January 2004

Opportunistic Infections of the CNS in Patients with AIDS

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Patient Encounter

- HD is a previously healthy 32 y.o. man who presents to ED with progressive decline in mental status, N/V, decreased PO intake, and severe unremitting headache for the past three days

- The differential diagnosis is broad, so what do you do in the ED?

Patient Encounter

- Physical Exam – Afebrile, VS within normal limits
  Physical exam otherwise unremarkable
- Neurological Exam – HD is somnolent,
  A&O to person only with dysmetria, gait instability, ? of L facial droop
- Toxicology Screen – no toxins
- CBC – showed WBC of 3.0 with Hct of 39.9
- Electrolytes – within normal limits

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Patient Encounter

- Lumbar Puncture showed 31 WBC's/uL, and 621 RBC's/uL in 3rd vial. On Gram Stain, no microorganisms seen

- What imaging would you recommend?

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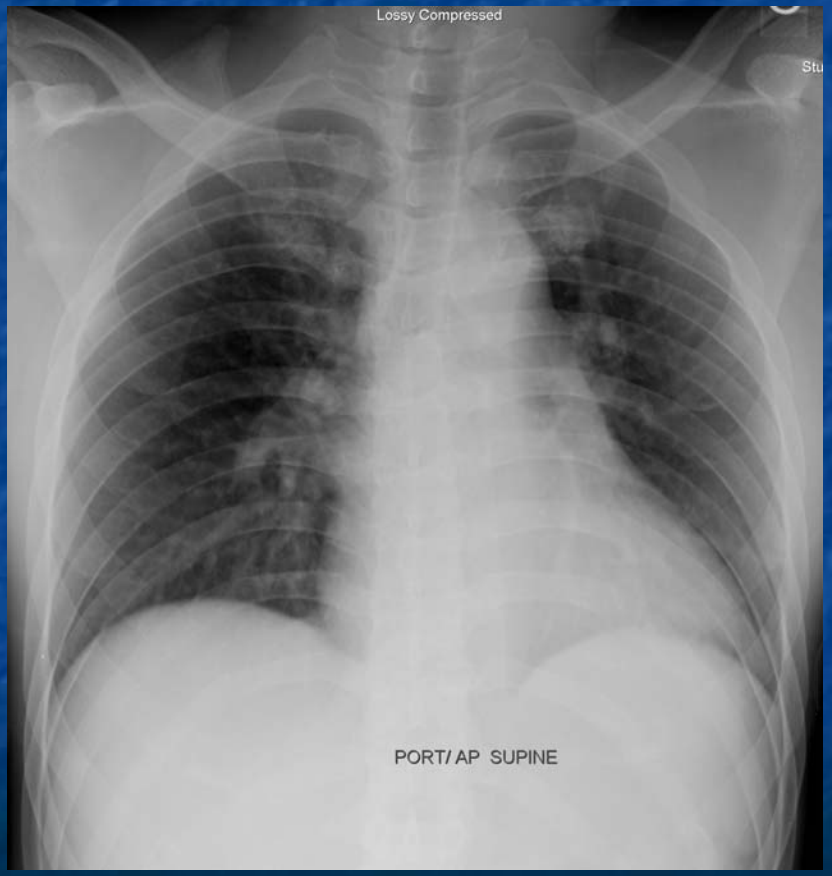
Portable CXR



No evidence of consolidation or active infection

Image from BIDMC PACS

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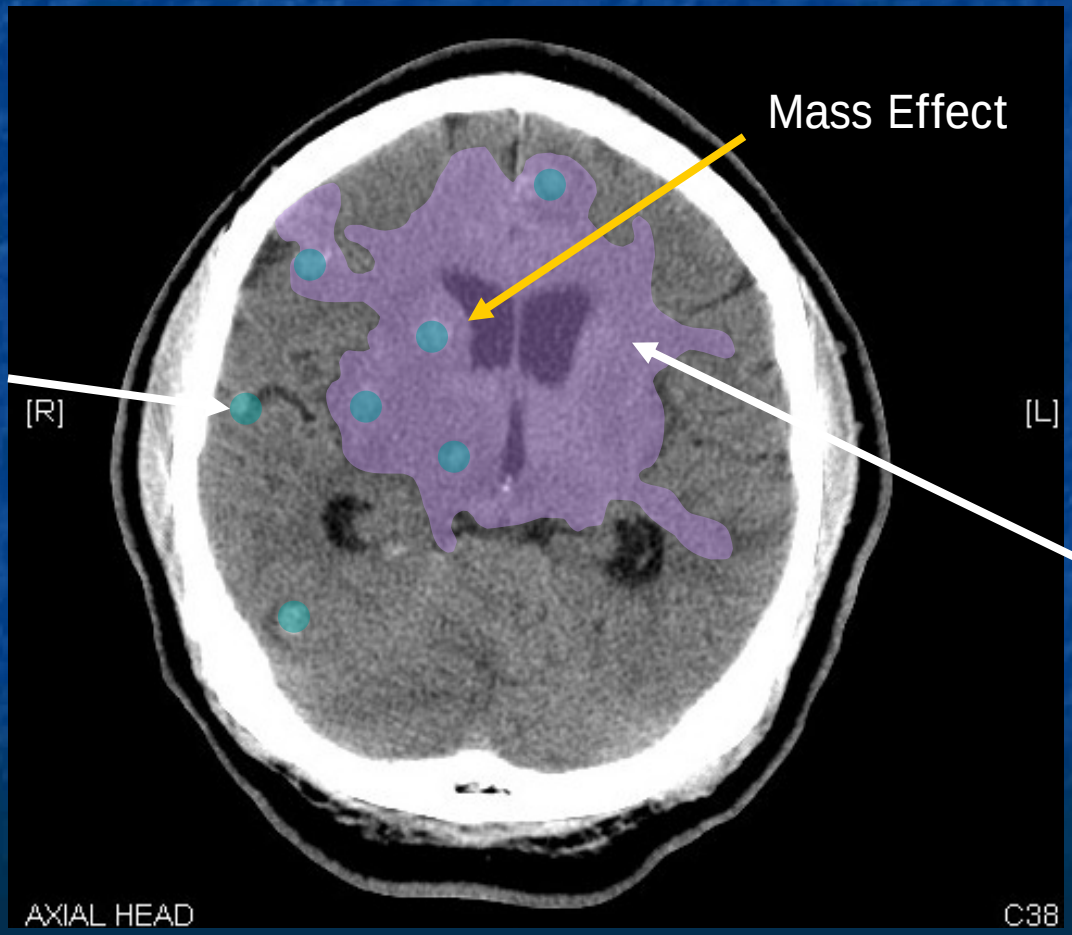
Our Patient – Axial CT

Multiple high-attenuation lesions spread throughout both hemispheres representing hemorrhagic foci



Areas of edema surrounding the lesions

Image from BIDMC PACS

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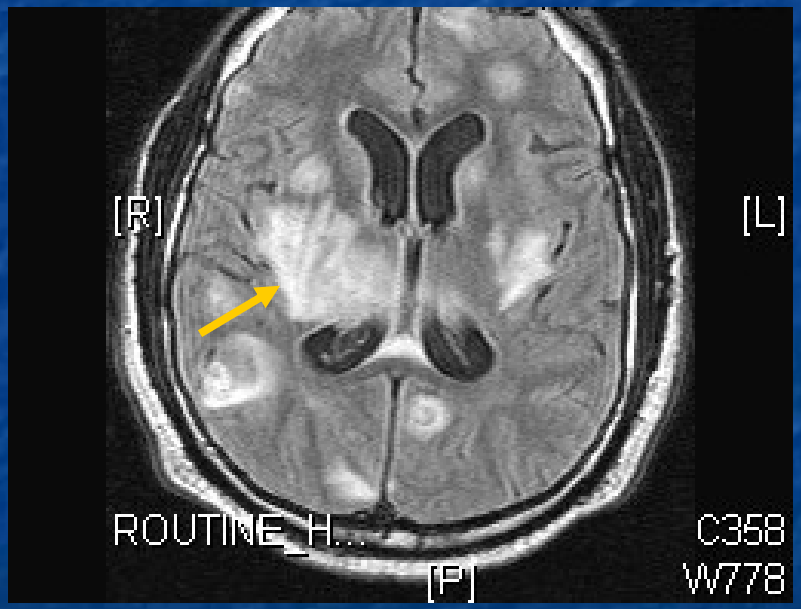
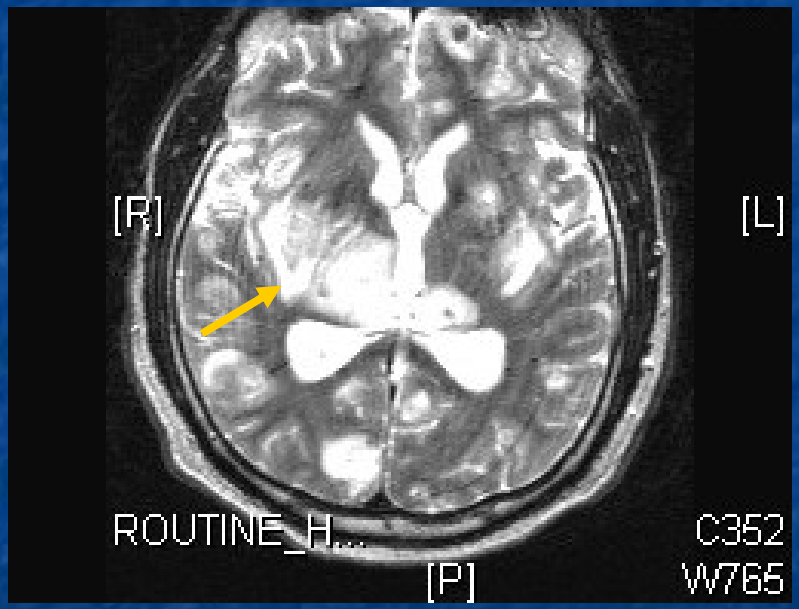
Our Patient – Axial MR

T1 Image	T2 Image
	

Both T1 and T2 scans show multiple hyper-intense lesions scattered throughout the cortex

Images from BIDMC PACS

Our Patient - Workup

- Anti-HIV antibodies were found in the patient's serum
- CD4 count was found to be 53 and the viral load later found to be >100,000 copies/mL
- Anti-toxoplasma IgG antibodies were subsequently found confirming the diagnosis of Toxoplasmosis
- HD was subsequently admitted to BIDMC where his condition rapidly improved on anti-protozoal medications and supportive care

Toxoplasmosis

- Most common CNS infection in patients with AIDS
- Caused by the organism *Toxoplasma Gondii* a protozoa that colonizes up to 15% of people
- 30% chance of reactivation when CD4 count <100
- Feline required for *Toxoplasma* lifecycle

Our Patient – Treatment and F/U

- HD was empirically treated with Pyrimethamine, Sulfadiazine, and Leukovorin for suspected Toxo
- He improved somewhat but had a recurrence of acute MS change on the floor
- Rapid treatment with Mannitol and Dexamethasone averted possible uncal herniation
- HD has since markedly improved and is currently on HAART with an undetectable viral load and CD4 > 100

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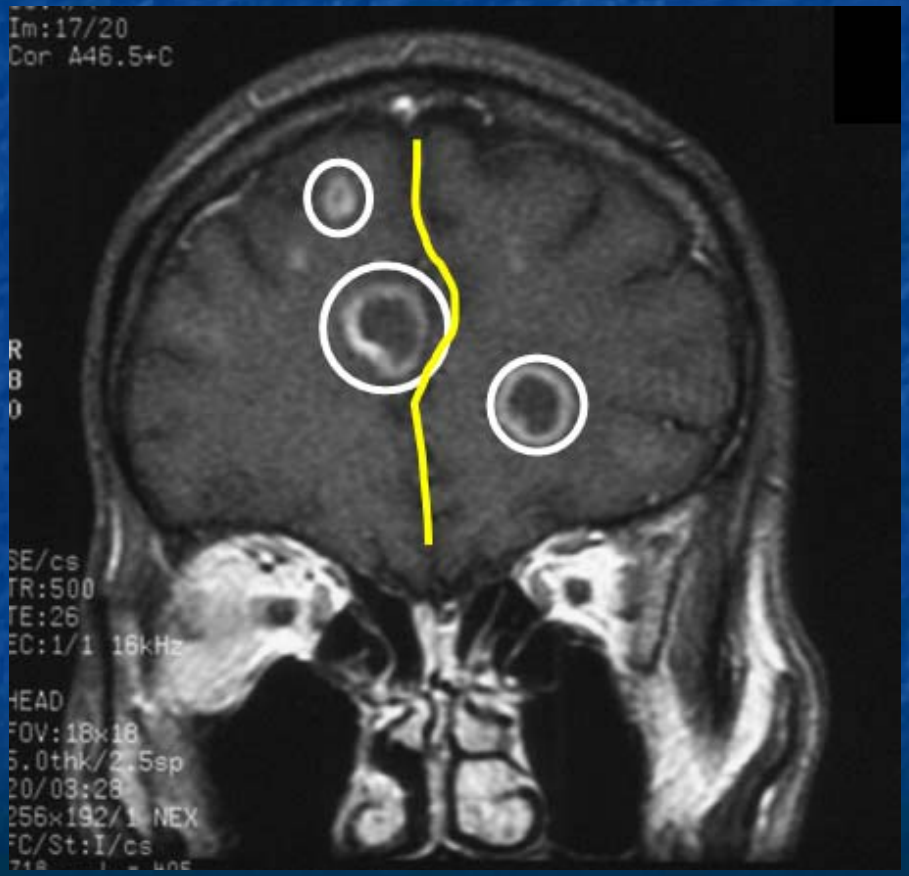
Patient #2 - Toxoplasmosis



Characteristic Findings

Ring enhancing lesions on MRI with surrounding edema

Evidence of mass effect, but no herniation

Image courtesy of S. Reddy, MD

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Other Opportunistic Infections of the CNS

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CNS Opportunistic Infections Overview

Mass Effect	No Mass Effect
• *Toxoplasma Gondii* • AIDS-related CNS lymphoma • CMV • TB • Fungal infections • Neurosyphilis	• Progressive Multifocal Leukoencephalopathy • HIV encephalopathy • *Cryptococcus Neoformans*

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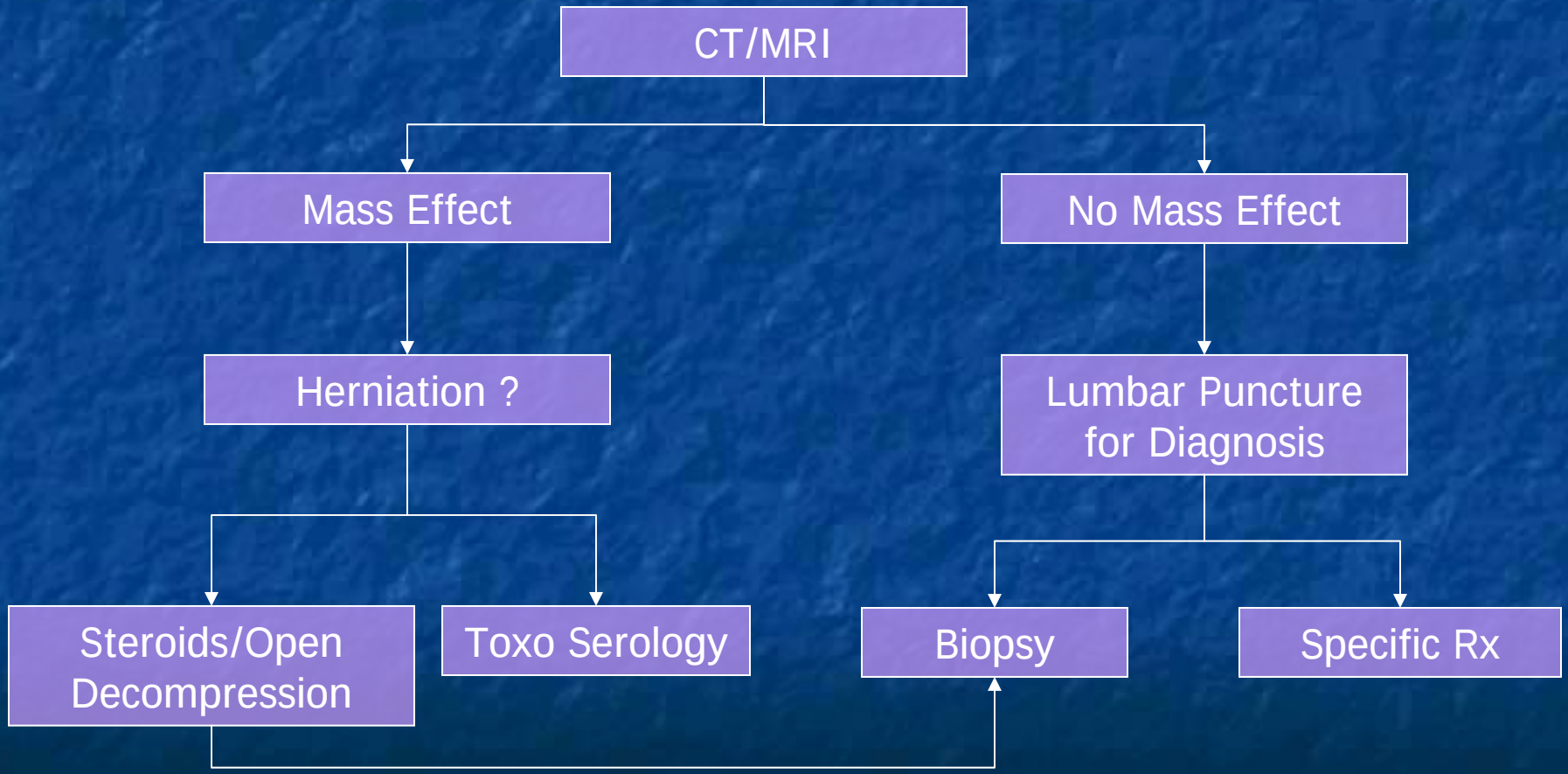
CNS Opportunistic Infections Overview



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CNS Opportunistic Infections Overview

CD4 Count	CNS Pathology
>500 cells/uL	CNS neoplasms (likely unrelated to HIV disease)
<200 cells/uL	TB, HSV
<100 cells/uL	Toxoplasmosis, Cryptococcus, CMV, PML, Fungi

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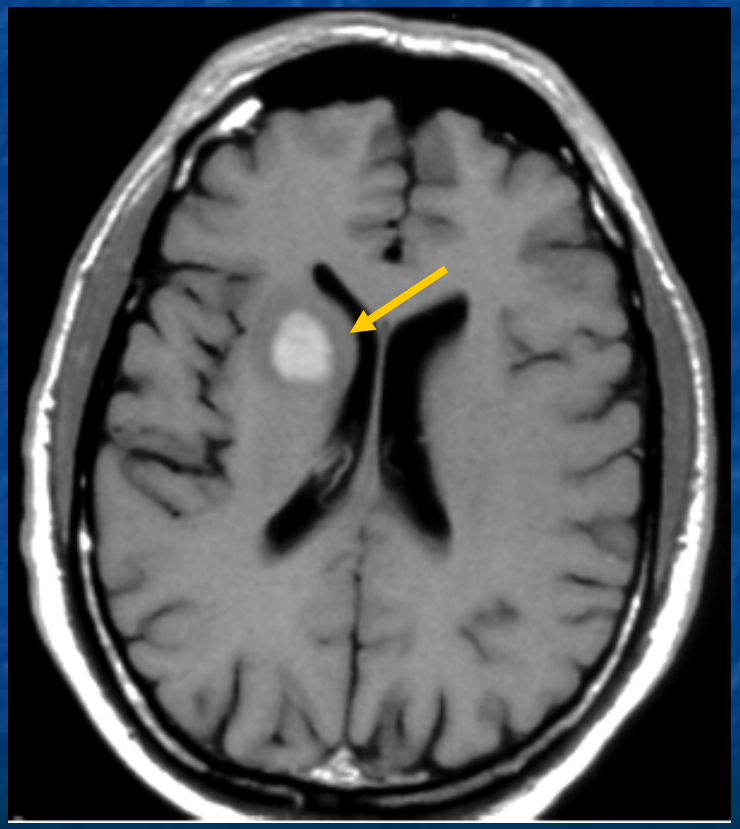
AIDS-related CNS Lymphoma



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- Nearly 100% of lesions are EBV positive by PCR
- Typically have some mass effect
- Difficult to differentiate from Toxoplasmosis

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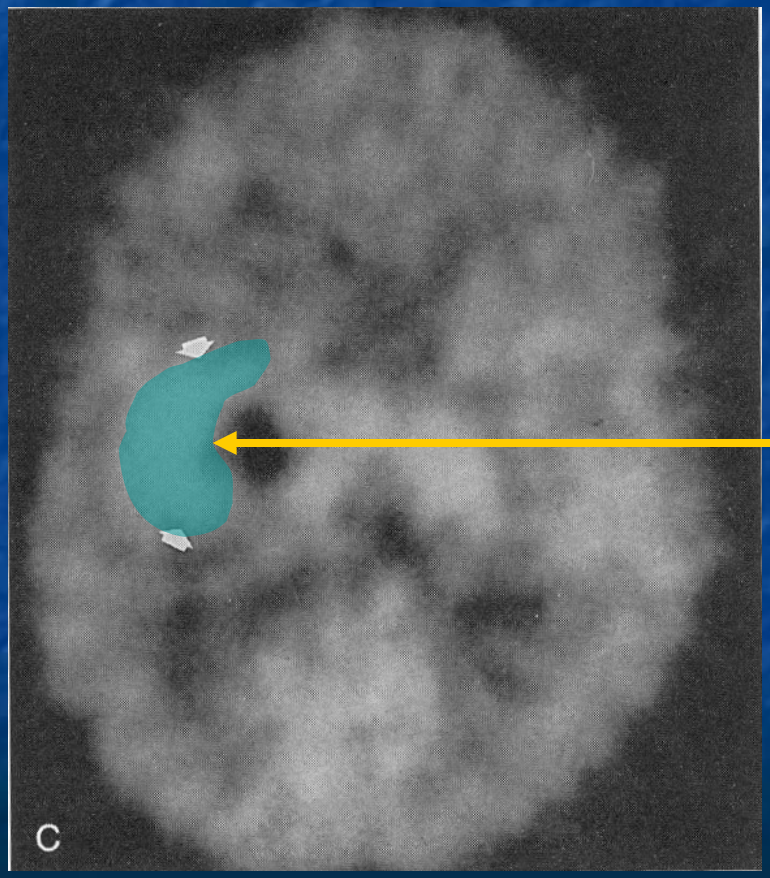
Toxo or CNS Lymphoma?



- Nuclear Imaging with FDG-PET shows areas of increased metabolic activity
- Suggestive of lymphoma vs. Toxoplasmosis

Images from Goodman, PC (Ed). *The Radiologic Clinics of North America: Imaging of the Patient with AIDS.* W.B. Saunders Co, Philadelphia, PA. 1997

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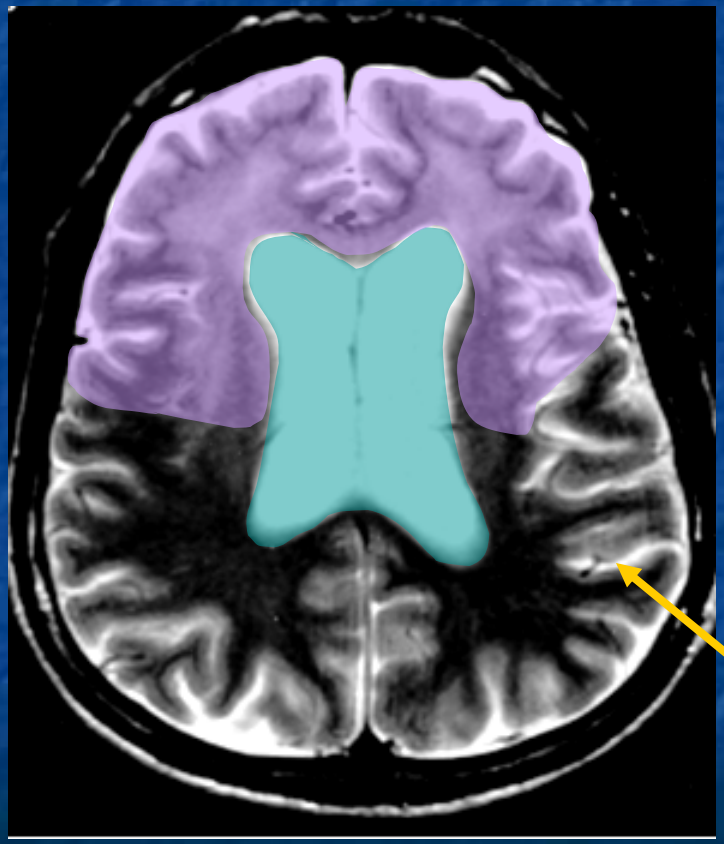
HIV Encephalopathy



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- Primary infection of neural cells with HIV, which have tropism for CNS

Which causes...

Cortical and subcortical atrophy

Ventricular enlargement

Widening of the Sulci

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HSV Encephalitis

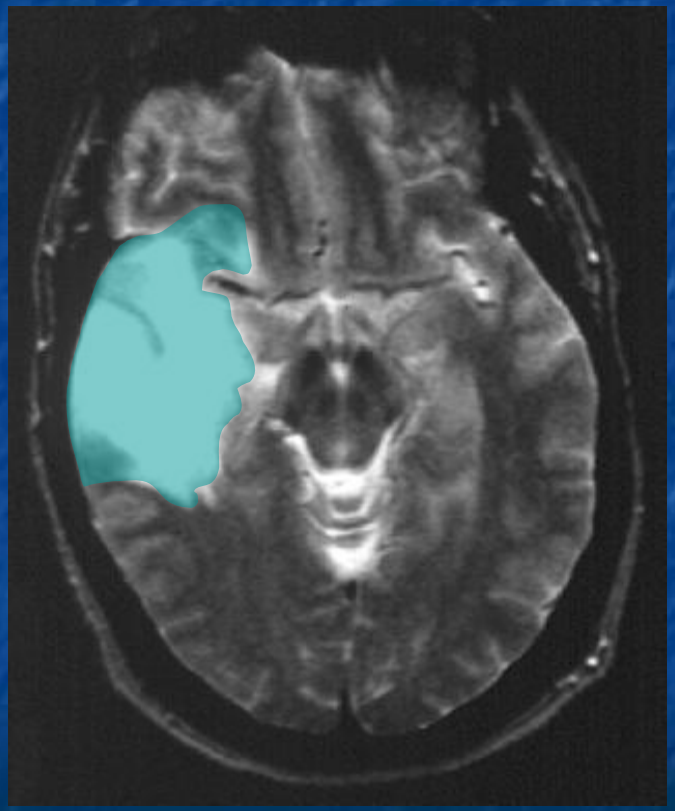

Image courtesy of S. Reddy, MD

- Increased risk in immunosupressed hosts
- Predilection for medial temporal lobe
- Destruction mediated by virus and host immune response

Progressive Multifocal Leukoencephalopathy

- Rare demyelinating disease caused by DNA Papovirus (a.k.a. polyomavirus)
- Route of transmission unclear
- 1%-4% of AIDS patients will develop PML if left untreated
- In one trial, 81% of patients with focal brain lesions without mass effect had PML

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Progressive Multifocal Leukoencephalopathy

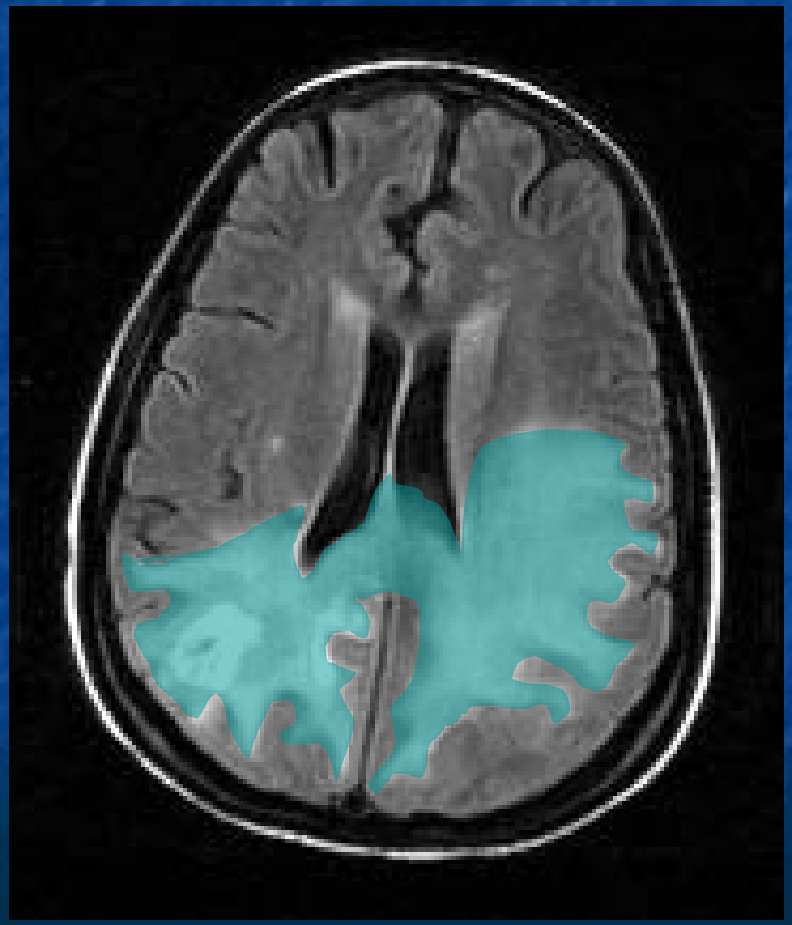

Image courtesy of B. Appagnani, MD

Characteristic Findings

Diffuse hyperintensities within the white matter with relative sparing of gray matter and no evidence of mass effect

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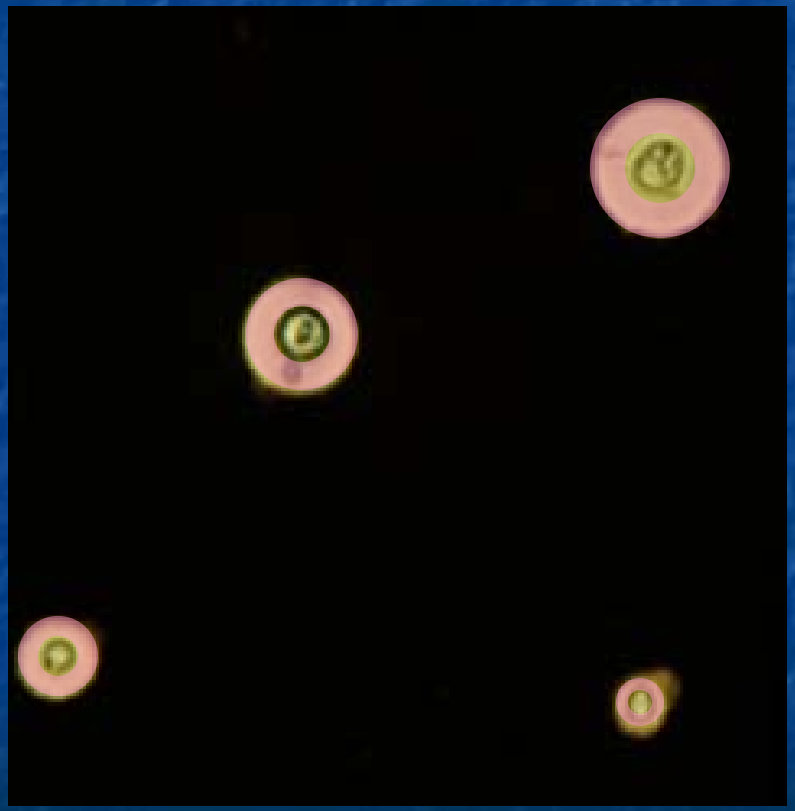
Cryptococcal Meningoencephalitis



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- AIDS defining illness in 40-60% of patients
- Diagnosed with Lumbar Puncture
- Indolent course with symptoms of fever, malaise, and headache

Prophylaxis

Opportunistic Infection	Prophylaxis
• Toxoplasmosis	• TMP/SMX (doubles for PCP prophylaxis
• CMV	• Gancyclovir
• HSV	• Acyclovir
• Cryptococcus	• Azoles (Fluconazole)

Acknowledgements

- Steve Reddy, MD
- Barbara Appignani, MD
- Martina Morrin, MD
- Larry Barbaras
- Pamela Lepkowski
- Gillian Lieberman, MD
- Jared Kesselheim
- Margot Albeck (a.k.a. lifesaver)

References

- Koralnik, Igor. *Approach to HIV-infected patients with CNS Mass Lesions.* In: UpToDate, Rose, BD (Ed), UpToDate, Wellesley, MA, 2003
- Porter, SB, Sande, MA. Toxoplasmosis of the central nervous system in the acquired immunodeficiency syndrome. *N Engl J Med* 1992; 327:1643
- Wallace, MR, Rossetti, RJ, Olson, PE. Cats and toxoplasmosis risk in HIV-infected adults. *JAMA* 1993; 269:76
- Demeter, Lisa. *Epidemiology of JC and BK virus infection.* In: UpToDate, Rose, BD (Ed), UpToDate, Wellesley, MA, 2003
- Demeter, Lisa. *Clinical manifestations and diagnosis of JC, BK, and other polyomavirus infections.* In: UpToDate, Rose, BD (Ed), UpToDate, Wellesley, MA, 2003
- Goodman, PC (Ed). *The Radiologic Clinics of North America: Imaging of the Patient with AIDS.* W.B. Saunders Co, Philadelphia, PA. 1997.
- Klein, RS. *Herpes Simplex Type I Encephalitis.* In: UpToDate, Rose, BD (Ed), UpToDate, Wellesley, MA, 2003
- Guterman KS; Hair LS; Morgello S Epstein-Barr virus and AIDS-related primary central nervous system lymphoma. Viral detection by immunohistochemistry, RNA in situ hybridization, and polymerase chain reaction. Clin Neuropathol 1996 Mar-Apr;15(2):79-86.
- Antinori A, et al. Diagnosis of AIDS-related focal brain lesions: a decision-making analysis based on clinical and neuroradiologic characteristics combined with polymerase chain reaction assays in CSF. *Neurology* 1997 Mar;48(3):687-94.
- Doweiko, JP, Groopman, JE. AIDS-related lymphoma: Primary Central Nervous System Lymphoma. In: UpToDate, Rose, BD (Ed), UpToDate, Wellesley, MA, 2003
- Kovacs, JA and Masur, H. Prophylaxis Against Opportunistic Infections in Patients with Human Immunodeficiency Virus Infection. N Engl J Med 2000 May; 342(19); 1416-29
- Gladwin, M and Trattler W. Clinical Microbiology Made Ridiculously Simple. Third Edition. Medmaster Inc. Miami, FL. 2001.