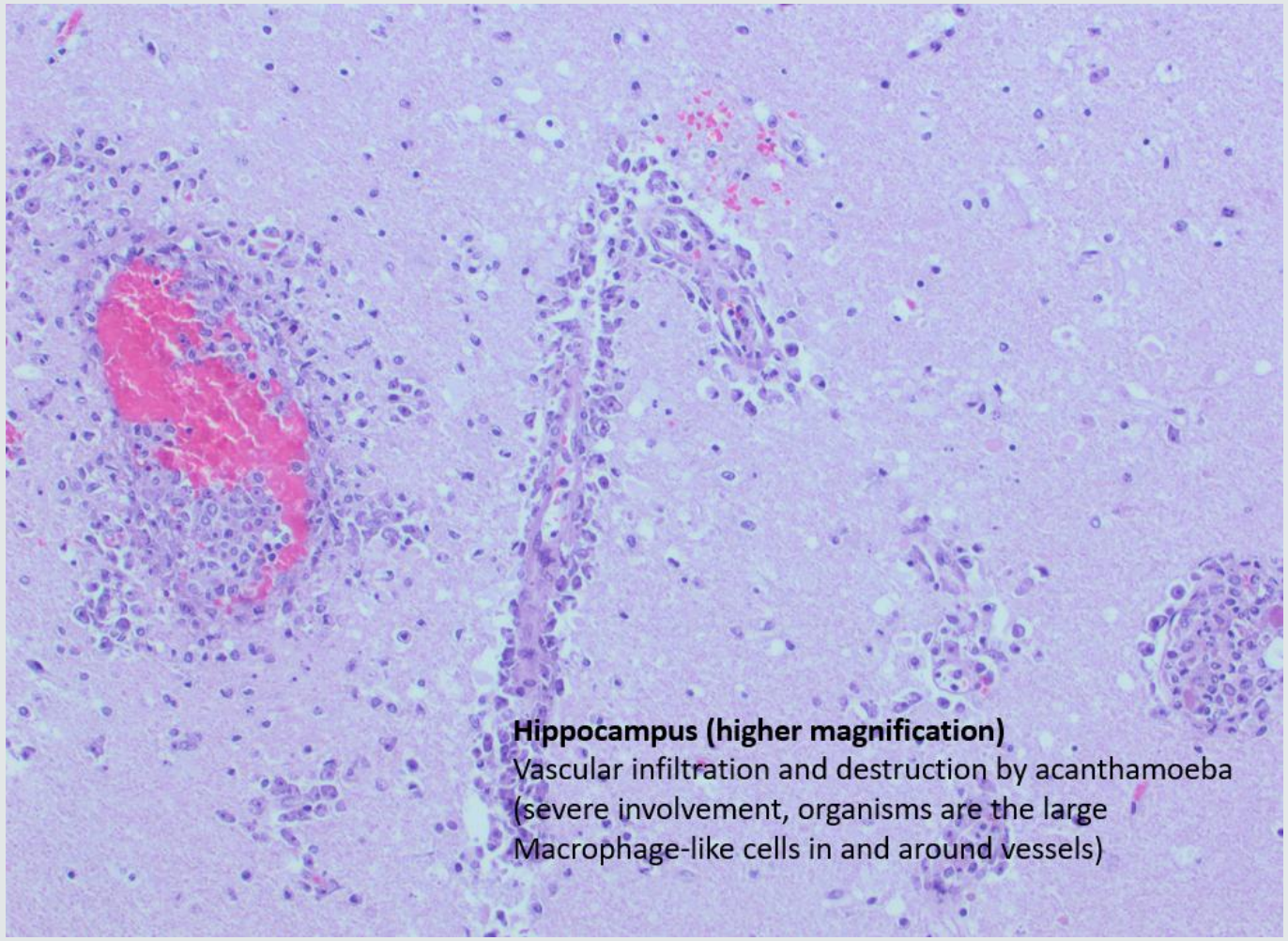


AUTOPSY



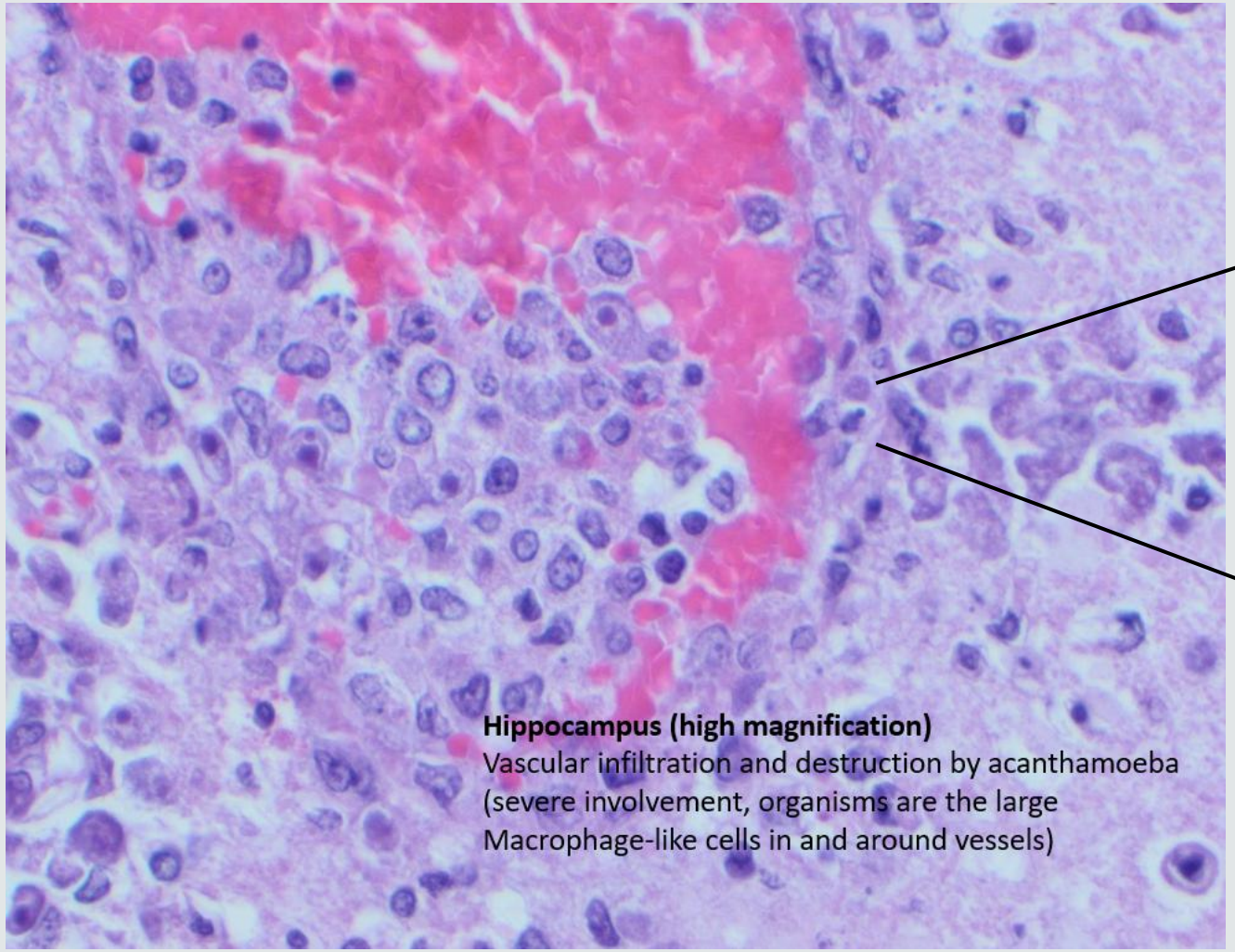
Photos courtesy of Drs. Matthew Wood, Randy Woltjer, Sam Jones and others in OHSU Dept of Pathology

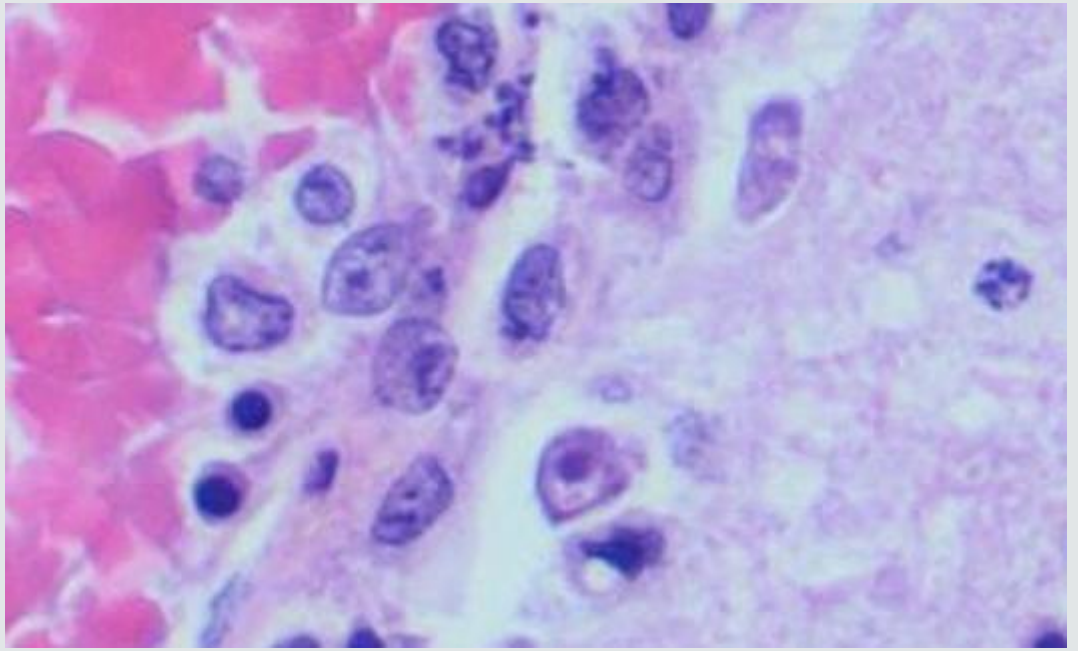
AUTOPSY (2)



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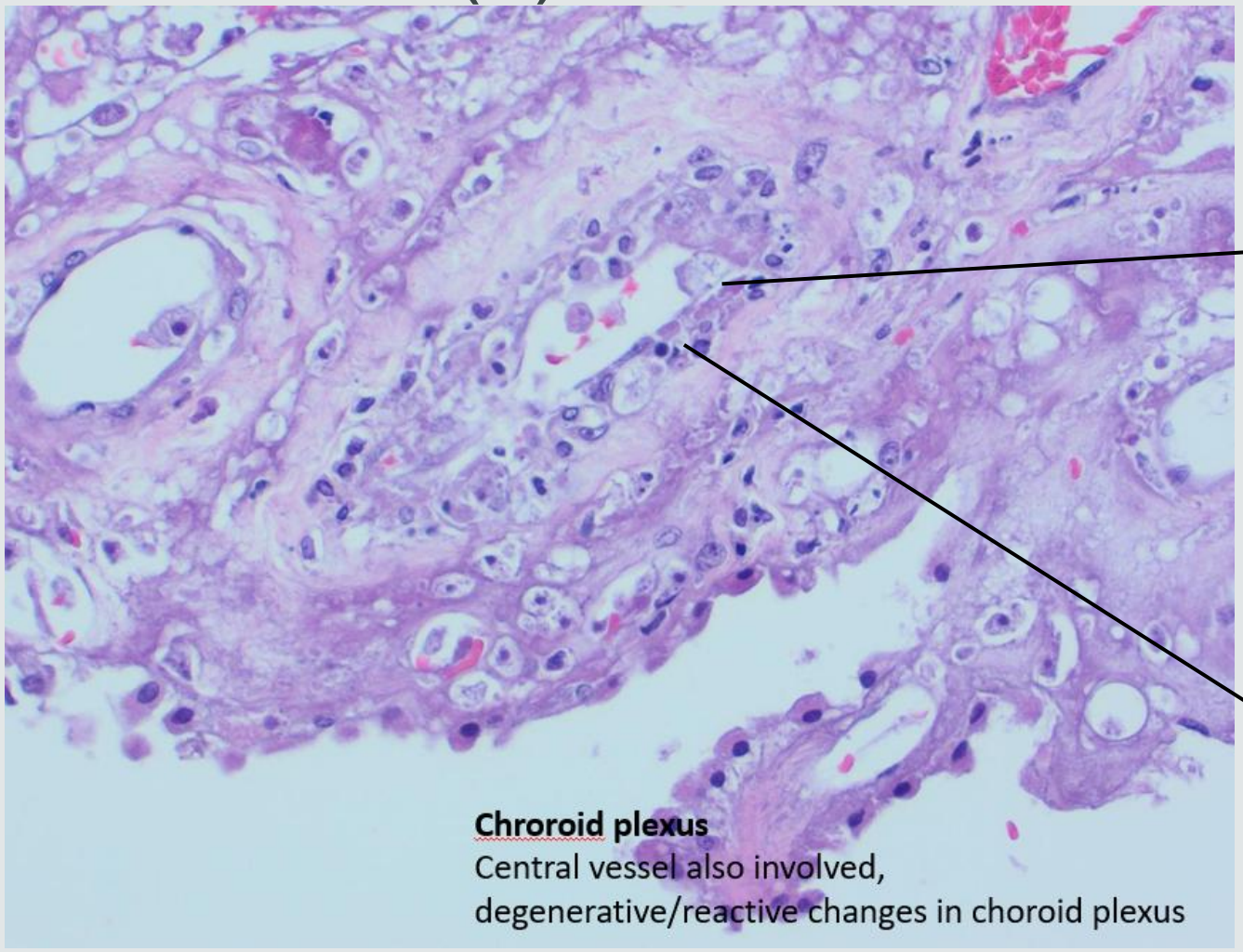
AUTOPSY (3)

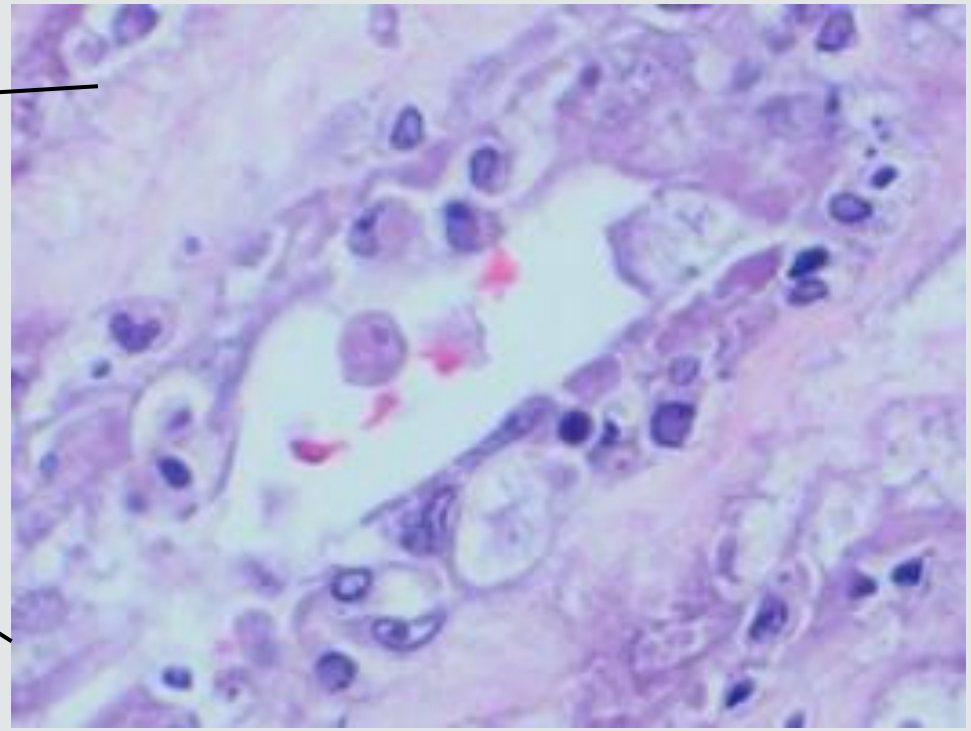




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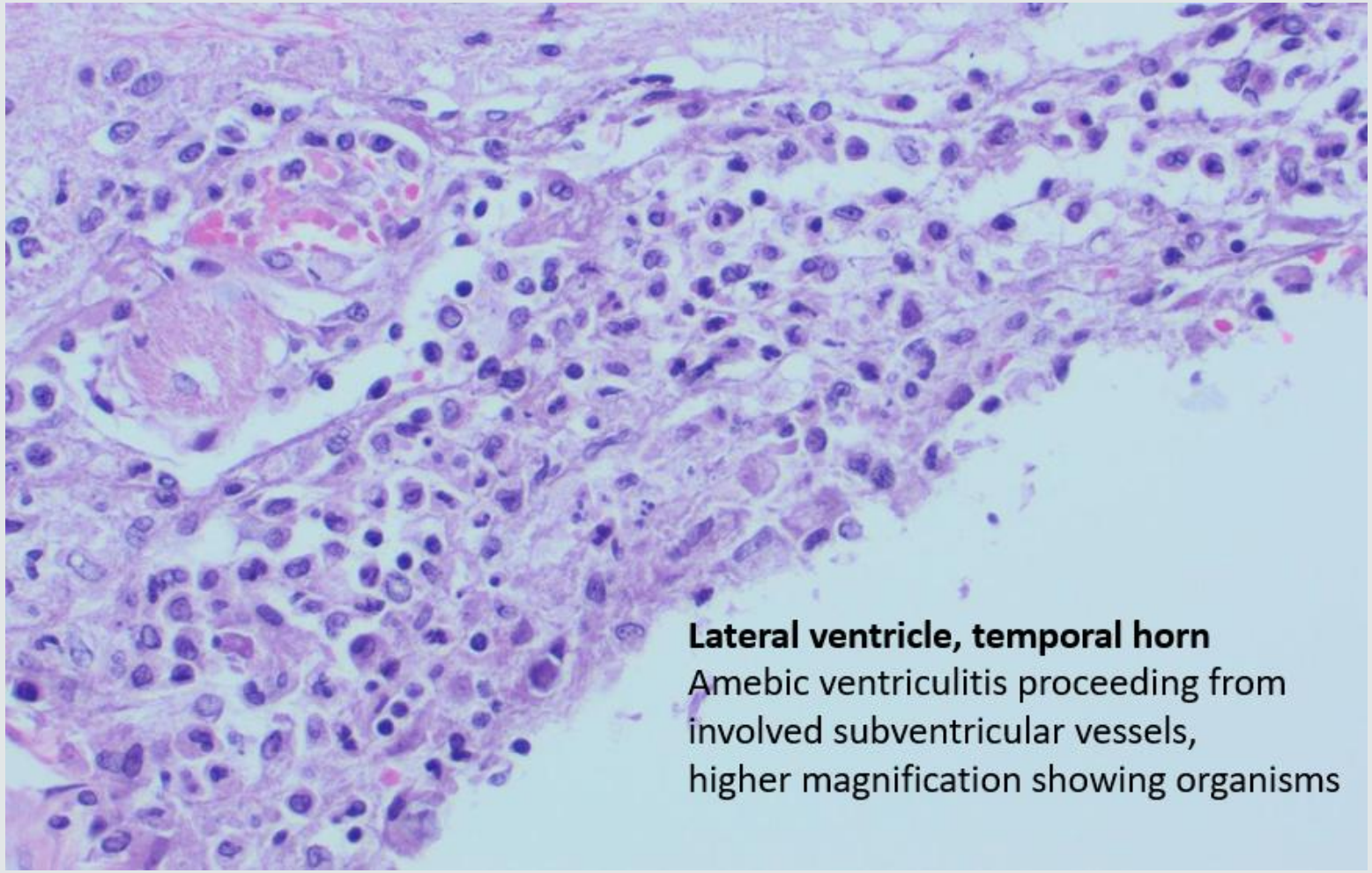
AUTOPSY (4)





Photos courtesy of Drs. Matthew Wood, Randy Woltjer, Sam Jones and others in OHSU Dept of Pathology

AUTOPSY (5)



Photos courtesy of Drs. Matthew Wood, Randy Woltjer, Sam Jones and others in OHSU Dept of Pathology

FINAL DIAGNOSIS –

ACANTHAMOEBA ENCEPHALITIS

DÉJÀ VU!
West Coast TID 11/1/2023: Dr. Poornima Ramanan

A 64-year-old male lung transplant recipient..

So, to recap..

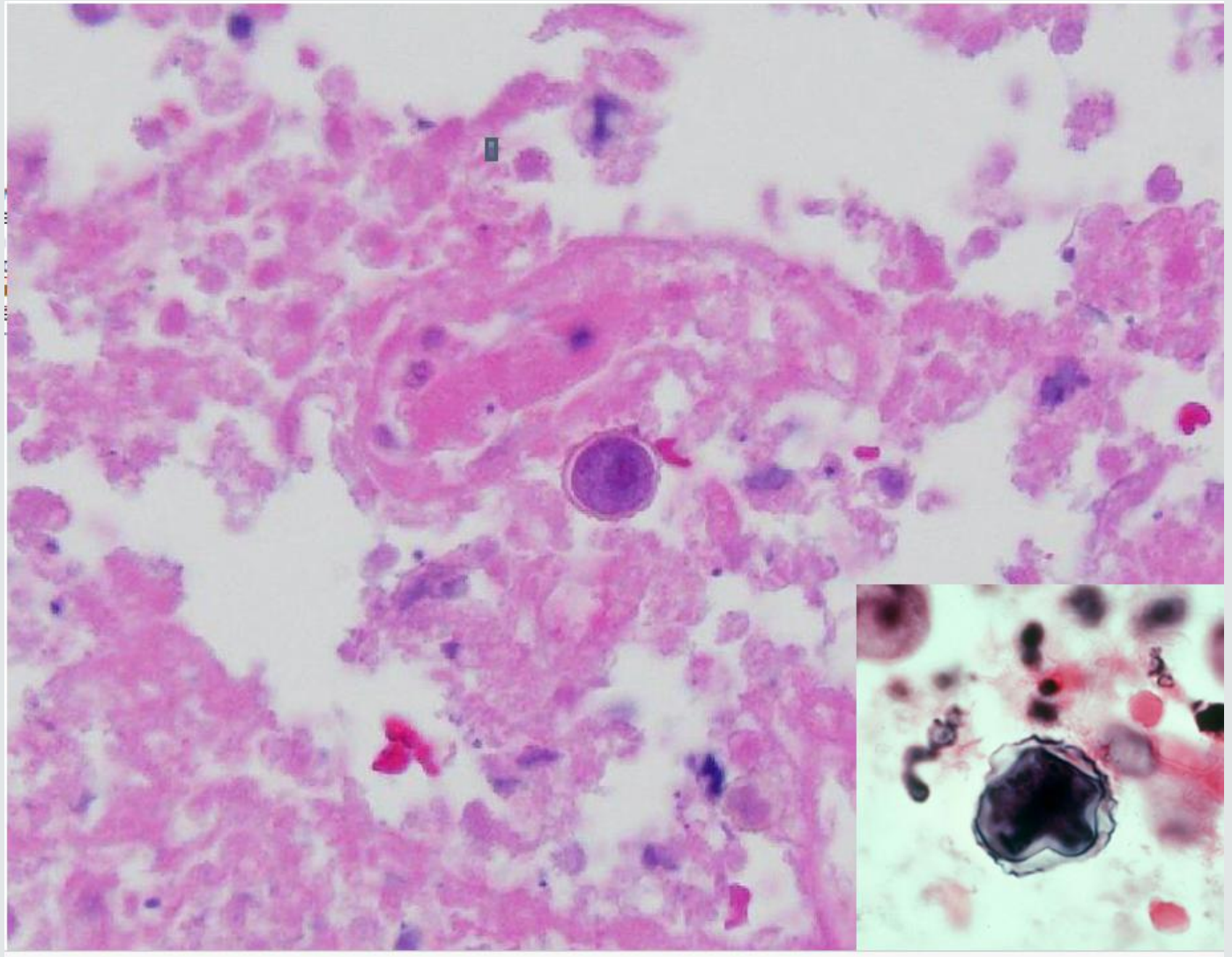
We have a single lung recipient from Mexico with known native lung *Aspergillus* mycetomas on therapeutic level of voriconazole who presented with intermittent fevers, encephalopathy with CSF lymphocytic pleocytosis, new multiple ring enhancing brain lesions , new GGO and nodular opacities in lung allograft (BAL + for Influenza A and *Aspergillus flavus*) and CMV viremia

At this point, patient is on the following antimicrobial therapy:

1. **Ambisome** – for presumed disseminated aspergillosis (remember, he received ambisome at OSH)
2. IV **ganciclovir** + **cytogam** – reactivation breakthrough CMV viremia (CMV drug resistance testing showed pan-sensitive virus)
3. **Oseltamivir** (10-day course for Influenza A LRTI)
4. **Meropenem** (empiric)

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WORSE ON MRI 10D LATER → BRAIN BX



- CSF studies pre-Biopsy:
  - Free-living amoeba PCR negative
  - Broad-Range PCR negative

Final diagnosis

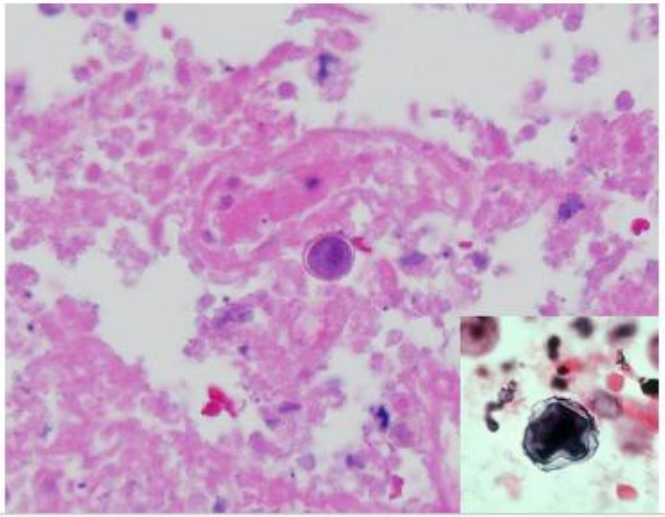
(confirmed by PCR, culture and histopath of brain tissue)

I. **Granulomatous Amebic Encephalitis due to *Acanthamoeba* sp.**

II. CMV viremia

III. Probable pulmonary aspergillosis in allograft + native lung mycetomas

IV. Influenza A LRTI



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Back to our patient…

- After consulting with CDC, patient was started on a cocktail of IV pentamidine + miltefosine + flucytosine + sulfadiazine + posaconazole
- Patient and [redacted] declined brain surgery for debridement of lesions
- [redacted] continued to clinically deteriorate and eventually opted for home hospice
- [redacted] was discharged on oral regimen of miltefosine + Bactrim + posaconazole
- [redacted] passed away ~ 3 weeks later

Diagnosis of free-living amebae infection is often challenging

A If you don't think about it, you will likely miss the diagnosis

1. Histopathology
2. PCR of brain tissue, CSF or skin or lung or sinus
3. Amoebic culture on non-nutrient agar plates overlaid with E.coli
4. Wet mount or Giemsa stain of CSF may show trophozoites

5. NGS – serum or CSF

Test

Free-living Ameb

Specimen Sourc

Acanthamoeba sp

Critical resu

Naegleria fowl



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ANOTHER RECENT CASE

- 58 yo M presented ~1 month post-SPK Tx
- Had received HD while in Dominican Republic
- Similar aggressive presentation
- HD13 – Acanthamoeba Dx via plasma metagenomic sequencing

  @1155 DNA molecules/microliter
- Declared brain dead next day
- Post-mortem – confirmed Dx

Case Reports > Transplant Proc. 2026 Jun;58(5):899-902. doi: 10.1016/j.transproceed.2026.05.005. Epub 2026 May 22.

Fulminant Acanthamoeba Encephalitis Diagnosed By Cell-Free DNA in a Renal Transplant Patient: A Case Report

Scott M Wilson [1], Armghan A Munir [2], Marie Le [3], Enver Akalin [4], Roger A Fecher [5], Judah Burns [6], Victoria Muggia [7], Luz E Liriano-Ward [4]

Affiliations + expand

PMID: 42173703 DOI: 10.1016/j.transproceed.2026.05.005

Abstract

Granulomatous amoebic encephalitis (GAE) caused by Acanthamoeba spp. is a rare, nearly universally fatal central nervous system infection that predominantly affects immunocompromised individuals, including solid organ transplant (SOT) recipients. Early diagnosis is essential but often delayed due to nonspecific symptoms and the limited sensitivity of conventional diagnostic tests. We describe the case of a 58-year-old man who presented with fever and diarrhea one month after a simultaneous pancreas-kidney transplant. Despite broad-spectrum antimicrobial therapy, he developed status epilepticus and rapid neurologic deterioration. Extensive infectious workup, including cerebrospinal fluid studies, was non-diagnostic, and neuroimaging revealed multifocal infarcts and cerebral edema. Plasma microbial cell-free DNA sequencing identified Acanthamoeba spp., leading to a presumptive diagnosis of GAE that was later confirmed postmortem. This case represents the first reported use of plasma-based next-generation sequencing to diagnose Acanthamoeba GAE and highlights the clinical utility of noninvasive molecular diagnostics in immunocompromised hosts with unexplained encephalopathy. Earlier recognition of rare pathogens using these tools may facilitate more timely interventions and improve outcomes in transplant recipients with rapidly progressive neurologic syndromes

https://pubmed.ncbi.nlm.nih.gov/42173703/

THANK YOUS

- The OHSU/VA TID group
- Poornima Ramanan MD - check out her full past presentation here:

https://www.ohsu.edu/school-of-medicine/infectious-diseases/meeting-schedule-and-presentation-archive

- OHSU Dept of Pathology –special thanks to Drs. Matthew Wood, Randy Woltjer, Samuel Jones.