DSS 2019-5

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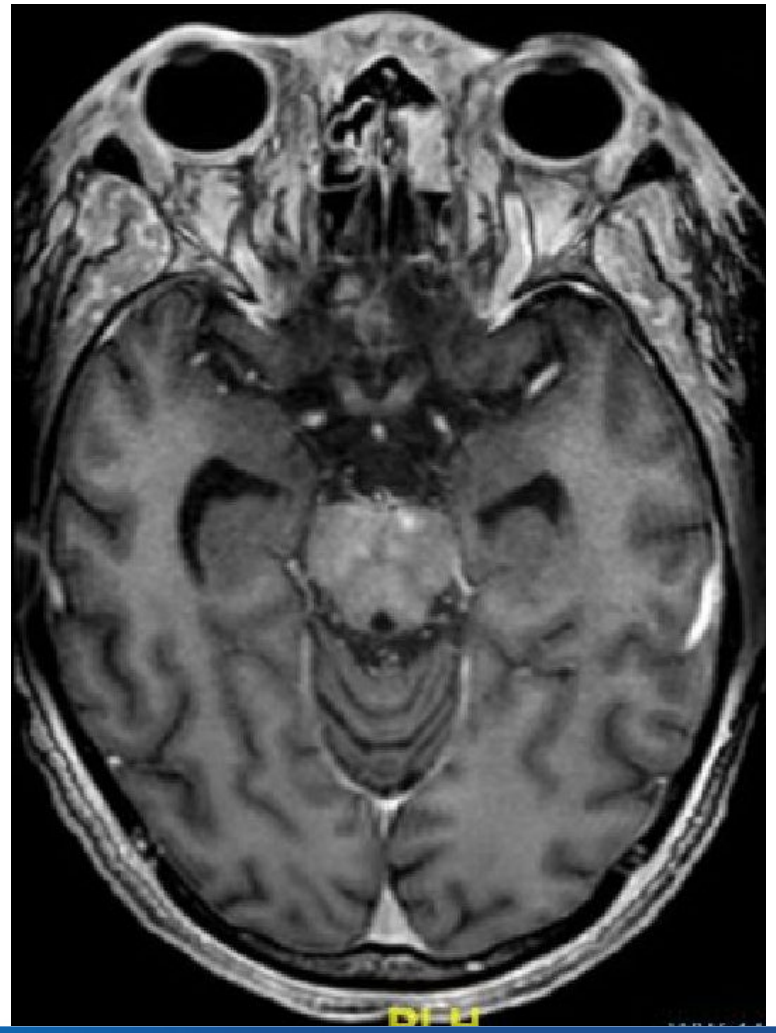
Disclosures

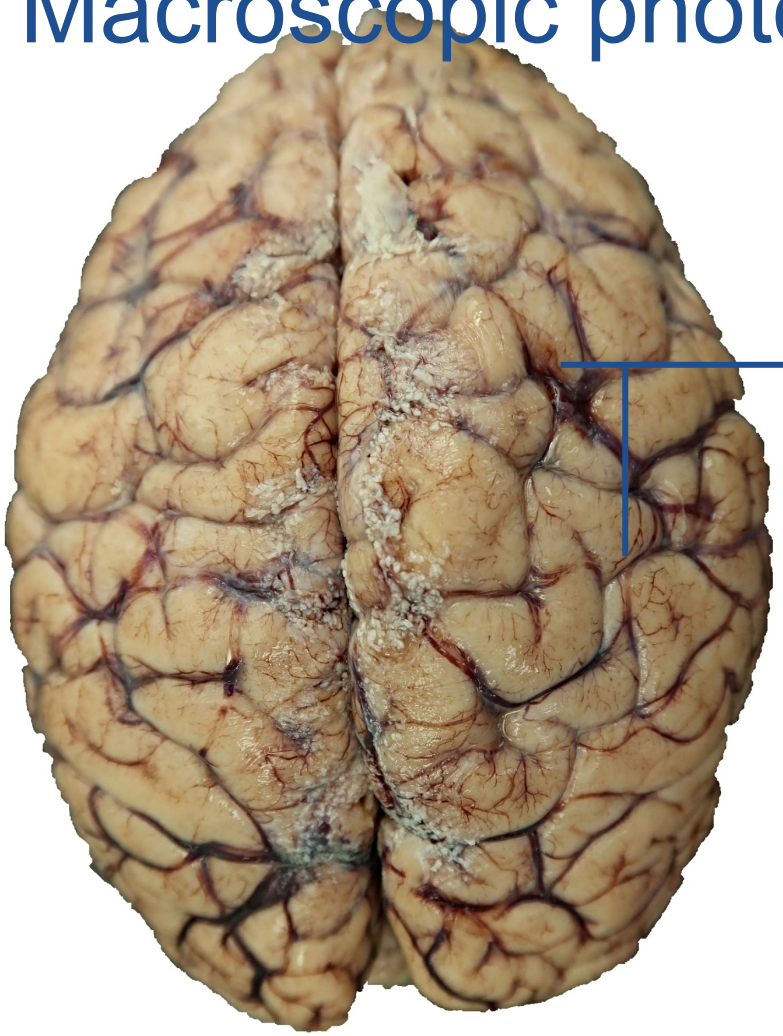
- None to declare

Presentation

- 39-year-old, HIV+ man
- **Repeated bouts of fevers** and **altered mental status**, requiring multiple admissions at an outside hospital.
- On the most recent admission, cranial imaging revealed a **'brainstem mass'** at an outside hospital and the patient was transferred to our institution.
- CSF infectious workups were negative.
- Despite antibiotic therapies, he passed away (**approx. 4 month course since initial presentation to death**).
- A brain/ spinal cord autopsy was requested to ascertain the cause of death.



Macroscopic photographs

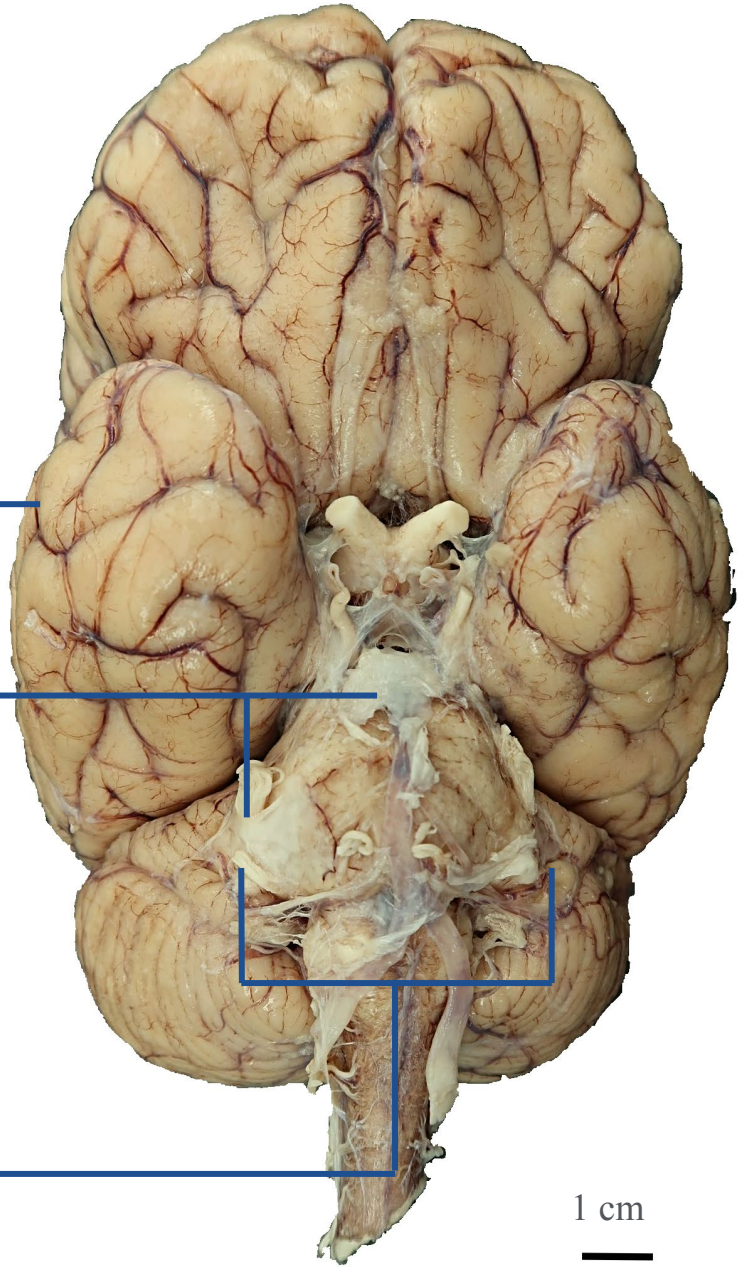


Fresh brain weight: 1525 grams

Swollen gyri and sulcal compression in bilateral cerebral hemispheres

Thickened leptomeninges at the base of the brain

Significantly widened pons



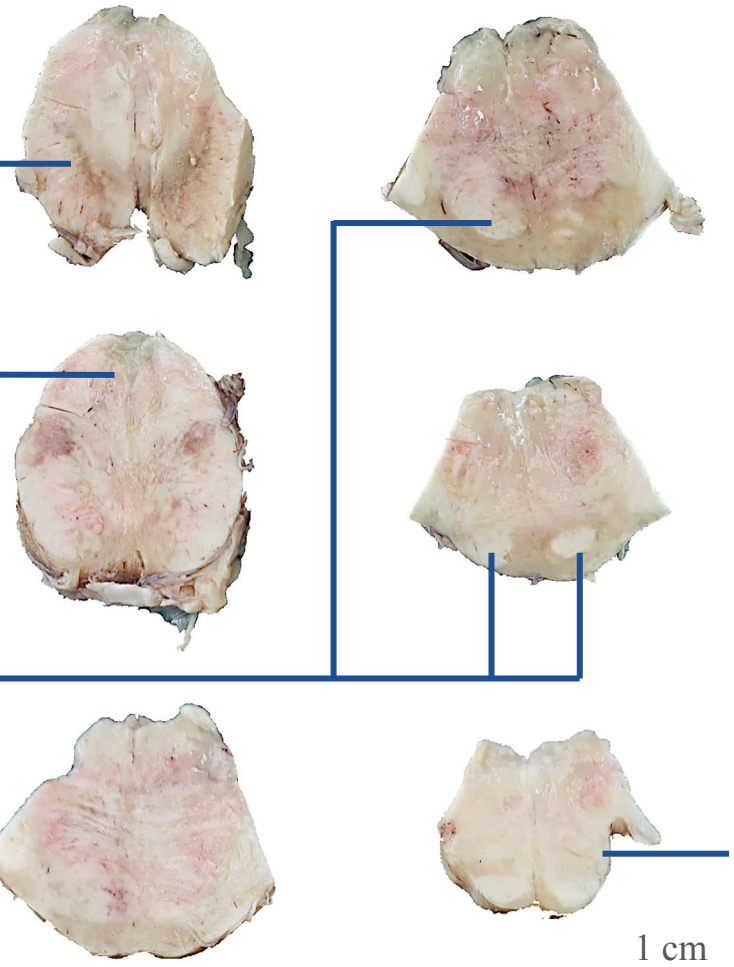
Macroscopic photographs

Diffuse swelling of the brainstem

Pale substantia nigra

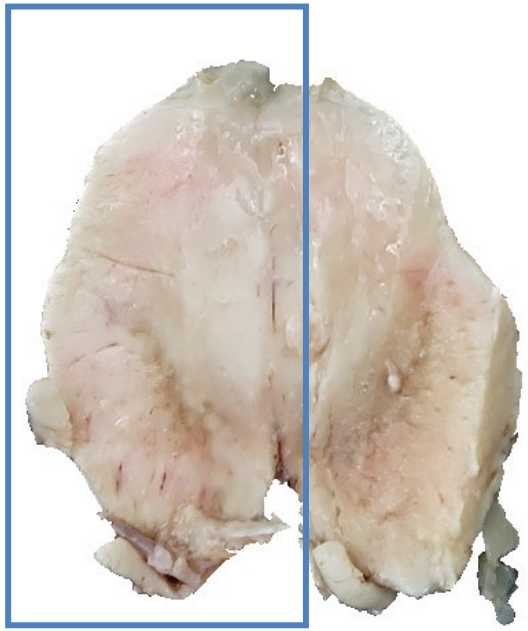
Obliteration of cerebral aqueduct

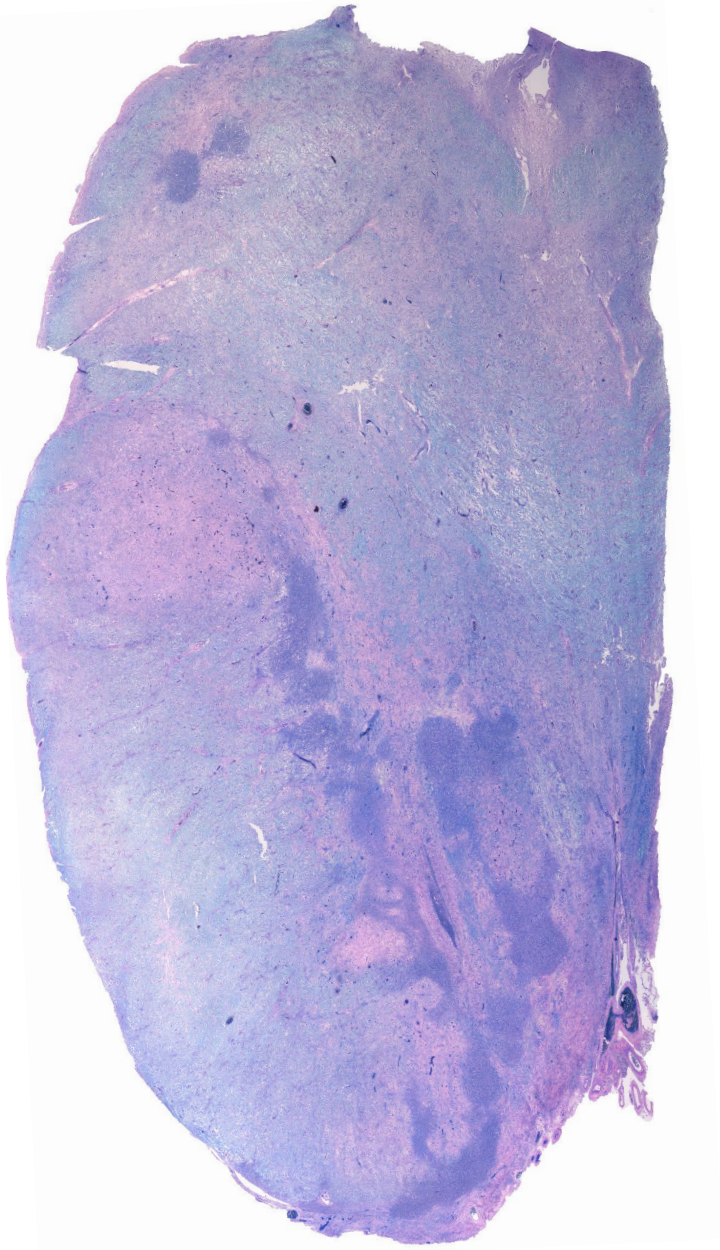
Mottled and hyperemic discoloration with white patches over basis pontis

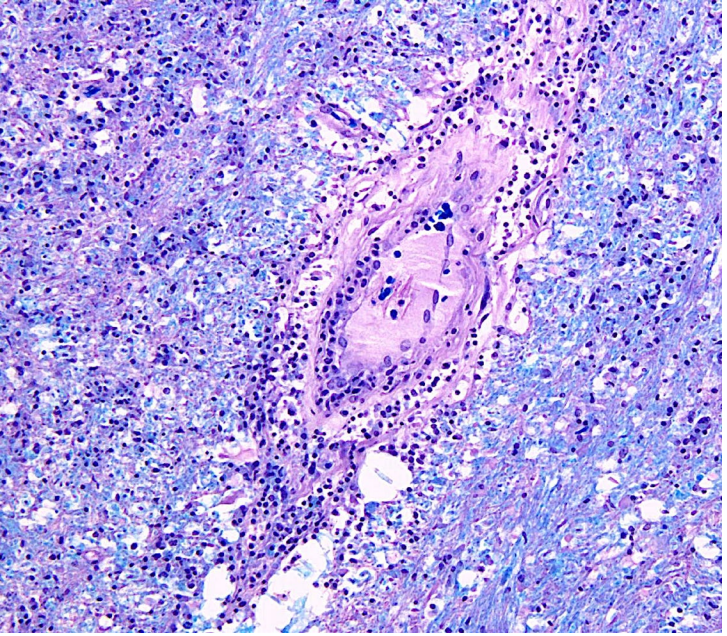


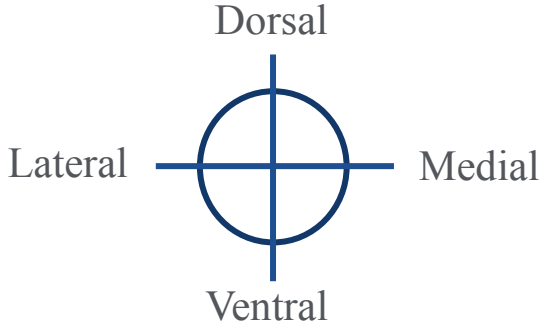
Poor demarcation of inferior olivary nuclei

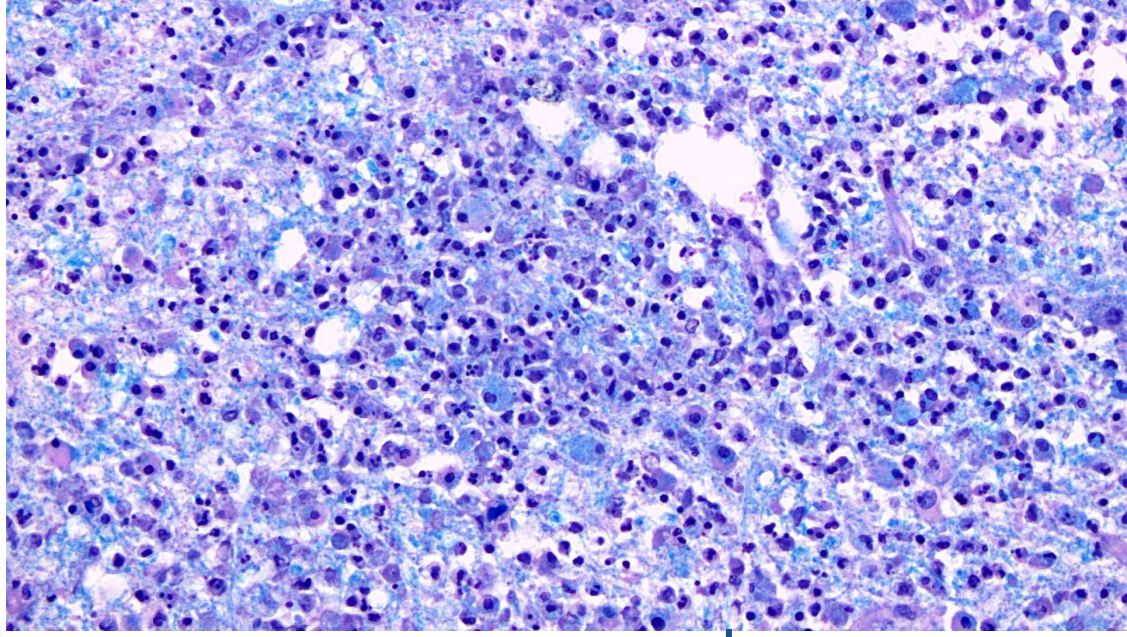
Diagnostic slide

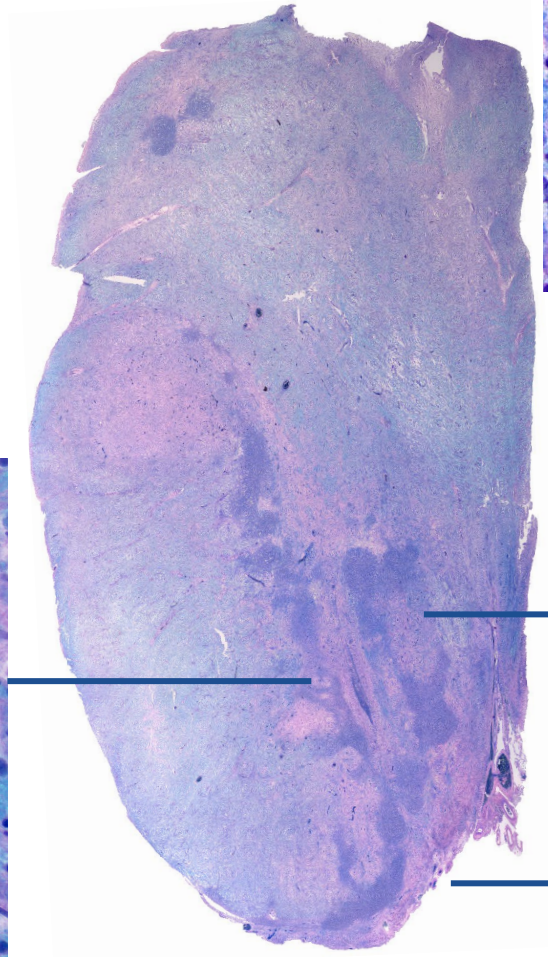


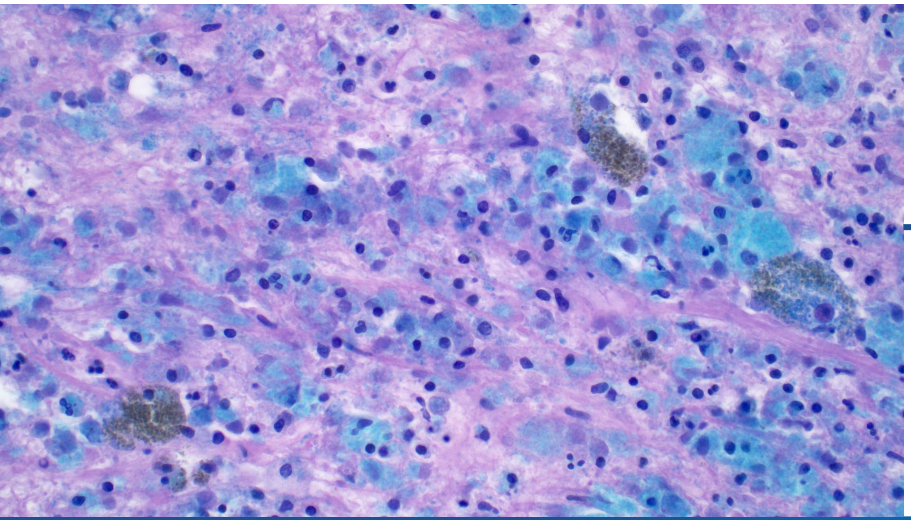


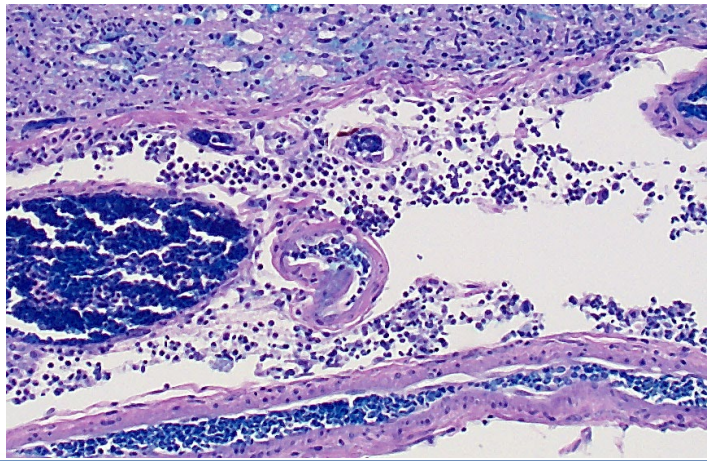


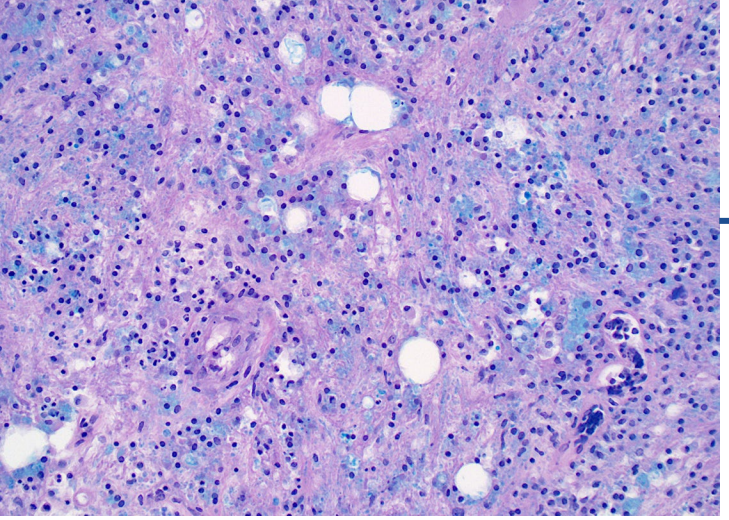

Dorsal
Lateral
Medial
Ventral

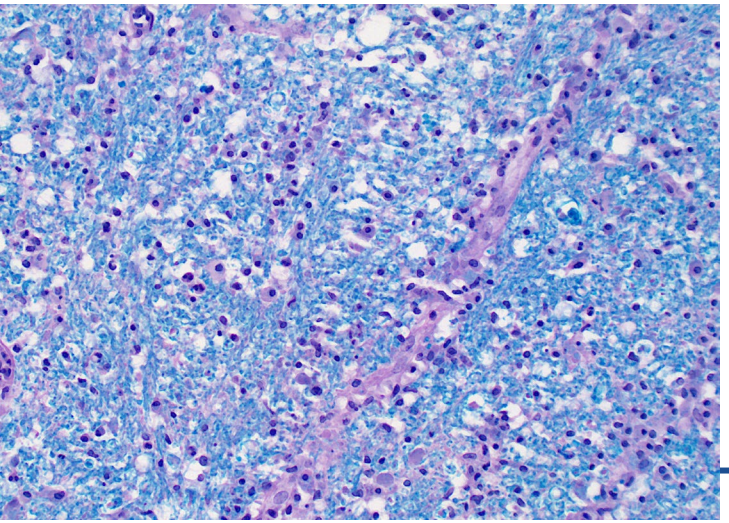


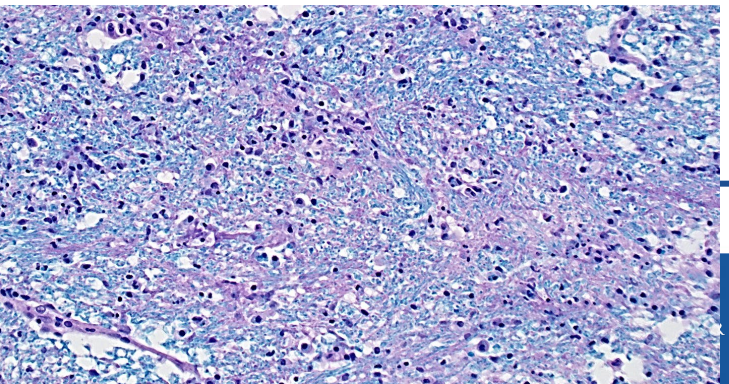










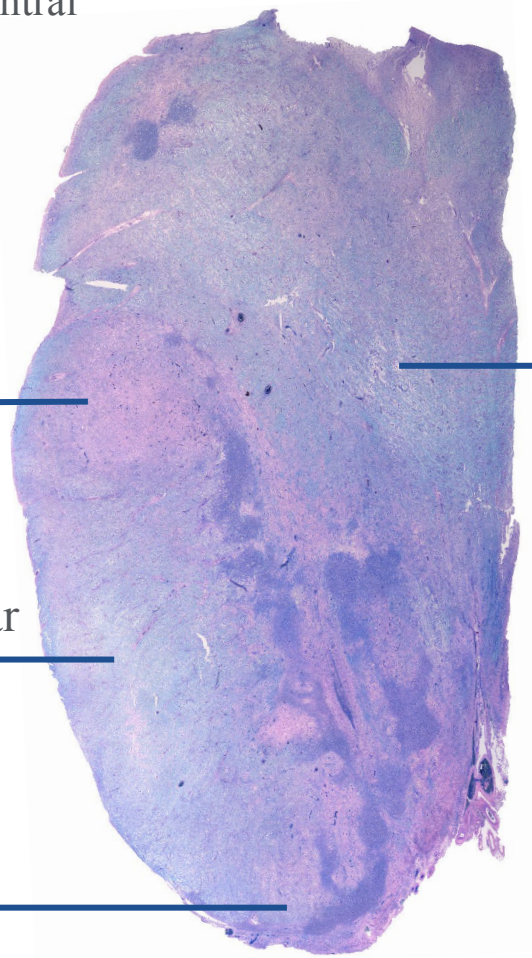


Dorsal

Lateral

Medial

Ventral

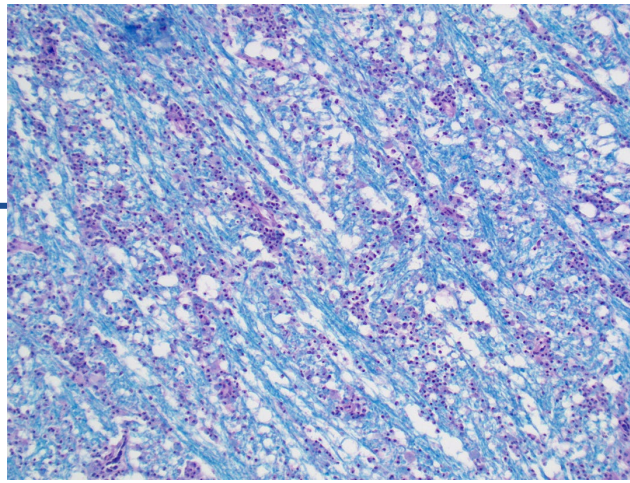


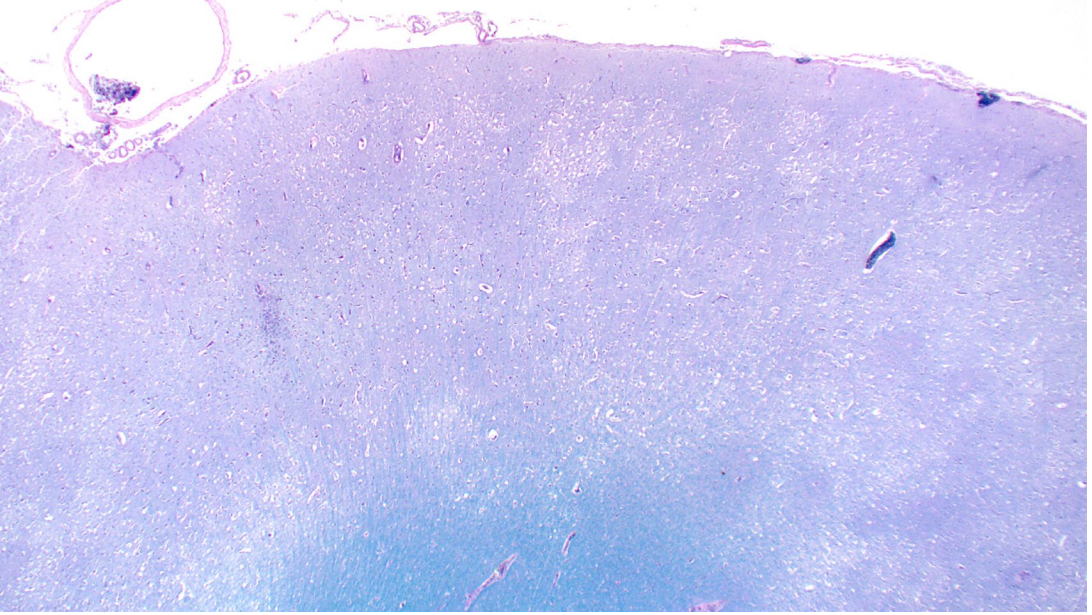
Occipitopontine

Corticospinal/bulbar

Frontopontine

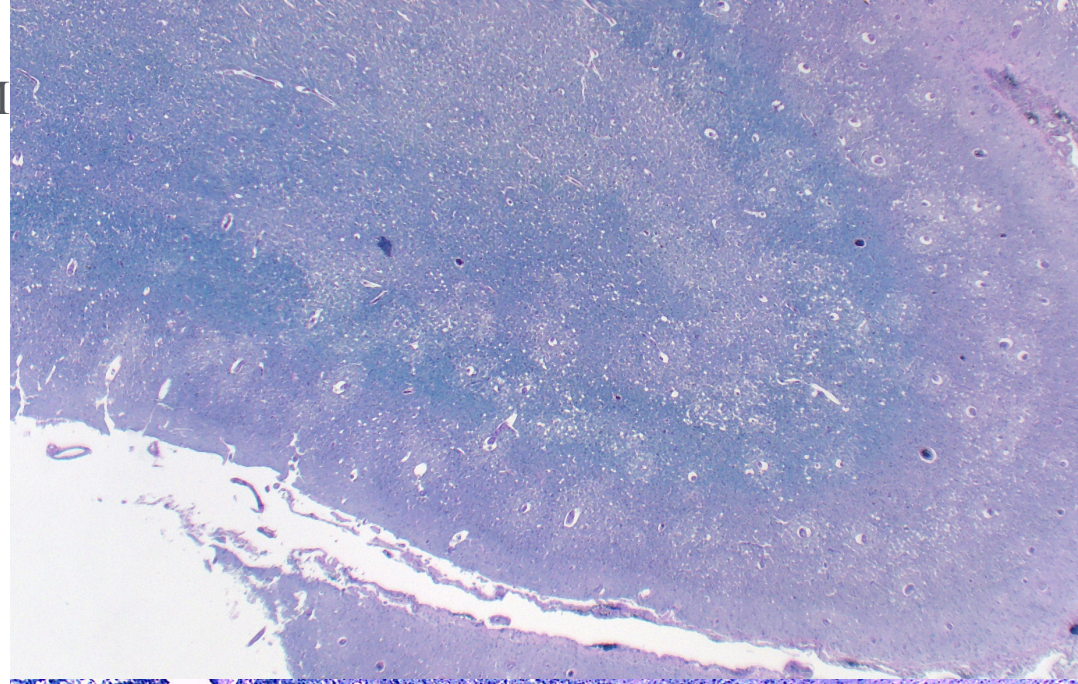
Superior cerebellar peduncle

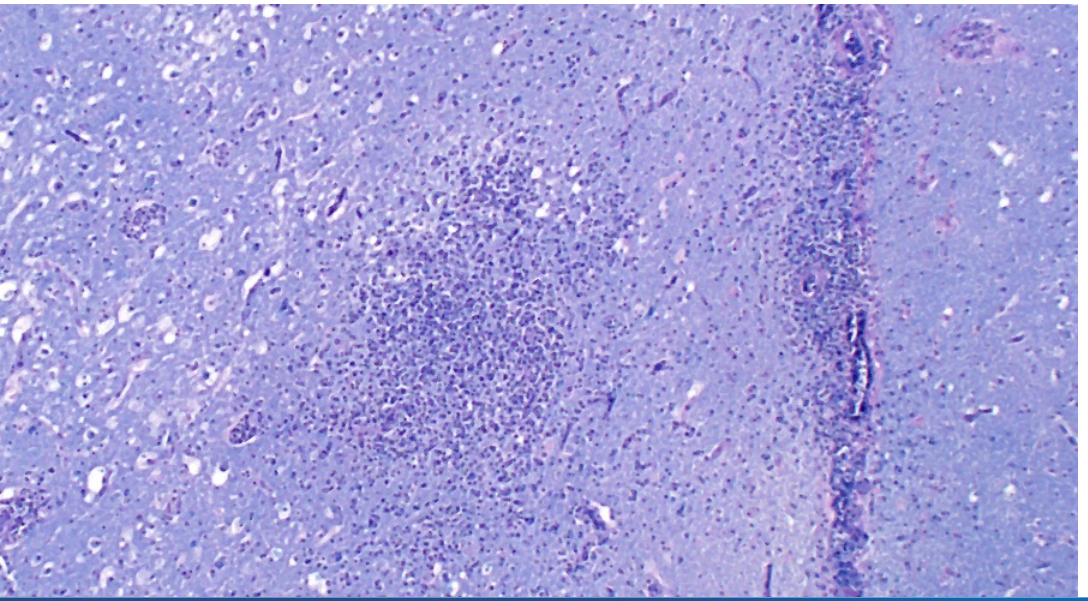




Prefrontal cortex

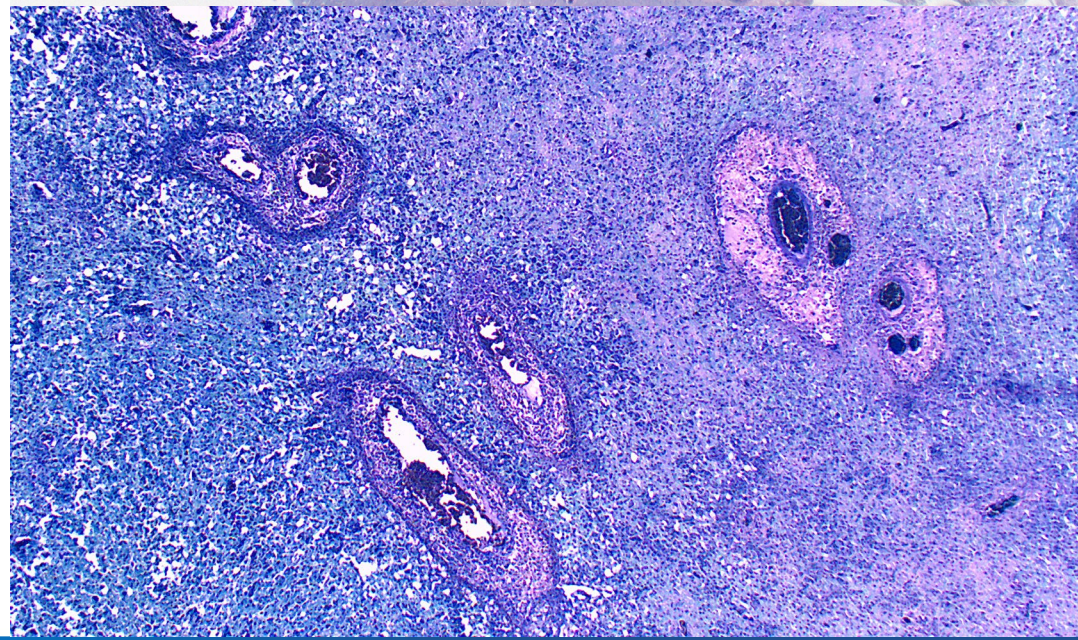
Occipital Cortex/WM





Prefrontal cortex

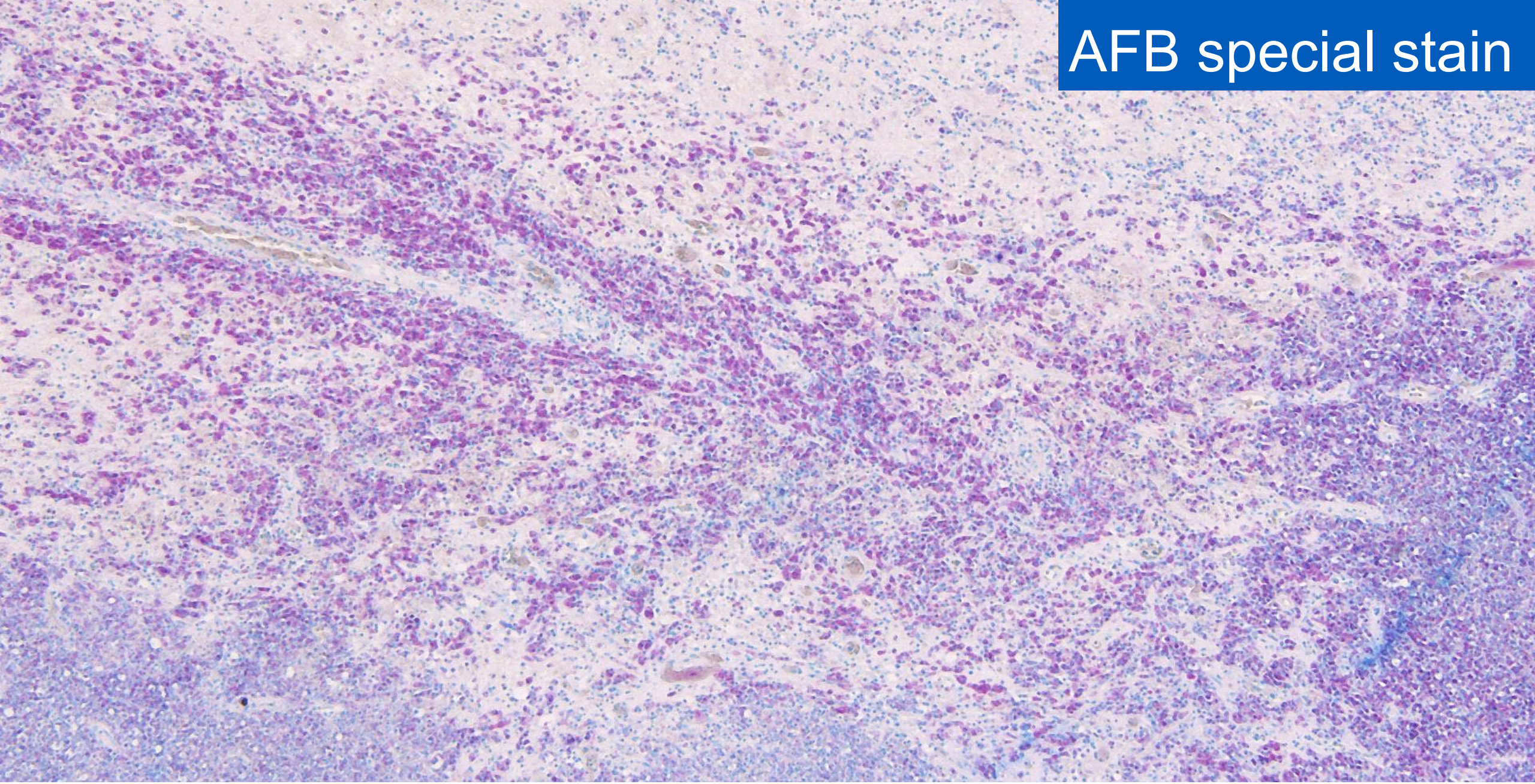
Hilum of cerebellar dentate nucleus



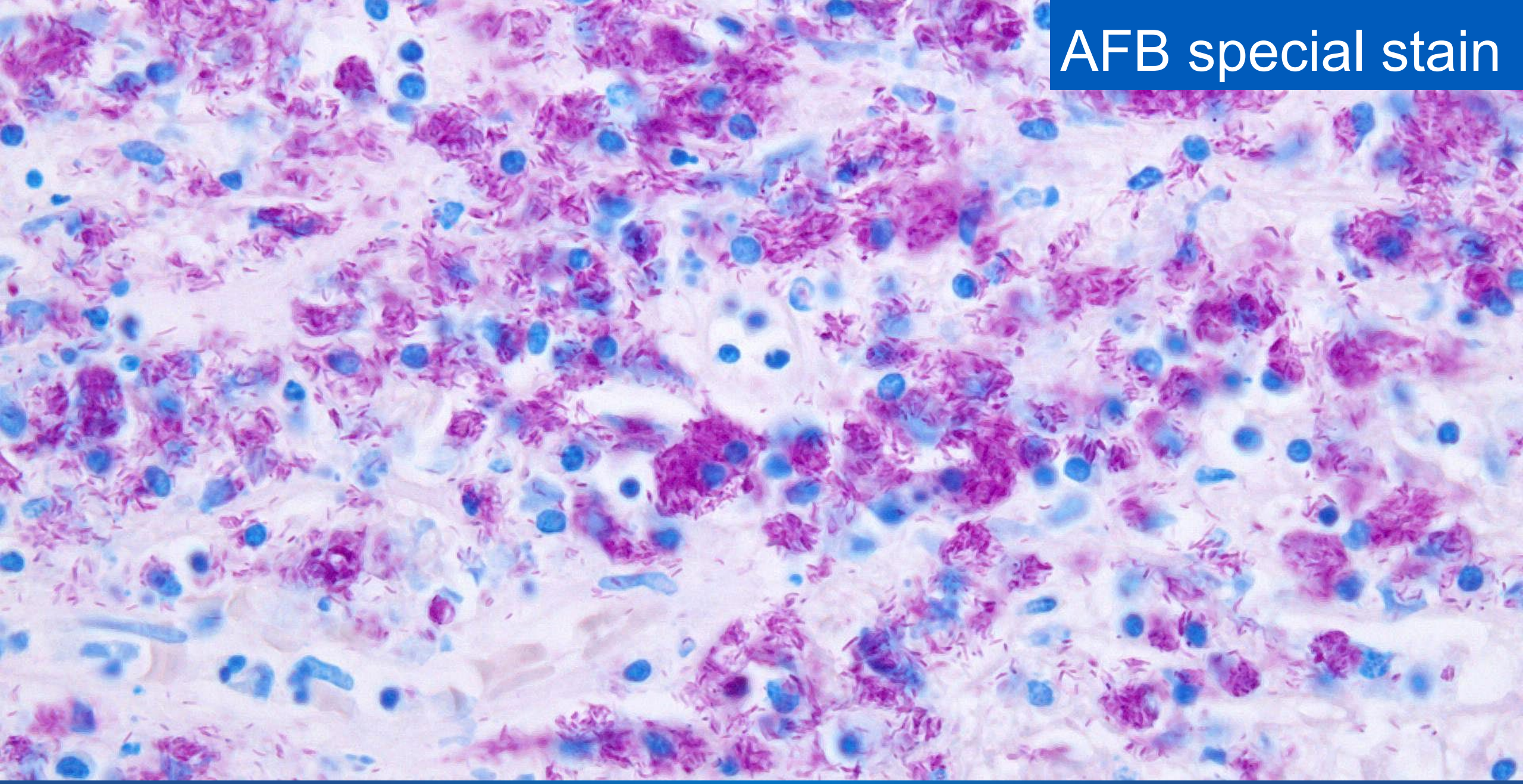
Differential diagnosis and ancillary tests?

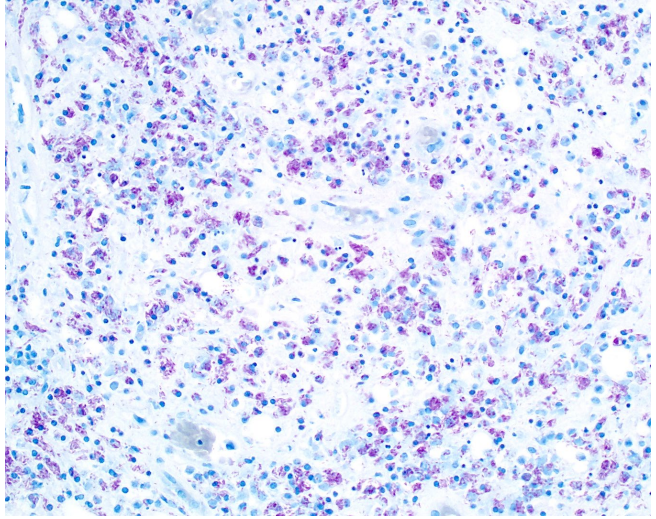
Category	Differential diagnosis
Infectious	Rhomboencephalitis: *Listeria monocytogenes*, tuberculosis, non-tuberculous mycobacteria
Inflammatory/ demyelinating	Acute Demyelinating Encephalomyelitis Multiple Sclerosis Central Pontine Myelinolysis/ osmotic demyelination syndrome Immune Reconstitution Inflammatory Syndrome
Vascular	Infarction
Neoplastic	Histiocytic disorder, Lymphoma

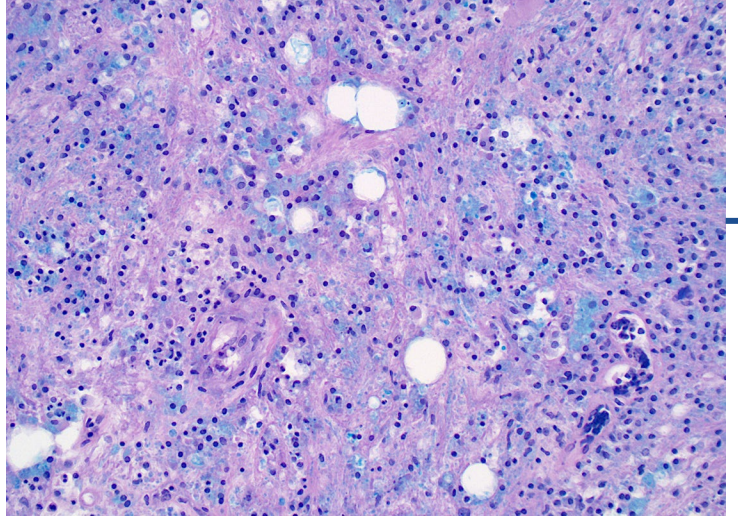
AFB special stain

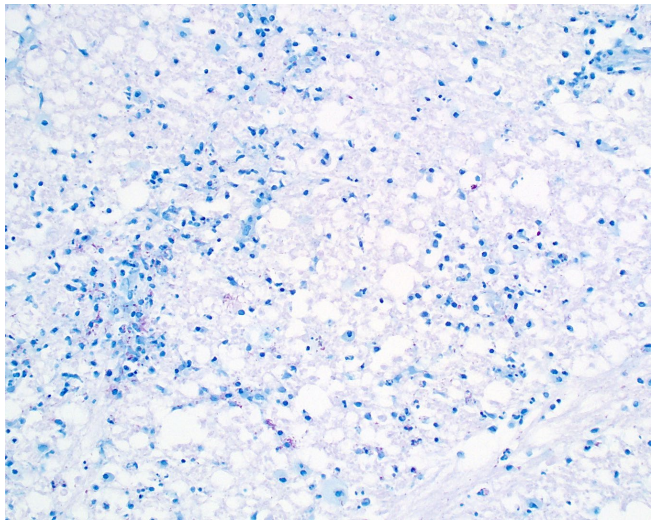


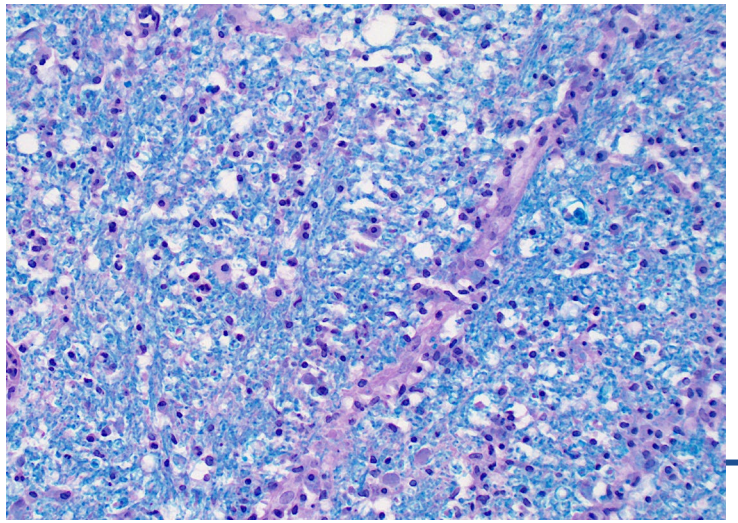
AFB special stain

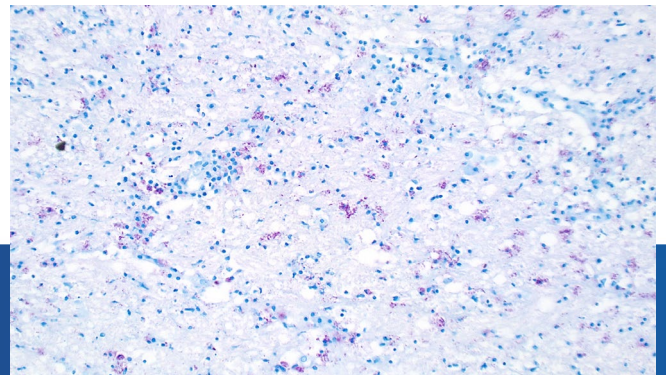


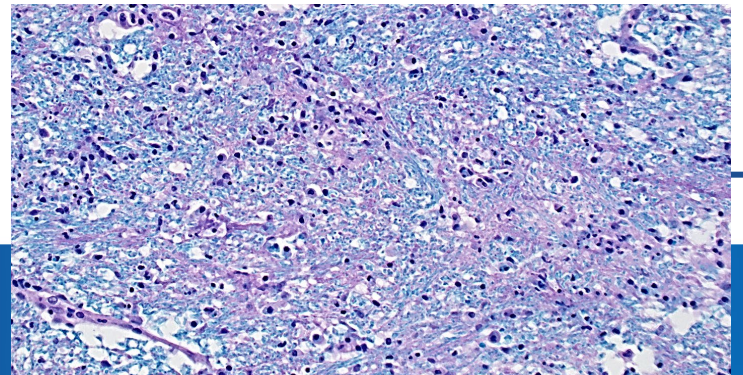


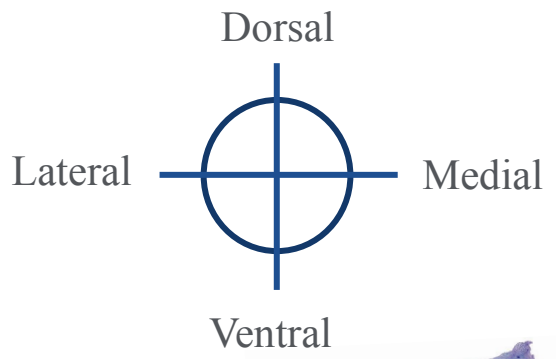











Dorsal
Lateral
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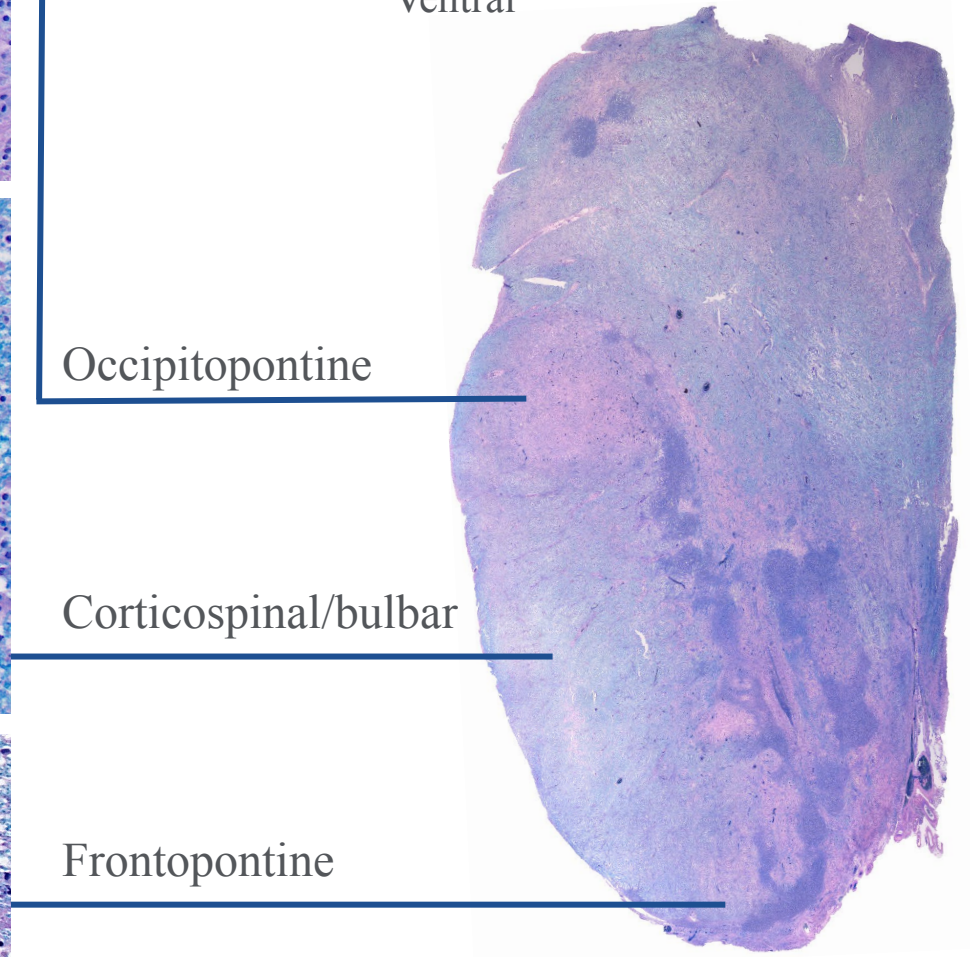
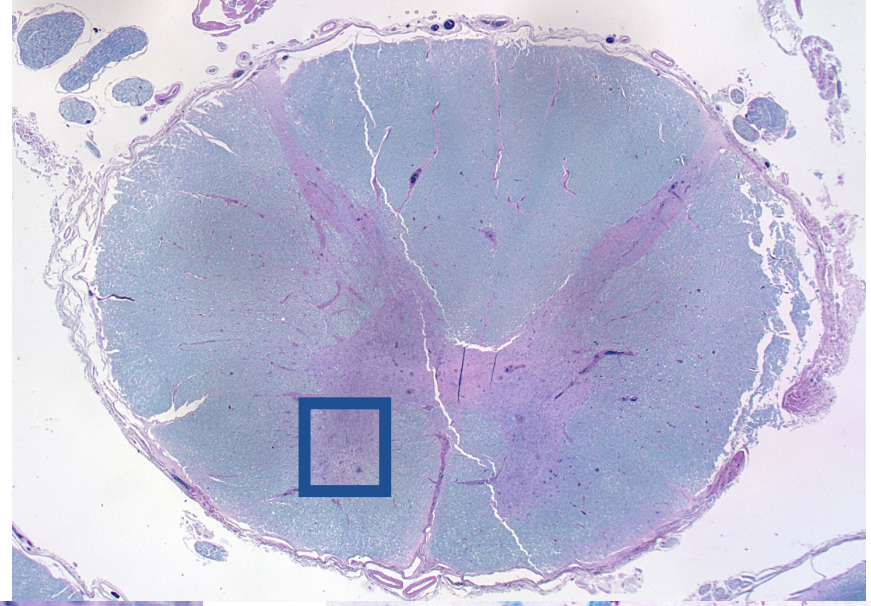
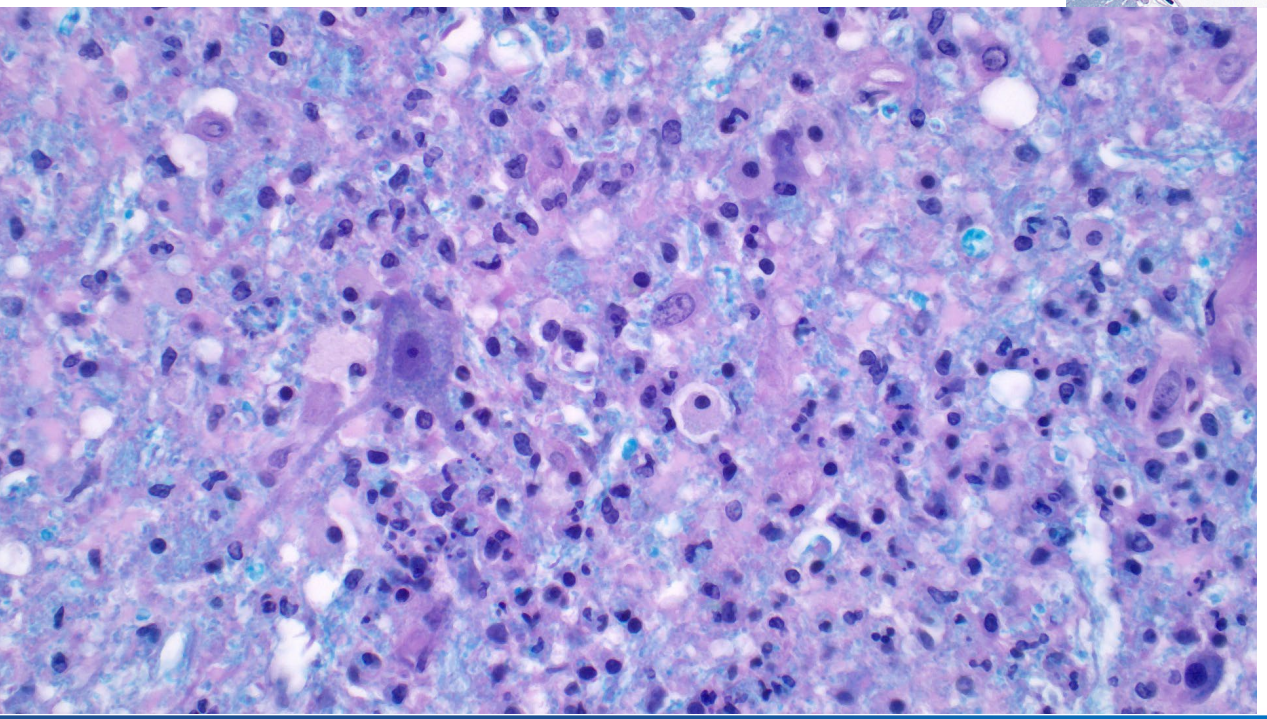
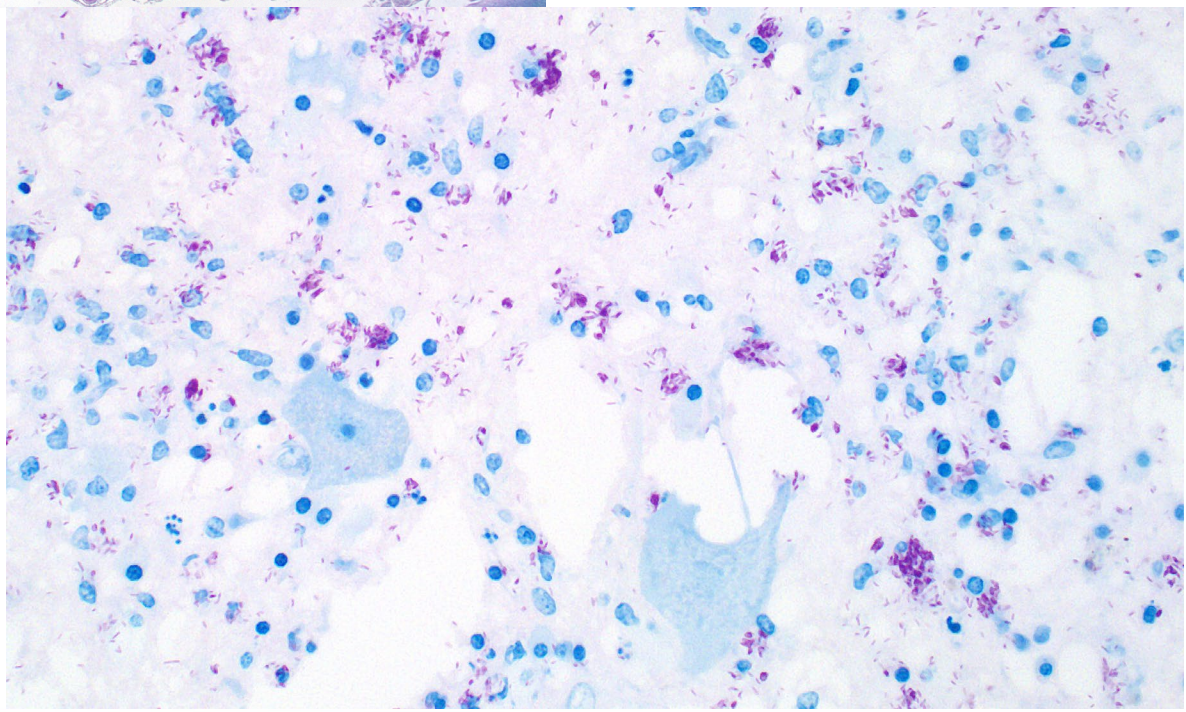

Occipitopontine
Corticospinal/bulbar
Frontopontine

Thoracic spinal cord- myelitis







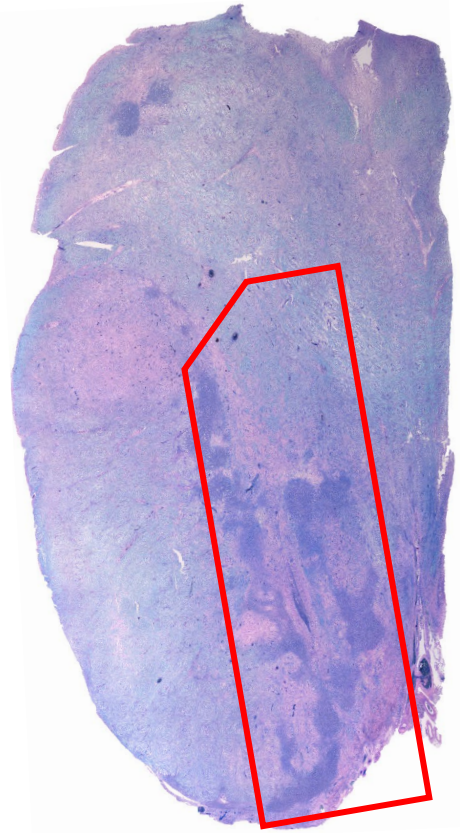
Diagnosis

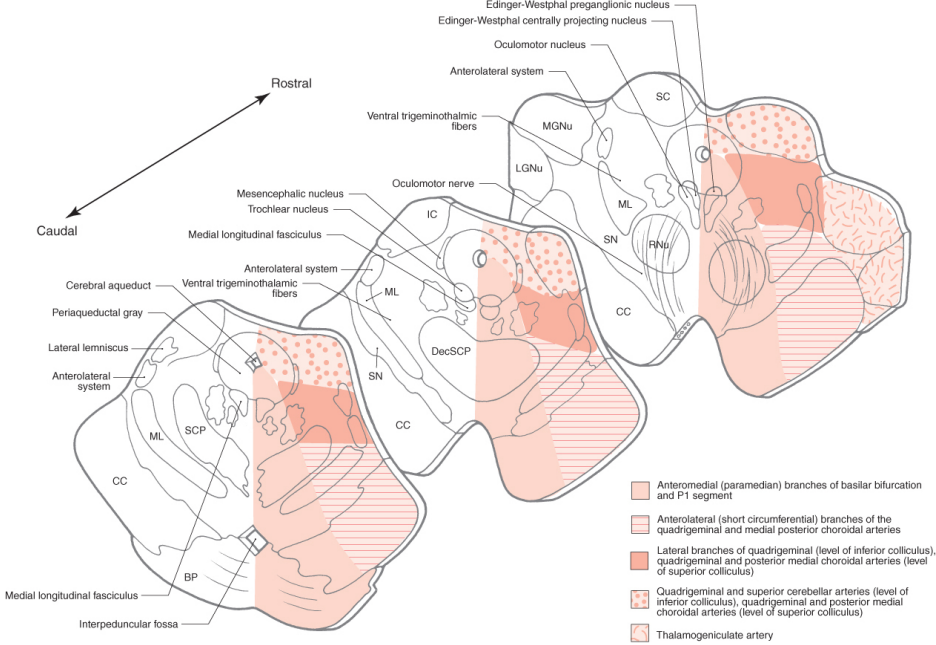
Meningomyeloencephalitis secondary to atypical mycobacterium

Atypical Mycobacteria infection

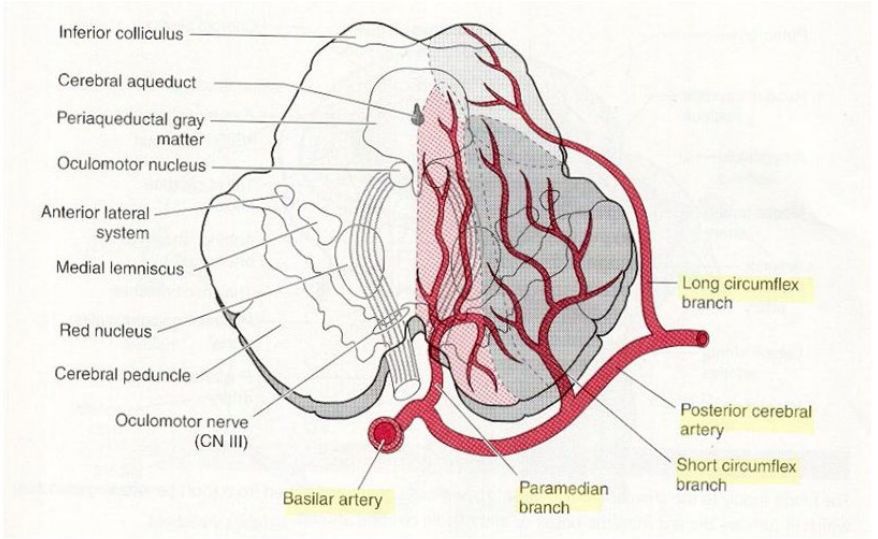
- Classically seen in the immunocompromised, notably those with HIV infection, but also in patients with steroid use.
- In a retrospective autopsy study of 450 patients who died with HIV/AIDS, the brain was the **second** most commonly affected organ after the respiratory system, with 32% of cases exhibiting lesions within the CNS.

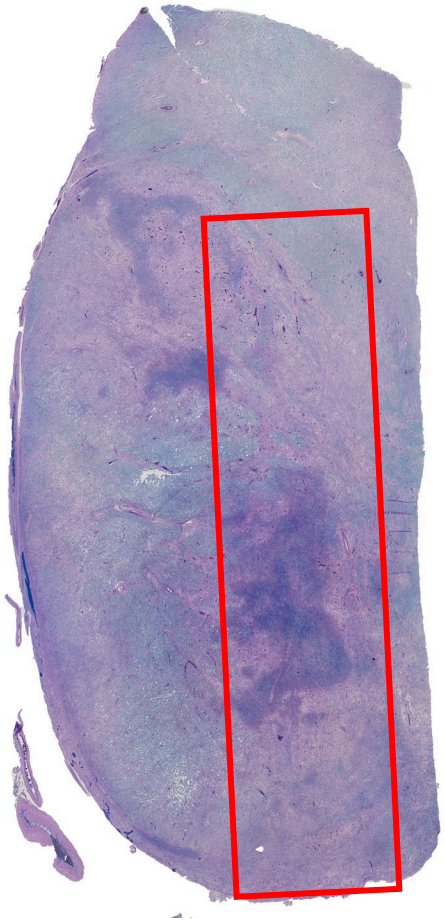
  Jellinger KA et al.. Neuropathology and general autopsy findings in AIDS during the last 15 years. Acta Neuropathol. 2000;100(2):213-20.
- CNS involvement is thought to arise from hematogenous spread of bacilli from the lungs or gastrointestinal tracts.

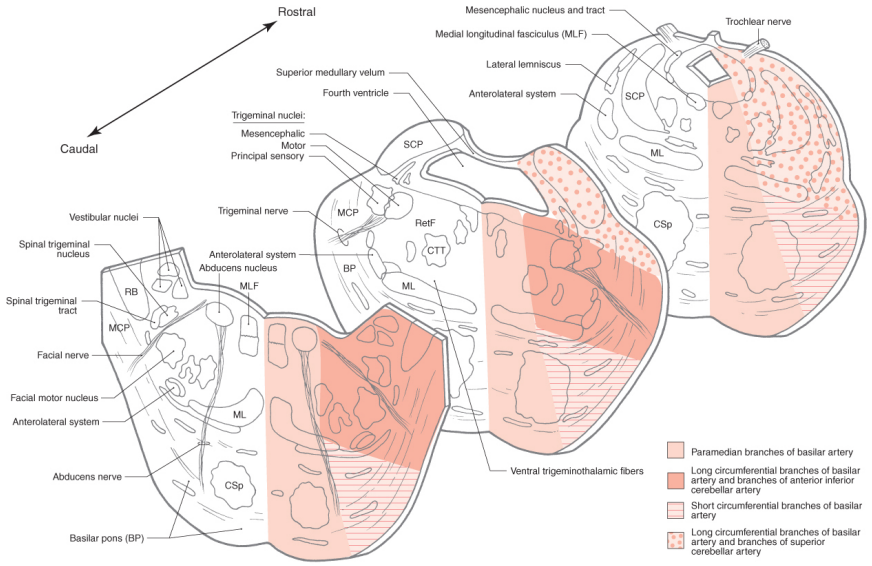


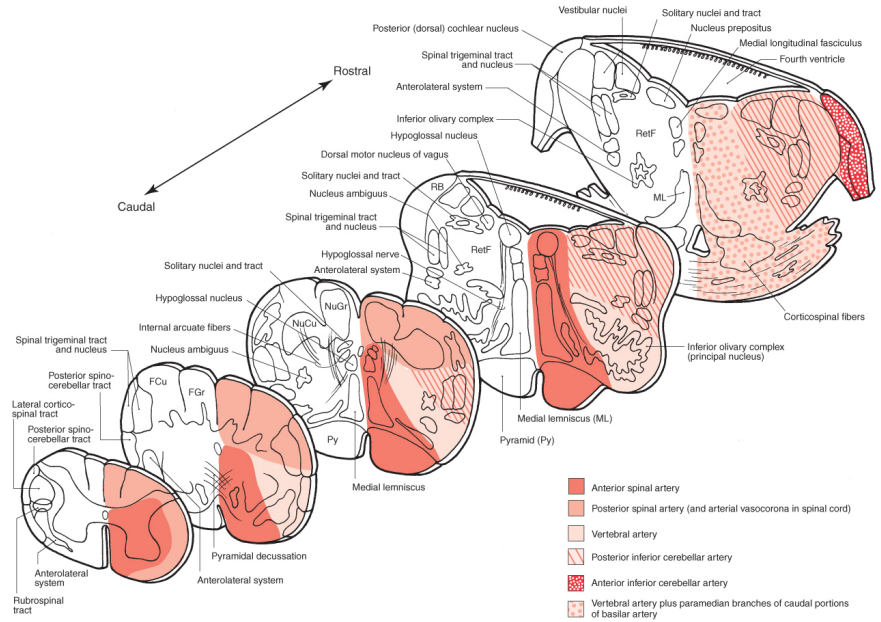


Haines DE. Neuroanatomy: An atlas of structures, sections, and systems. Lippincott Williams & Wilkins; 2010.









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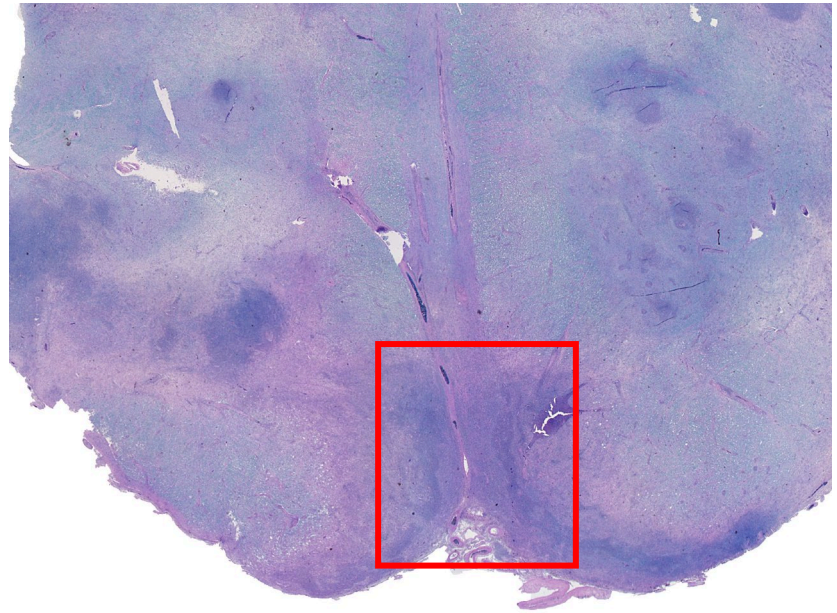


Types of atypical Mycobacteria/ nontuberculous Mycobacteria

Over 170 species of atypical Mycobacteria. Common pulmonary infections:

- *Mycobacterium avium*
- *Mycobacterium kansasii*
- *Mycobacterium abscessus*

16S rRNA sequencing on FFPE tissue of the brainstem provided a 99% base-pair match (V3/V4 regions) to two classifiable mycobacterial species:

- *Mycobacterium haemophilum*
- *Mycobacterium riyadhense*

Microbiome core facility- Anne-Catrin Uhlemann & Katharina Thoene

Learning points/ summary

Consider atypical mycobacteria as a cause of rhomboencephalitis in the immunocompromised

Histologic features of atypical mycobacterial infection:

- Meningitis/ subacute meningoencephalitis
- Perivascular lymphocytic infiltrate
- Demyelinating foci
- Granulomata are sparse, if present at all

References

1. Jones Jr HR, Ho DD, Forgacs P, Adelman LS, Silverman ML, Baker RA, et al. Acute fulminating fatal leukoencephalopathy as the only manifestation of human immunodeficiency virus infection. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1988;23(5):519-22.

2. Jubelt B, Mihai C, Li TM, Veerapaneni P. Rhombencephalitis/brainstem encephalitis. Current neurology and neuroscience reports. 2011;11(6):543.

3. Petito CK, Cho ES, Lemann W, Navia BA, Price RW. Neuropathology of acquired immunodeficiency syndrome (AIDS): an autopsy review. Journal of neuropathology and experimental neurology. 1986;45(6):635-46.

4. Cegielski JP, Wallace RJ, Jr. Central Nervous System Infections with Nontuberculous Mycobacteria. Clinical Infectious Diseases. 1997;25(6):1496-7.

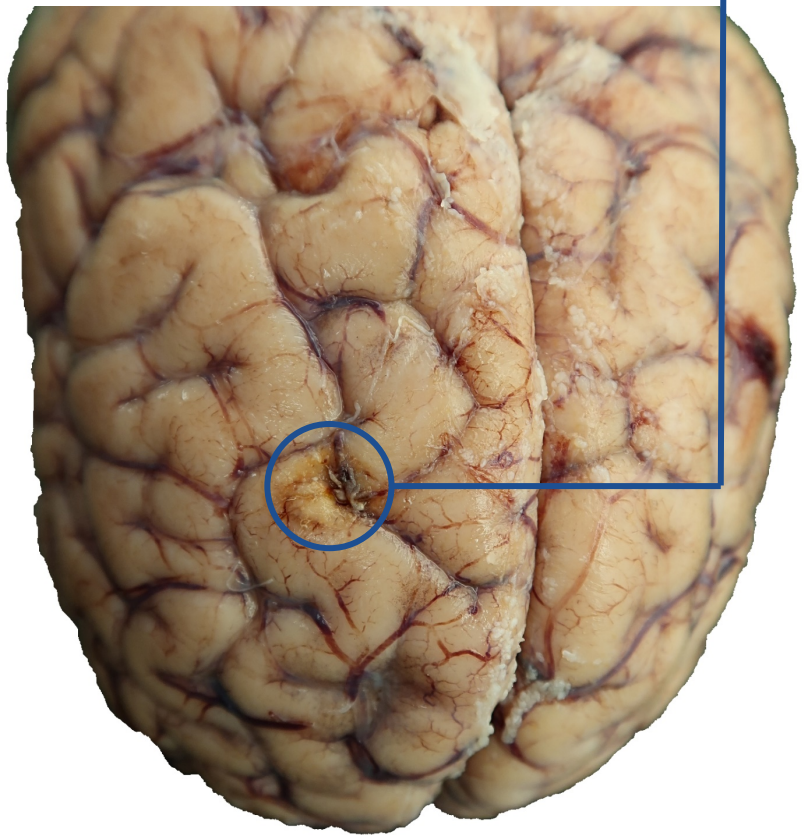
5. Jellinger KA, Setinek U, Drlicek M, Bohm G, Steurer A, Lintner F. Neuropathology and general autopsy findings in AIDS during the last 15 years. Acta Neuropathol. 2000;100(2):213-20.

Carol Petito, 1942-2018
Provided significant contributions to the neuropathology of HIV infection

Any questions?

Extra slides

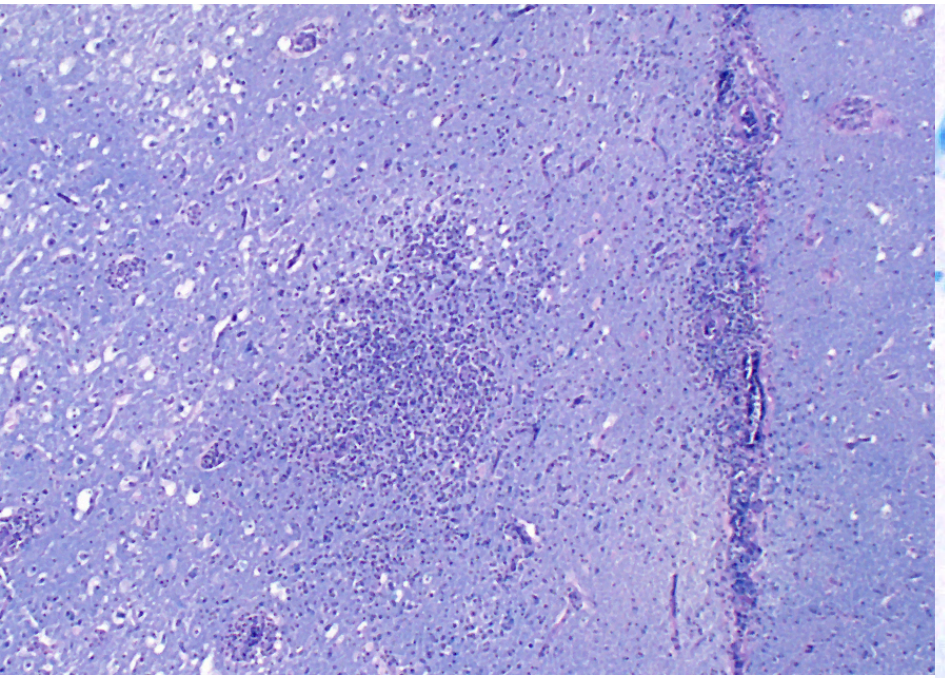
Macroscopic photographs

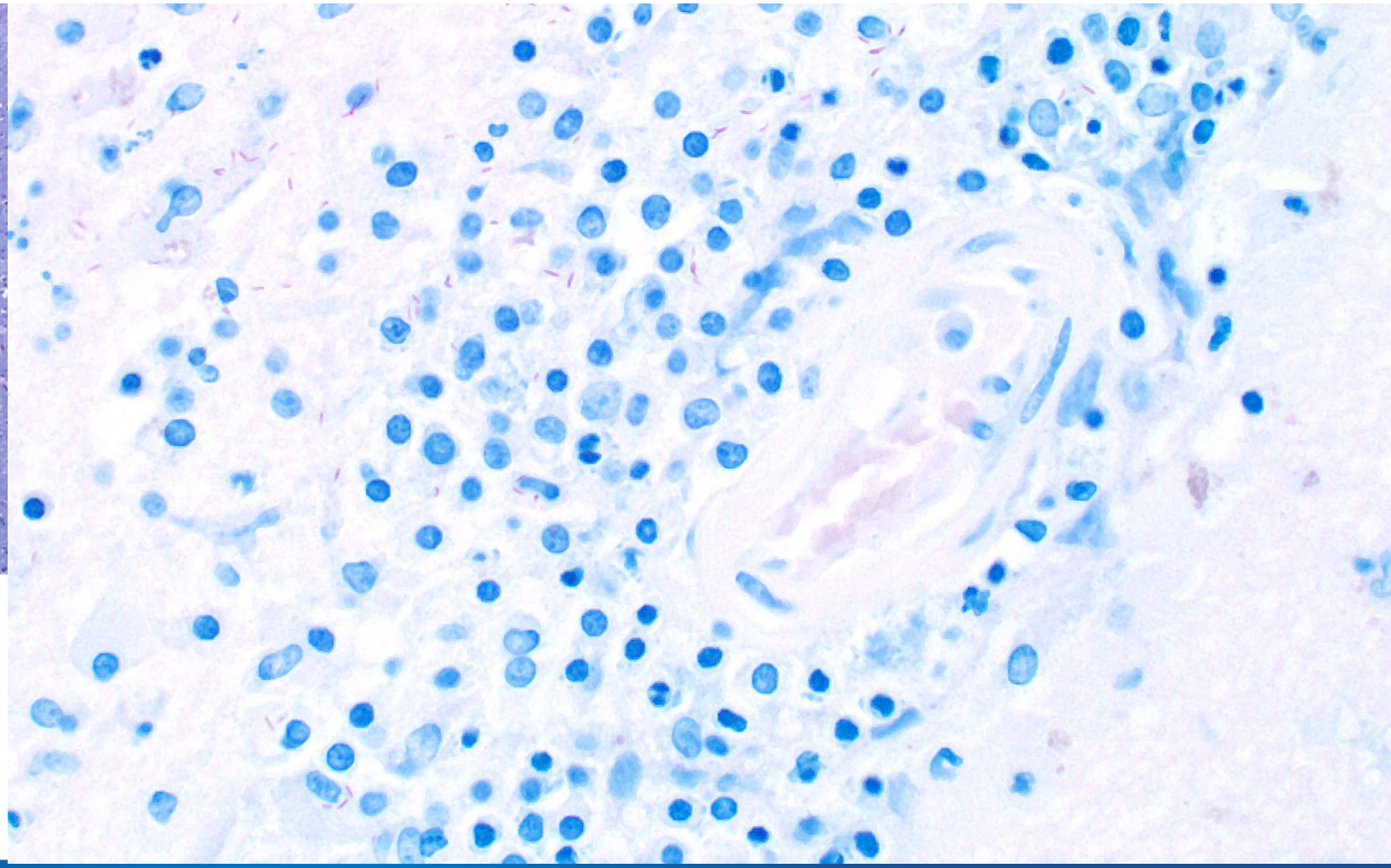


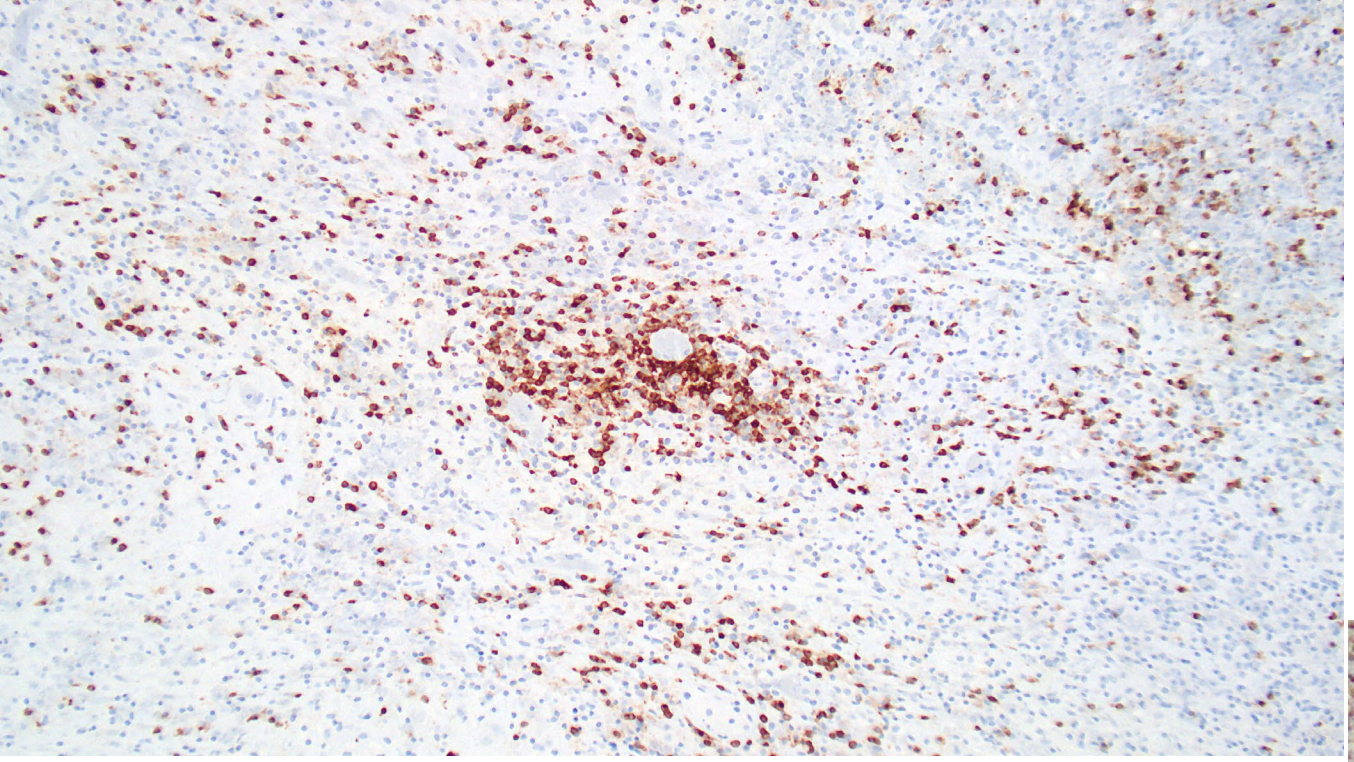
s/p VP shunt p

Hydrocepl

Prefrontal cortex-meningoencephalitis

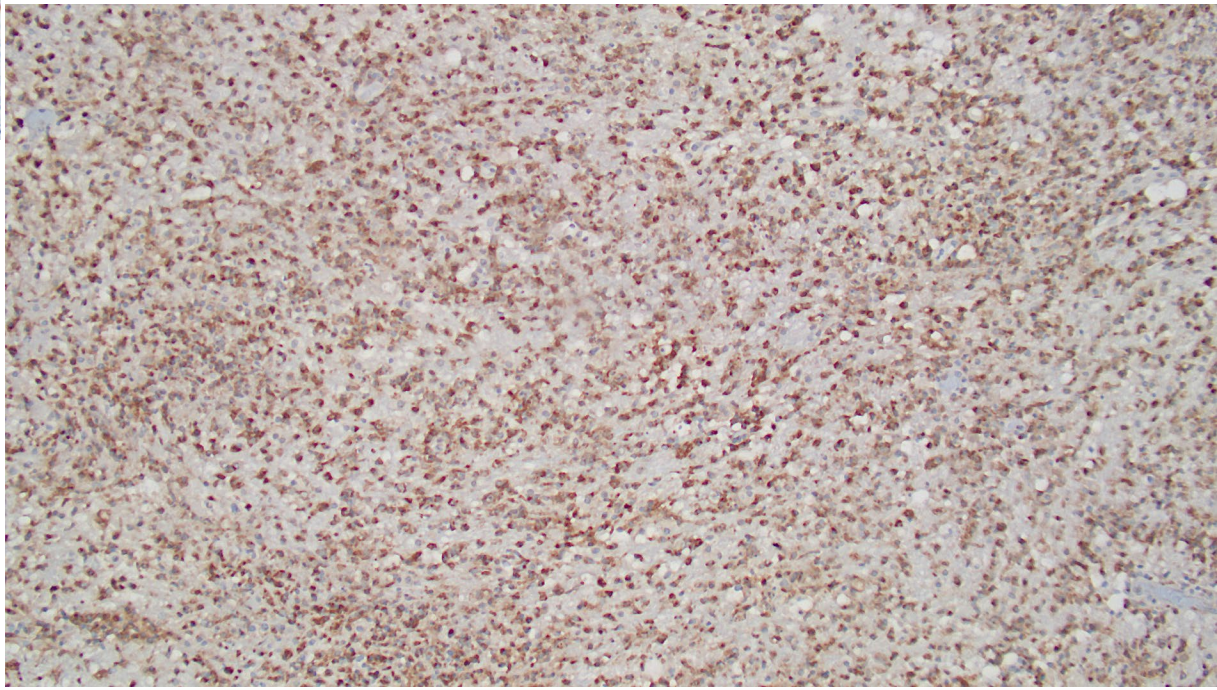






Perivascular accumulation and parenchymal CD3+ lymphocytes

Diffuse CD68+ macrophages within parenchyma

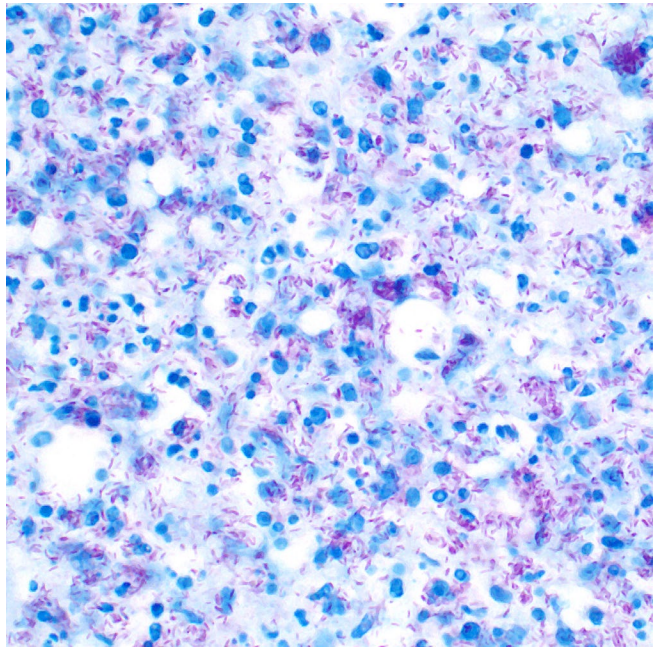


Additional stains

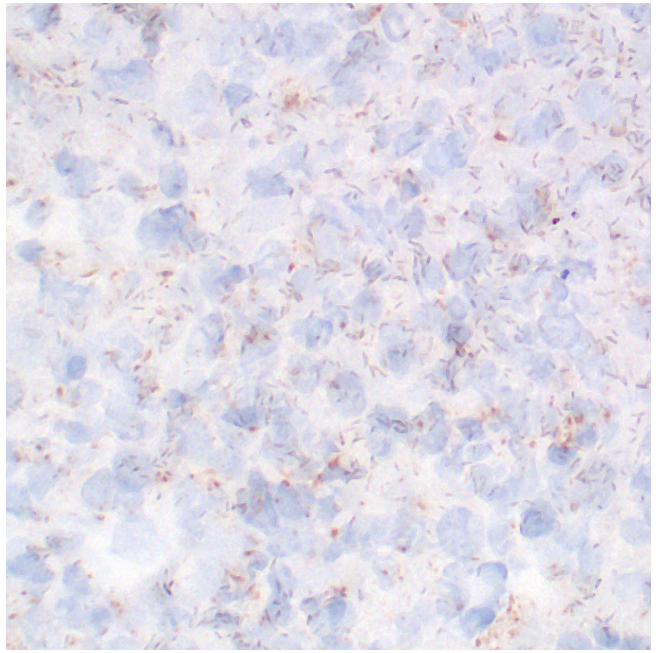
Phosphorylated neurofilament shows widespread axonal loss and spheroid formation

Micro-organism stains- negative for other organisms, including CMV, JC virus, and Toxoplasma

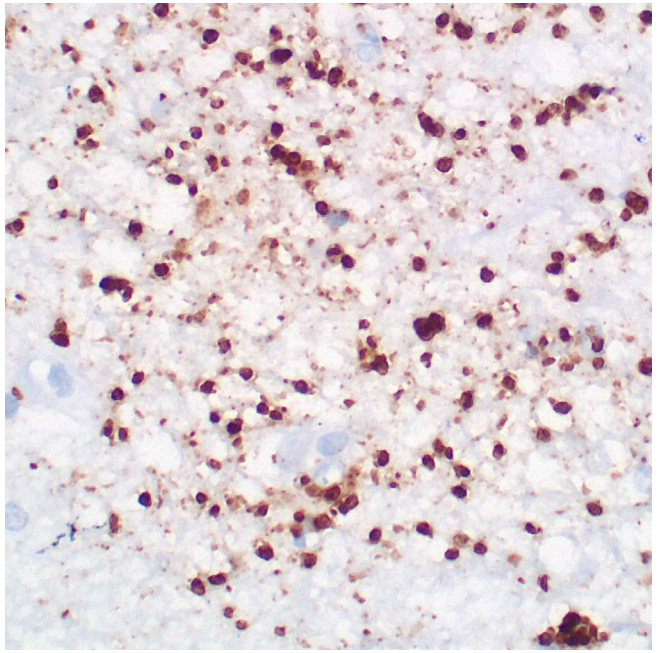
AFB



Toxoplasma immunostain



Toxoplasma +ve control



An example of cross-reactivity of Toxoplasma immunostain and another organism: Sundermann CA, Estridge BH, Branton MS, Bridgman CR, Lindsay DS. Immunohistochemical diagnosis of Toxoplasma gondii: potential for cross-reactivity with Neospora caninum. Journal of Parasitology. 1997 Jun 1;83(3):440-3.