



NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Central Nervous System (CNS) Opportunistic Infections in HIV

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Last Updated: 7/31/12

Approach to Diagnosis

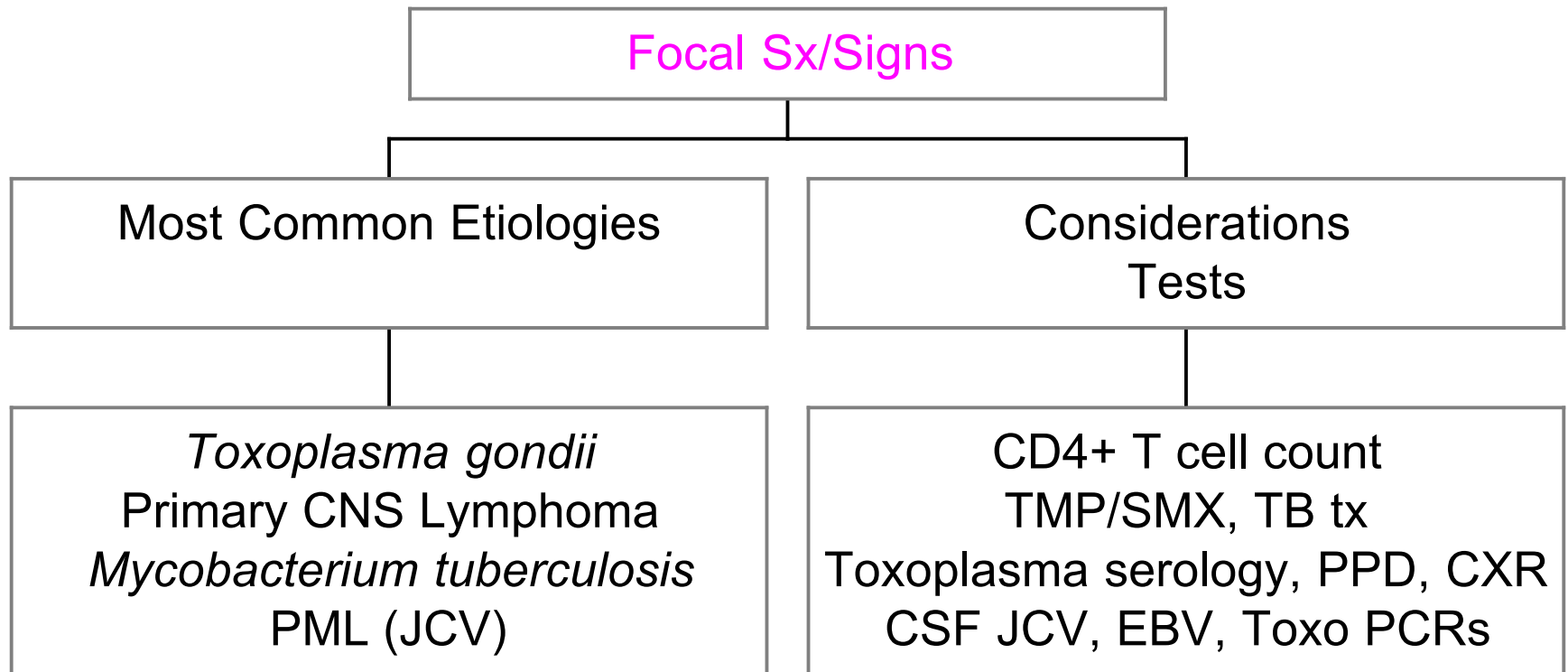
- Nonfocal parenchymal symptoms and signs
 - HIV-associated dementia
 - CMV encephalitis
- Focal parenchymal symptoms and signs
 - Toxoplasmosis, TB, primary CNS lymphoma
 - Progressive multifocal leukoencephalopathy
- Meningeal symptoms and signs
 - Cryptococcus, TB, syphilis

Susceptibility to CNS OIs

	CD4 cells/ul		
	500-200	<200	<100
CNS Syphilis	X	X	X
TB	X	X	X
HIV Dementia		X	X
Crypto, Toxo		X	X
PCNSL, PML			X
CMV encephalitis			X

PCNSL, primary CNS lymphoma; PML, progressive multifocal leukoencephalopathy

Approach to Diagnosis



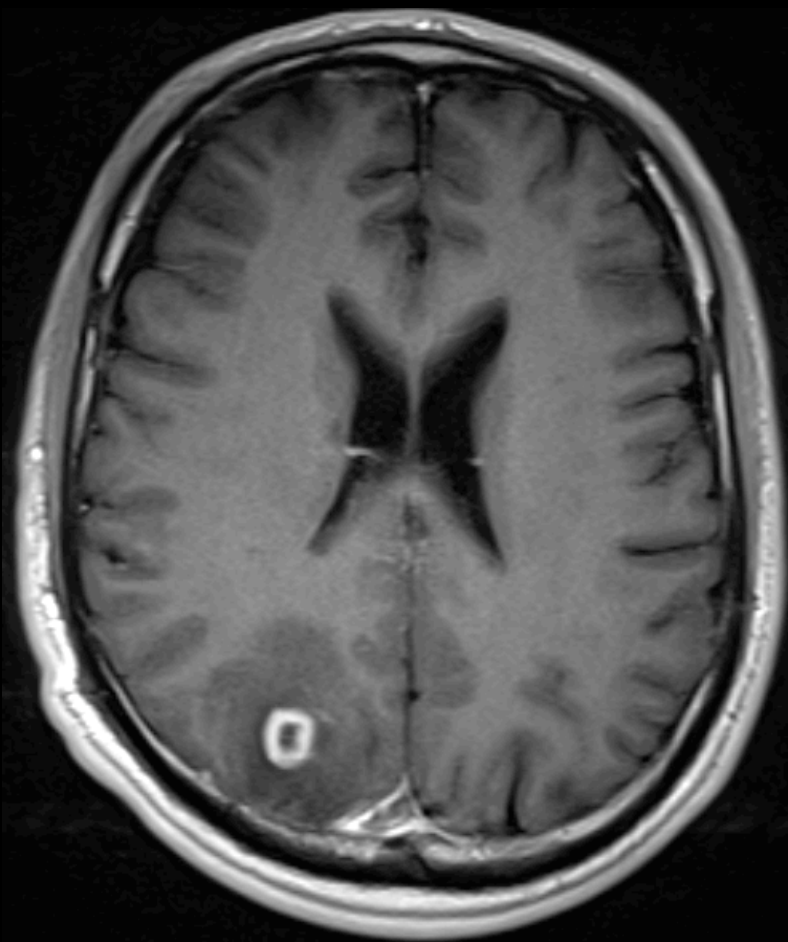
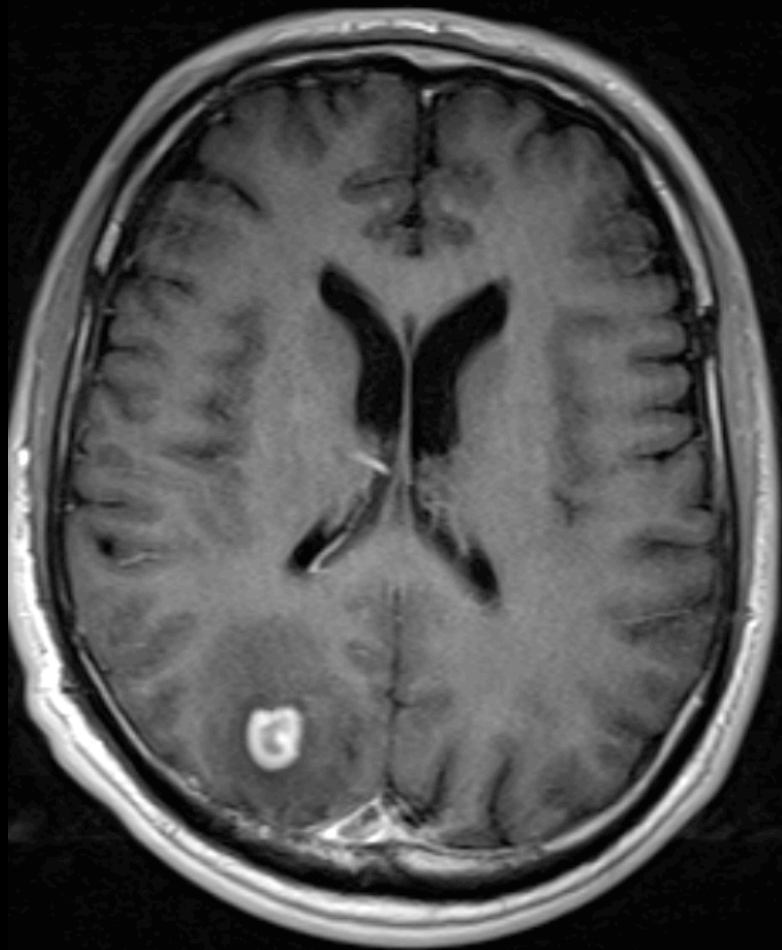
AB

- 35 year old HIV+ woman
- Left face and arm weakness X 5 days
- Off HAART since 2007
 - CD4 56 cells/ul, 4%
 - Plasma HIV RNA 917,200 c/ml
- Anti-*Toxoplasma* IgG seropositive 10 yrs ago
- Not receiving TMP/SMX prophylaxis

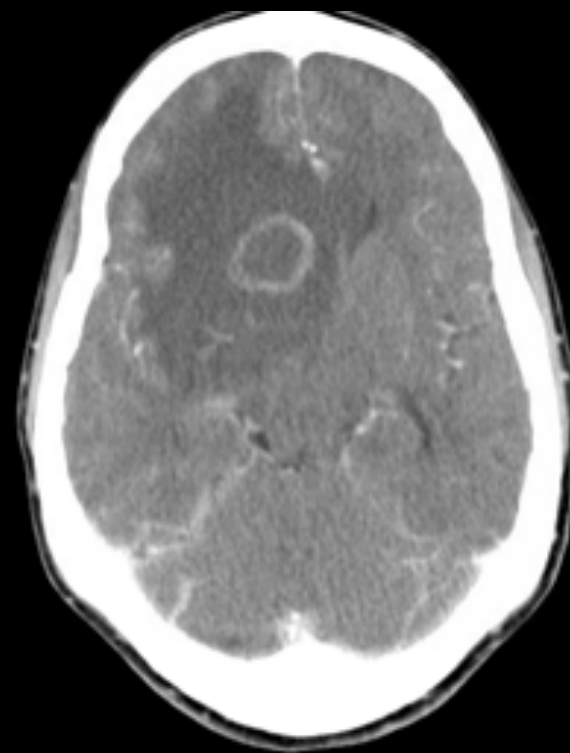
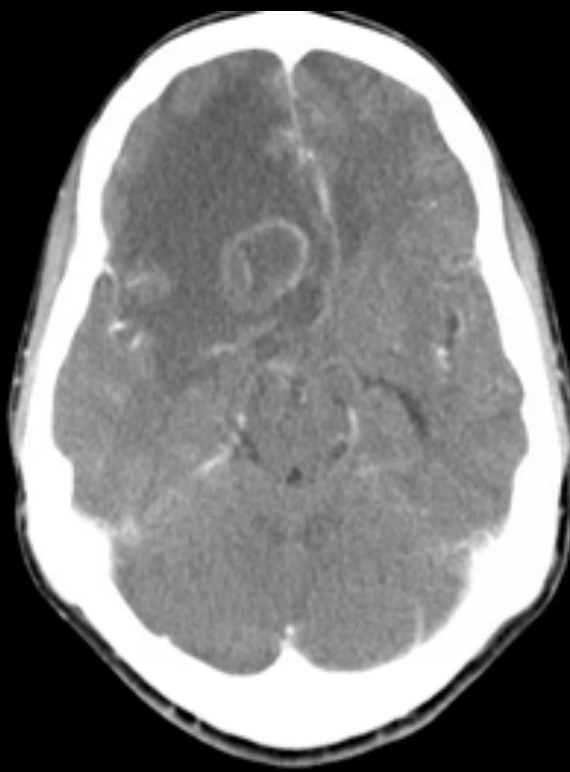
Clinical Findings in CNS Toxo

Symptoms	%	Signs	%
Headache	55	Altered sensorium	42
Confusion	52	Hemiparesis	39
Fever	47	Psychomotor retardation	38
Seizures	29	Cranial nerve palsies	28

Toxo



Toxo



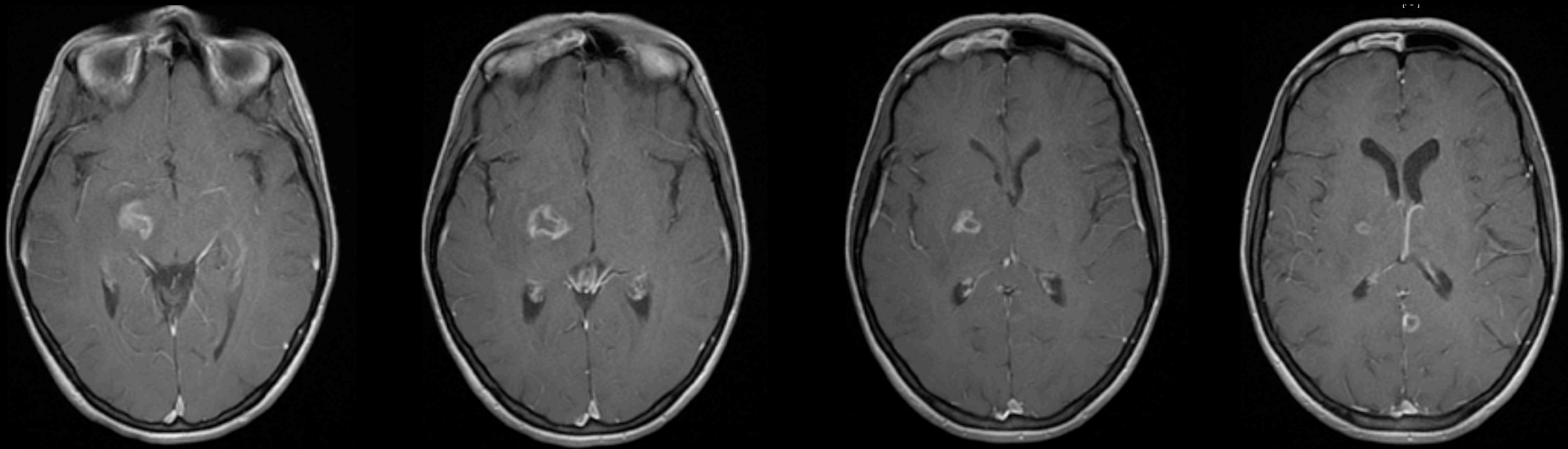
Treatment Trial

- Most appropriate candidates
 - More than one enhancing lesion
 - Detectable serum anti-*Toxoplasma* IgG
 - Not receiving TMP-SMX
 - No other more likely diagnosis
- Improvement supports *Toxoplasma* encephalitis (TE) dx
 - 10-14 day trial

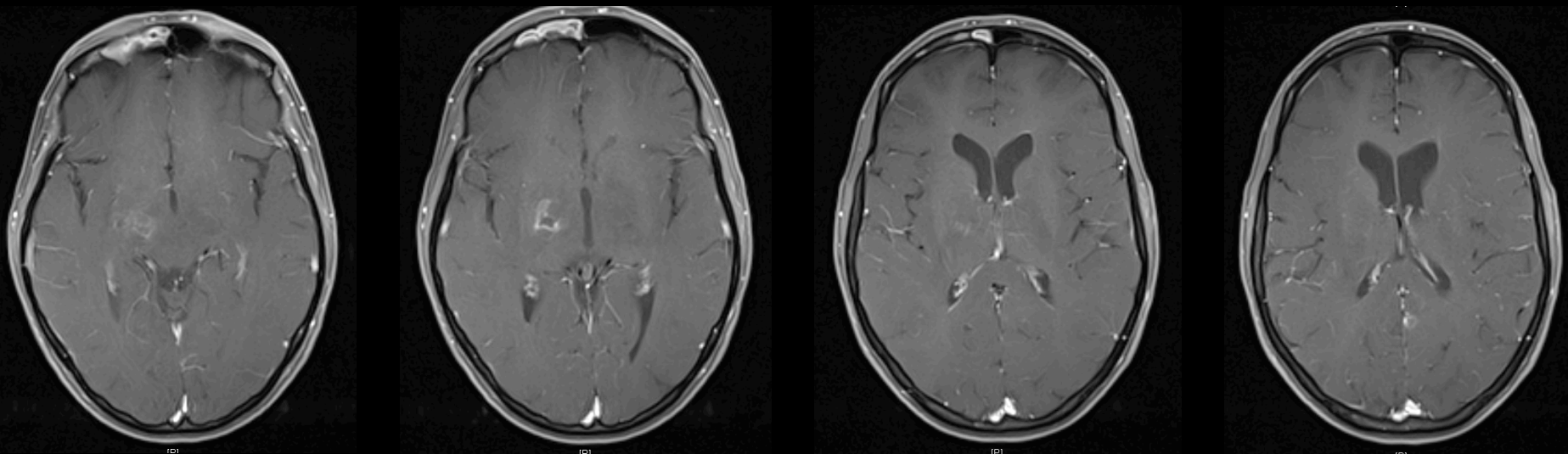
Primary Toxo Therapy

Pyrimethamine		100-200 mg PO load, then 75-100 mg PO/d
	plus	
Sulfadiazine		1.5-2.0 g PO qid
	or	
Clindamycin		600-900 mg PO qid
	plus	
Folinic Acid		10-50 mg PO/d

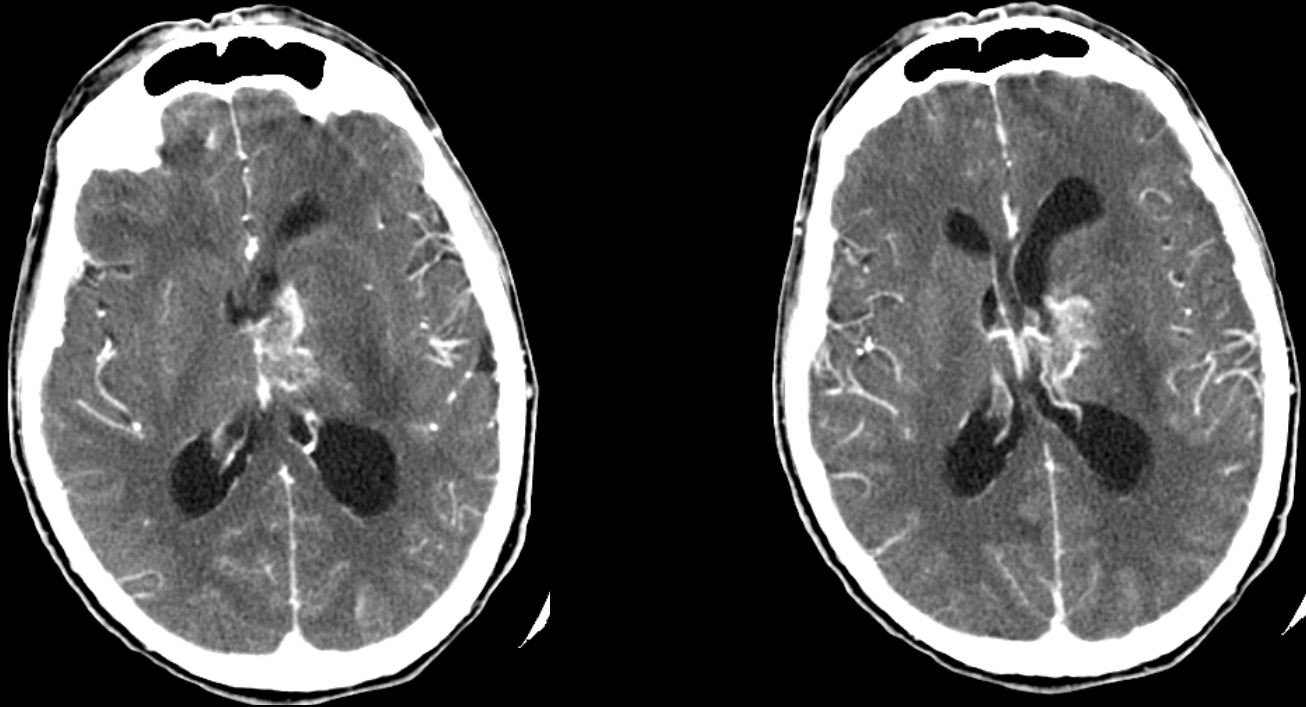
Pretreatment



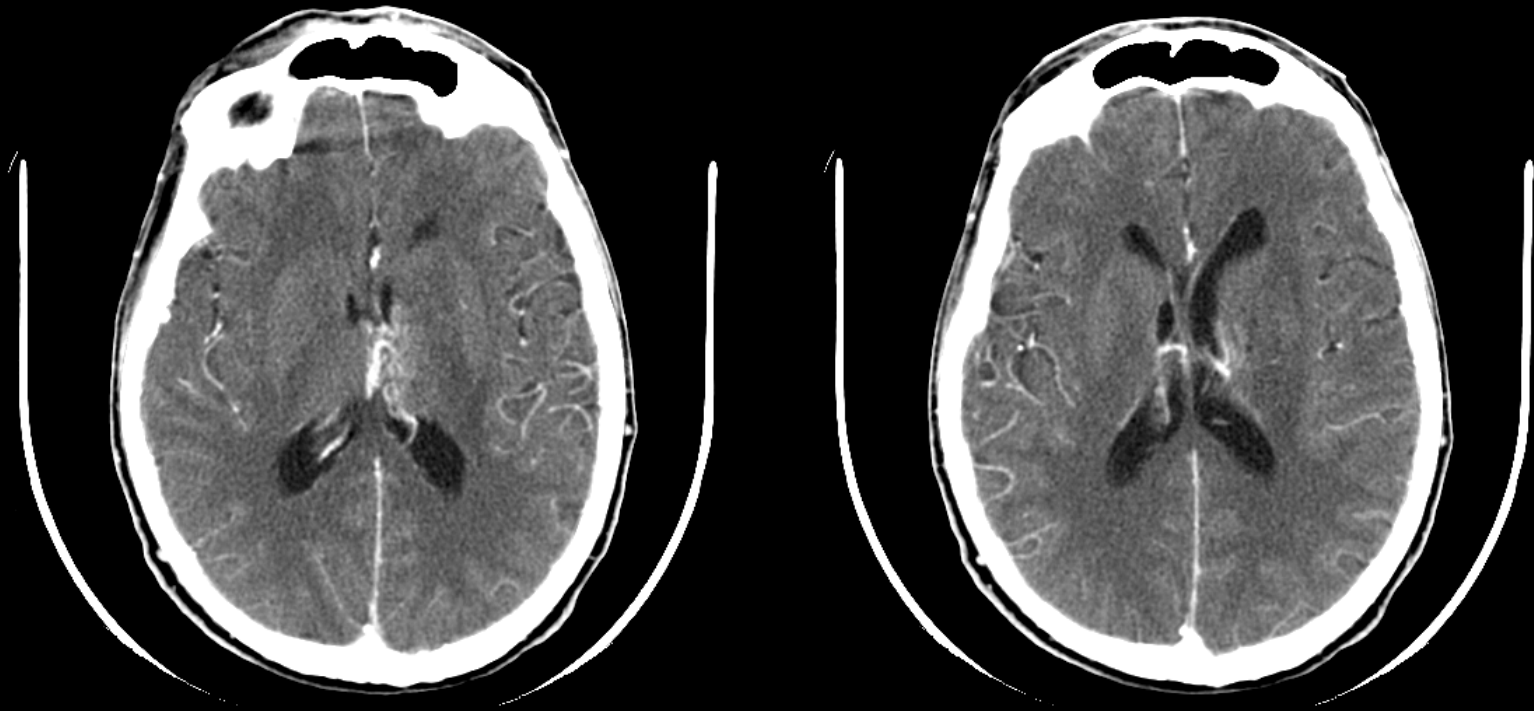
11 days later



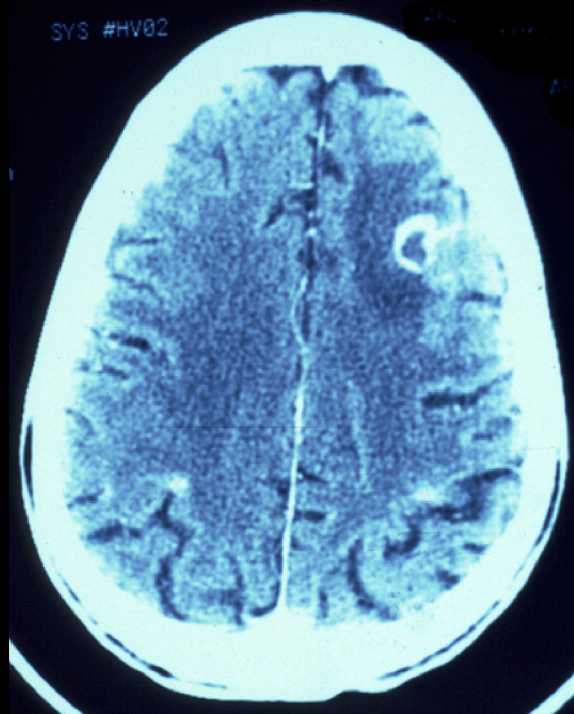
CNS Toxo Before Tx



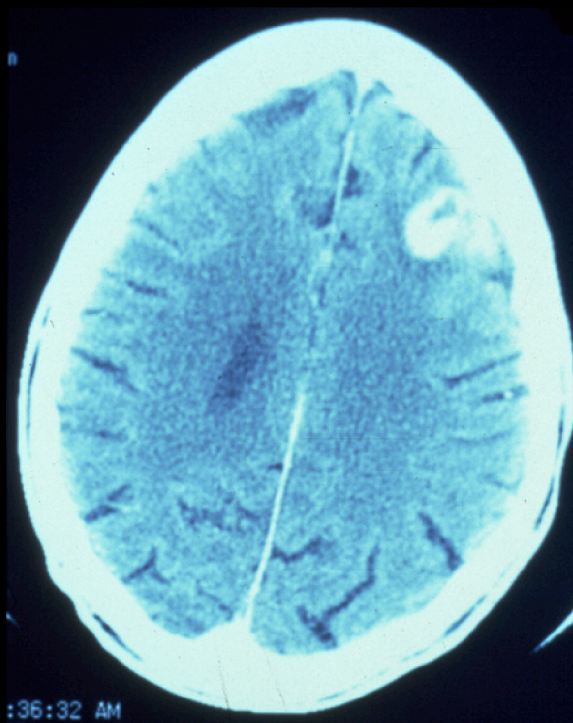
CNS Toxo After 10 d Tx



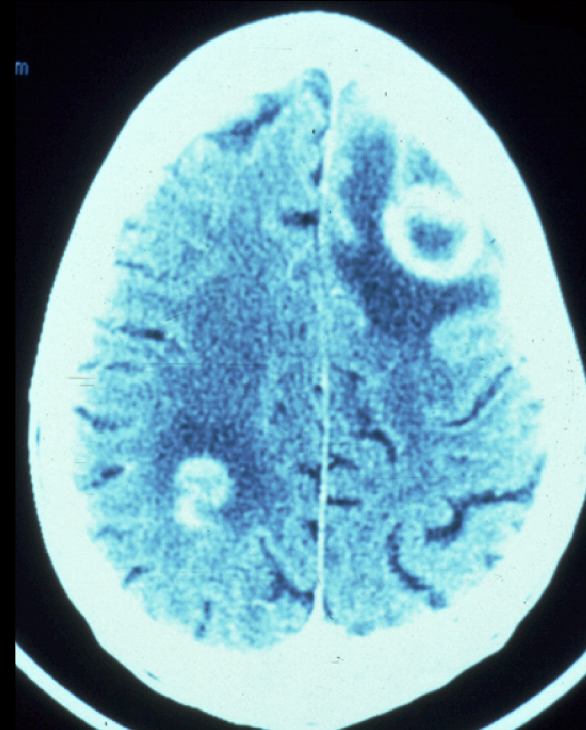
Failed Toxo Tx Trial



Baseline



10 Days TE Tx



6 Weeks TE Tx

Maintenance Toxo Therapy

Pyrimethamine		25-50 mg PO/d
	plus	
Sulfadiazine		1.0 g PO tid-qid
	or	
Clindamycin		300-450 mg PO qid
	plus	
Folinic Acid		10-50 mg PO/d

IRIS and TE

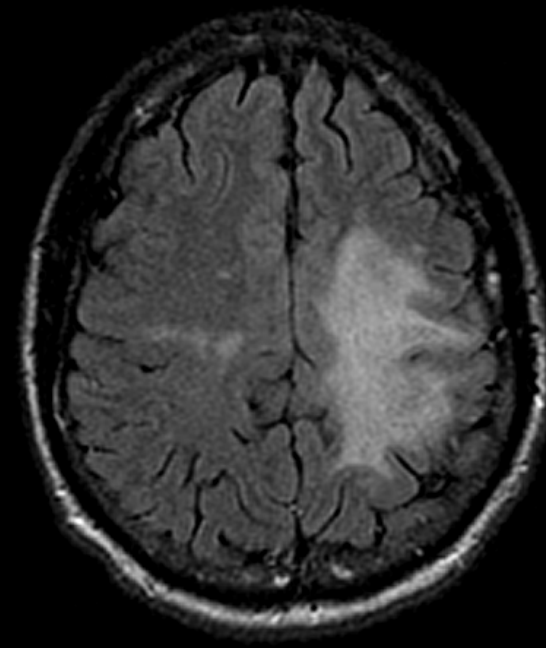
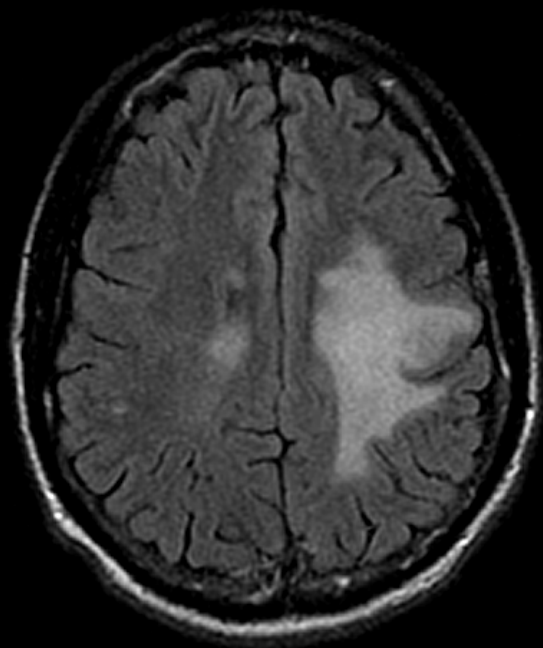
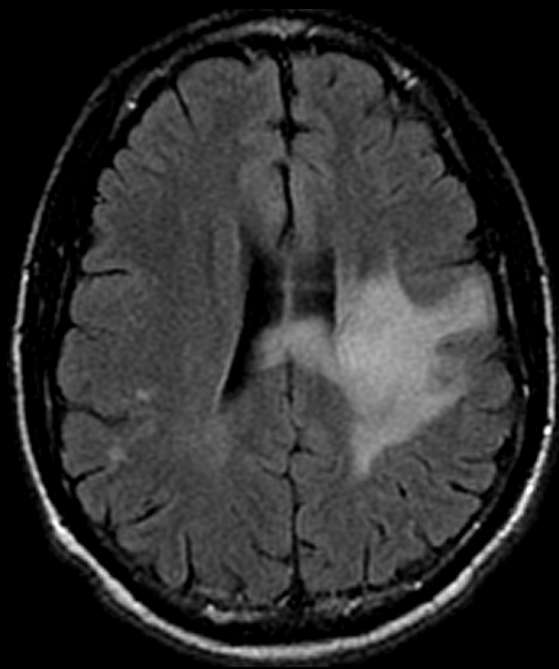
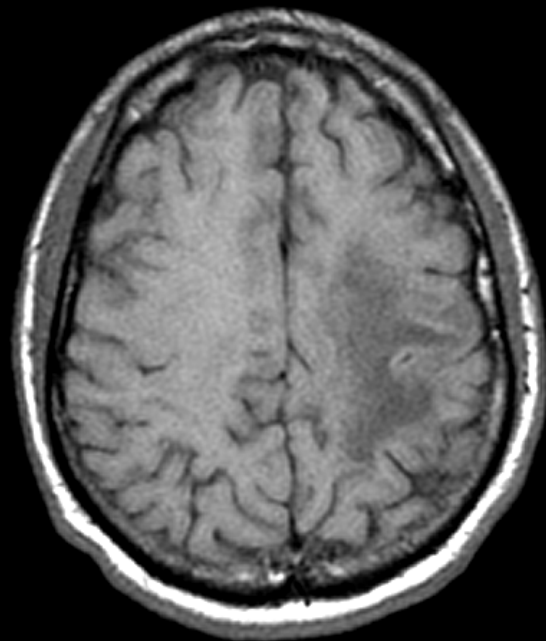
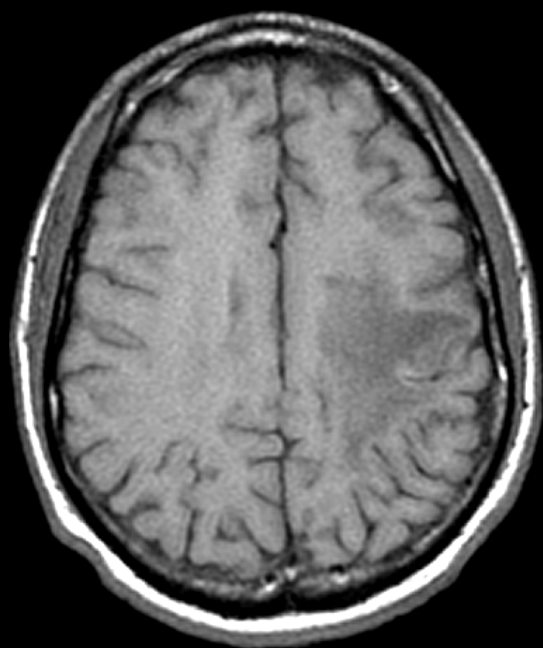
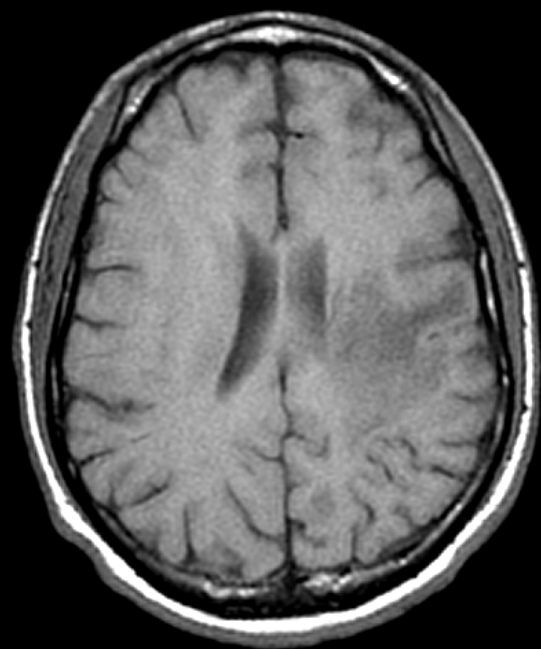
- Martin-Blondel et al. (JNNP 2011;82:691)
 - 3/65 cases of TE over 9 years
 - All developed on ART (unmasking)

HAART and Toxo

- Start HAART as soon as feasible
- DC secondary prophylaxis when “immune reconstituted”
 - CD4 > 200/ul for 6 months after completion of primary therapy

DS

- 27 year old HIV+ man
- 3 month history of trouble using his (dominant) right arm and hand
- Exam shows right UE decreased tone and weakness
- Just started HAART
 - CD4 6/uL, 1%
 - Plasma HIV RNA 26,856 c/ml
- CSF PCR for JCV positive



Clinical Findings in PML

- Visual field loss
- Limb weakness
- Gait disturbance
- Coordination difficulties
- Cognitive dysfunction
- Seizures in about 20%

PML Diagnosis in HIV

- Non-enhancing focal lesion on CT/MR -> 68%
 - With positive CSF JCV PCR -> 99%
 - With negative CSF JCV PCR -> 27%
- CSF JCV PCR less likely to be positive in patients on HAART

Treatment for PML

- Potent antiretroviral therapy
- No proven benefit
 - Ara C
 - Interferon gamma
 - IL-2
 - Cidofovir
 - Mefloquine
 - IL-7?

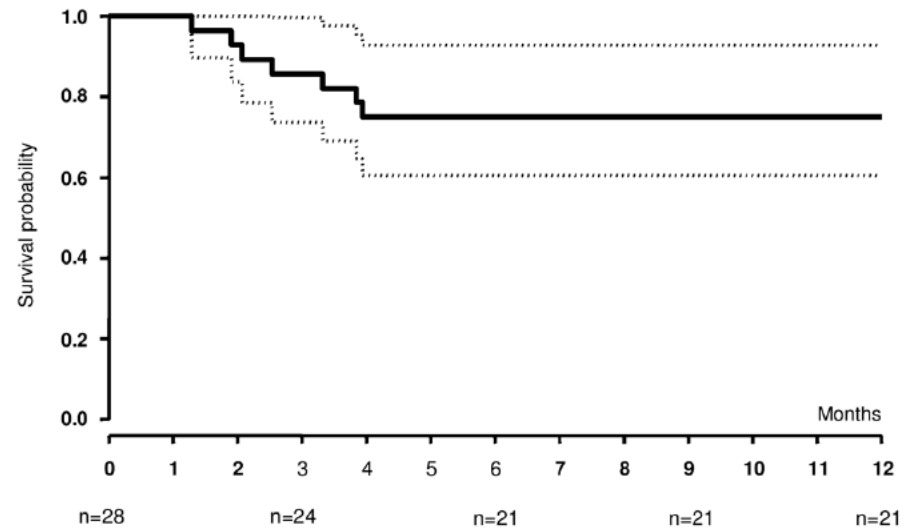
Outcome

- Before HAART
 - Mean survival 18 weeks
 - 10% recovered spontaneously
- After HAART
 - Mean survival > 1yr
 - 50% die in the first 6 months after dx
 - Moderate to severe disability

Treatment for PML

Gasnault et al. (PLoS ONE 2011;6)

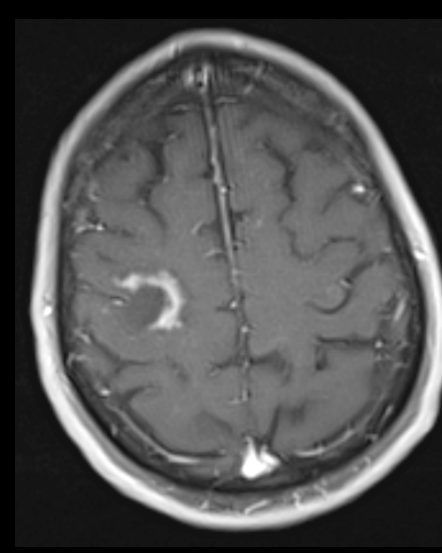
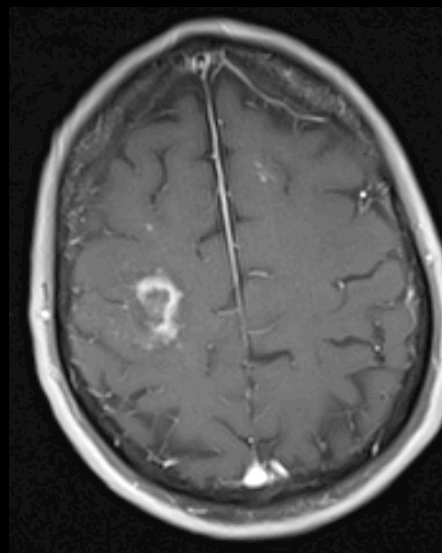
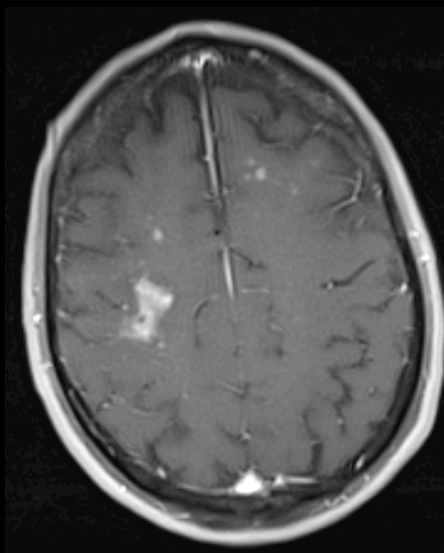
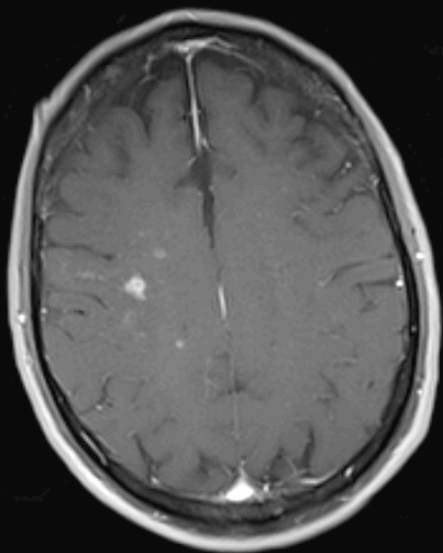
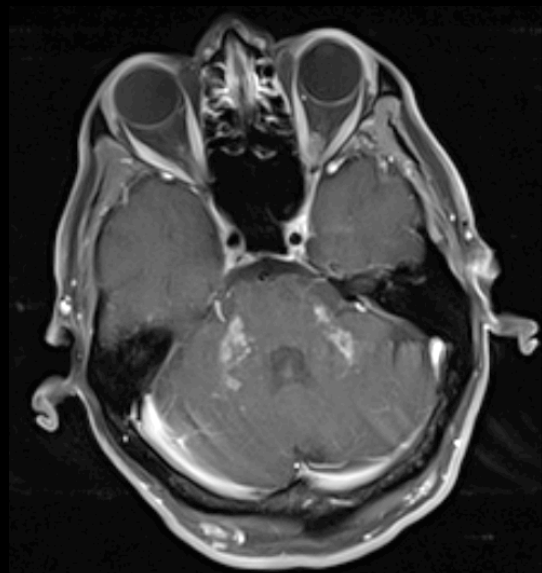
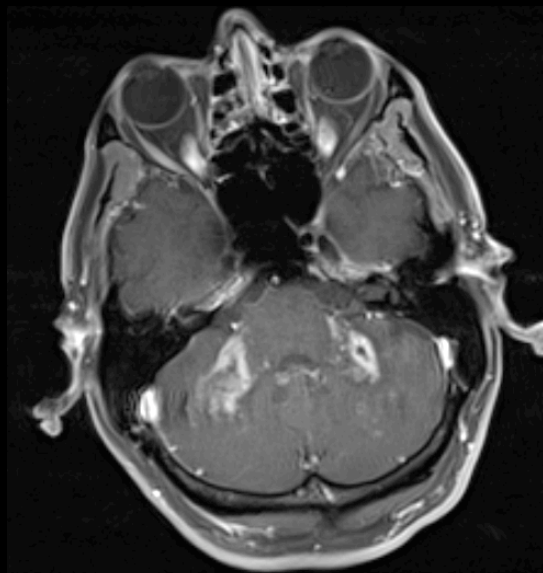
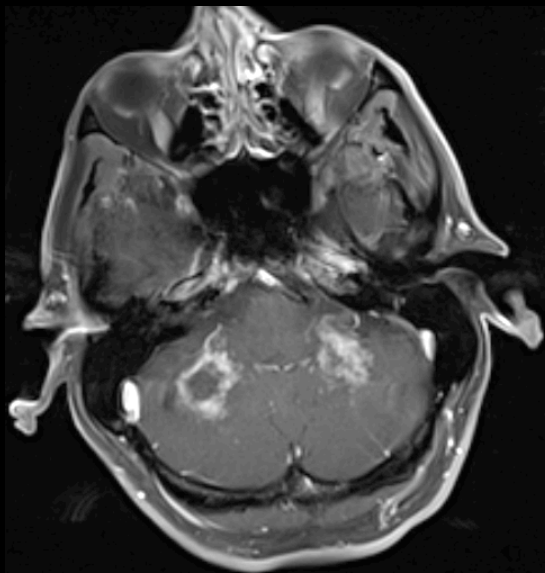
- Open label, prospective multicenter study of 5 ARVs on PML outcome
 - Enfuvirtide X 6 months
- 28 patients
 - 12 ART-naive
- One year survival 75% (61-93%)
 - 7 deaths, all before 4 months



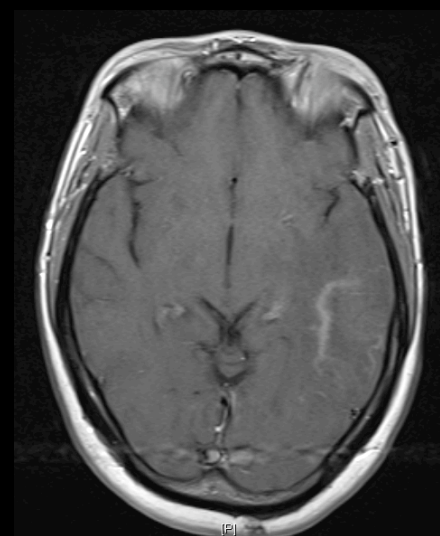
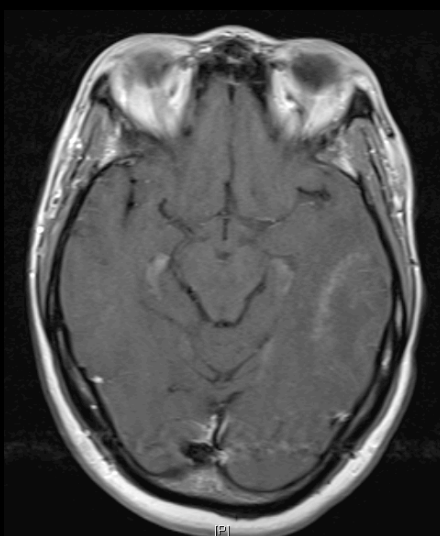
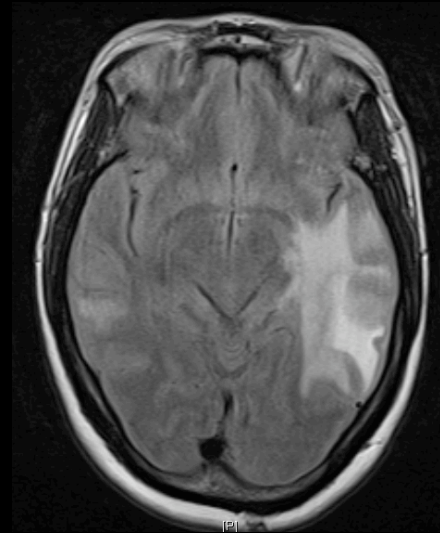
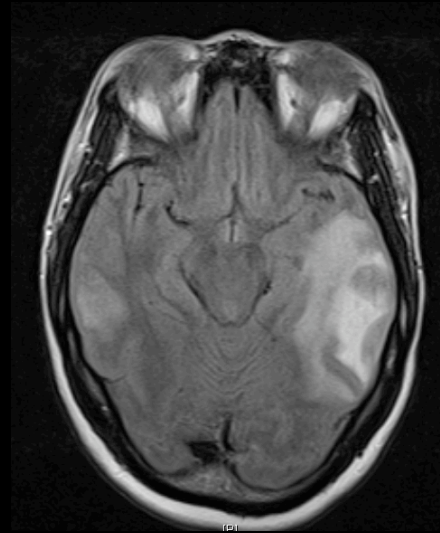
PML IRIS

- Falcó et al. (JAIDS 2008;49:26)
 - Observational study at 7 Barcelona hospitals 2002-2006
 - 61 new diagnoses of PML
 - 14 (23%) IRIS
 - 6 paradoxical
 - 8 after starting HAART
 - Contrast enhancement on neuroimaging more common with IRIS
 - Only seen in 30% of IRIS patients
 - IRIS did not impact survival

PML IRIS



PML IRIS



Better Prognosis in HIV PML

- CD4 \geq 100/uI
- HIV RNA < 500 c/ml
- HAART
- AIDS-defining illness
- Inflammation
 - CT/MR, MRS or biopsy
 - CSF pleocytosis
- Low CSF JCV DNA