West Coast Transplant ID Society Meeting 12/3/2025

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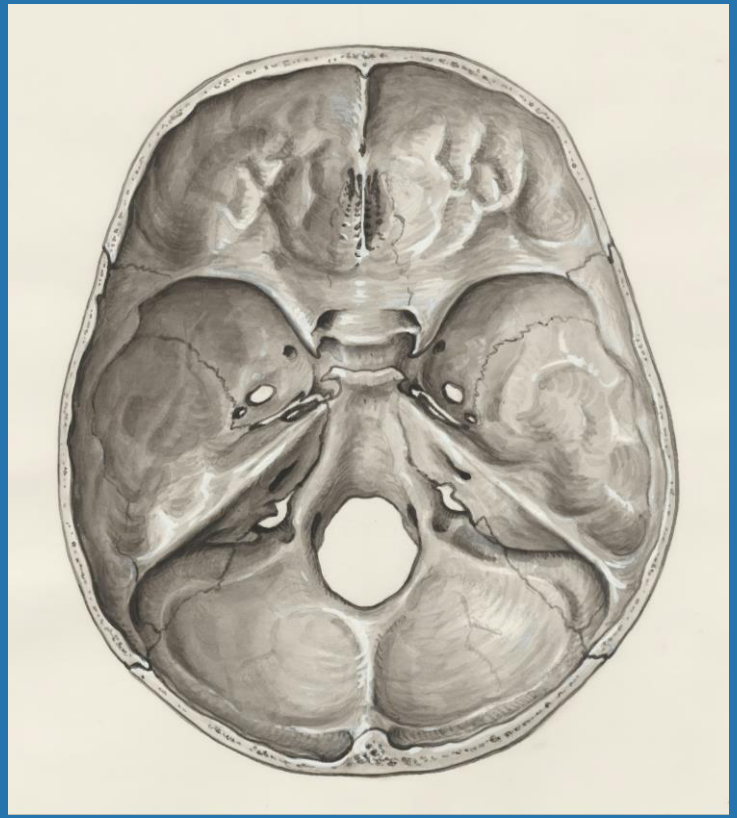

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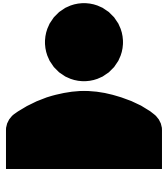
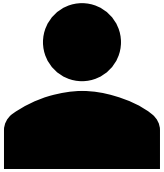
Case Presentation: Introduction



[redacted]-year-old [redacted] with a history of membranous and diabetic nephropathy s/p DDRT (1/[redacted]/2024), CMV R+ presents with acute encephalopathy and weakness.

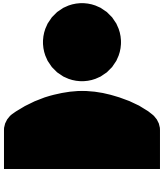
- 1 day of headache and nausea/vomiting, then difficulty with ambulation and lack of response to commands and questions

Medications



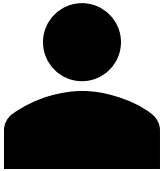
- Tacrolimus
- Prednisone 5 mg qday
- *MMF had been held due to recent BK viremia

Social History



- Born in Seoul, South Korea
- Immigrated to Los Angeles in 197[redacted]
- Lives in Glendale, CA with [redacted]
- No pets or regular animal exposure
- Retired. Previously worked in a restaurant
- Last travel was to Korea a few weeks before admission for vacation
- No prior abnormal TB testing nor known TB contacts

Physical Examination



Tmax 39.6 BP 162/99 HR 82 RR 20 SpO2 95% on RA

General: alert, non-verbal, not responsive to commands, no purposeful movement
HEENT: PERRLA, does not track with eyes, poor dentition
Neuro: face symmetry, 4-5/5 motor strength in RUE, RLL, LUE, LLE, normal reflexes, not able to assess orientation

Labs

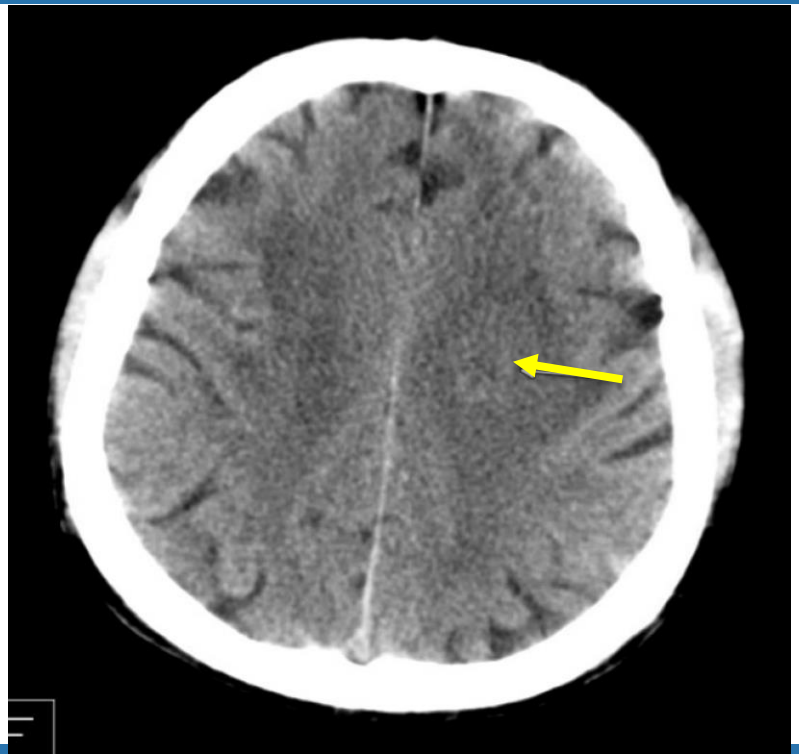
Admission:

- WBC 19.59 cells/μL (no differential available)
- Creatinine 1.56
- Glucose 291
- Tacrolimus 3.2
- COVID and influenza PCRs negative

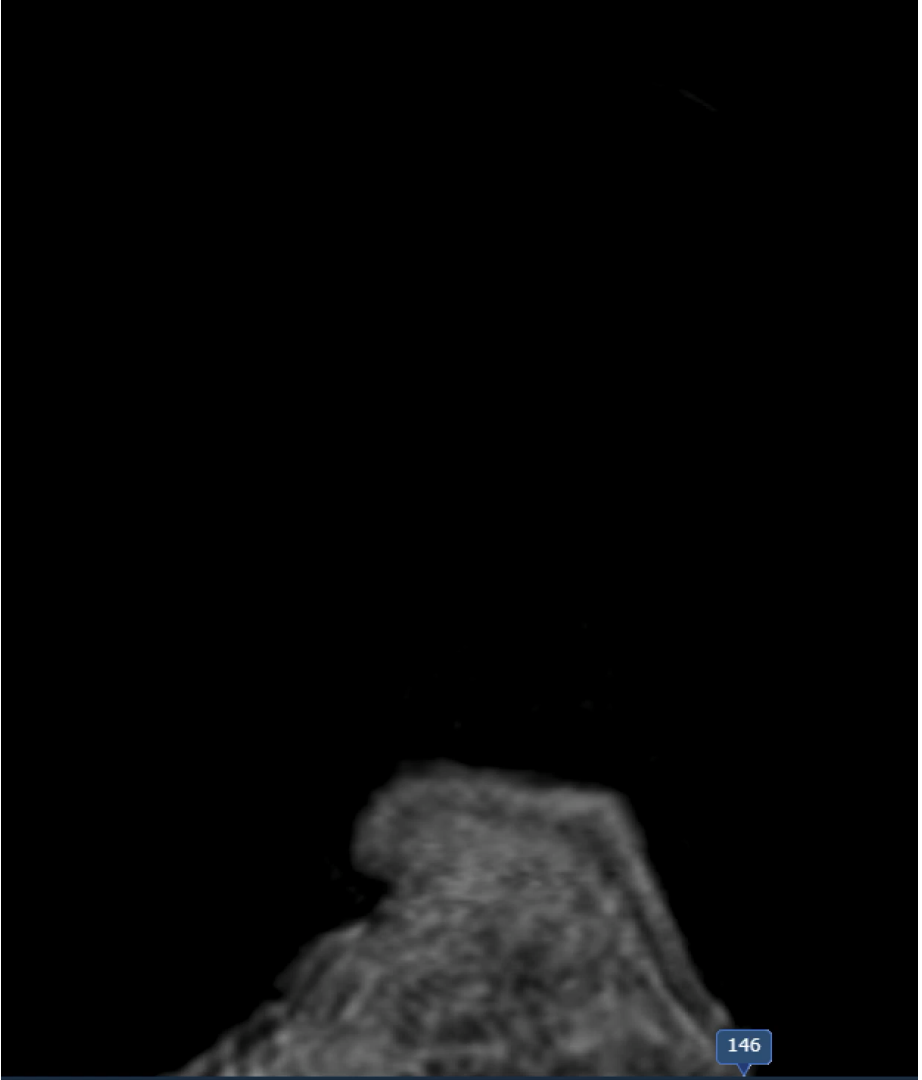
Transplant Serologies:

- Toxoplasma IgG negative
- Quantiferon Gold negative
- Strongyloides IgG negative
- HIV Ag/Ab negative
- Cocci EIA negative
- CMV IgG positive

Imaging: Non-contrast head CT



IMPRESSION:
Limited partially motion-degraded examination.
Heterogenous lesion with surrounding edema suggested in left frontal lobe measuring 17 x 12 mm. No mass effect or acute intracranial hemorrhage. This can represent an evolving neoplasm such as metastasis or glioma, with infectious or other inflammatory process or less likely subacute/early chronic hematoma included in the differential.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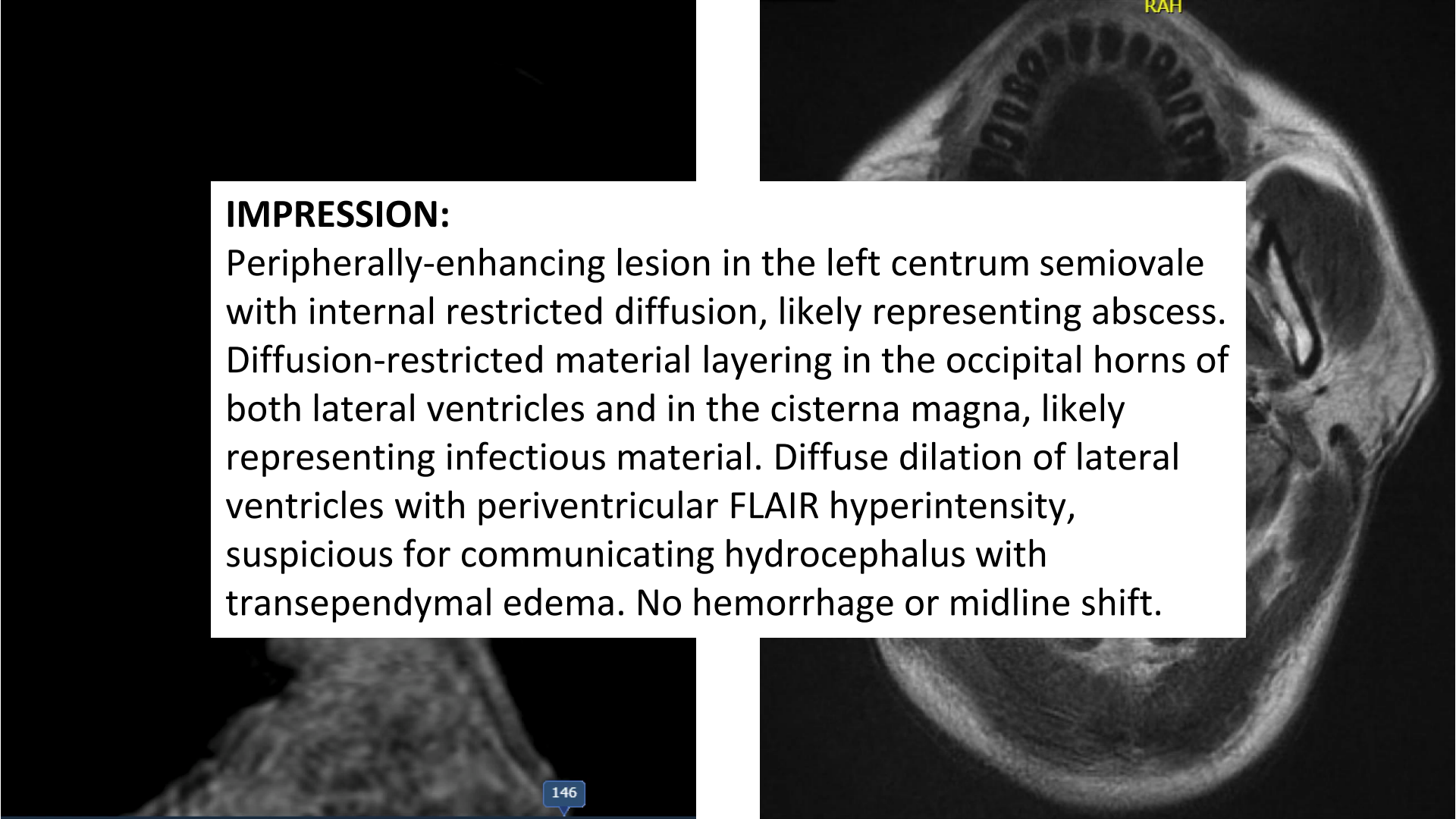
RAH



IMPRESSION:

Peripherally-enhancing lesion in the left centrum semiovale with internal restricted diffusion, likely representing abscess. Diffusion-restricted material layering in the occipital horns of both lateral ventricles and in the cisterna magna, likely representing infectious material. Diffuse dilation of lateral ventricles with periventricular FLAIR hyperintensity, suspicious for communicating hydrocephalus with transependymal edema. No hemorrhage or midline shift.

Additional Imaging:

- CT chest wo contrast: biapical pleural-parenchymal scarring

Clinical Course

Neurology and Transplant ID were consulted. Admitted to NeuroICU.

Underwent lumbar puncture.

Neurosurgery was consulted. EVD was placed.

Started on methylprednisolone and empiric antimicrobials.

CSF Evaluation

CSF from LP

- Opening pressure: 35 cm H20 (in left lateral recumbent position)
- Bloody, cloudy CSF
- 181,000 RBCs
- 18,019 TNC uncorrected, 17,657 corrected / 95% segmented neutrophils / 3% lymphocytes / 2% monocytes
- Glucose 31
- Protein 1,355

CSF from EVD

- Opening pressure: 7 cm H20
- Cloudy, xanthochromic CSF
- 2,000 RBCs
- 316 TNC uncorrected, 312 corrected/ 2% segmented neutrophils / 83% lymphocytes / 15% monocytes
- Glucose 68
- Protein 377

Initial Differential

Bacterial

- Oral bacteria (strep species, anaerobes)
- Staph aureus
- Nocardia spp.
- Listeria monocytogenes
- Gram negative rods
- MTB

Viral

- Less likely given neutrophil pleocytosis

Parasitic

- Less likely, low concern for Toxoplasmosis

Fungal

- Aspergillus spp.
- Cryptococcus spp.
- Coccidioides
- Mucorales
- Fusarium
- Scedosporium

Poll #1: Which empiric antimicrobials would you start?

a) Vancomycin + cefepime + ampicillin + triazole
b) Vancomycin + cefepime + ampicilin + triazole + TMP-SMX
c) Ceftriaxone + metronidazole + ampicillin + triazole + TMP-SMX
d) Ceftriaxone + metronidazole + ampicillin + triazole
e) None

Additional Laboratory Evaluation:

- Serum CrAg
- Serum T.gondii PCR
- Serum Cocci EIA

- Blood cultures

All **NEGATIVE**

- CSF ARUP meningitis/encephalitis panel
- CSF bacterial culture
- CSF fungal culture
- CSF AFB culture
- CSF MTB PCR
- CSF HSV 1/2
- CSF CMV PCR
- CSF Aspergillus Ag
- CSF CrAg
- CSF Miravista Cocci Ag
- CSF T.gondii PCR
- CSF Nocardia PCR

Clinical Course (continued)

Started vancomycin, ampicillin, ceftriaxone, metronidazole. Linezolid added. Ampicillin discontinued.

Encephalopathy persists.

Given negative ME panel and CSF cultures to date and pending mNGS, microbial cell-free DNA is sent.

Started on valacyclovir PO for severe mucocutaneous HSV.

Obligate & Opportunistic Pathogens[2] May cause disease in humans at any concentration

Fungi	***Aspergillus flavus/oryzae*** Alert result	341	

Microbes with Pathogenic Potential & DNA Viruses[2] Can cause disease and may also represent normal human microbiota

Fungi	***Candida tropicalis***	1,327	
	Kluyveromyces marxianus (Candida kefyr)	626	
Bacteria	***Enterococcus faecalis***	7,834	• **AMR marker: *vanA* and *vanB* not detected** Consistent with susceptibility to vancomycin and other glycopeptides.
Viruses	**Herpes simplex virus type 1 (HSV-1)**	7,678	
	BK polyomavirus (Betapolyomavirus hominis)	813	

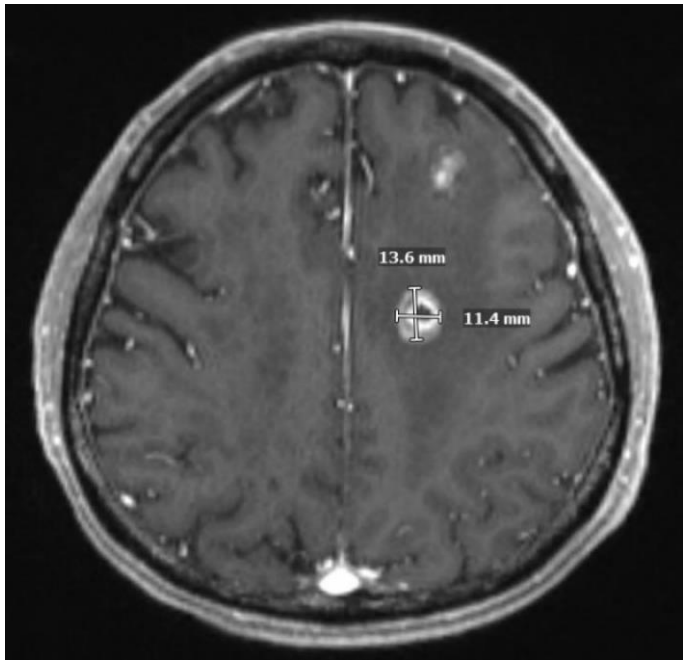
Microbes of uncertain significance Unresolved species identity[2] or emerging literature[3] associated with clinical significance

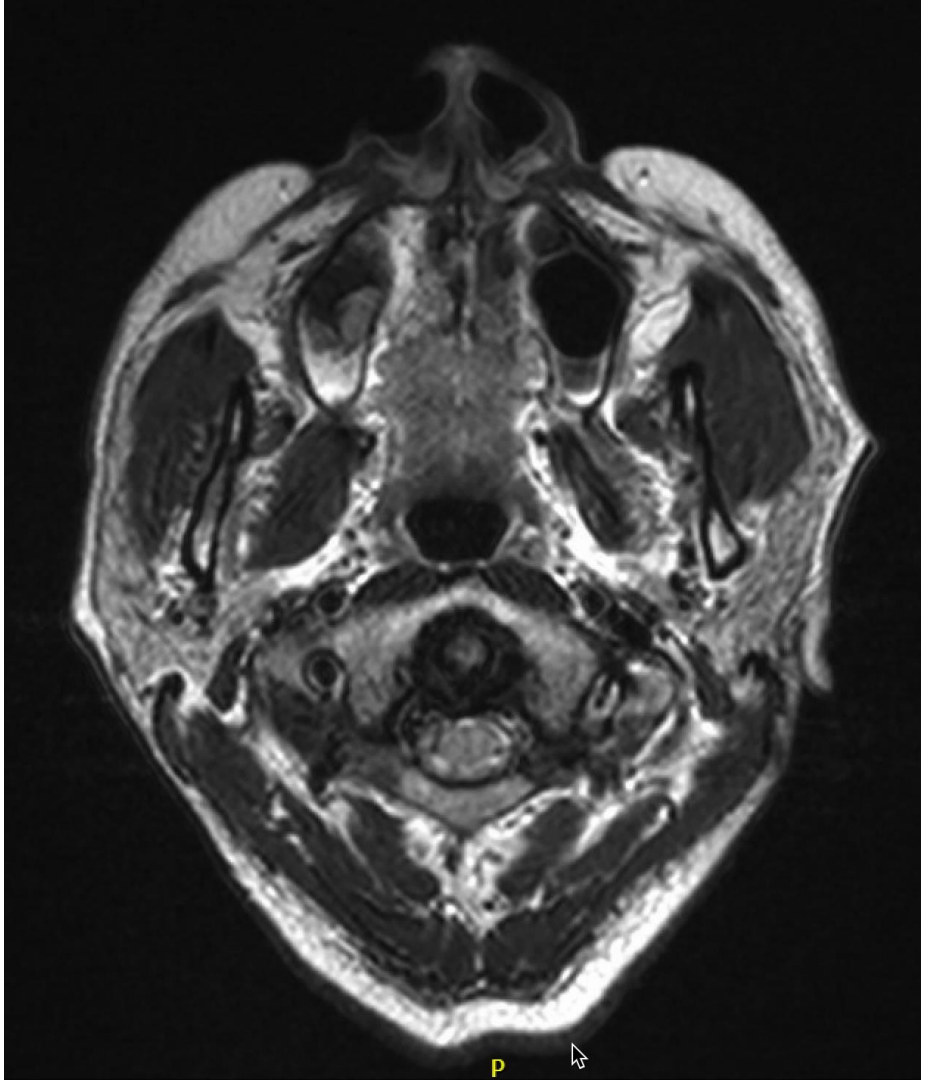
Fungi	***Aspergillus species*** Alert result	338	

Clinical Course (continued)

- Isavuconazole added to ceftriaxone, metronidazole, and linezolid.
- EVD removed after 8 days.
- CSF from EVD and first LP result with no growth.
- NSG re-consulted for consideration of stereotactic brain biopsy. Not pursued.
- Linezolid discontinued due to low concern for CNS Nocardiosis and cytopenias.
- Patient shows slow improvement in cognitive function, but still not at baseline.

Repeat brain MRI w/contrast (2 weeks after initiation of antibiotics and 1 week after initiation of isavuconazole)





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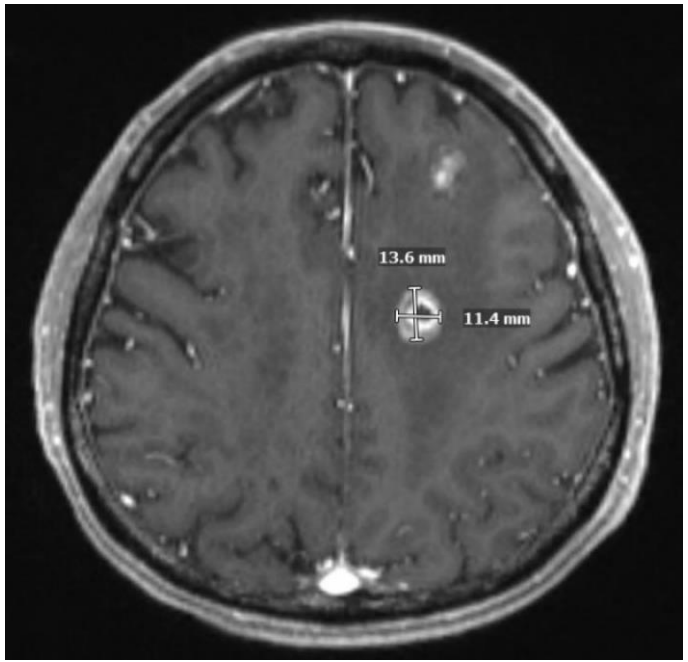

IMPRESSION:

Interval removal of left ventriculostomy catheter.

Stable size of small left centrum semiovale abscess (14 mm x 11 mm).

Suspect new subcentimeter developing abscess along genu of corpus callosum adjacent to left frontal horn and near ventriculostomy catheter tract, measuring up to 8 mm.

Ventriculitis with increased ependymal enhancement along left atrium.

CSF mNGS (UCSF) results 2 weeks later...

Component Ref Range & Units	
Bacteria {\par} Not Detected	Not Detected
Comment: Sample contains high DNA background; there is decreased sensitivity for detection of DNA viruses, bacteria, fungi, and parasites.	
DNA Viruses {\par} Not Detected	Not Detected
Comment: Sample contains high DNA background; there is decreased sensitivity for detection of DNA viruses, bacteria, fungi, and parasites.	
RNA Viruses {\par} Not Detected	Not Detected
Comment: Sample contains high RNA background; there is decreased sensitivity for detection of RNA viruses.	
Fungus {\par} Not Detected	Not Detected
Comment: Sample contains high DNA background; there is decreased sensitivity for detection of DNA viruses, bacteria, fungi, and parasites.	
Parasites {\par} Not Detected	Not Detected
Comment: Sample contains high DNA background; there is decreased sensitivity for detection of DNA viruses, bacteria, fungi, and parasites.	
Comments {\par}	
Sample is hemolyzed. There is a decrease in sensitivity for metagenomic detection of pathogens due to increased human host background and/or potential assay inhibition.	
Comment: High levels of human nucleic acids in samples can decrease the test sensitivity for organism detection.	

Patient has a diminishing brain abscess and ventriculitis with slow clinical response.

What etiologies are you considering at this point?

Clinical Course (continued)

NSG re-consulted. No surgical intervention recommended. New abscess thought to be sequelae from EVD removal.

Repeat LP performed given lack of microbiologic diagnosis. Cytology, flow cytometry, and mNGS sent.

After 4 weeks of metronidazole, patient develops tinnitus. Metronidazole discontinued.

Repeat mNGS is negative and cytology also negative. Flow cytometry limited by high background.

Discharge with meropenem (for continued broad coverage and optimal CNS penetration) and isavuconazole.

- Cloudy CSF
- < 1 RBC
- 444 TNC / 2% segmented neutrophils / 83% lymphocytes / 15% monocytes
- Glucose 60
- Protein 182

2 weeks later in clinic…

- Patient is back to his neurologic baseline on meropenem and isavuconazole. Has mild intermittent left sided headaches which occur transiently and self-resolve.
- Brain MRI w/contrast was obtained at 8 weeks, showing decrease in left centrum semiovale abscess to 8 mm; resolution of ependymal enhancement; and no visible abscess along prior tract of ventriculostomy catheter

Poll #2: At this point, what is your next step in management?

a) Continue meropenem pending repeat imaging
b) Narrow to ceftriaxone
c) Step down to oral antimicrobial
d) Stop antimicrobials and watch
e) Other

Pyogenic Brain Abscess

- Focal area of pus/inflammation within brain parenchyma
- Sources
  - Contiguous infection related to otitis media, mastoiditis, sinusitis, or meningitis
  - Hematogenous spread from endocarditis, pulmonary infection, dental infection
  - Direct inoculation from surgery or trauma
- Symptom onset often acute and non-specific (headache and neurologic deficits >> fever, nausea)

Epidemiology of Pyogenic Brain Abscesses in SOT

- The overall prevalence of brain abscess in the post-transplantation period is unknown due to paucity of data
- Some longitudinal and retrospective studies estimate prevalence of 0.53-0.61% in SOT recipients (Selby *et al*., Qin *et al*.)

Etiology of Pyogenic Brain Abscesses in SOT

Immunocompetent Patients

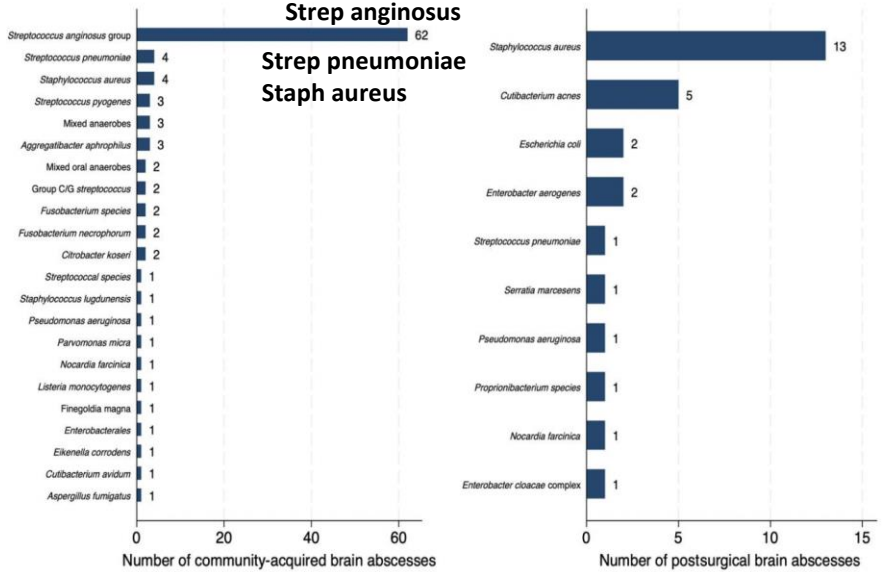

Figure 1. Frequency of causative pathogens of community-acquired and postsurgical brain abscess. For polymicrobial infections only, the primary pathogen is included.

Allen et al. OFID, 2025

Kidney Transplant Recipients

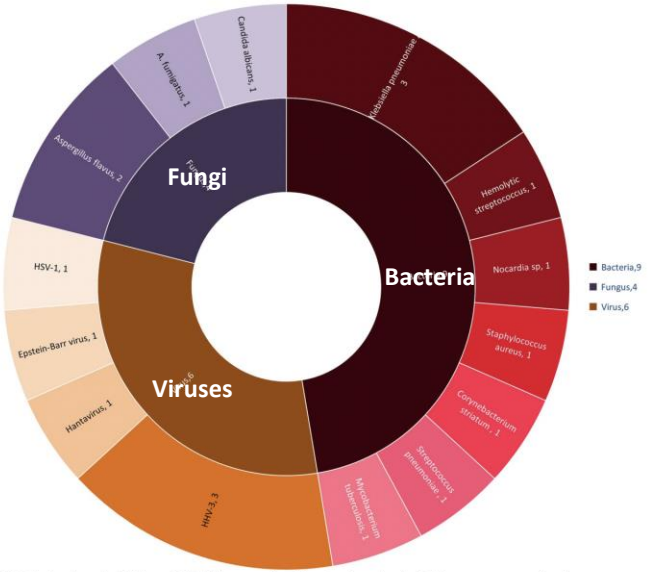

Fig. 2 Pathogenic result of CSF. Bacteria: 3 Klebsiella pneumoniae, 1 Mycobacterium tuberculosis, 1 Streptococcus pneumoniae. 1 Corynebacterium striatum, 1 Staphylococcus aureus, 1 Nocardia sp and 1Hemolytic streptococcus. Virus: 3 HHV-3, 1 HSV-1,1 Epstein-Barr virus and 1 Hantavirus. Fungus: 2 Aspergillus flavus, 1 Candida albicans and 1 Aspergillus fumigatus

Qin et al. BMC Infectious Diseases, 2025

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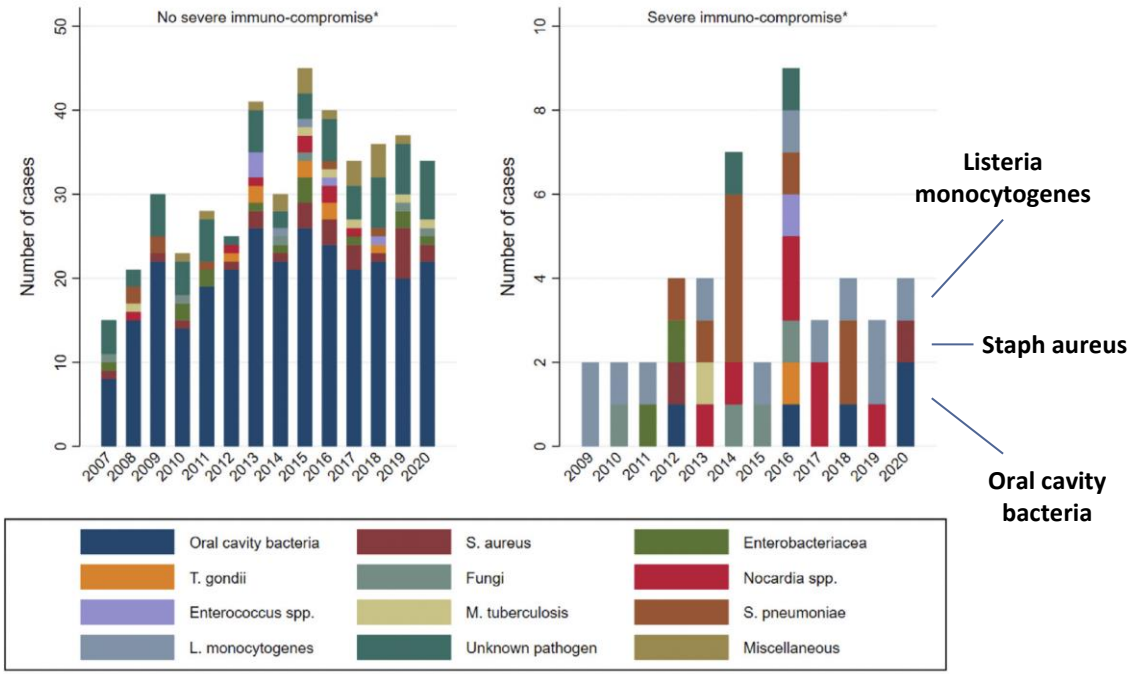
Etiology of Pyogenic Brain Abscesses in SOT



- Danish population-based cohort study with 485 cases from 2007-2014
- Median age 59
- 40% of cohort was immunocompromised, only 1% were transplant recipients

Bodilsen et al. Brain, 2023
Bodilsen et al. Clinical Microbiology and Infection, 2024

Etiology of Pyogenic Brain Abscesses in SOT

Clinical Characteristics of Brain Abscesses by Allografted Organ Type

Organ Type*	Transplantation Frequency	No. of Major Subsequent Operations	Organism Frequency*	No. of Patients Who Were		Outcome*
				Ventilator Dependent	Hemodialysis Dependent	
Liver (15)	1.8 Livers per patient	9	*Aspergillus* sp (13); *Mucorales* sp (1); and *Toxoplasma* sp (1)	14	12	Dead (14), alive (1)
Heart and heart-lung (7)	1.1 Hearts per patient	3	*Aspergillus* sp (4); *Nocardia* sp (2); and *Toxoplasma* sp (1)	4	4	Dead (5), alive (2)
Kidneys (6)	1.3 Kidneys per patient	5	*Aspergillus* sp (5) and *Candida* sp (1)	6	5	Dead (5), alive (1)

*The number in parentheses indicates the number of patients.

Selby et al. Arch Surg, 2011

- Aspergillus spp., Nocardia spp., and Toxoplasma spp. are common opportunistic pathogens in SOT recipients
- Scedosporium, Mucorales, MTB, and Cladophilaophora have also been identified in case reports

Pyogenic Brain Abscess Timeline in SOT

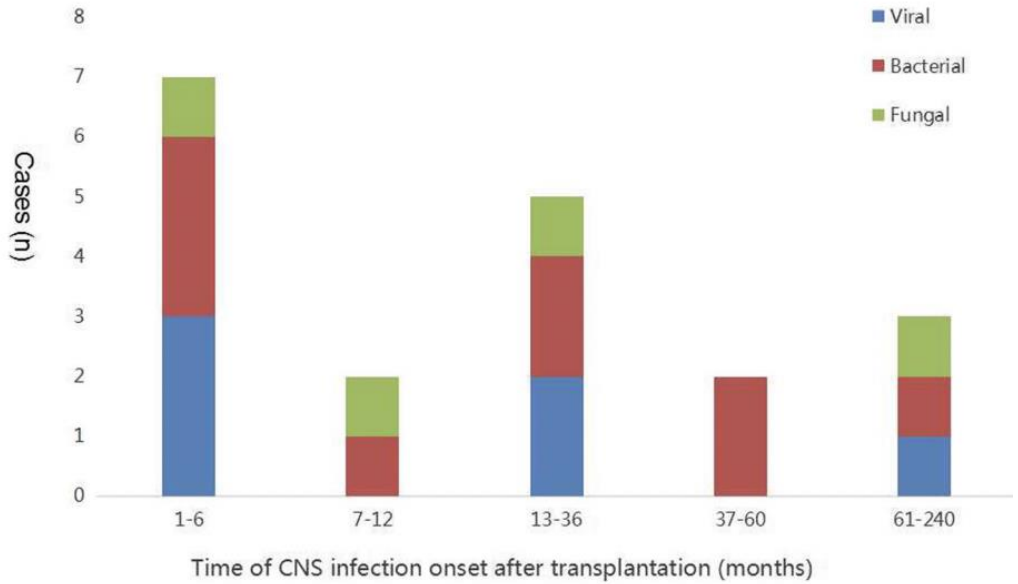


Fig. 1 Onset time of CNS infections. 1–6 months after transplantation is a higher-incidence period of CNS infections

Qin et al. BMC Infectious Diseases, 2025

Diagnostics: Role of Molecular Diagnostics

- Guidelines per Bodilsen et al.: pooled analysis of 9 studies
  - Concordance of molecular diagnostics with cultures: 67%
  - Discordance: 8%
  - Positive molecular diagnostics and culture negative: 13%
  - Culture positive and negative molecular testing: 9%
  - Identified other oral cavity bacteria and other Nocardia spp. in 66% of cases
- Qin et al: mNGS diagnosed 100% (6/6) of viral CNS infection, 67% (6/9) of bacterial, 75% (3/4) of fungal in KTRs
- Allen et al: 16s RNA gene PCR identified pathogen in 56% of culture negative cases (14/25)

Diagnostics: Role of microbial cell free DNA (mcf-DNA)

- Overall, low yield for CNS infections
  - Kaur et al.: No significant impact on diagnosis of CNS infection (though did not include abscess) or deep seated infections including abscess
- Two case reports (1 SOT recipient) identified fungal pathogen via mcf-DNA

Treatment: Duration?

- Limited data to guide the optimal duration of antimicrobials for pyogenic brain abscess
- European Society of Clinical Microbiology and Infectious Diseases guidelines (2024) : 4 single-center retrospective cohort studies
- Conditional recommendation, low certainty of evidence: <u>6-8 weeks of IV antimicrobials for aspirated abscess or conservatively managed abscess</u>, possibly 4 weeks if surgically resected
- No recommendation for timing of stepdown to PO antimicrobials

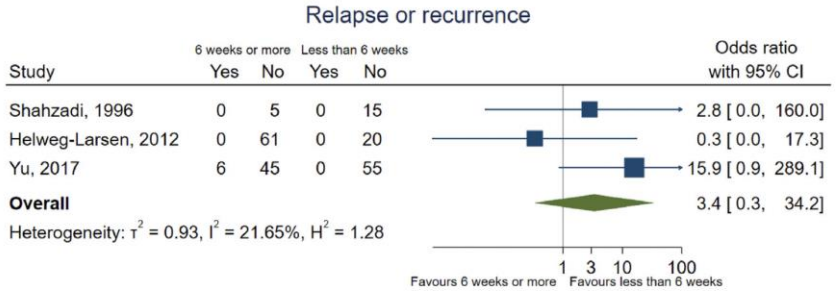


Fig. 13. Risk of relapse or recurrence according to treatment duration.

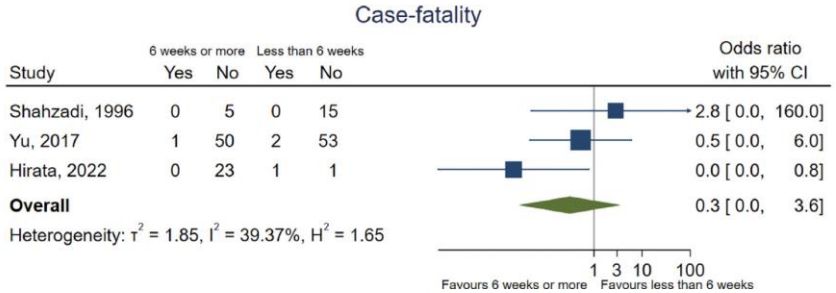


Fig. 14. Risk of death according to treatment duration.

Clinical Update

- Continued clinical stability on levofloxacin and isavuconazole. Tolerating well
- 4 months after initiation of antimicrobials, repeat head CT w/ contrast showed stable size of left frontal lobe abscess (8 mm) with mild surrounding edema
- Isavuconazole level at 2.8
- Remains on levofloxacin and isavuconazole with plan for repeat imaging in 3 months

Poll #3: Assuming the next brain imaging study is stable or slightly improved, what would your next step be?

a) Stop oral antibiotic, continue isavuconazole, and repeat imaging in a few months
b) Stop all oral antimicrobials and repeat imaging
c) Continue all oral antimicrobials and repeat imaging

Key Takeaways

- Identification of organisms in pyogenic brain abscesses can be challenging even in immunocompetent hosts. Aspiration of fluid is recommended as CSF yield is lower
- Molecular testing may increase diagnostic yield especially in culture negative cases, but sensitivity is still limited
- Lack of strong evidence to guide nuance in treatment approaches (surgical and antimicrobial, IV vs. PO), even less in immunocompromised
- 8 weeks of intravenous antimicrobials are currently recommended depending on clinical improvement and surgical candidacy

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