CITYWIDE CONFERENCE

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Jefferson
Thomas Jefferson University
HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

27 years old female presents with

- Altered Mental Status

HPI

- 27 y/o female with past medical history of Anxiety, Depression and ?remote history of genital herpes presented with acute onset of altered mental status to our ED in July, 2019.

- The night before, she went to sleep in her usual state of health.

- Her boyfriend woke up around 2:00 am hearing her moan and found her unresponsive in bed. He called 911 and she was brought to the ED.

- Patient was a flight attendant and 6 days prior to her presentation, she had returned from her first International flight to Ireland.

- On her return, she had sore throat and “swollen tonsils”; was taking OTC ibuprofen and cough drops.

- No fever or headache was reported at home. ROS could not be obtained.

- **Past Medical History:** Anxiety, Depression, genital HSV and chlamydia
- **Past Surgical History:** None
- **Family History:** Dementia (Grandfather)
- **Allergies:** No known allergies
- **Medications:** Ibuprofen, IUD

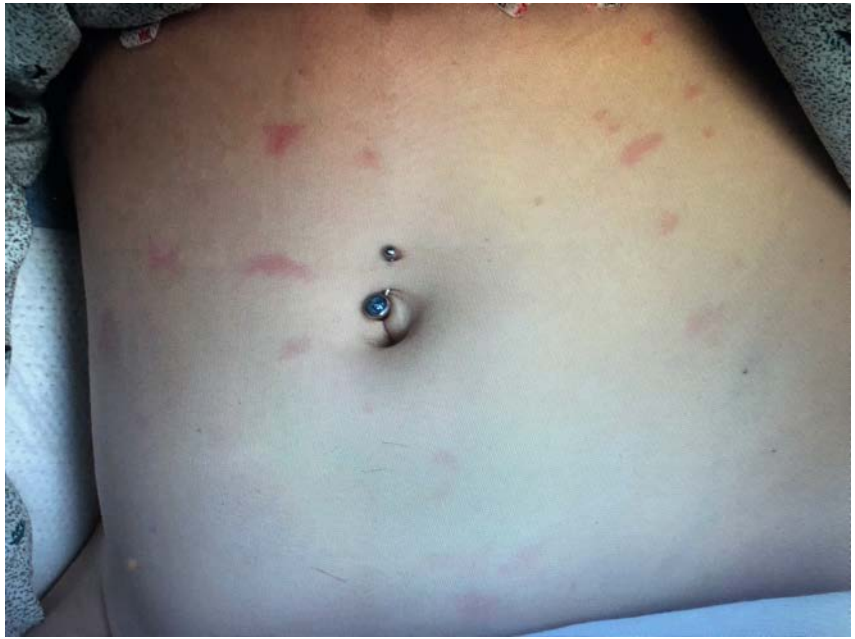
Social History

- Born and raised in California. Up to date on vaccinations per mother. H/O seasonal allergies and frequent swollen tonsils as a child.
- Moved to Philadelphia 2 months ago; lives in Fishtown with roommates
- Started new job as a flight attendant and had first international trip to Ireland; stayed in Dublin for 2 days. No unusual exposures reported.
- Patient's sister mentioned that she had a **spider bite** 5 weeks ago while traveling to Dallas. Developed a **rash** on her chest over the next few weeks.
- No h/o smoking or IVDA. Occasional alcohol.
- In a monogamous relationship with boyfriend of 2 months.

PHYSICAL EXAMINATION

- A young, well-developed female lying in bed, appears lethargic and uncomfortable.
- **Vitals:** T **104ºF**, HR 110 bpm, BP 100/50 mmHg, RR 21/min, O2 Sat 99 % on RA
- **HEENT:** normocephalic, atraumatic, mild pharyngeal erythema without exudates or ulcerations
- **Eyes:** no conjunctival pallor/ injection, no scleral icterus, PERRLA (3 mm B/L), EOMI
- **Neck:** No cervical adenopathy, mild nuchal rigidity
- **Cardiovascular:** Normal rate and normal heart sounds
- **Respiratory:** Normal vesicular breathing B/L

- **Abdomen:** soft, non-tender, non-distended, normoactive bowel sounds
- **GU:** Foley catheter noted
- **Extremities:** No edema
- **Skin:** Maculopapular rash on torso and neck



- **CNS:** non-verbal but arousable by verbal and tactile stimuli and responsive to noxious stimuli, Cranial nerves intact, no focal deficits on motor/ sensory exam, increased tone B/L upper extremities, equivocal plantars.

LAB DATA

- WBC: 8.7 (PMN: 90%, L: 3%, Mono: 6%)
- H/H: 13.0/ 39
- Platelets: 199
- Na/K: 130/4.5, Cl/CO2: 92/23, BUN/creat: 8/0.6, Ca: 9.3
- AST/ALT: 10/11, ALP: 58, TB/DB: 0.6/<0.2, TP/Alb: 7.7/3.9
- Lactate: 1
- TSH: 0.25, fT4: 1.0
- UA: 2+ protein but otherwise unremarkable
- Serum and urine drug screen negative
- BCx: drawn
- HIV negative

Lumbar Puncture

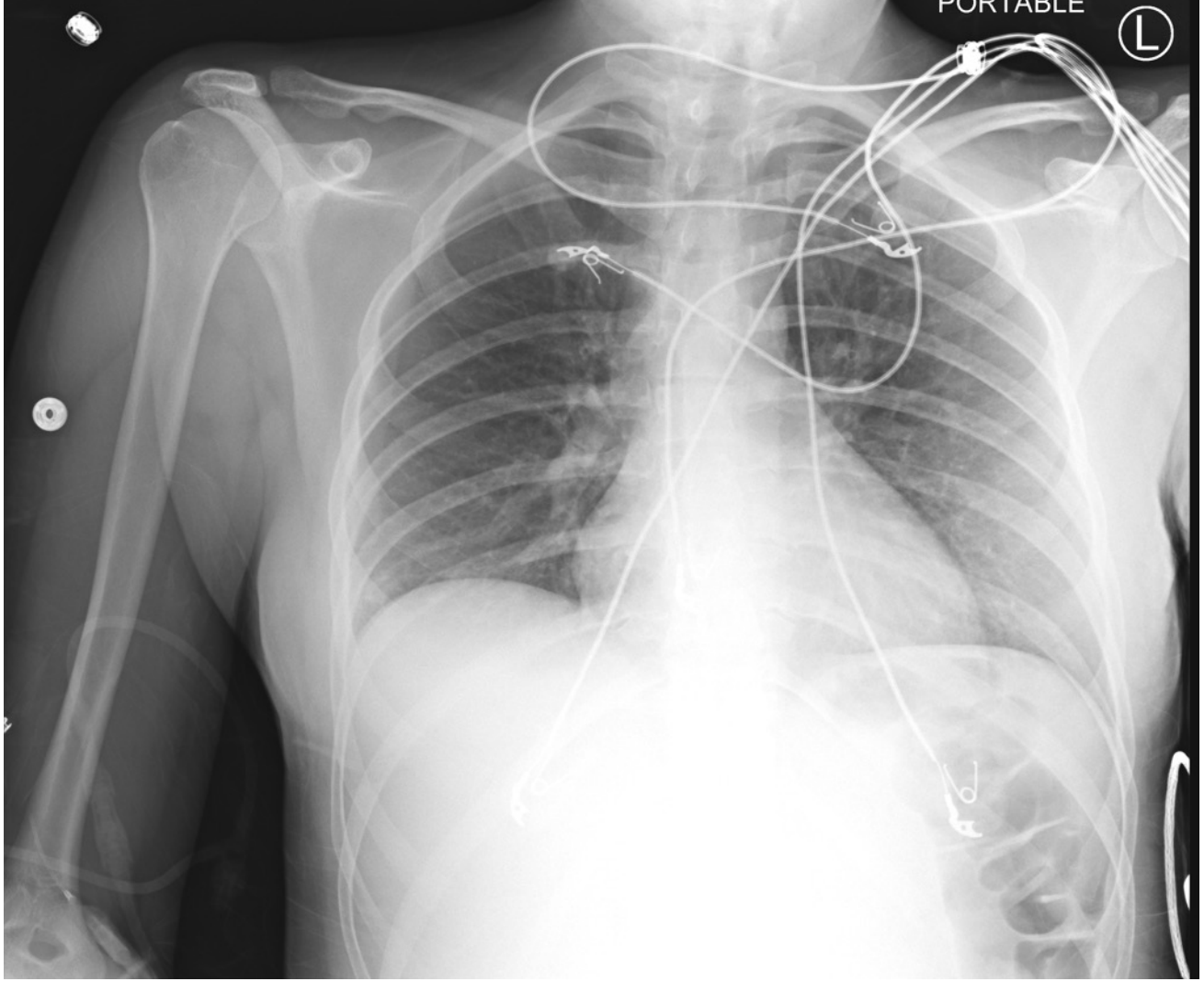
Opening pressure: 25

Protein: 107 , Glucose: 69

WBC: 13 (no RBCs), 16% PMNs, 74% lymphos, 10% mono

Meningitis/ Encephalitis panel: negative

NOS on GS


PORTABLE
L

CTH

- No ICH or mass effect
- Partially visualized prominent adenoids

Summary

- 27 years old female with a PMHx of ?HSV1 genital infection, chlamydia, now admitted with acute meningoencephalitis, preceded by sore throat.

- CSF analysis shows lymphocytic pleocytosis.

Differential Diagnosis

Differential Diagnosis

- Herpes viruses (HSV, VZV, EBV, CMV, HHV-6)
- Arthropod-borne viruses (West Nile virus, St. Louis encephalitis virus, La Crosse virus, eastern equine encephalitis virus)
- Non-polio Enteroviruses (echovirus, coxsackie virus)
- Tick-borne Powassan virus
- HIV
- Influenza virus
- JC virus
- Adenovirus
- Syphilis
- Lyme
- Anaplasma

- Bacterial Meningitis (Pneumococcus, Listeria, Mycoplasma pneumoniae)
- Mycobacterium tuberculosis
- Endemic mycoses
- Cryptococcus
- Toxoplasma
- Other protozoa (Acanthamoeba sp., Balamuthia mandrillaris)
- Autoimmune

Back to the patient…

In the ER, patient was started on IV Vancomycin, Ceftriaxone, steroids and Acyclovir

ID CONSULT

- MRI Brain
- EBV, CMV PCR
- West Nile IgM in CSF and serum, West Nile PCR in CSF
- Mycoplasma IgM and IgG
- Syphilis cascade, Lyme assay and western blot, Anaplasma serologies
- Start Doxycycline
- ID recommended to stop Vancomycin and Acyclovir, continue Ceftriaxone

- **MRI Brain:** No acute infarction, hemorrhage, mass or abnormal enhancement
- Her mental status worsened. Became more obtunded and she was intubated 24 hours after admission.
- A repeat CTH done after intubation showed no change.
- **Repeat CSF:**

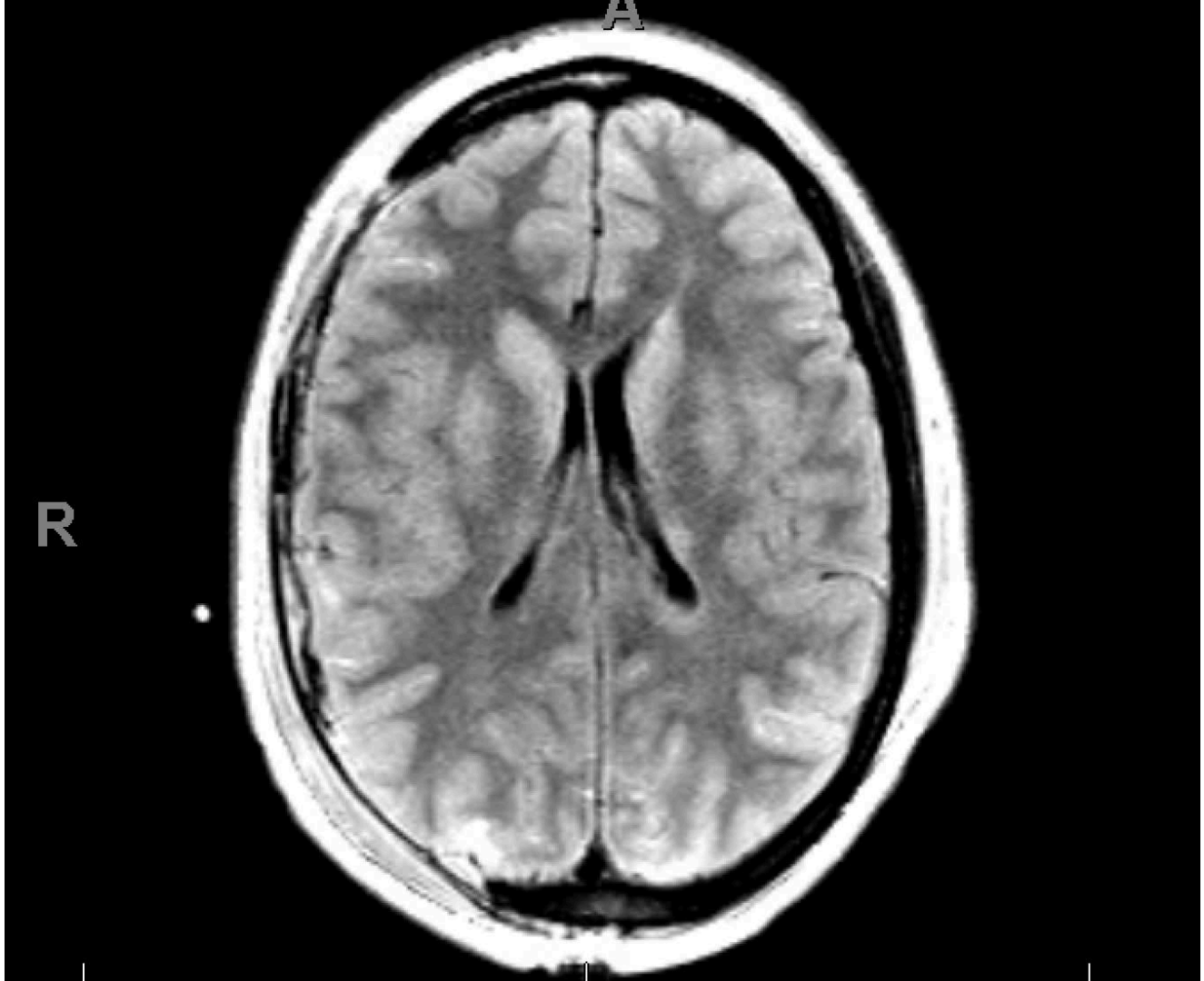
  WBC: 49 (RBC: 0); 16 % PMN, 78 % Lymph, 10 % Mono

  Protein: 107

  Glucose: 69

- Day 3, she became bradycardic and hypotensive and CTH showed generalized cerebral swelling

- Underwent emergent decompressive hemicraniectomy.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- Day 3, Respiratory pathogen panel (done on admission) resulted positive for **Adenovirus**.

- Any change in management?

ADENOVIRUS

- Most commonly adenovirus causes self limited disease- respiratory tract infections, pharyngitis, tonsillitis, pertussis like syndrome, otitis media, pneumonia, several outbreaks reported among military recruits and daycare

- Other infections: conjunctivitis, gastro enteritis, GU infections, notably hemorrhagic cystitis

- Sporadic cases of meningitis and meningoencephalitis, either as a primary infection or as a complication of pneumonia

- Most infections are asymptomatic, severe fatal infections rare in immunocompromised

- Important opportunistic pathogen in immunocompromised host, esp in HSCT and solid organ transplant recipients, esp in 1st 3 months

- **Diagnosis**
  - PCR: detects viral DNA- can be used in fixed tissue specimens, serum and blood
  - Other ways: 4 fold or greater rise in antibody titers in acute and convalescent sera
  - Typing usually not done in routine labs
  - CSF viral cultures are generally not recommended in patents who present with meningoencephalitis.

Disseminated Adenovirus Infections

- No approved antiviral agents for treatment
- Use of Cidofovir based on case reports and case series
- IVIG- adjunctive therapy
- Mostly studied in transplant recipients

Treatment

- **Cidofovir**

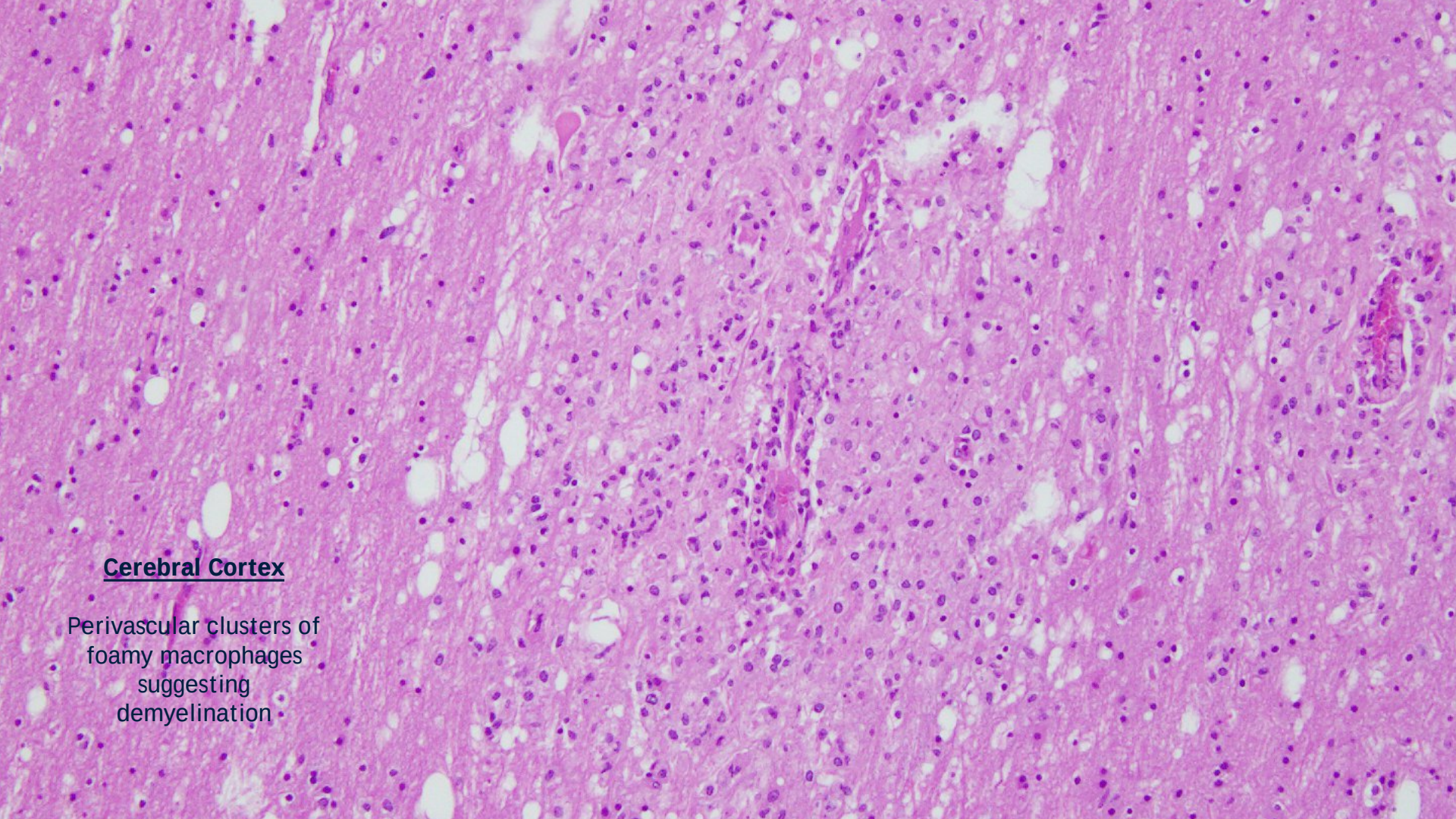
1 mg/kg 3 times a week OR 5 mg/kg/week for 2 weeks followed by 5 mg/kg every other week until resolution of symptoms and documentation of 3 negative samples, 1 week apart

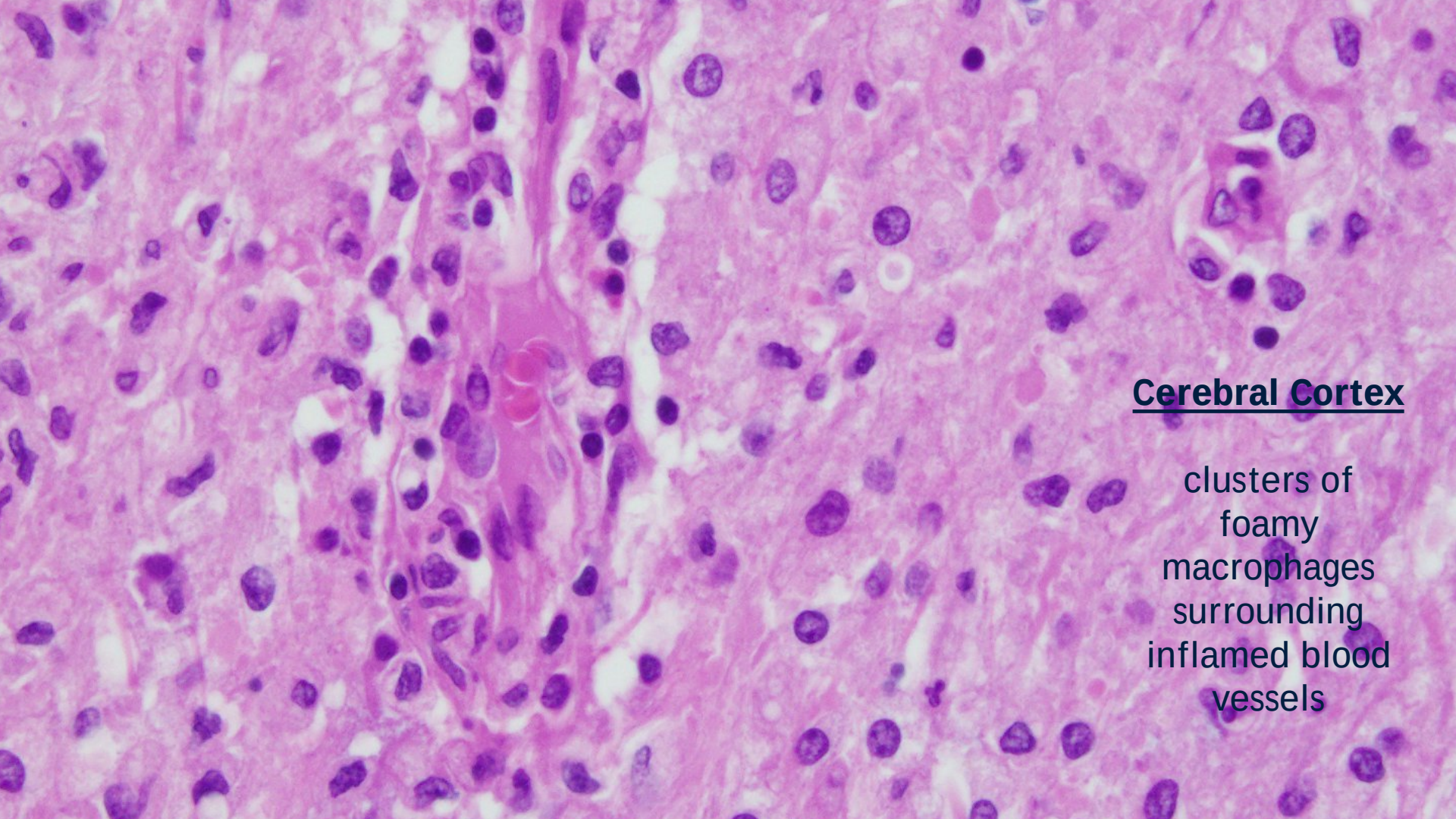
- Probenecid and IV hydration before and after Cidofovir

- Nephrotoxicity 50%– main limiting factor, given with Probenecid and aggressive hydration
- Neutropenia 20 %

- **Brincidofovir**

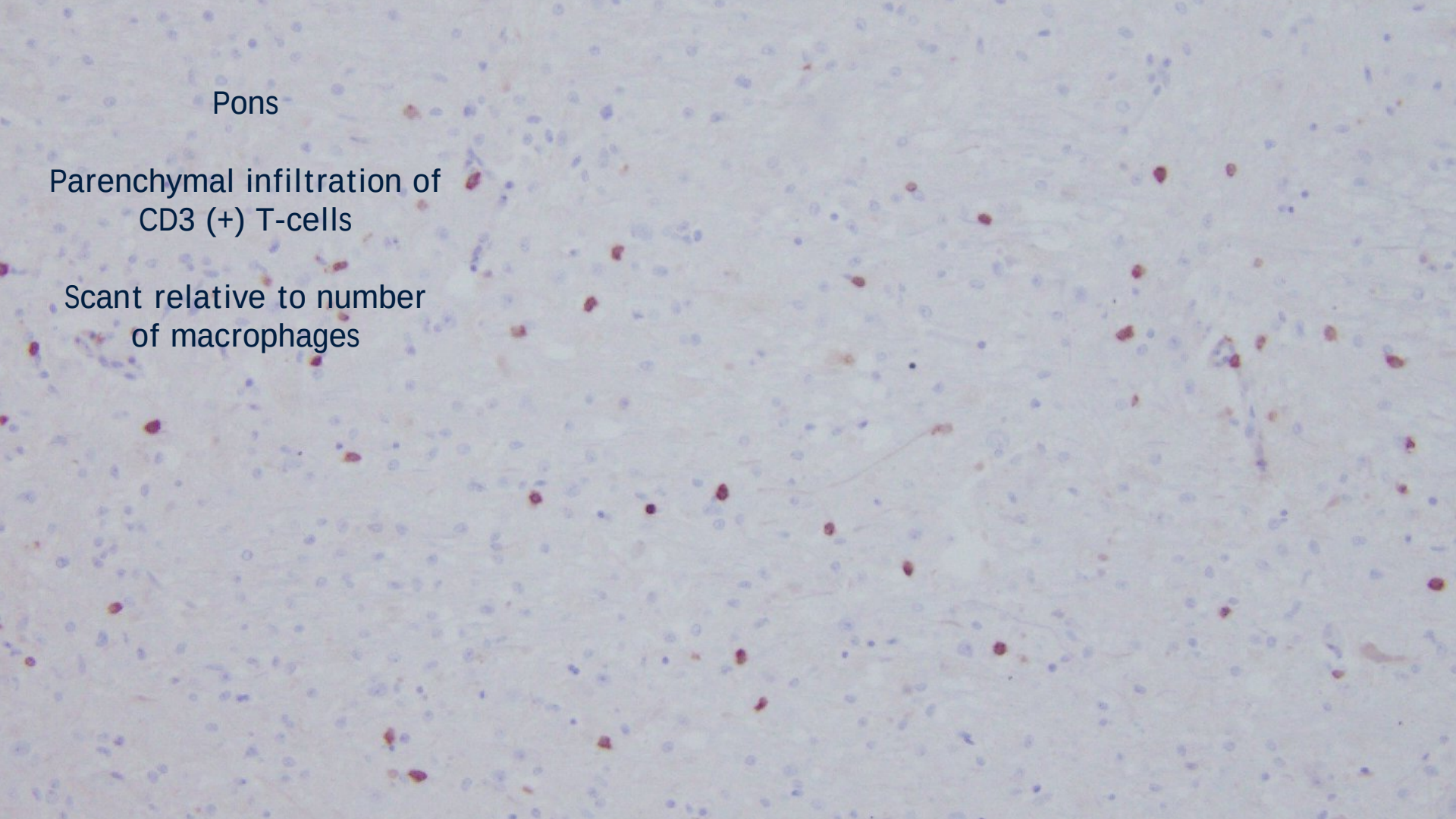
- Started on Cidofovir 5 mg/kg along with probenecid
- Adenovirus PCR in serum and CSF was negative
- Discussed with Microbiology to coordinate serotyping with CDC- Identified as serotype 4
- Her mental status continued to worsen and family decided to withdraw care on Day 10 of admission.
- Family requested autopsy

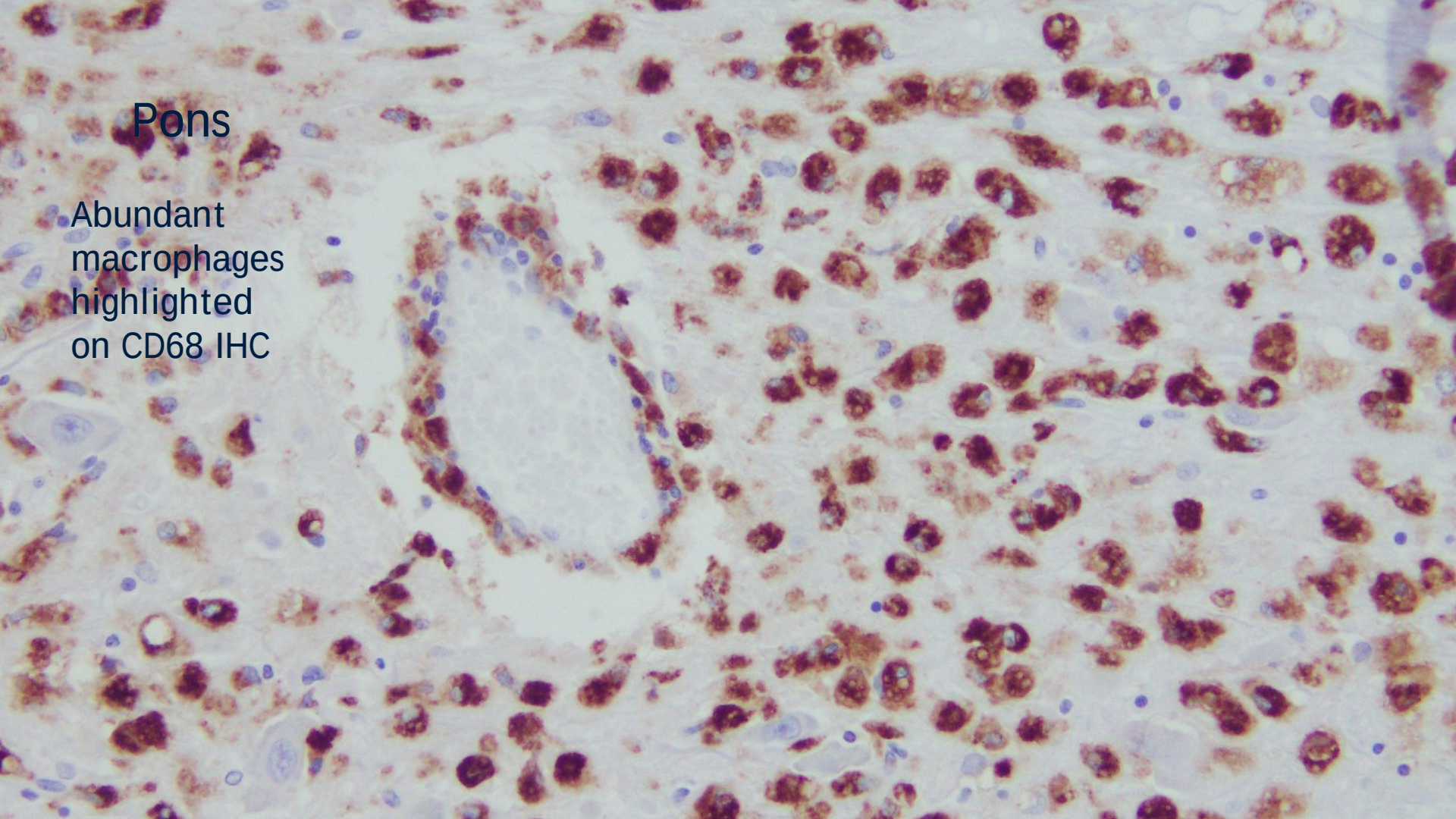

Cerebral Cortex
Perivascular clusters of foamy macrophages suggesting demyelination



Cerebral Cortex

clusters of foamy macrophages surrounding inflamed blood vessels


Pons
Parenchymal infiltration of CD3 (+) T-cells
Scant relative to number of macrophages


Pons
Abundant macrophages highlighted on CD68 IHC

Acute Disseminated Encephalomyelitis (ADEM)

- AKA Post infectious encephalomyelitis
- Autoimmune demyelinating disease that follows an infection or rarely vaccination typically after 1-4 weeks after the inciting event
- Infections- Influenza A and B, Hepatitis viruses, non specific flu-like URIs, non viral infections like Mycoplasma
- Presents with headache, fever, AMS (ranging from irritability to coma), may have motor deficits, brainstem involvement common- oculomotor deficits, dysarthria, motor deficits,aphasia, optic neuritis,
- Variant forms with variable peripheral nerve involvement

- CSF profile similar to viral encephalitis
- MRI if showing demyelinating lesions supportive of the diagnosis
- On pathology- perivenular inflammation and demyelination
- Encephalitis- perivascular and parenchymal inflammation , neuron and glial cell death and evidence of viral infection- viral inclusions, antigen staining
- Treatment: High dose steroids, IVIG, plasma exchange

Adenovirus Meningoencephalitis

- Among the more than 50 serotypes of adenovirus, serotype 2 is the most common serotype that has been reported to be associated with meningoencephalitis and disseminated disease.

- Published reports of the neuropathological features of adenovirus meningoencephalitis are scarce; reported cases show bilateral, sometimes symmetric, necrotizing lesions with a striking predilection for medial and paramedian structures and the ventricular system.

- Lymphocytic infiltrates, microglial nodules, and intranuclear inclusions are the most common microscopic findings.

- Involvement of the spinal cord and roots has only been reported in a couple of cases.

QUESTIONS?

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