

HIV and CNS

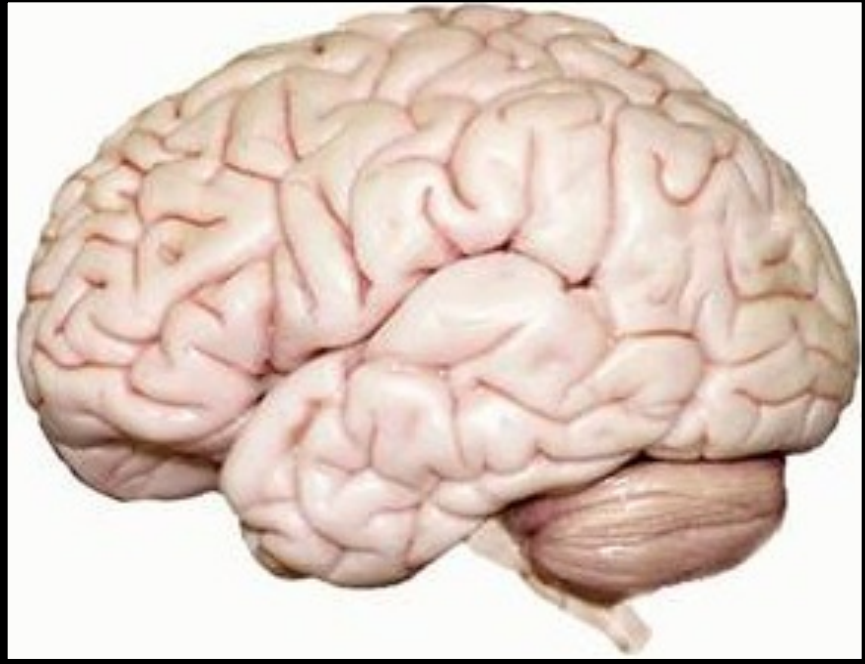
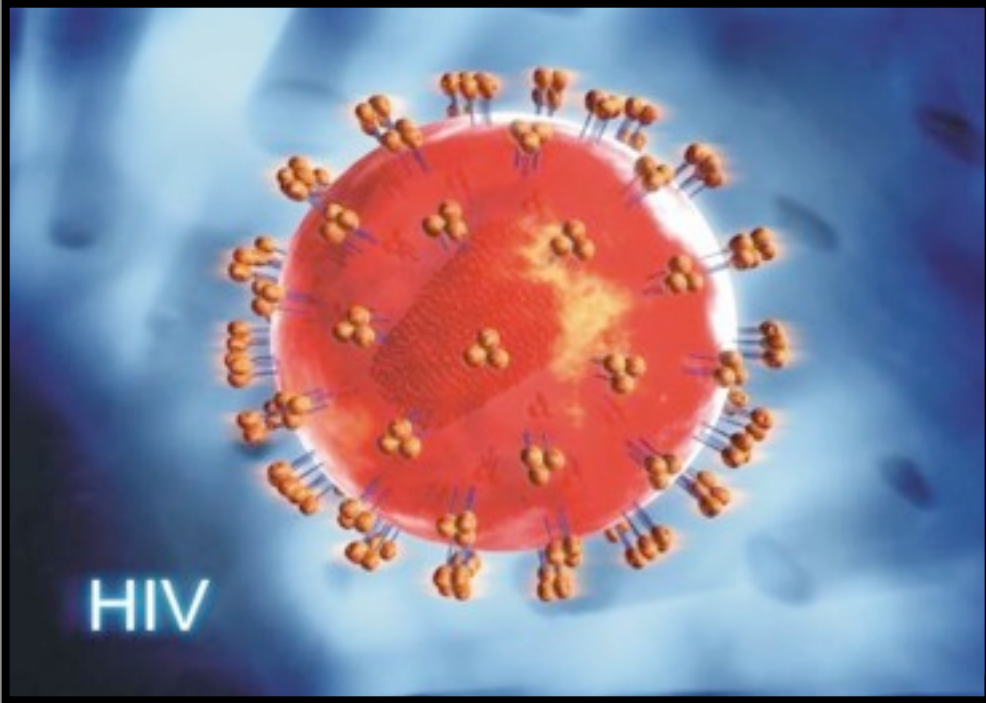
Stereotactic Biopsy in the diagnosis of brain lesions in AIDS patients

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Argentina

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Definition

✓ AIDS Patients

- Patients with high life risk due to HIV infection
- Associated pathologies or systemic diseases caused by the HIV

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Classification of patients infected with HIV-1

Clinical Subgroups

- ✓ **A : Acute infection/ Asymptomatic HIV+ patient**
- B : Symptomatic patients not included in A or C** (oropharyngeal or vulvovaginal candidiasis, cervical dysplasia or in situ carcinoma, peripheric neuropathy, LOV,VHZ,PTI, pelvic inflammation disease)
- C : Markers diseases of AIDS**

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Classification of patients infected with HIV-1

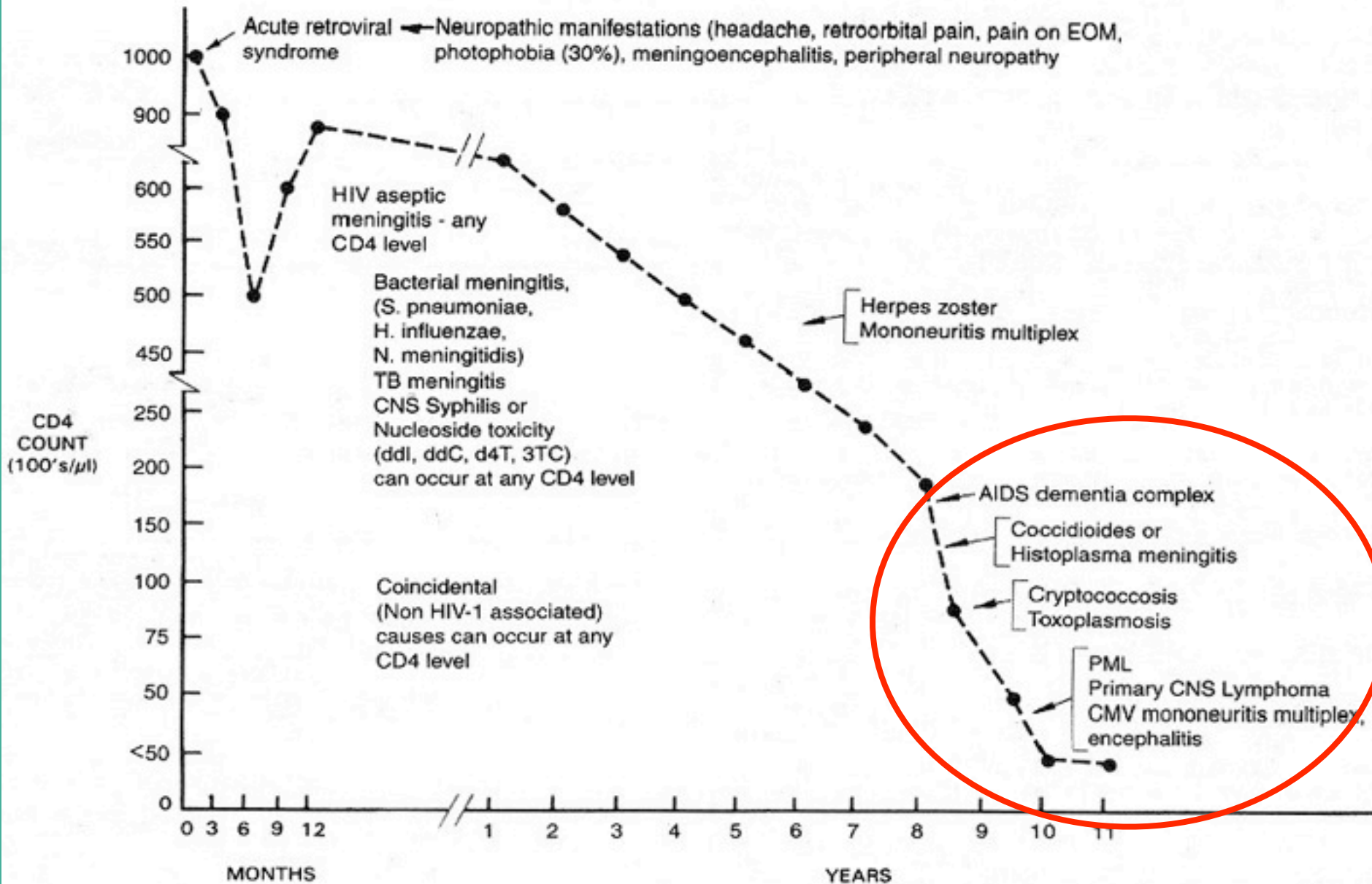
Clinical Subgroups

CD4 LEVELS	A	B	C
> 500/mm	A1	B1	C1
200-499/mm	A2	B2	C2
< 200/mm	A3	B3	C3

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COURSE OF NEUROLOGIC DISEASE AND HIV INFECTION IN ADULTS

— Clinical latency or mildly symptomatic disease —



Neurologic Symptoms in AIDS

- ✓ 50% develop neurologic symptoms
- ✓ 10% present initially with neurologic complaint
- ✓ 10-20% normal brain on autopsy

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*Neurological symptoms are very often found in HIV AIDS disease and it usually has a very high morbidity and mortality
It appears in any stage of the disease*

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CNS involvement

- ✓ First stage or Acute Retroviral Syndrome
 - aseptic meningitis, seroconversion acute myelitis, peripheral neuropathies, Guillain-Barré S.
- ✓ Middle or chronic stage :
Immune mediated neuropathies, Antiretroviral toxicity
- ✓ Final stage or AIDS :
 - CNS infections
 - CNS tumors

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CNS infections

PARASITIC INFECTIONS

Toxoplasmosis

Trypanosomiasis

- BACTERIAL INFECTIONS :
Tuberculosis
Micoabacterium a.i.
Treponema
Bacterial infections

- FUNGAL INFECTIONS :

Criptococcosis

Candidiasis

Aspergillosis

Histoplasmosis

- VIRAL INFECTIONS :
CMV
PML/JCV
HSV
VZV

Cláudio G. Tompowsky, MD.

CNS tumors

- ✓ Primary CNS Lymphoma
- ✓ Secondary Lymphoma
- ✓ Kaposi Sarcoma
- ✓ Gliomas ??

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Mechanism of action of HIV-1

Direct Mechanism

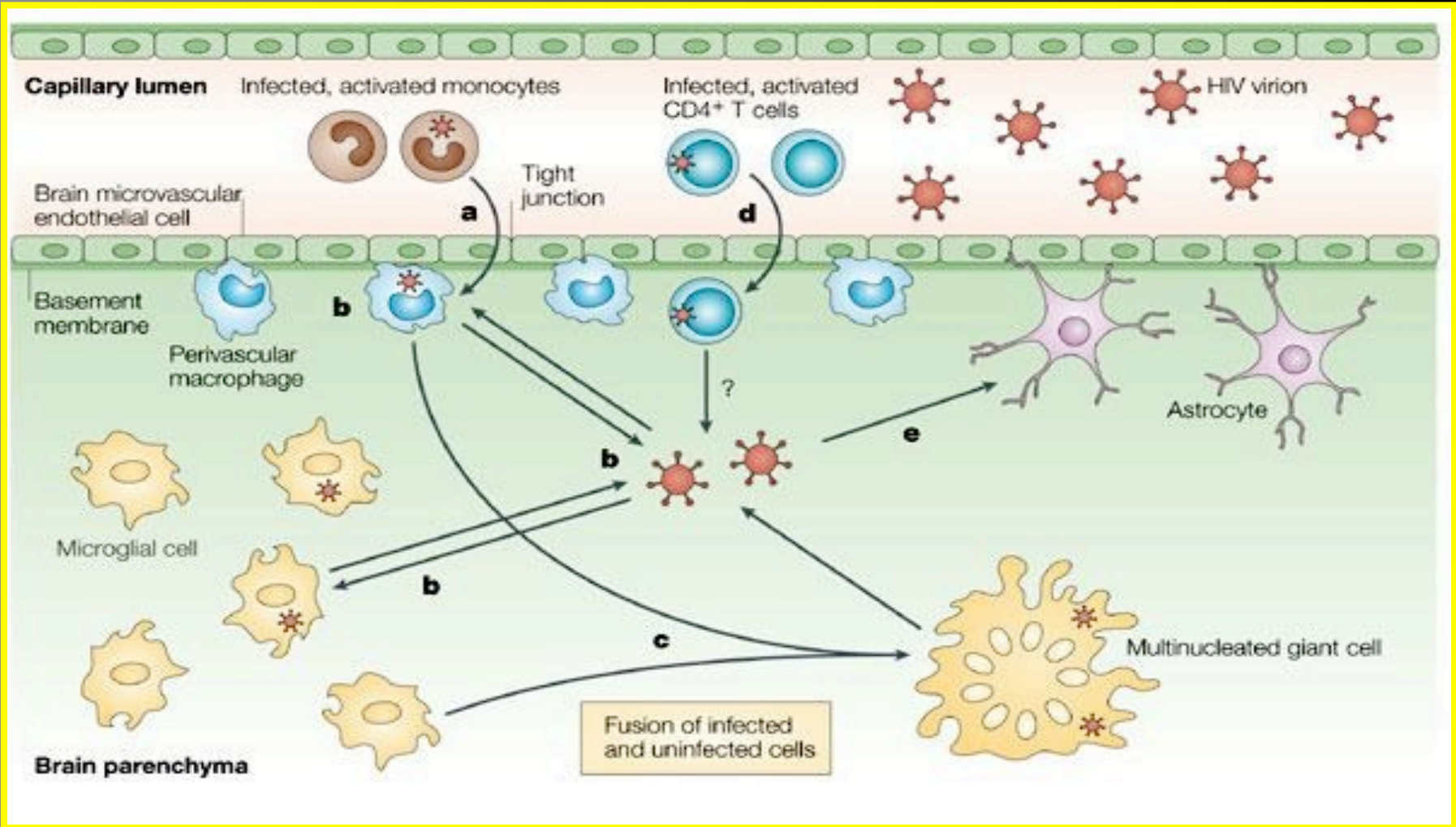
- HIV infection of cells

Indirect Mechanism

- Toxic effect of HIV-1 proteins over neuronal tissue
- Interaction between glial cells and infected macrophages
- result in neuronal damage
- NMDA receptor associated with neuronal damage

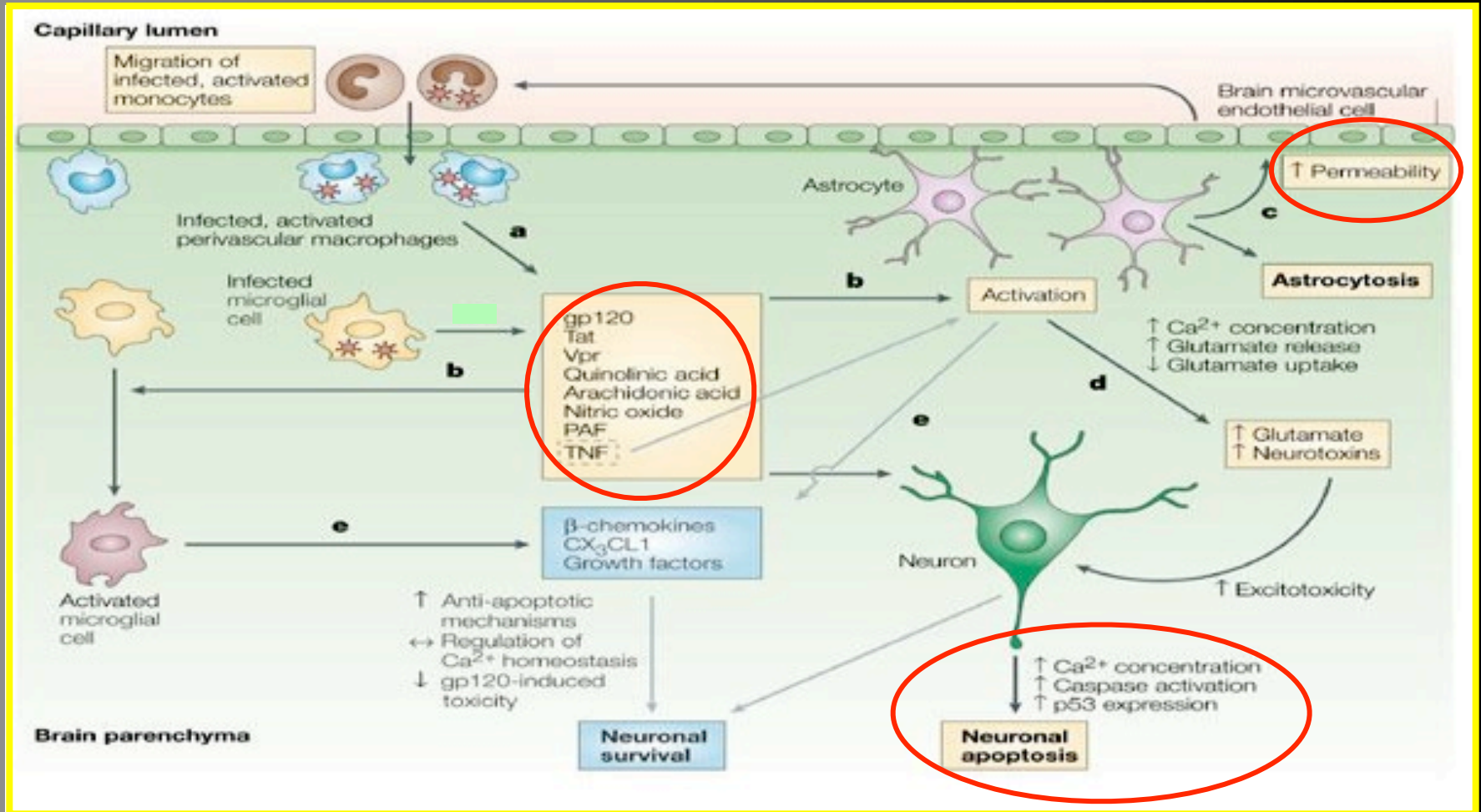
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HIV-CNS-Pathophysiology



Gonzalez-Scarano F et al. *Nat Rev Immunol* 2005;5:69-81 Claudio G. Yampolsky M.D.

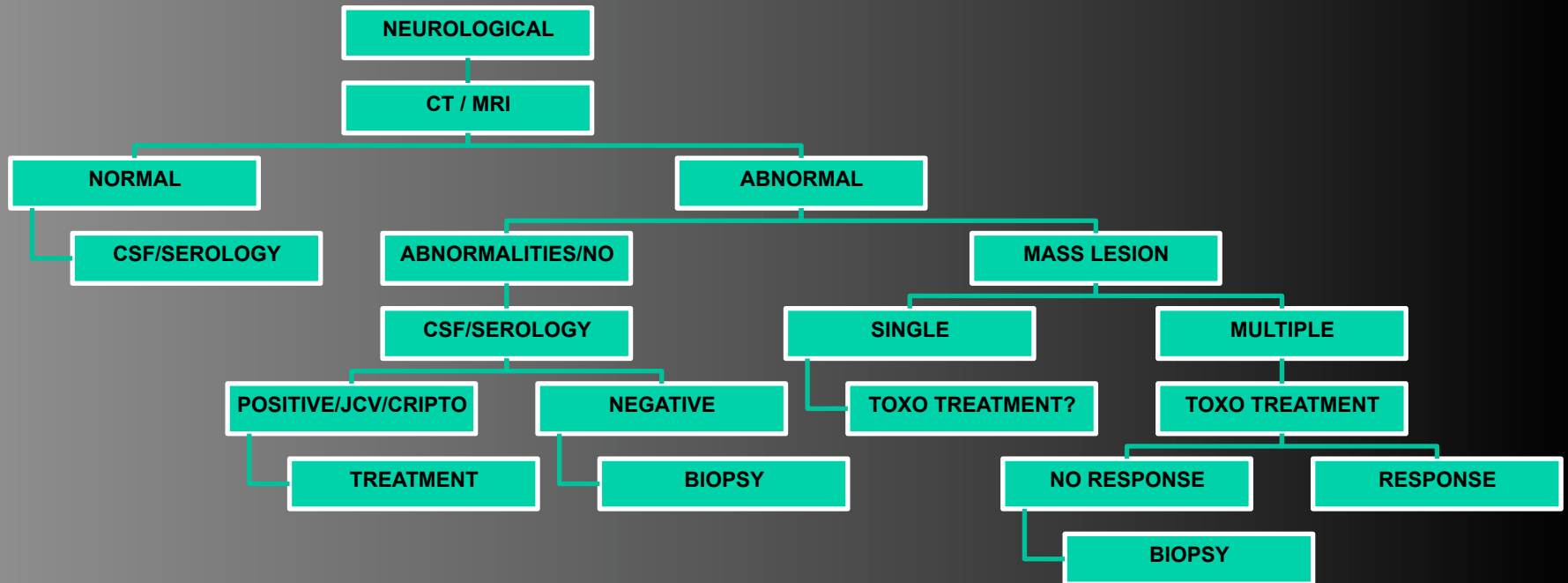
HIV-SNC-Pathophysiology



Gonzalez-Scarano F et al. Nat Rev Immunol 2005;5:69-81

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Diagnostic Algorithm



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Stereotactic brain biopsy

- ✓ Minimal Invasive Procedure
- ✓ Maximal efficacy
- ✓ Minimal morbidity

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Stereotactic brain biopsy

- ✓ When ?
- ✓ What for ?
- ✓ How ?
- ✓ Results

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Stereotactic brain biopsy

- ✓ When ?
- ✓ What for ?
- ✓ How ?
- ✓ Results

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Stereotactic brain biopsy

- ✓ When ?
- ✓ What for ?
- ✓ How ?
- ✓ Results

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Stereotactic brain biopsy

- ✓ When ?
- ✓ What for ?
- ✓ How ?
- ✓ Results

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Stereotactic brain biopsy

- **First step** : frame
- **Second step** : image aquisition (CT, MRI).
- **Third stepo** : planning.
- **Forth step** : biopsy

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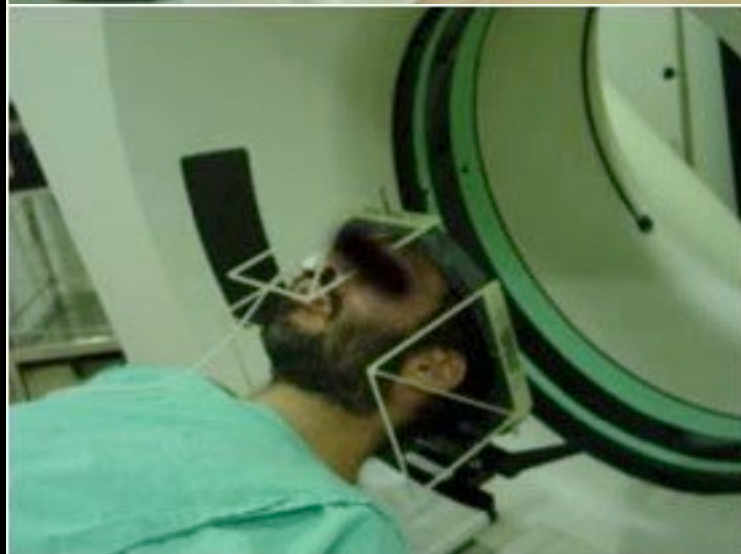
Frame



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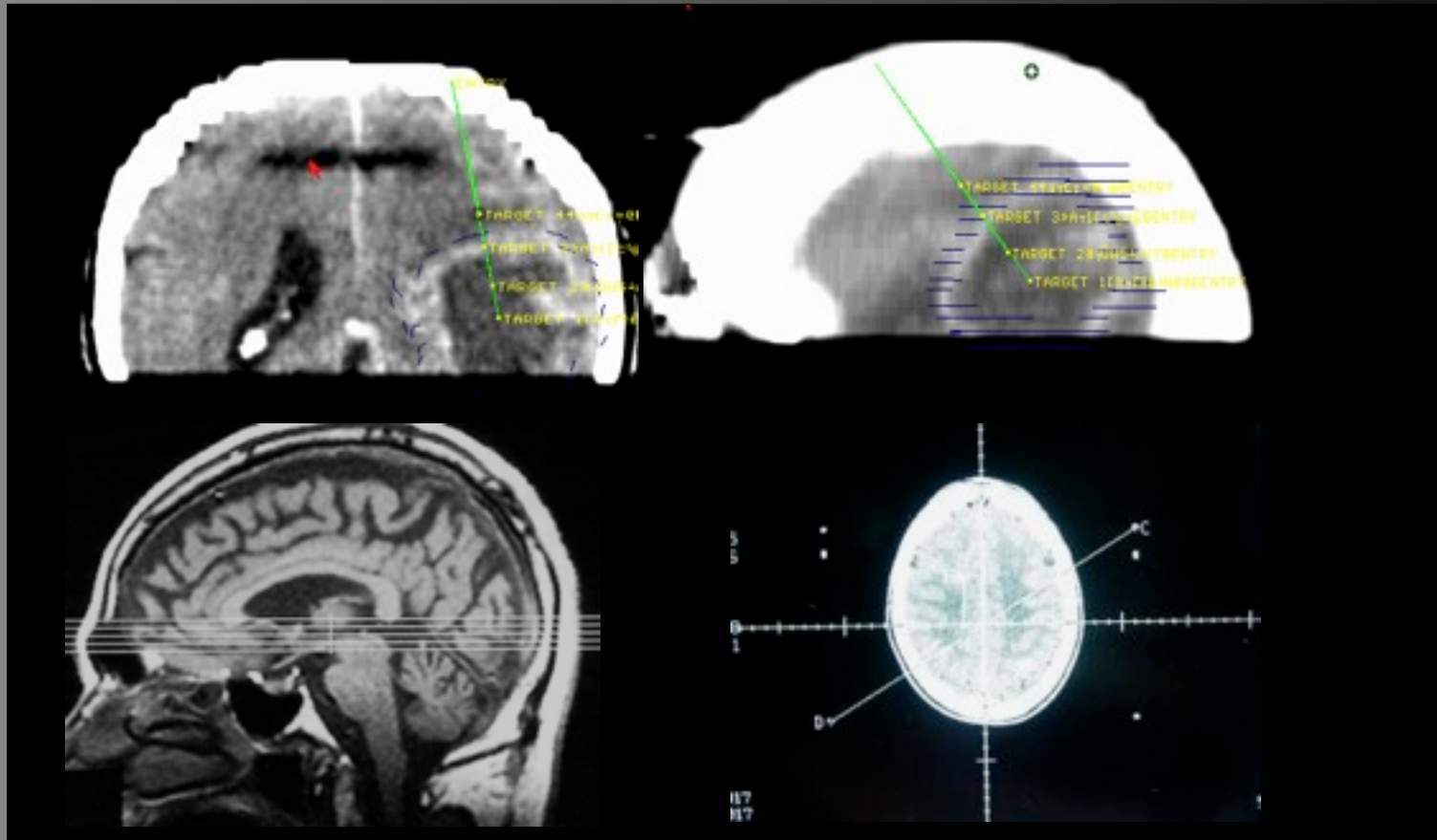
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Image aquisition



D.

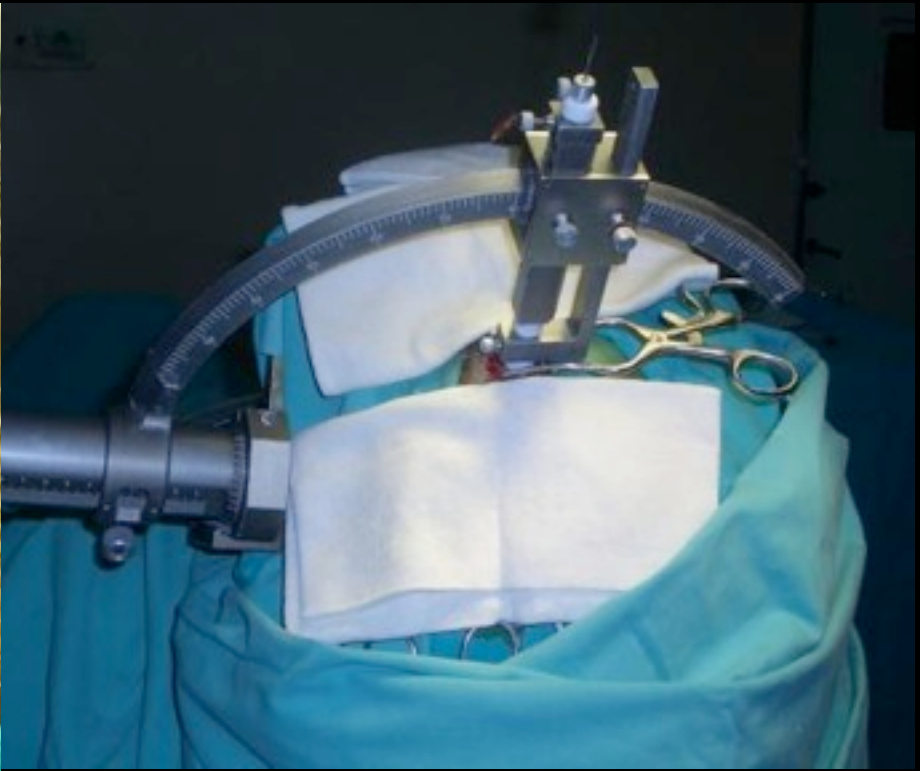
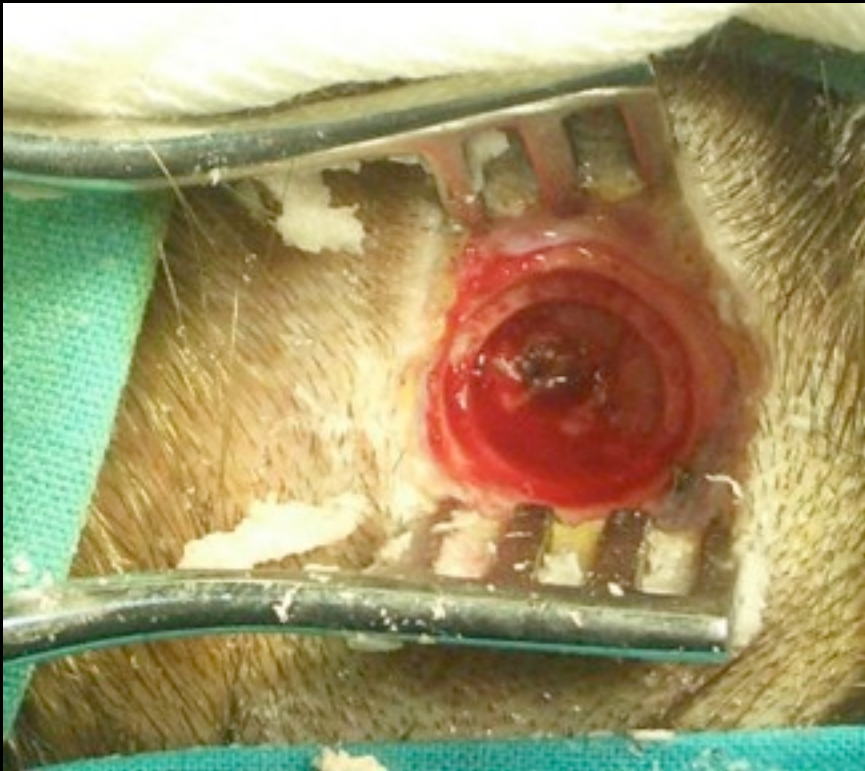
Planning



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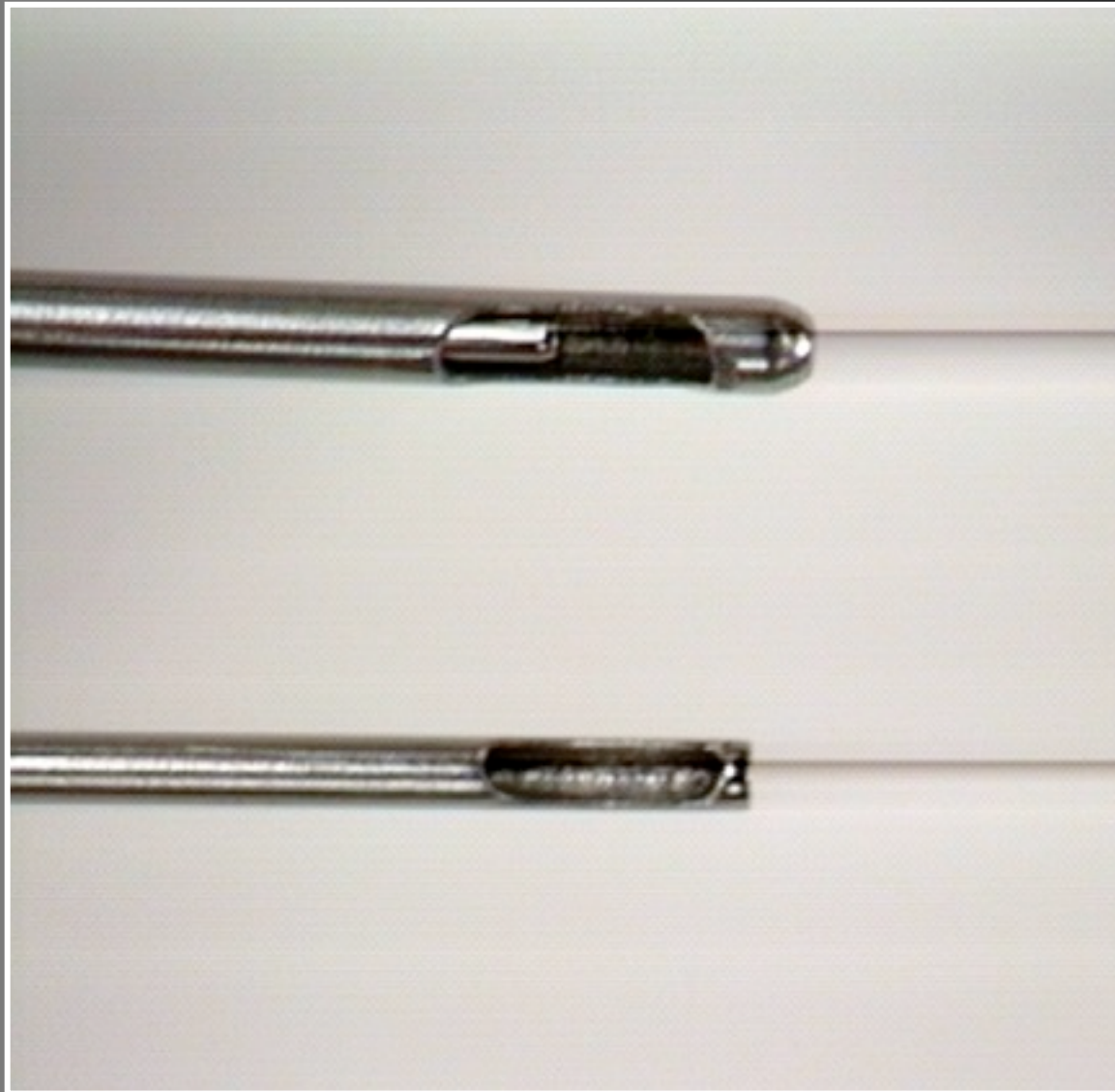
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Biopsy



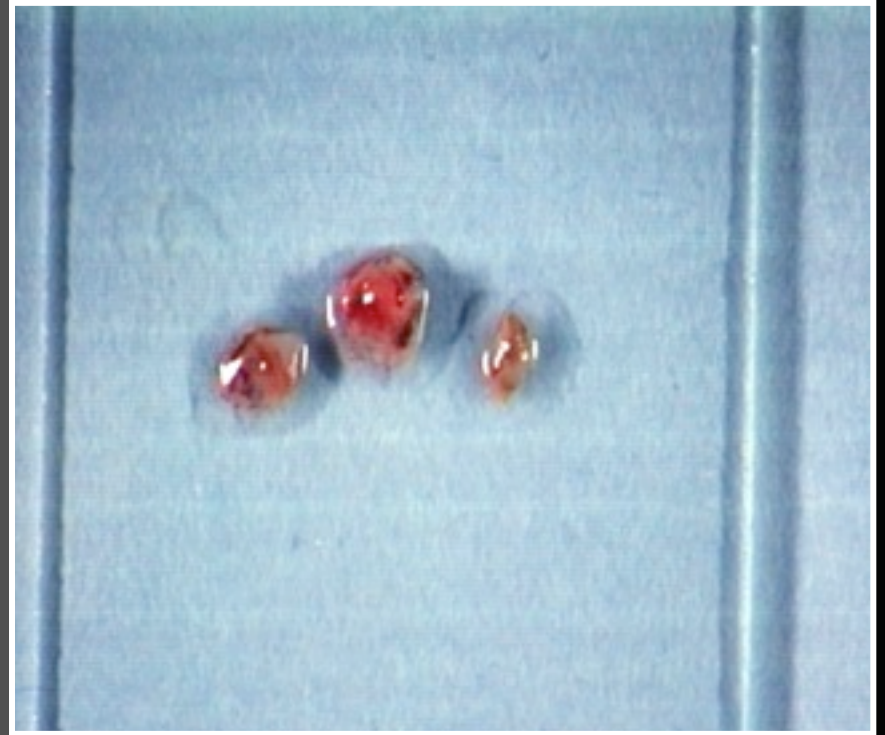
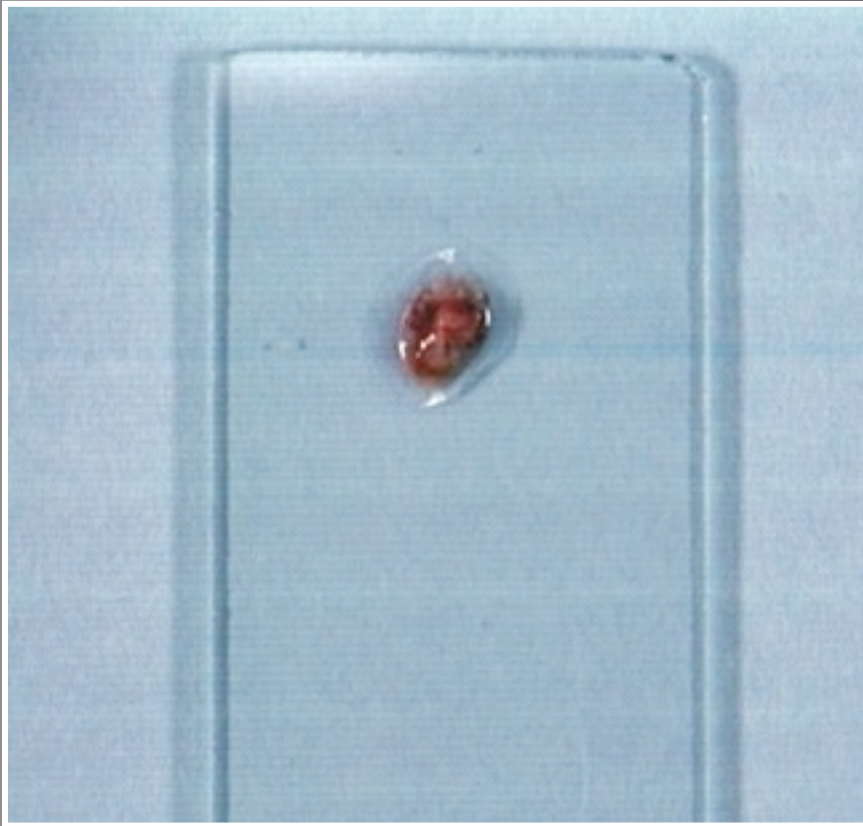
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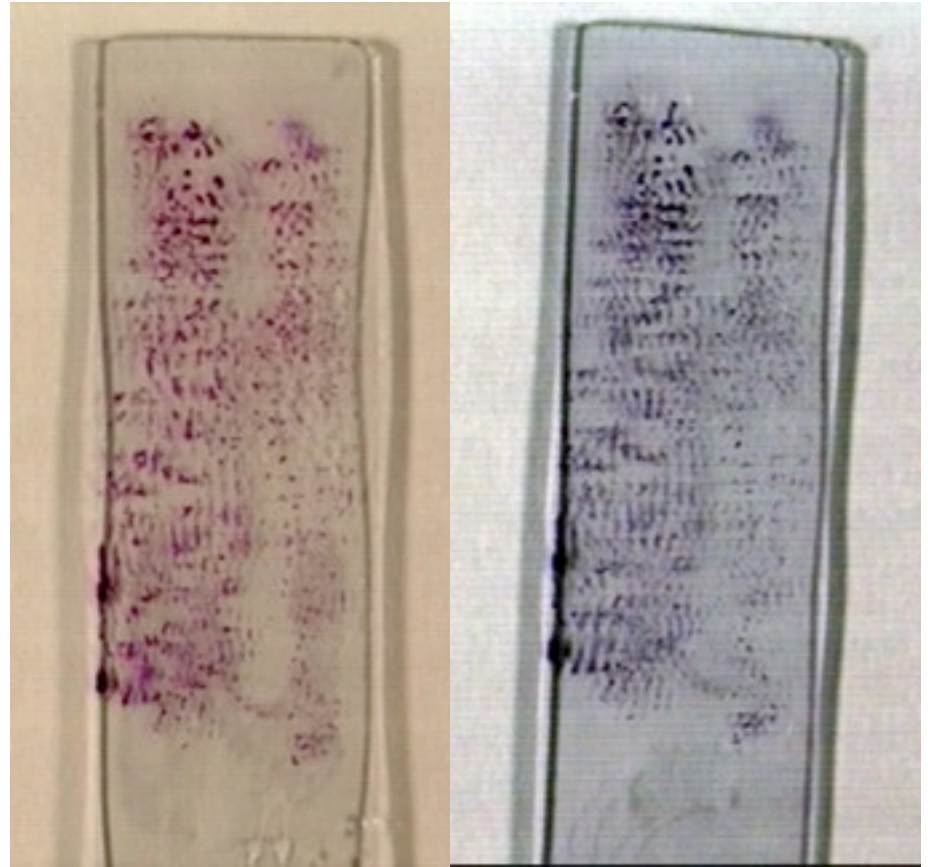
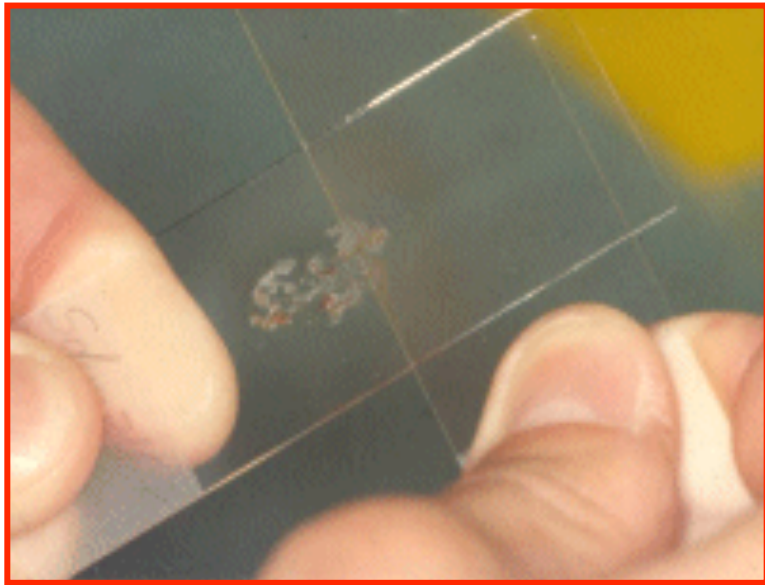
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Friday, 20 August 2010

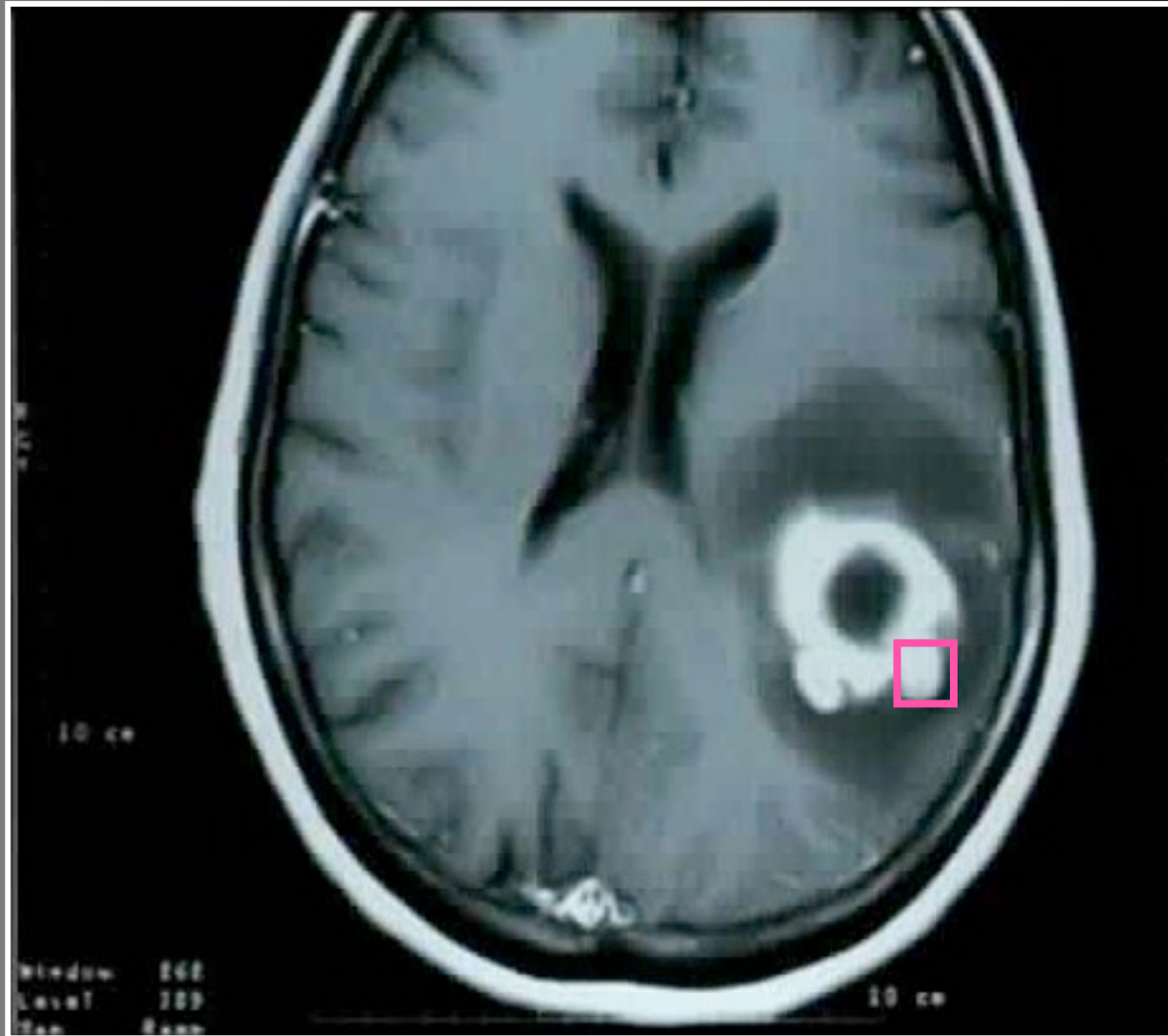


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- ¿¿ Is the biopsy representative of the lesion ???

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Diagnostic yield

Intraoperative:

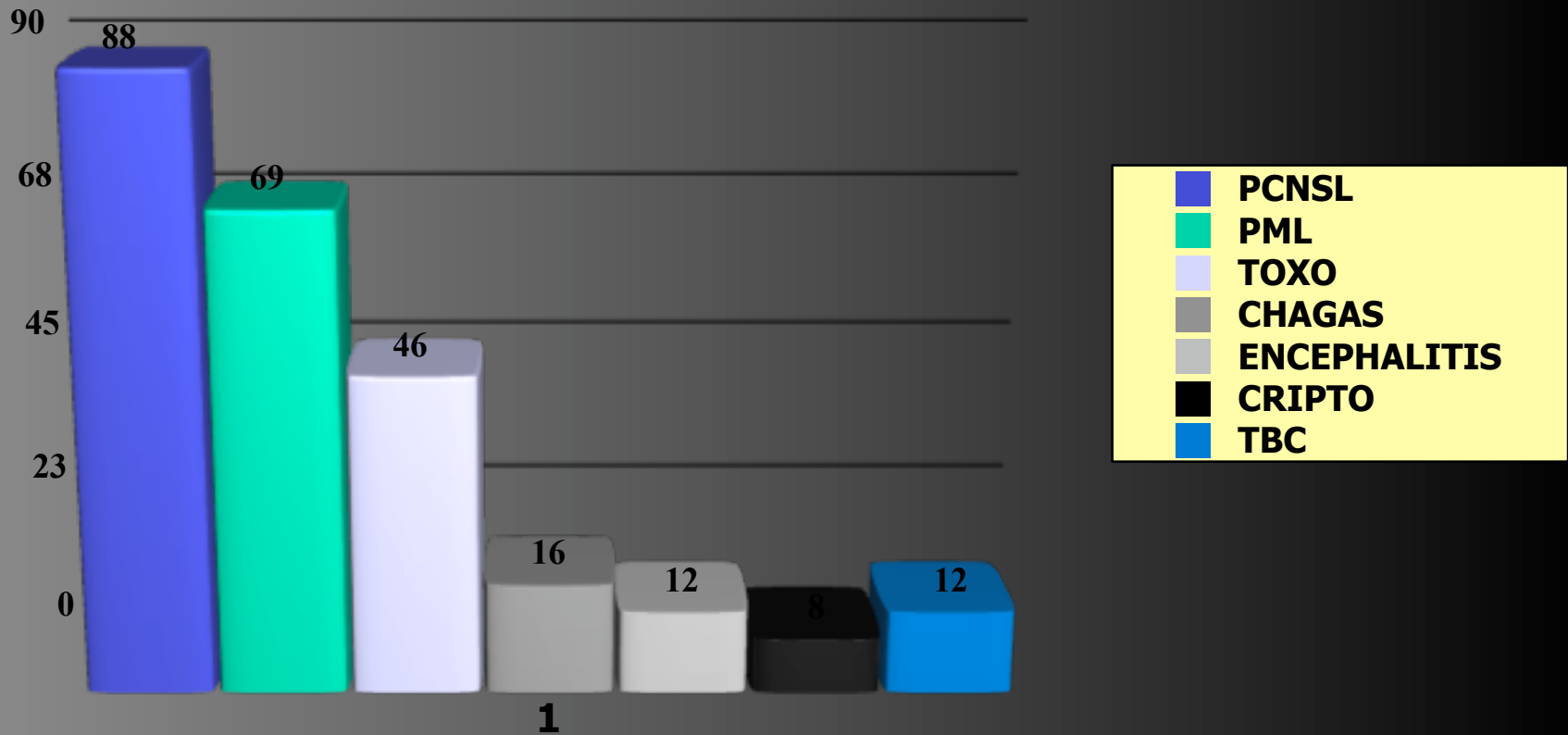
- sensitivity 78%;
- specificity 90%

Cytology:

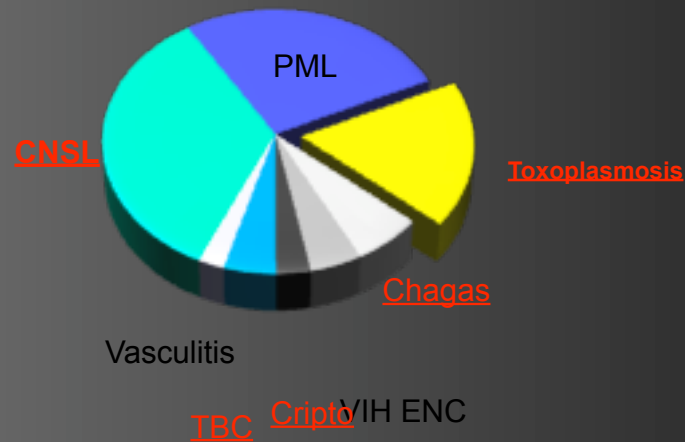
- sensitivity 88%
- specificity 90%

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STEREOTACTIC BIOPSY IN AIDS PATIENTS (N = 300)



STEREOTACTIC BIOPSY IN AIDS PATIENTS (N = 300)



Diagnosis N=300

PCNSL.....	88 (29,3%)
PML.....	69 (23%)
TOXOPLASMOSIS.....	46 (15,3%)
CHAGAS DISEASE.....	16 (5,3%)
TUBERCULOSIS.....	12 (4%)
ENCEPHALITIS-VIH.....	12 (4%)
CRIPTOCOCOMA.....	8 (2,7%)

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Diagnosis N=300

VASCULITIS.....	6 (2%)
NOCARDIOSIS.....	3 (1%)
HISTOPLASMOSIS.....	1 (0.3%)
PML -VZV+JCV.....	1 (0.3%)
GRANULOMA.....	1 (0.3%)
ENCEPHALITIS VIH+VZV.....	1 (0.3%)

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Diagnosis N=300

ASTROCYTOMA G IV.....	5 (1,7%)
GLIOSARCOMA.....	1 (0,3%)
OLIGODENDROGLIOMA	2 (0,7%)
HODGKIN LYMPHOMA	1 (0,3%)
BRAIN STEM MTS.....	2 (0,7%)
INCHARACTERISTICS FINDINGS.....	25 (8.3%)

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CNS lymphoma

- High incidence (1 a 10-12%)
- Most frequent non infectious disease found on AIDS patients
- Incidence: 2.7% in clinical series and 1 -15% in autopsies

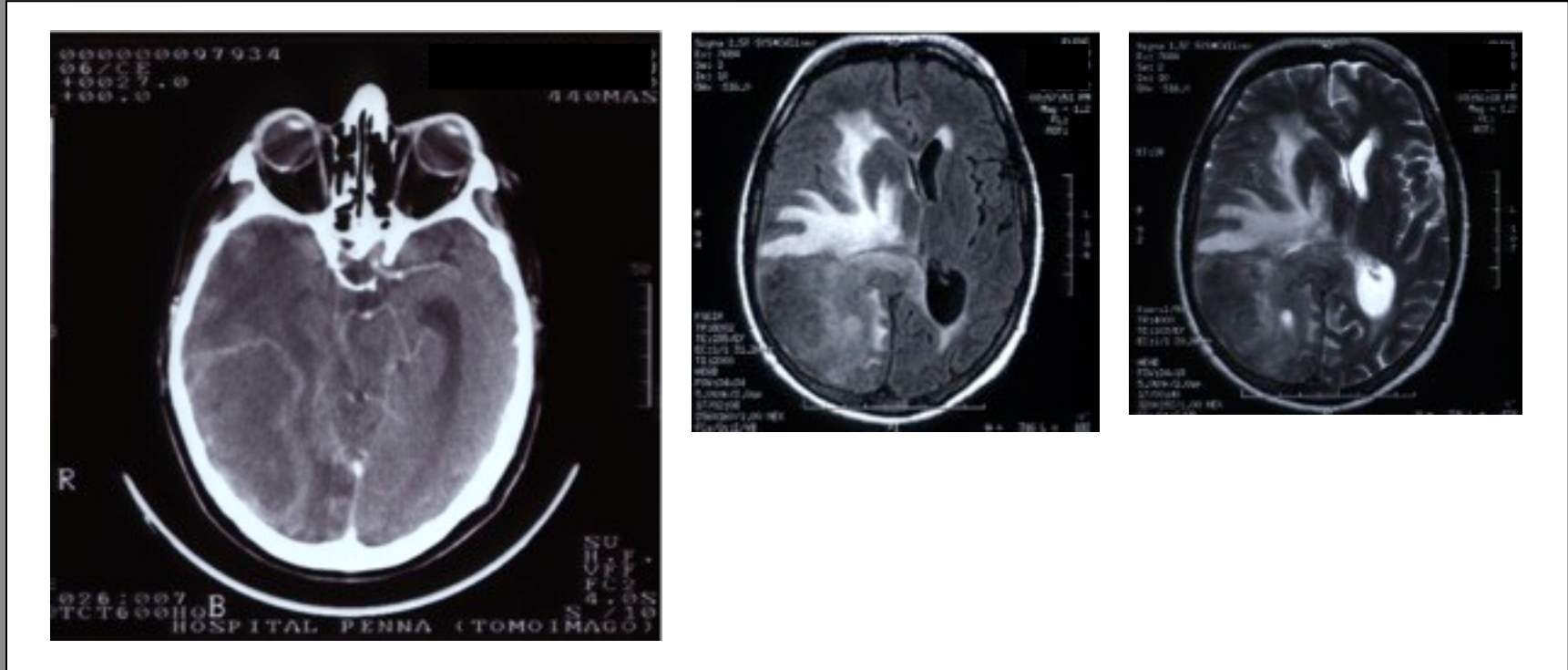
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CNS lymphoma

- Related with immunosuppression
- High grade, diffuse B- cells Tumors
- Multiple and bilateral
- Related with Epstein Barr Virus
- Single periventricular lesions
- Multiple infra and supratentorial lesions
- MRI Spectroscopy : high coline, low NAA and presence of fat and lactate

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35 years old male, headaches and seizures
CD4 < 50 cells



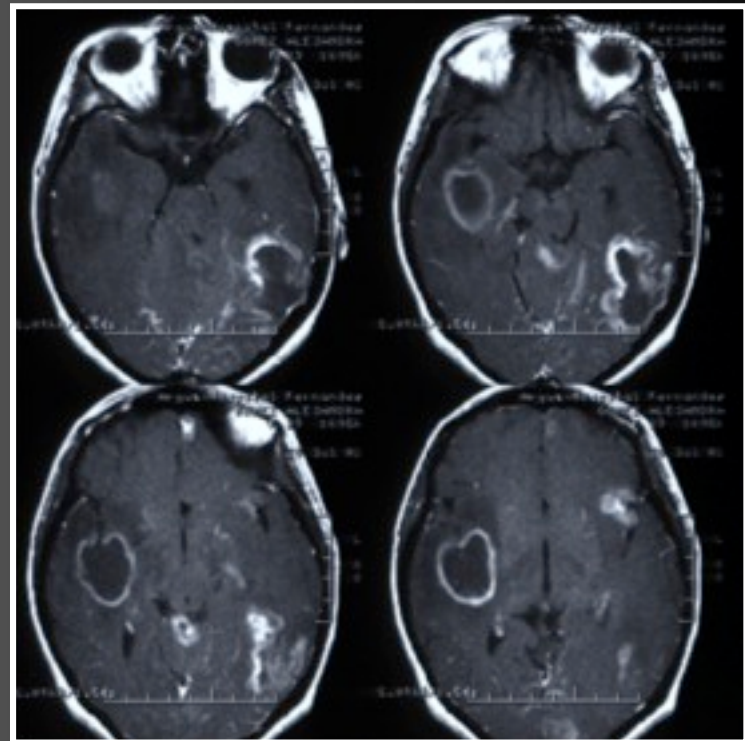
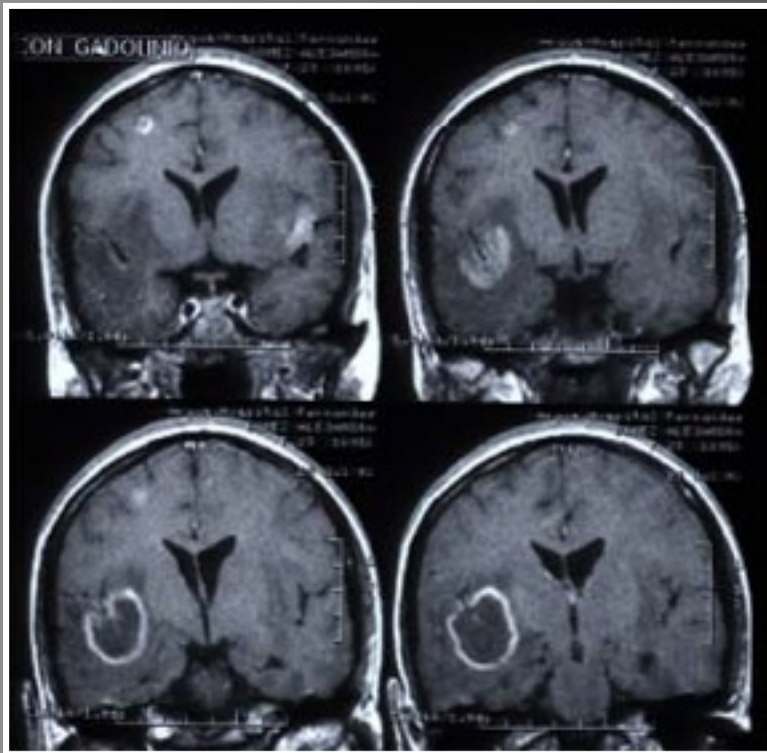
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28 years old male, right hemiparesia and seizures
CD4 < 50 cells



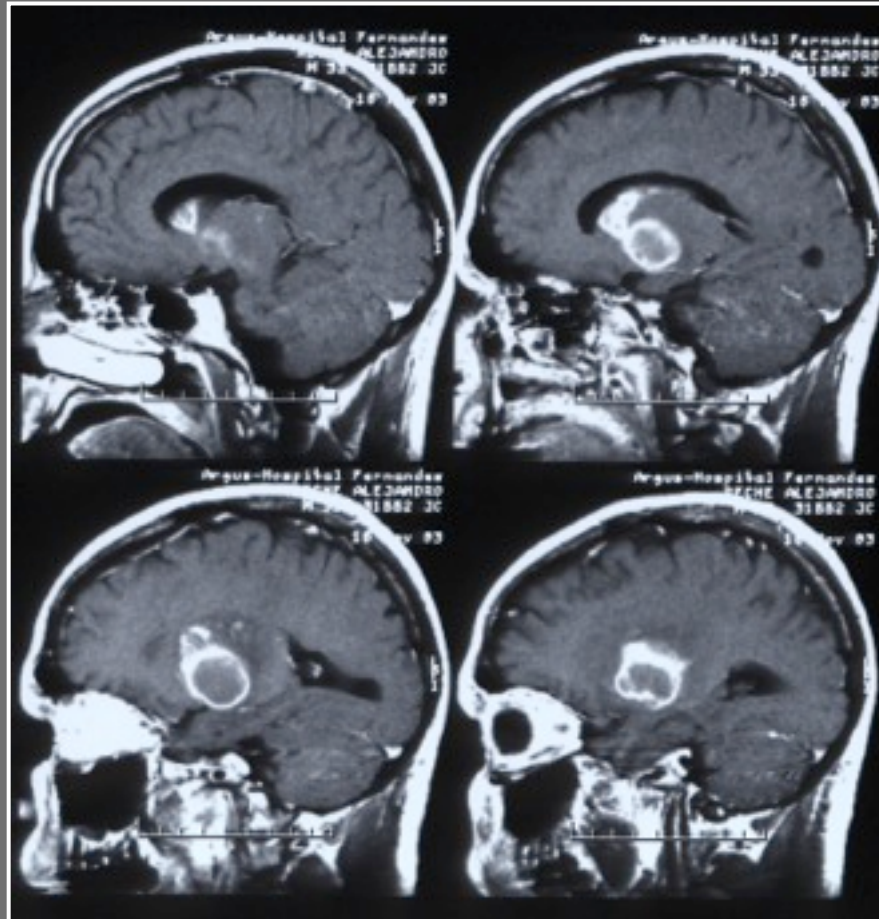
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25 years old female, seizures and headaches
CD4 < 50 cells



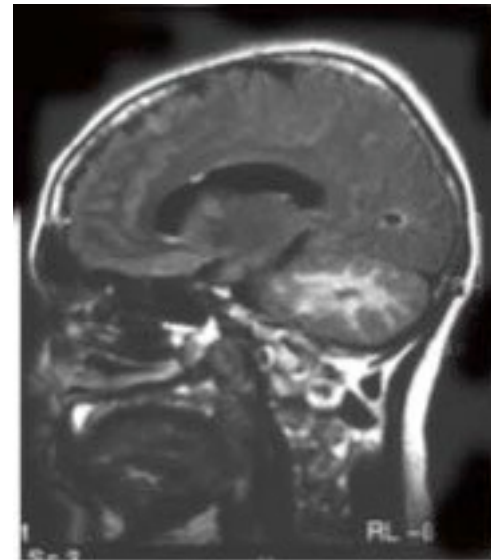
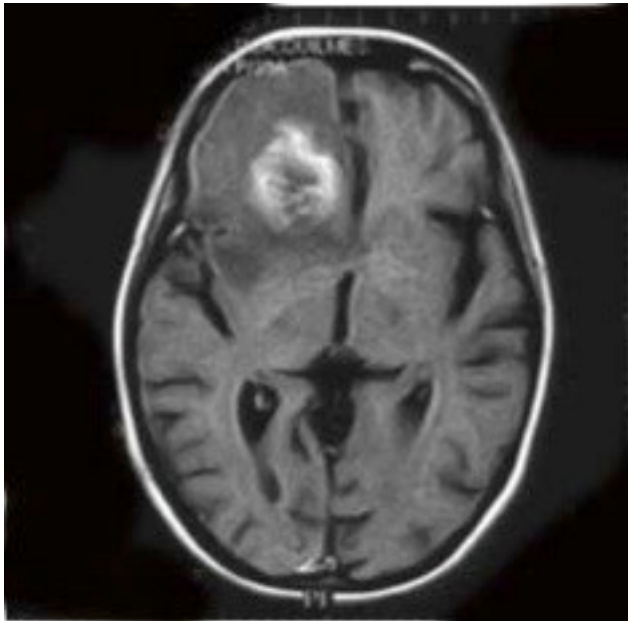
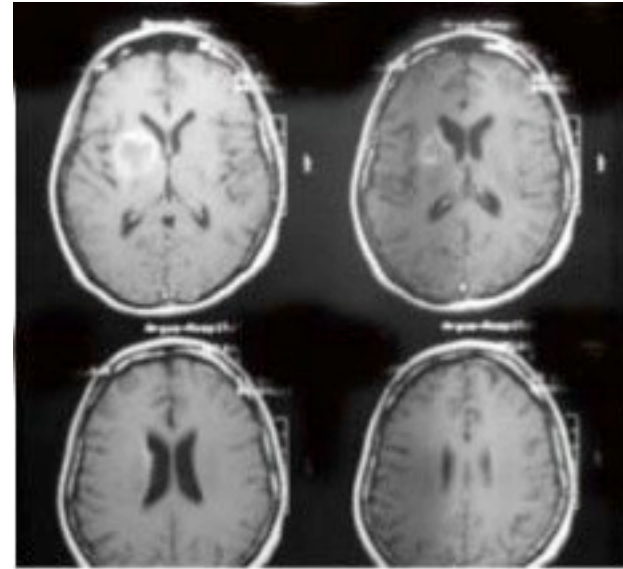
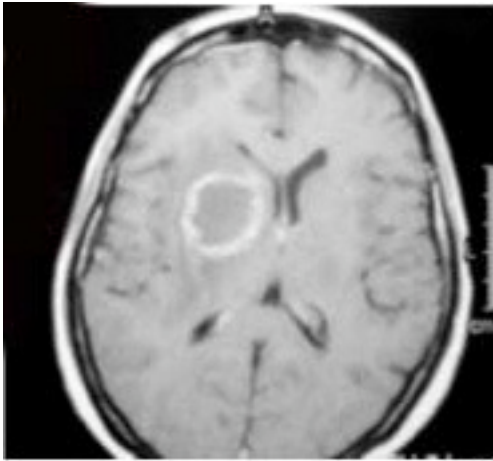
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CNS lymphoma



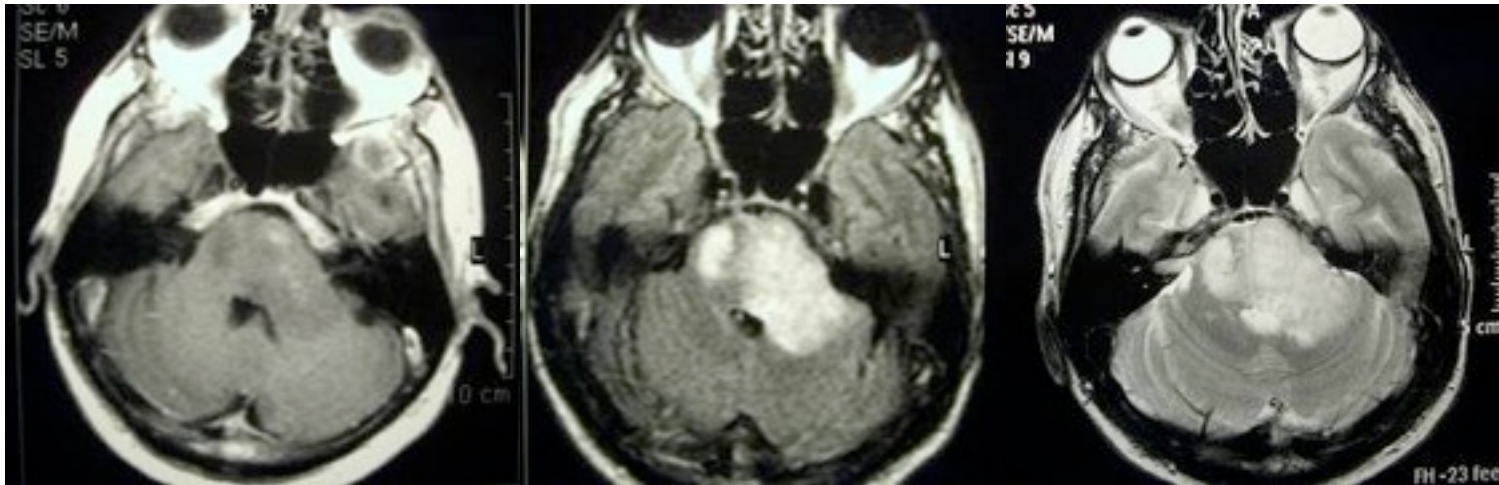
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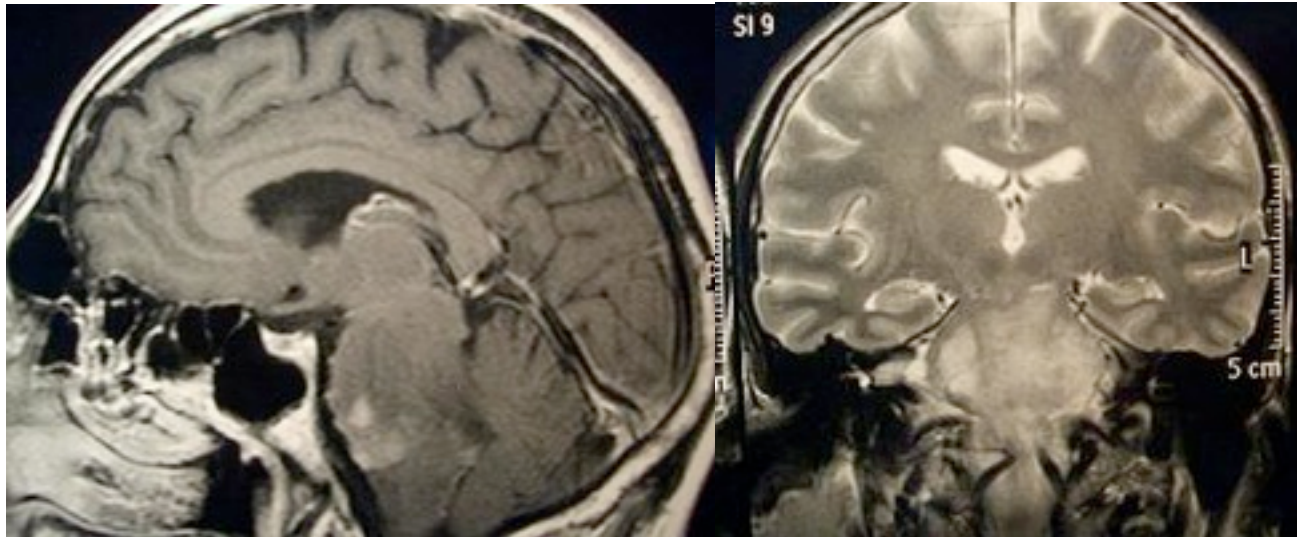
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CNS lymphoma



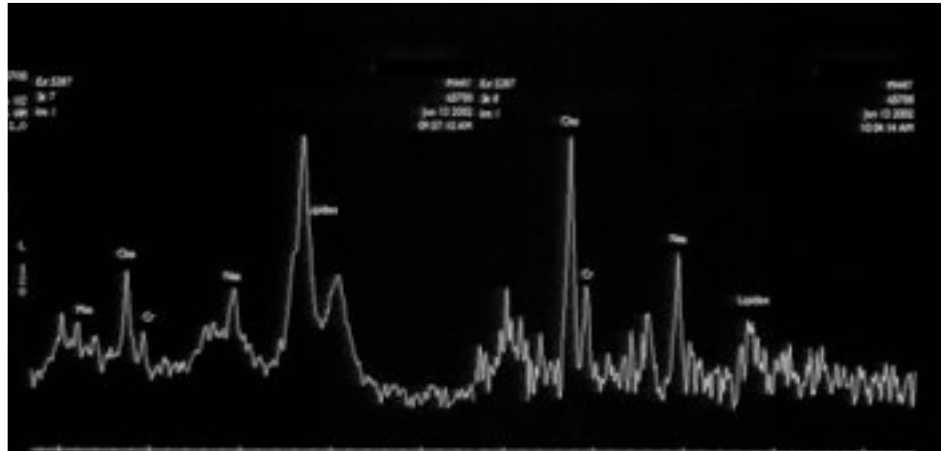
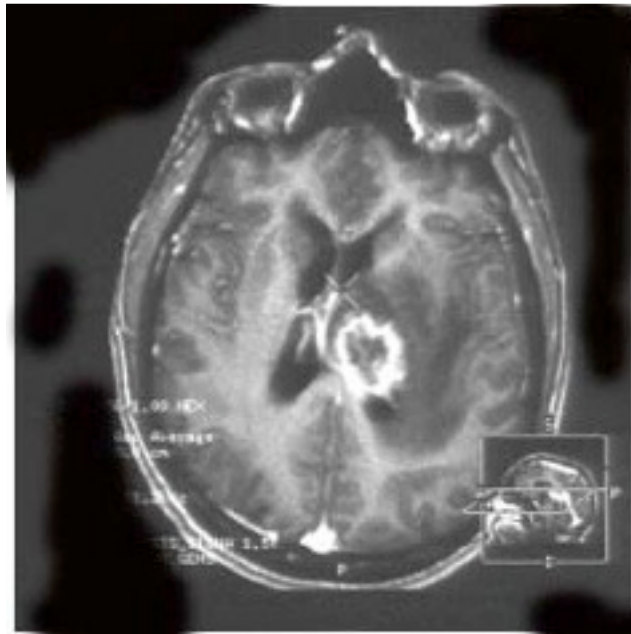
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CNS lymphoma



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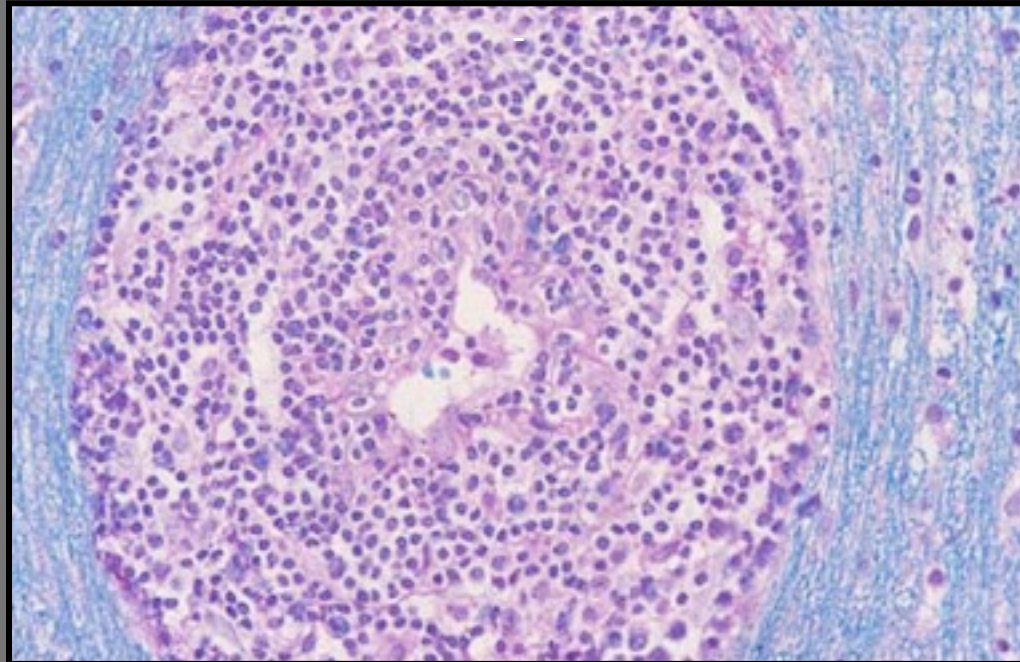
CNS lymphoma



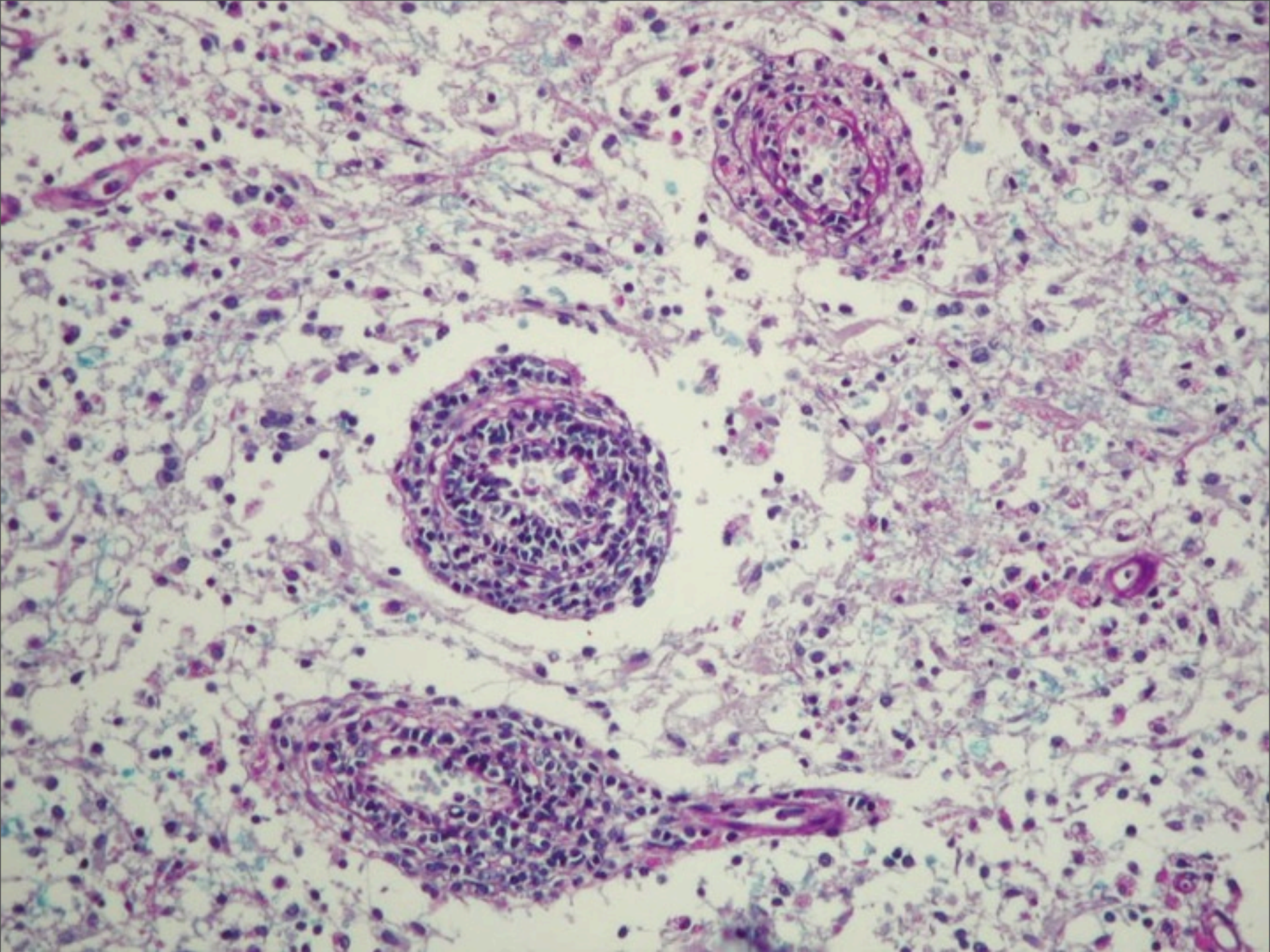
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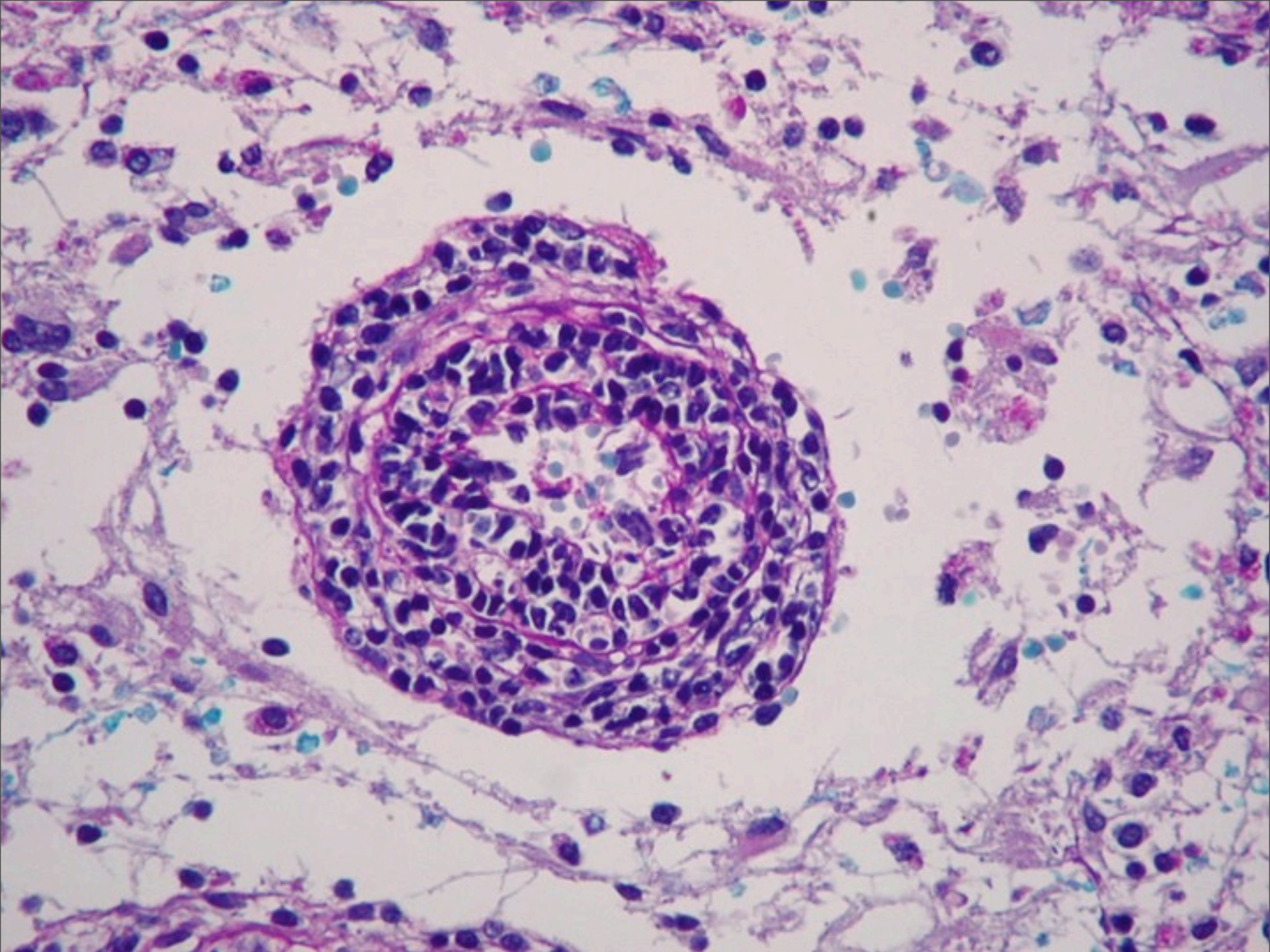
CNS lymphoma

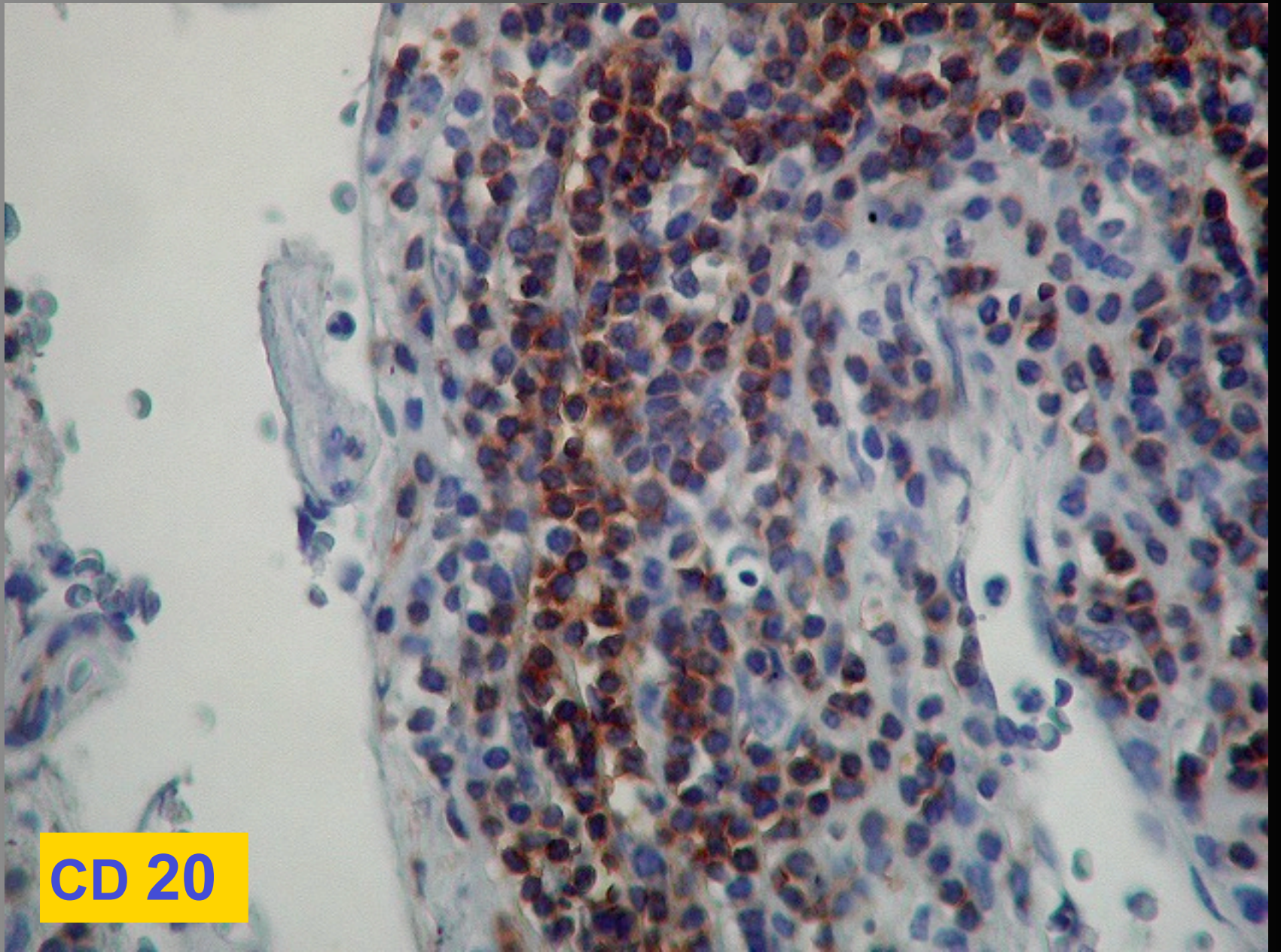
-Lymphoid cells in the perivascular space



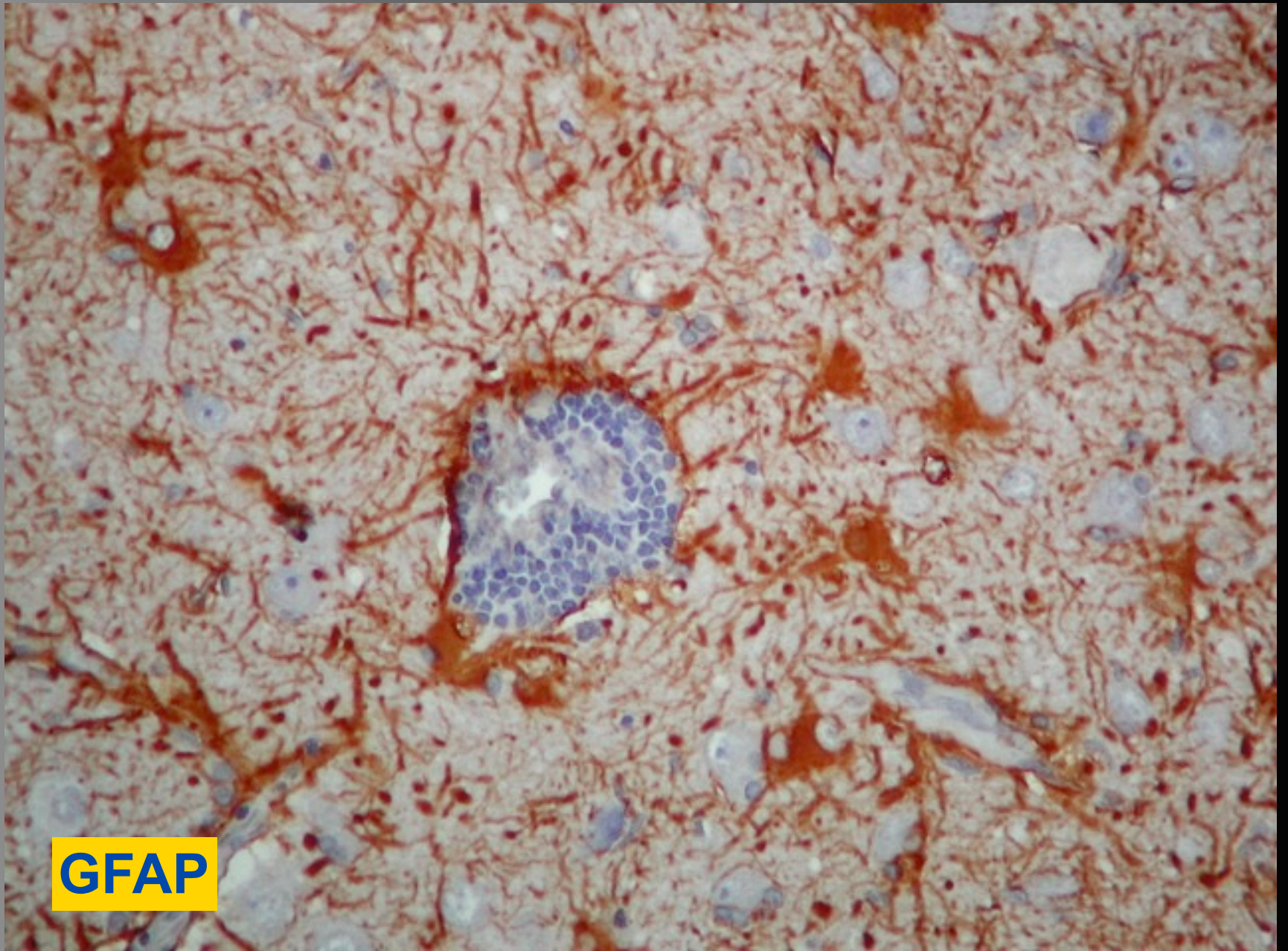
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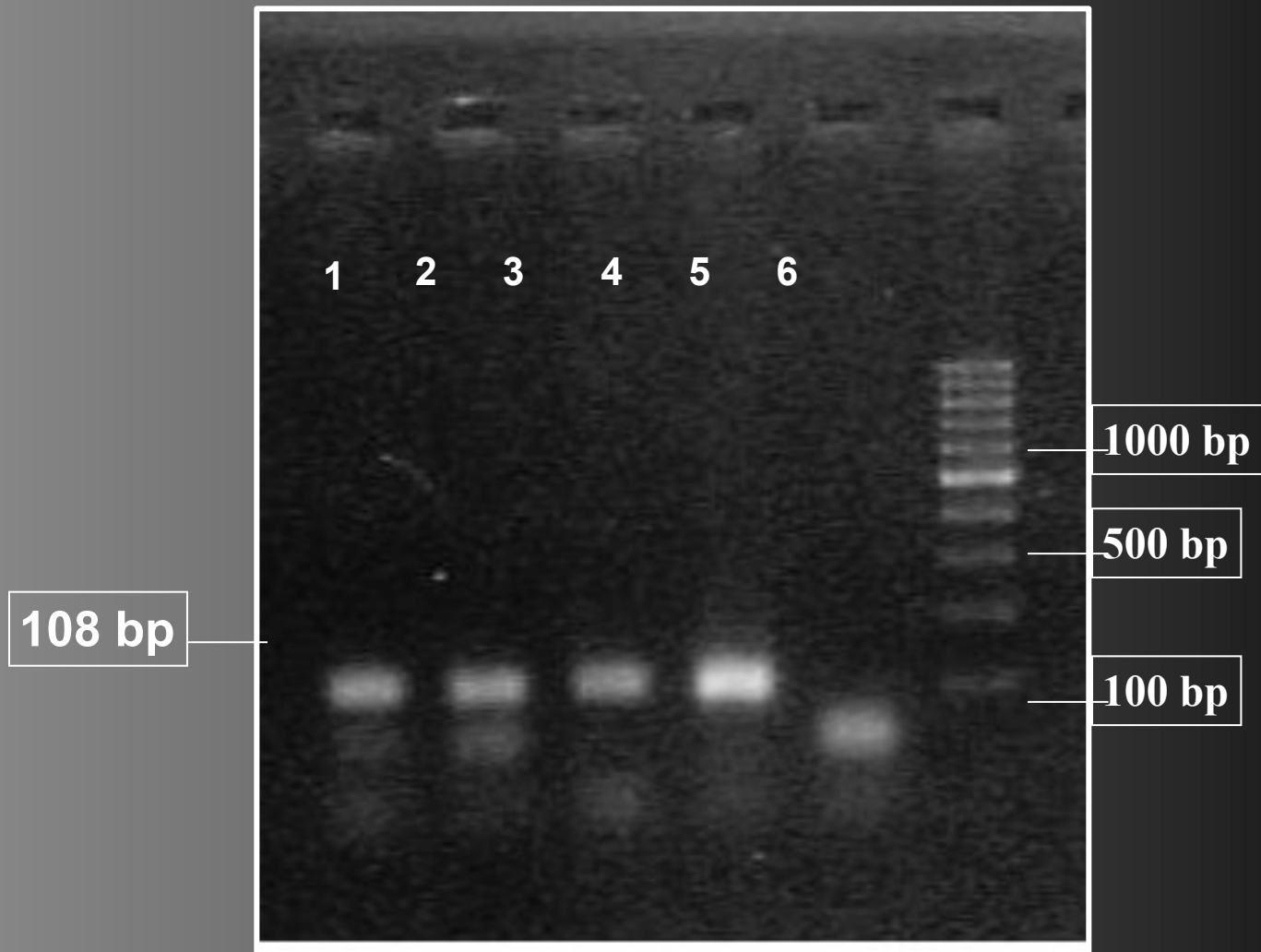




CD 20



GFAP



PCR- Epstein Barr

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- Circulating Epstein-Barr virus (EBV) in HIV-infected patients and its relation with primary brain lymphoma
International Journal of Infectious Diseases 11, 172-178 (2007)

- Epstein-Barr virus genotypes and LMP-1 variants in HIV infected patients
Journal of Medical Virology 79: 401-407 (2007)

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Glucocorticoid therapy obscures the diagnosis of cerebral lymphoma

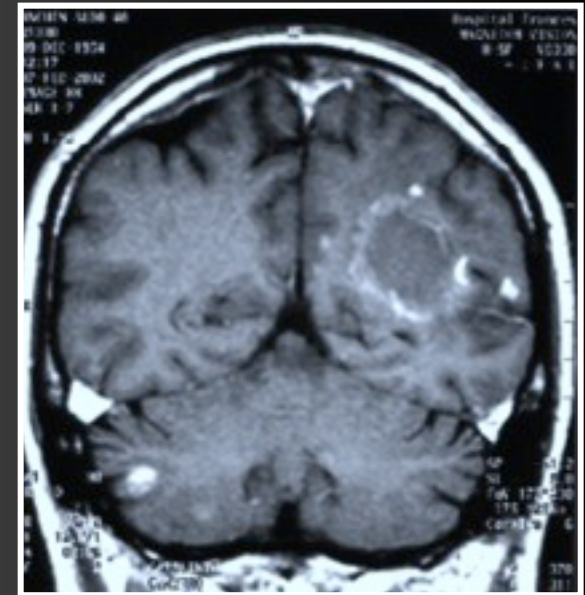
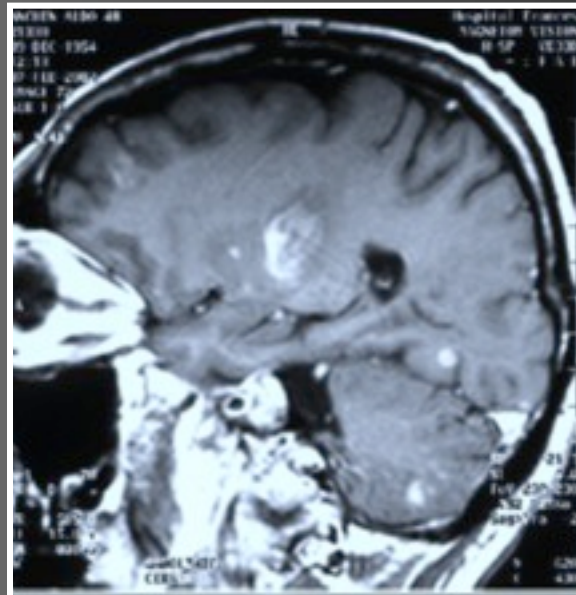
M. Geppert¹, CB. Ostertag², G. Seitz¹, and M. Kiessling¹

¹ Institut für Pathologie and ² Abteilung für Stereotaktische Neurochirurgie, Universitäts-Klinikum, Universität des Saarlandes, D-6650 Homburg, Federal Republic of Germany

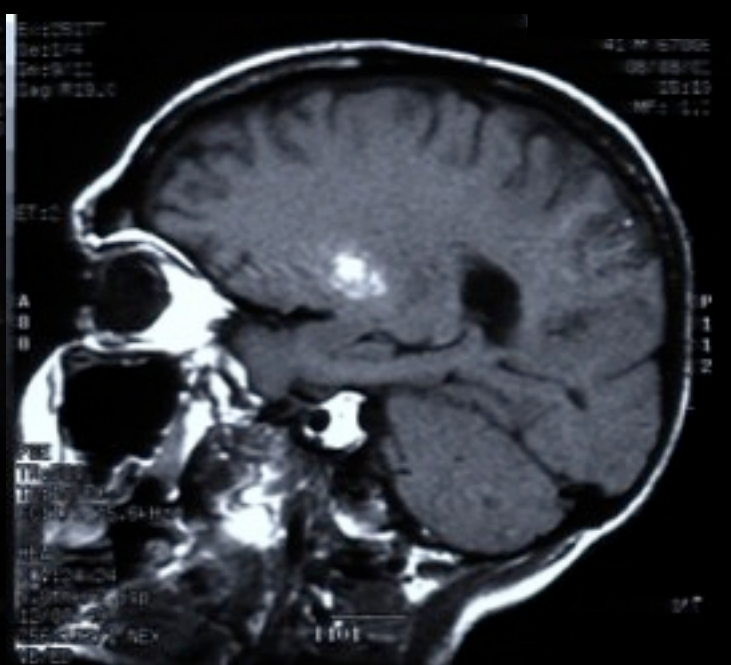
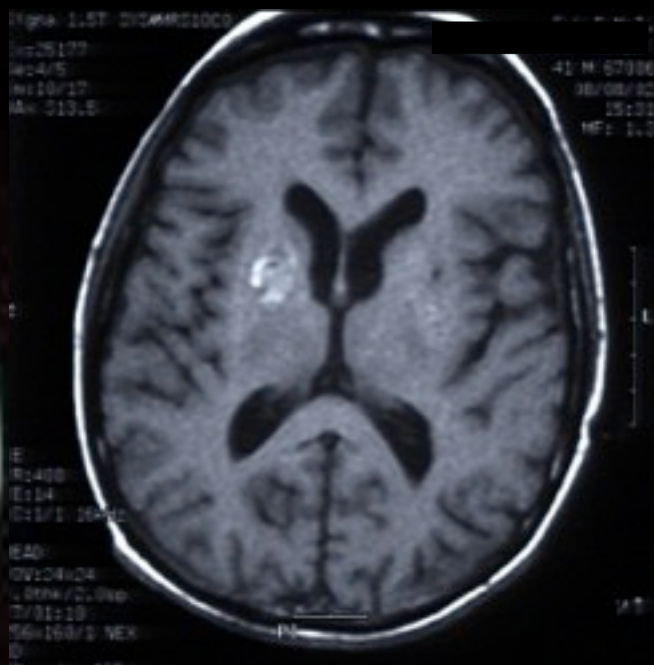
Received December 8, 1989/Revised, accepted April 25, 1990

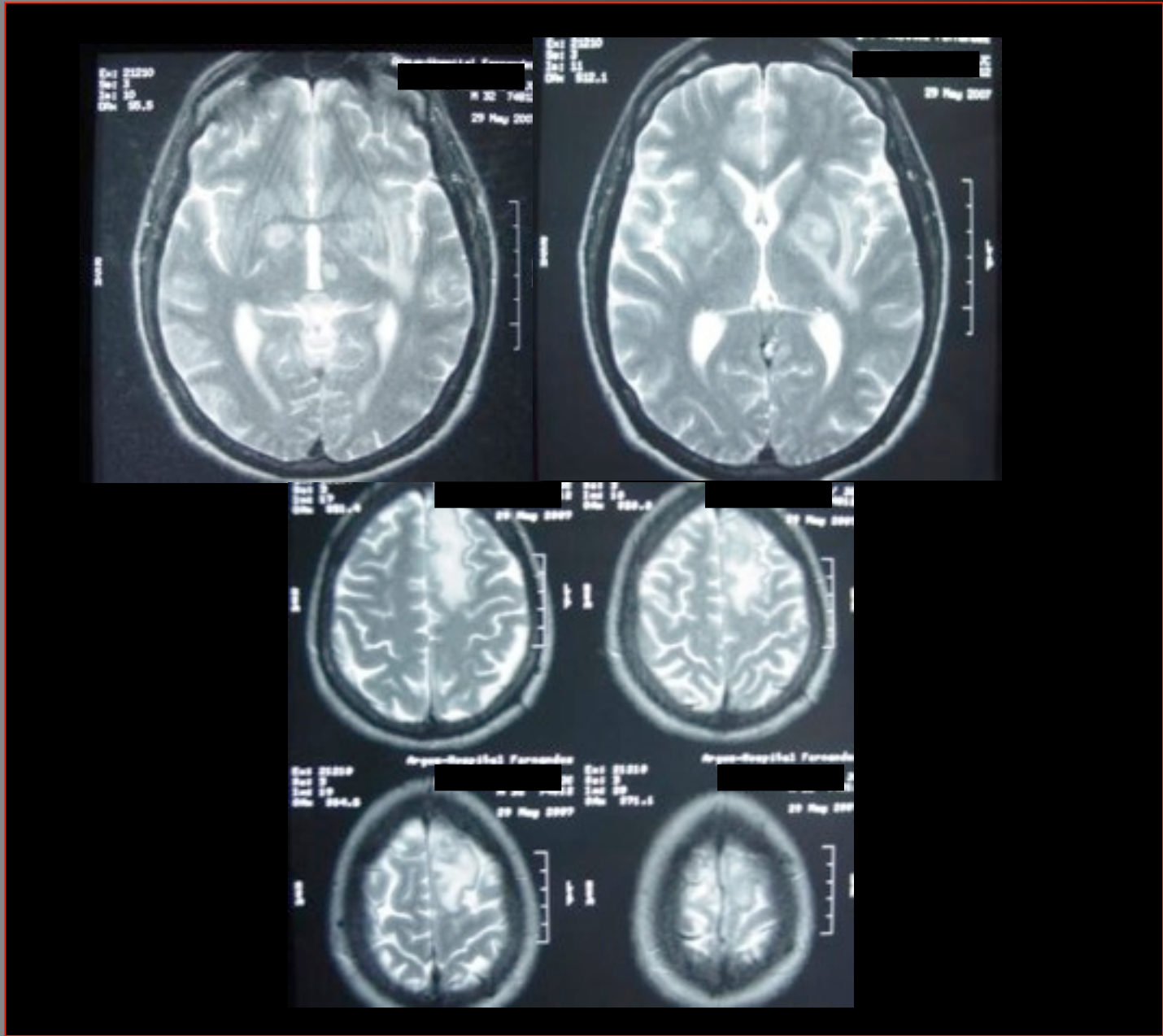
TOXOPLASMOSIS

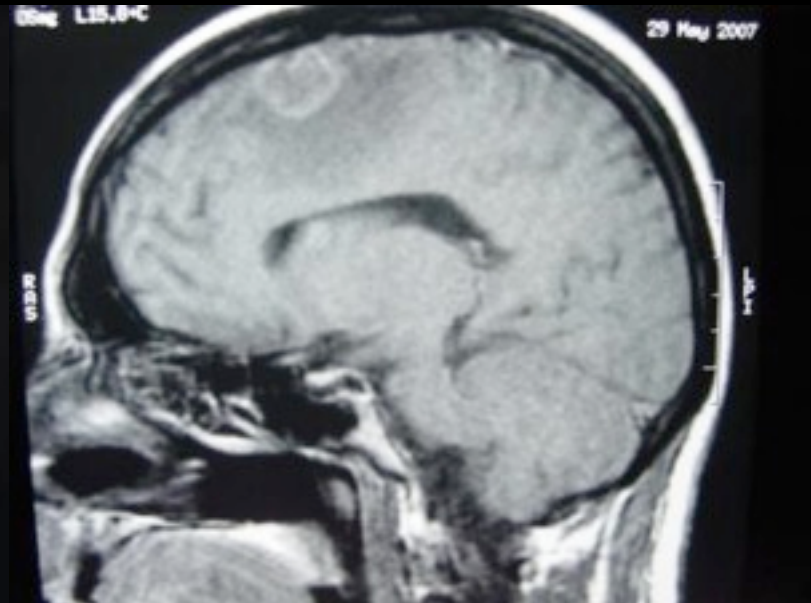
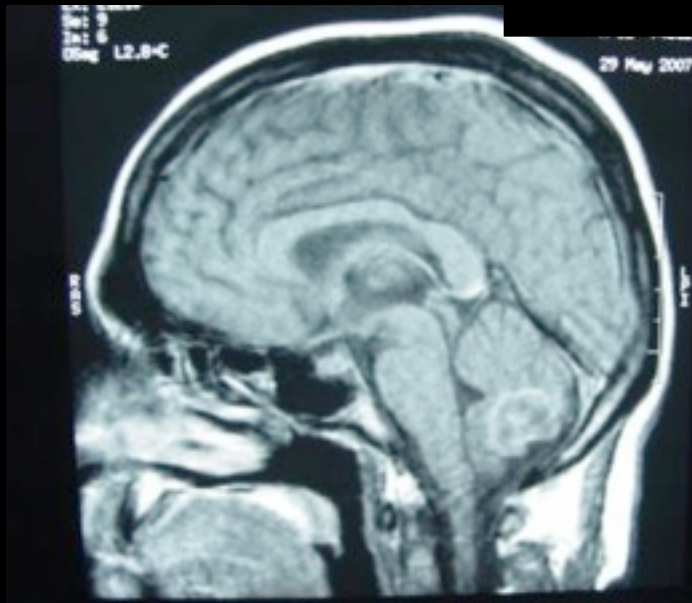
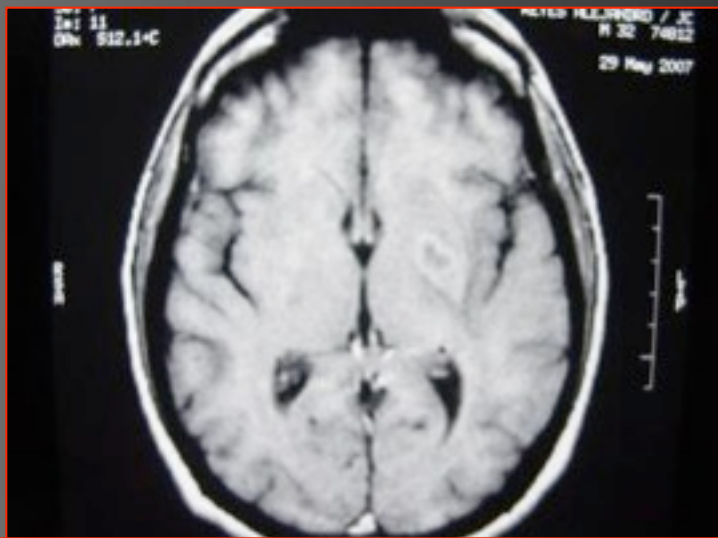
47 years old male, headaches and focal symptoms, CD4 < 50 cells

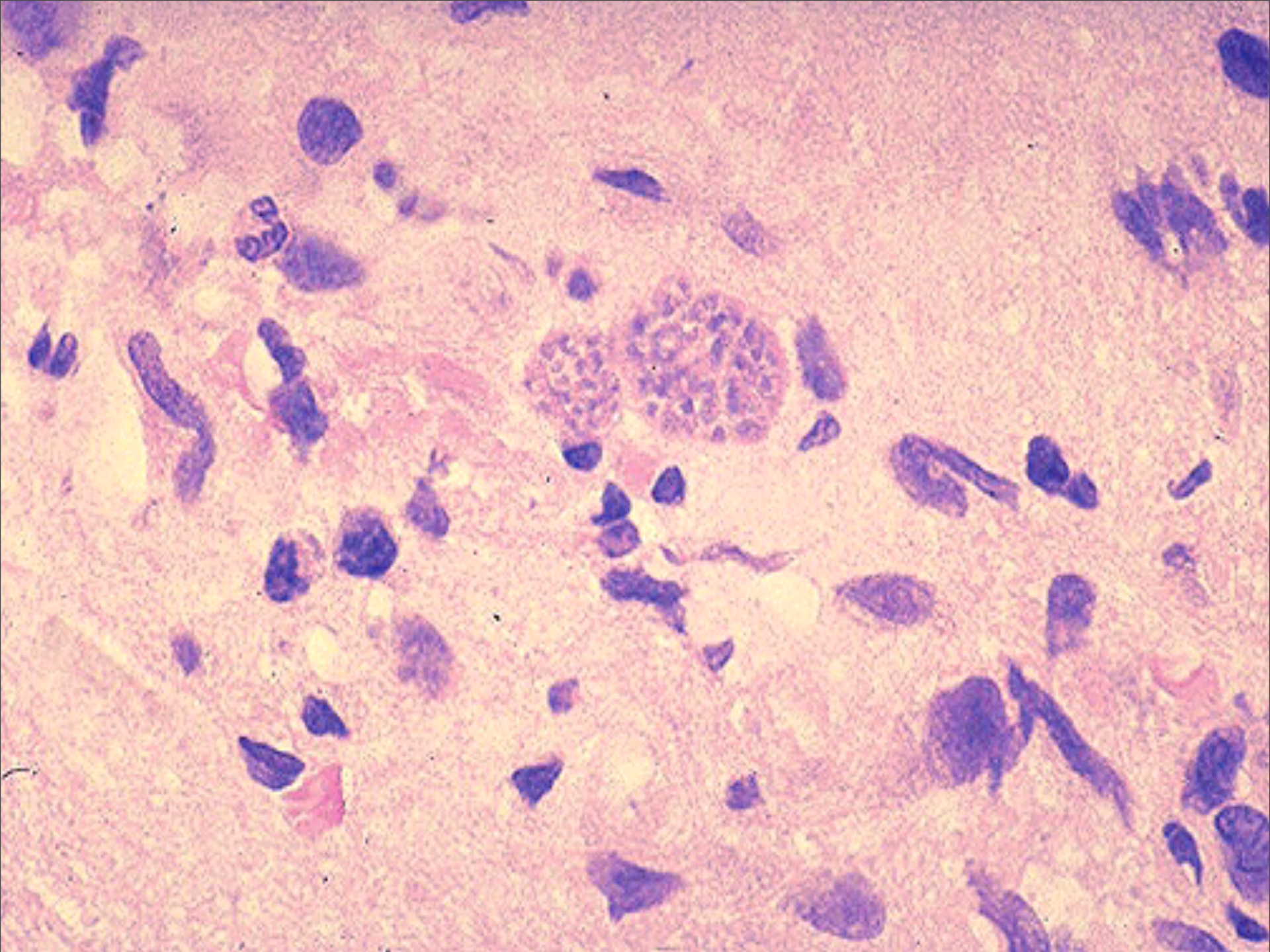


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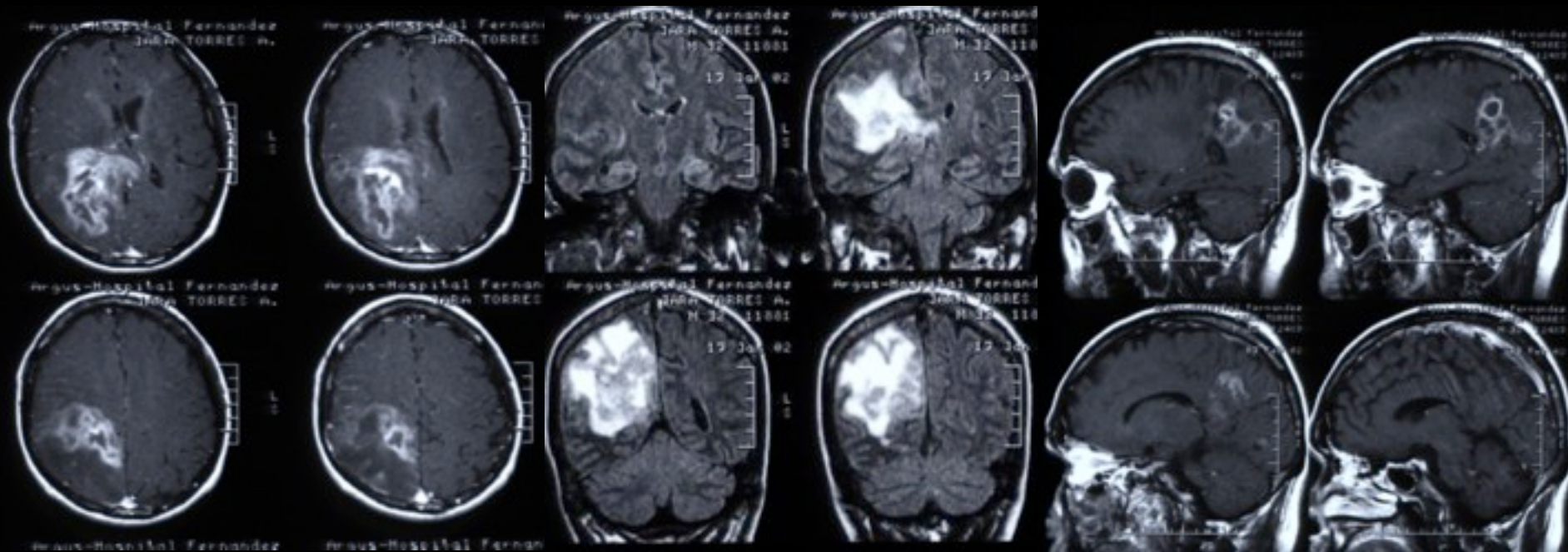




Chagas disease

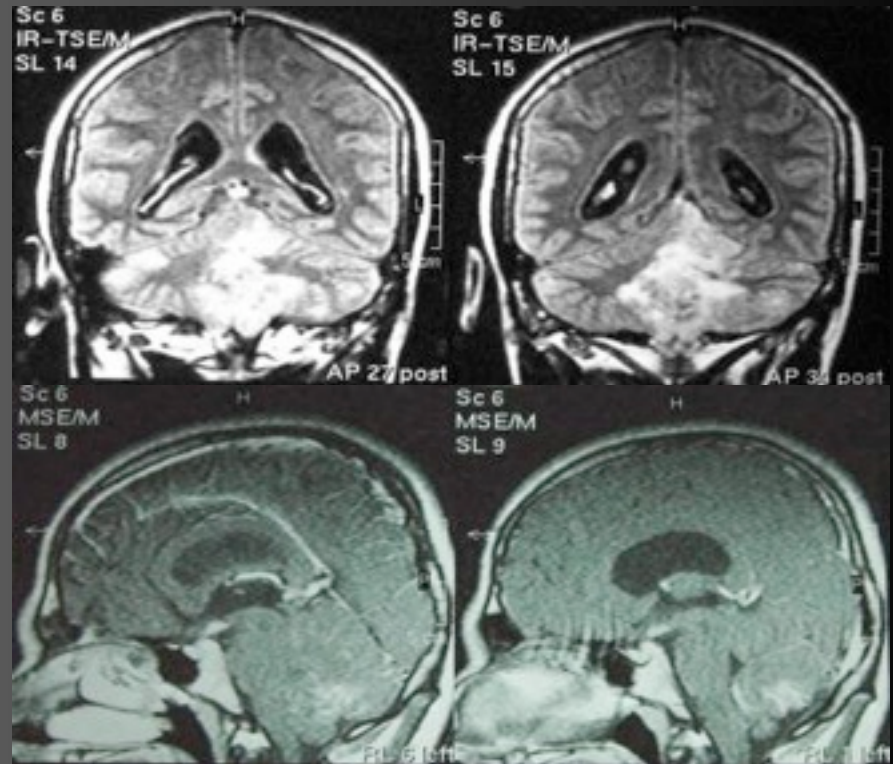
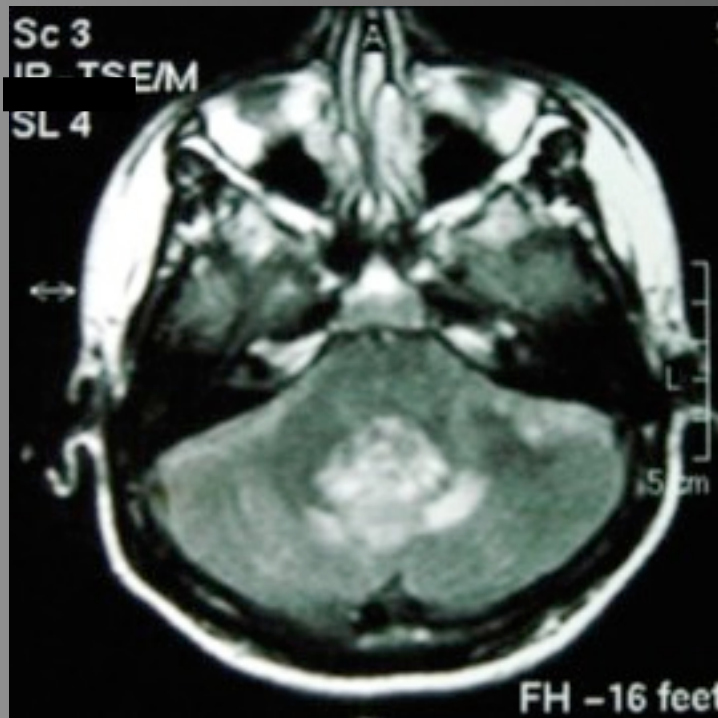
- Meningoencephalitis
- Brain Chagomas

32 years old male, headaches and left hemiparesia,
CD4 < 50 cells

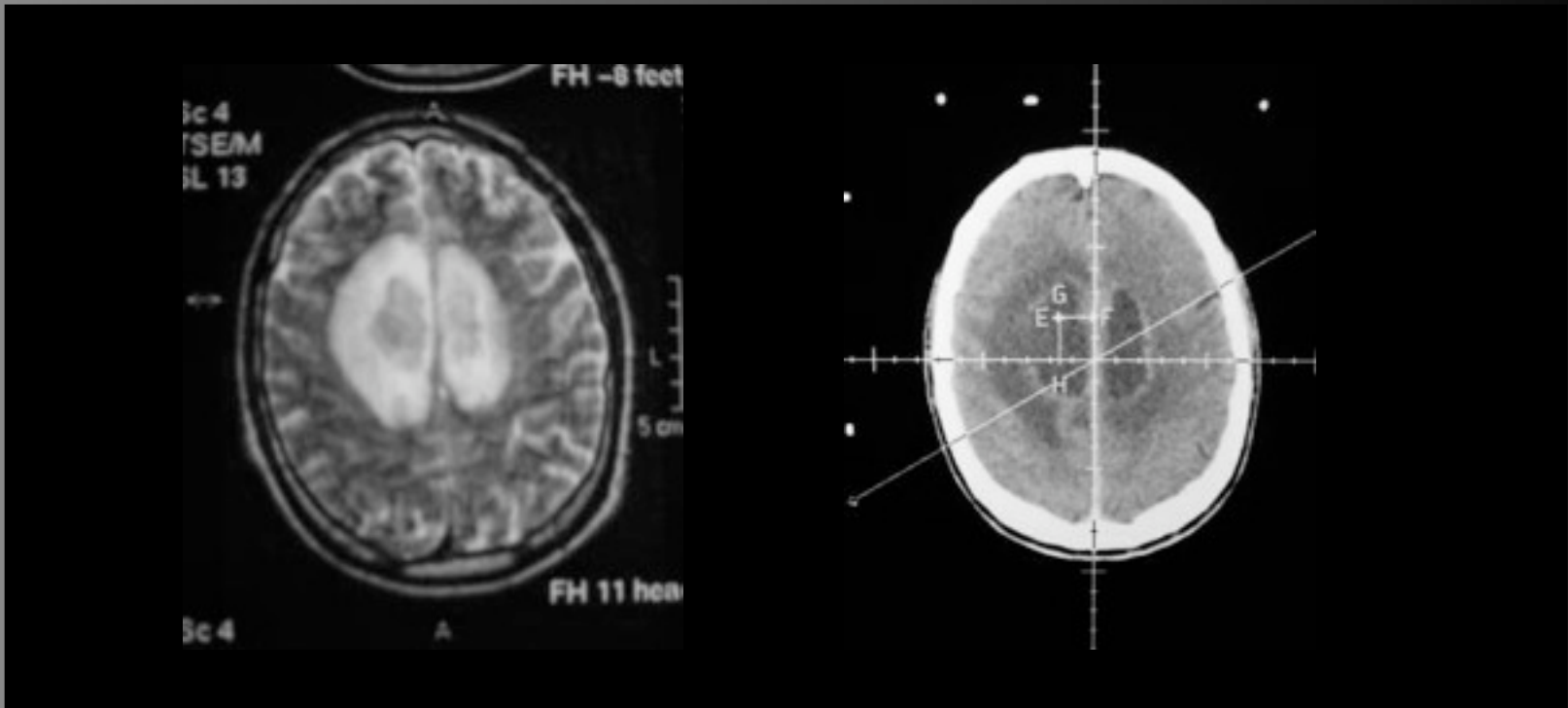


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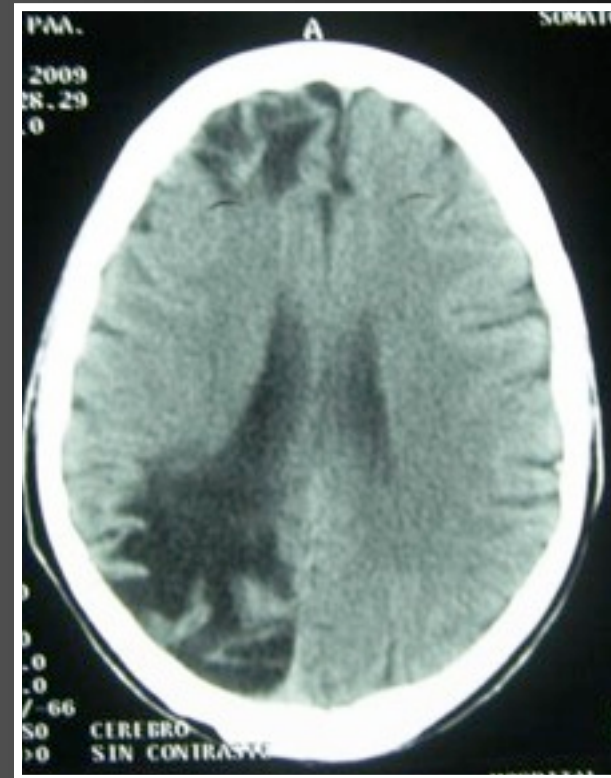
24 years old male, headaches. CD4 < 50 cells



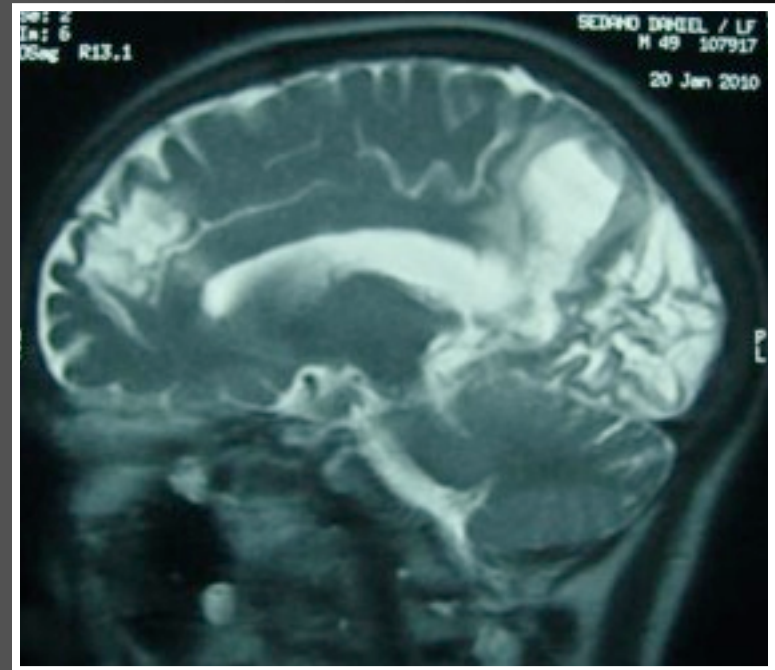
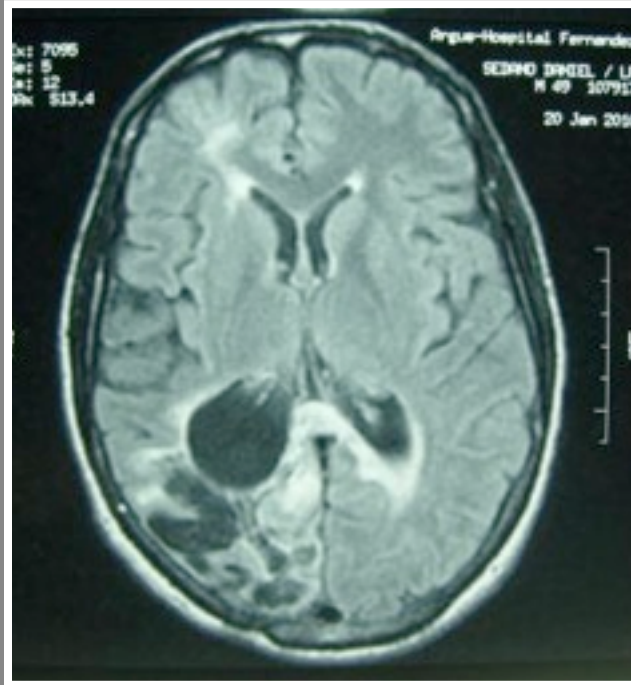
55 years old male. seizures CD 4 < 50 cells



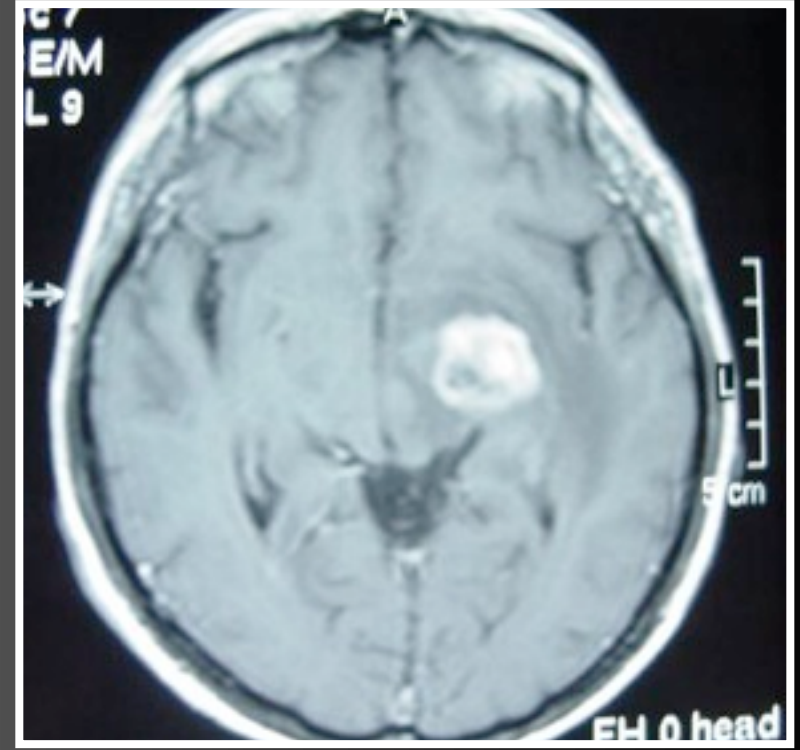
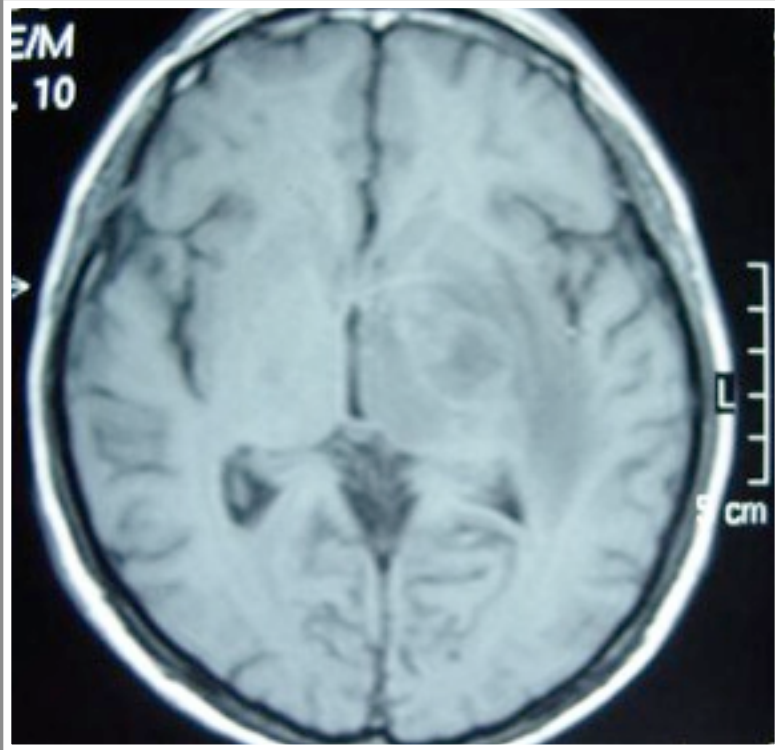
Chagas disease



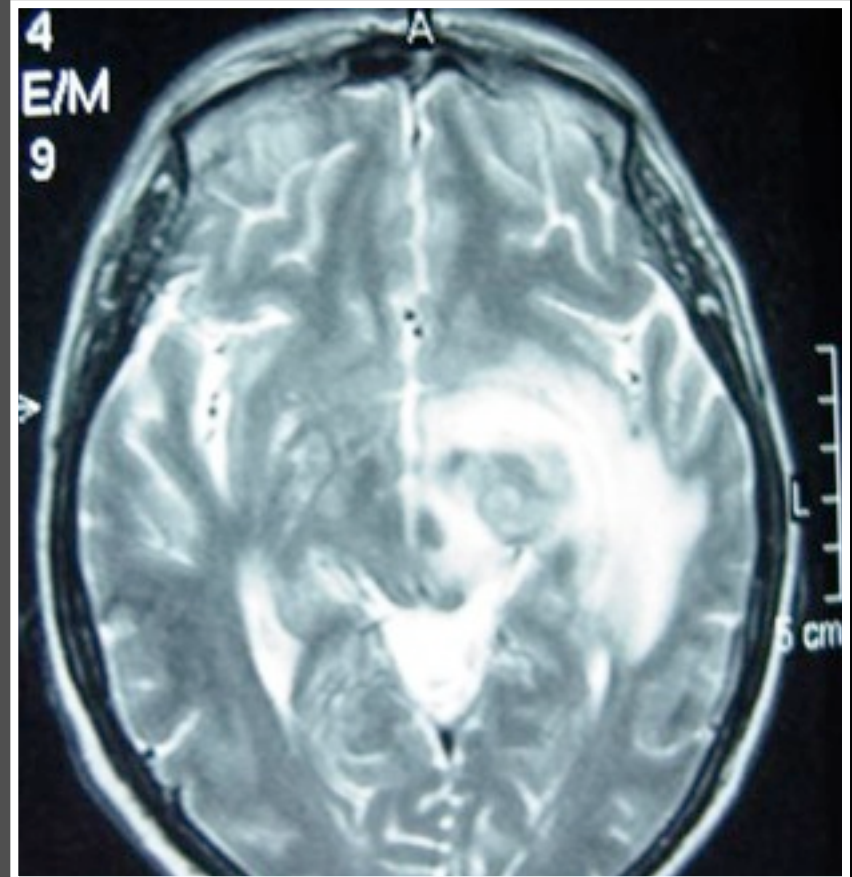
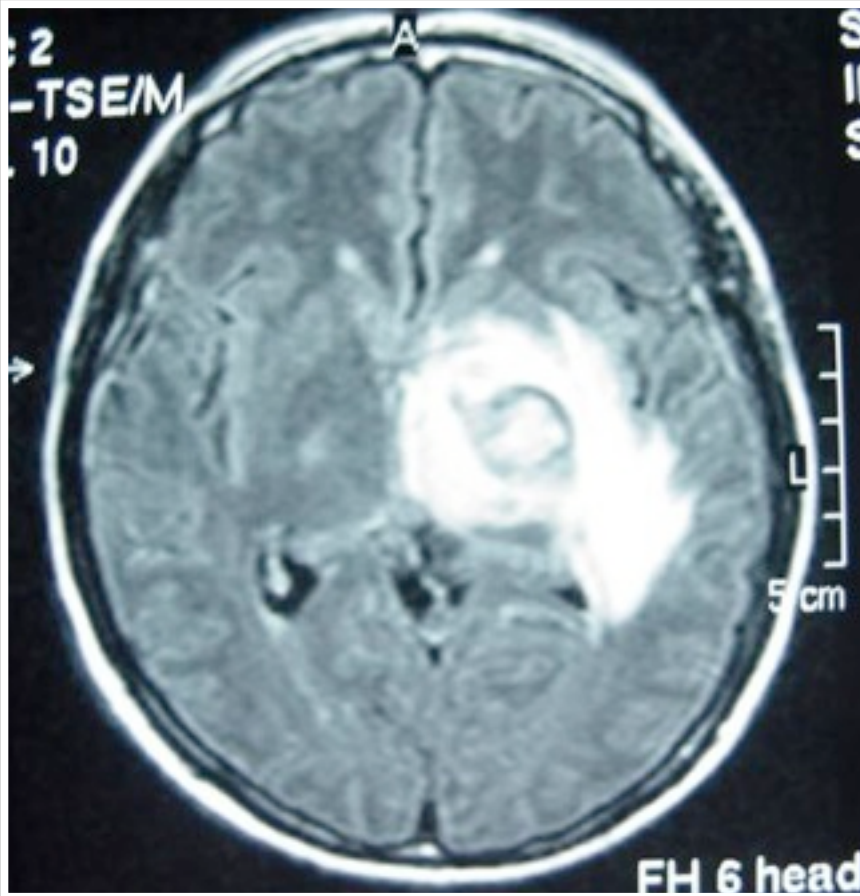
Chagas disease

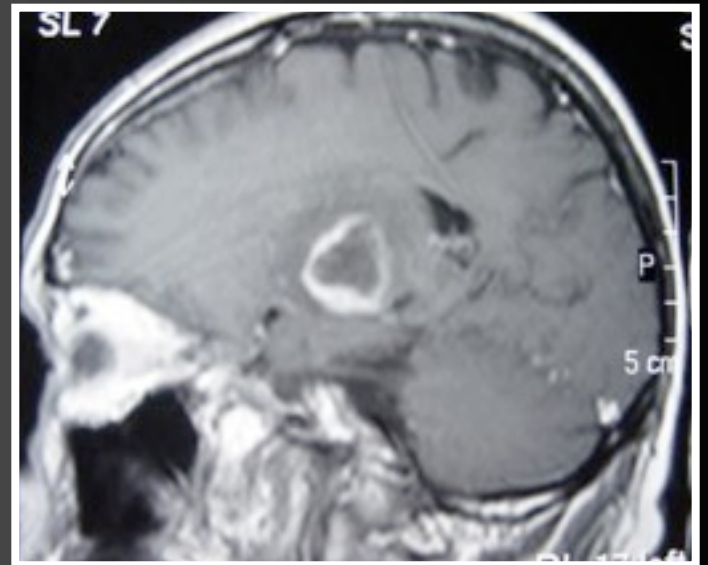
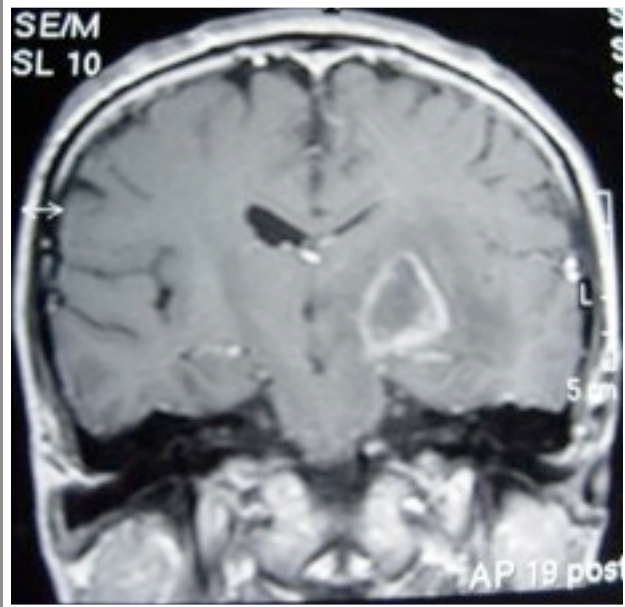
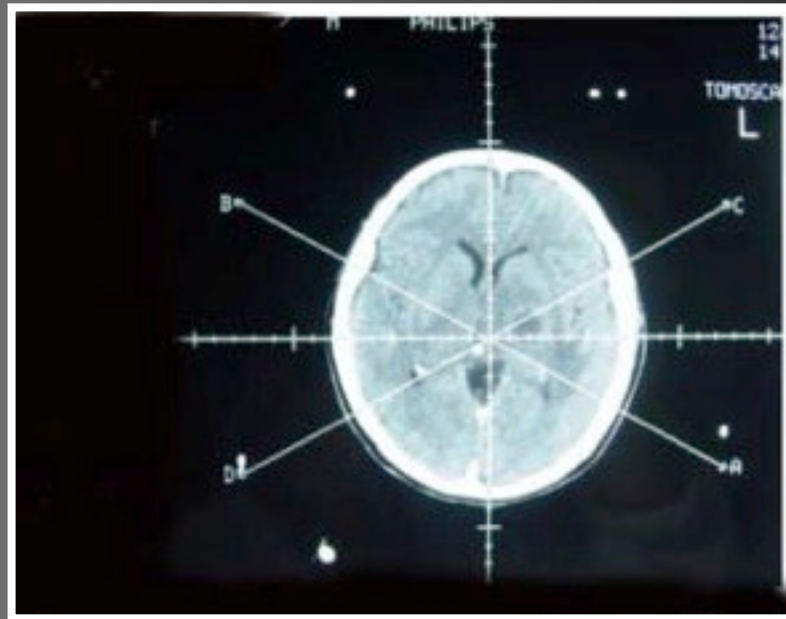


Chagas disease

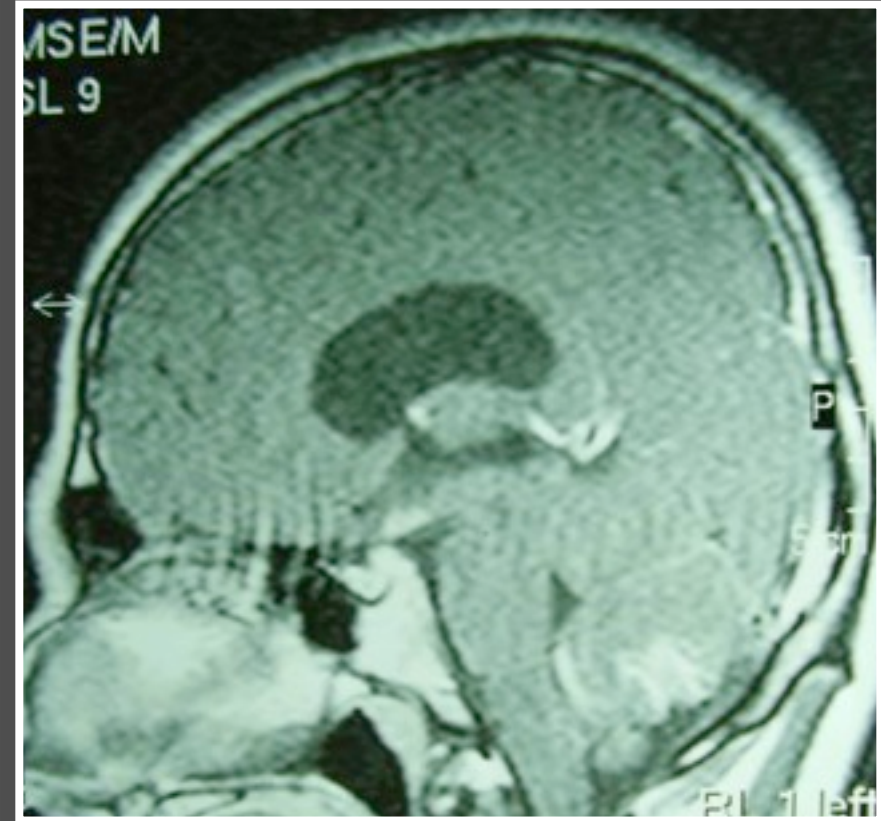
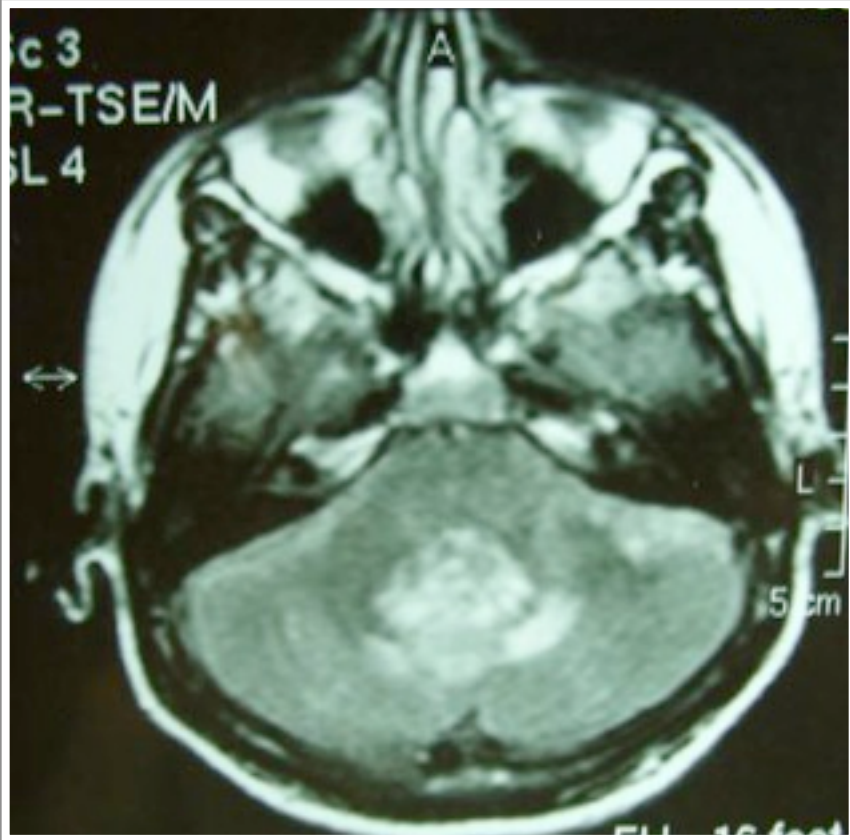


Chagas disease

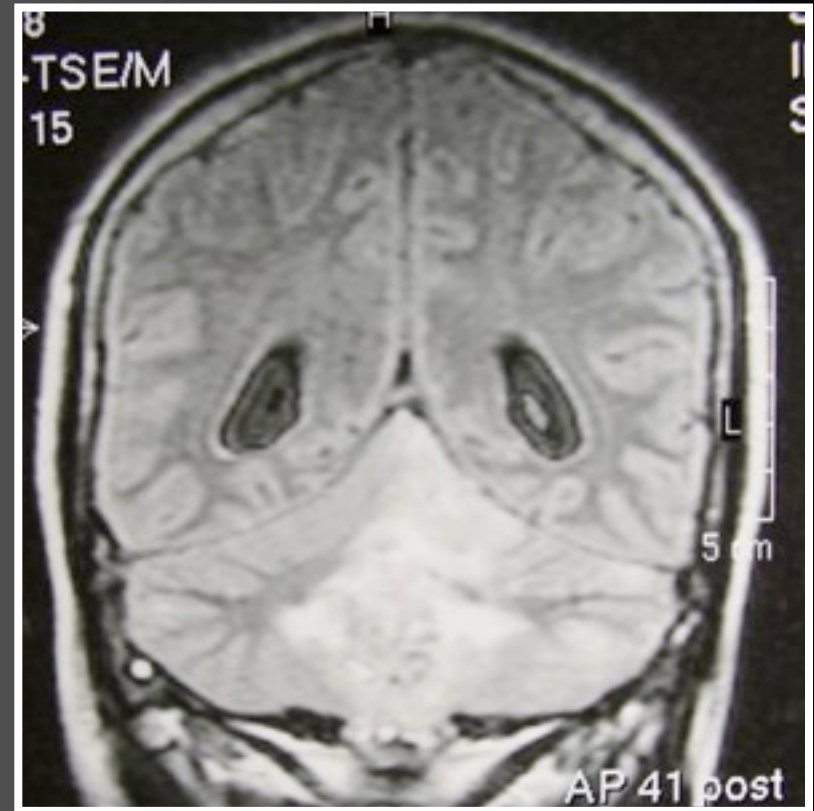
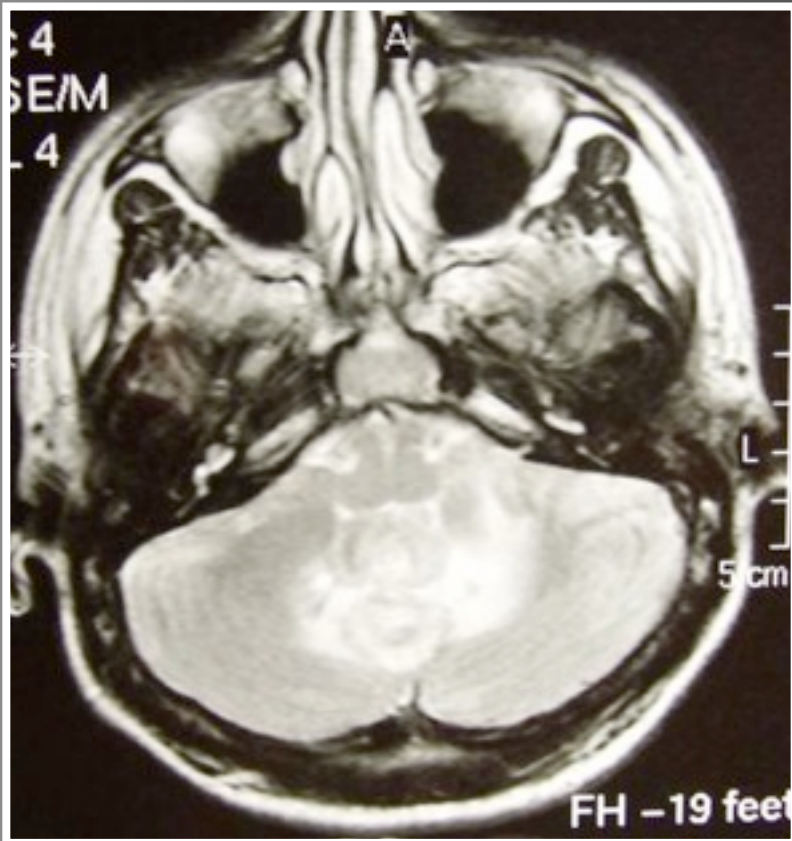




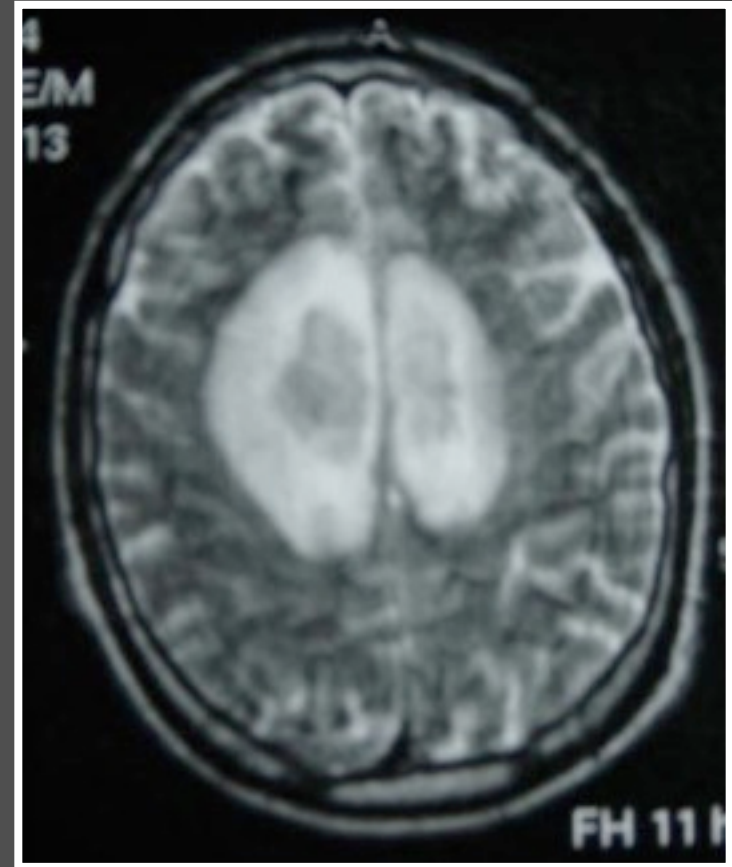
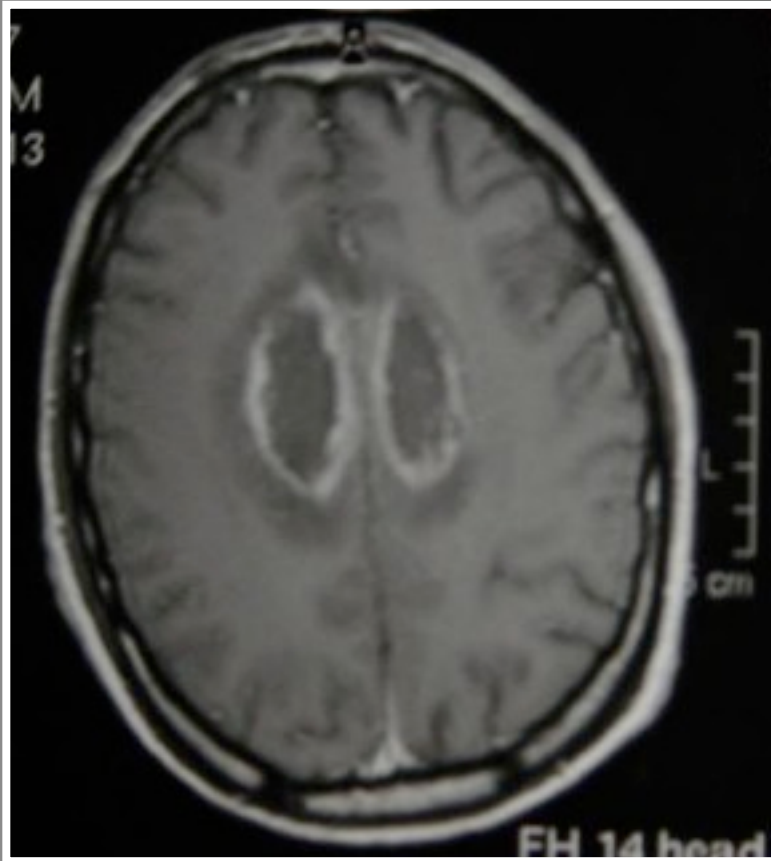
Chagas disease

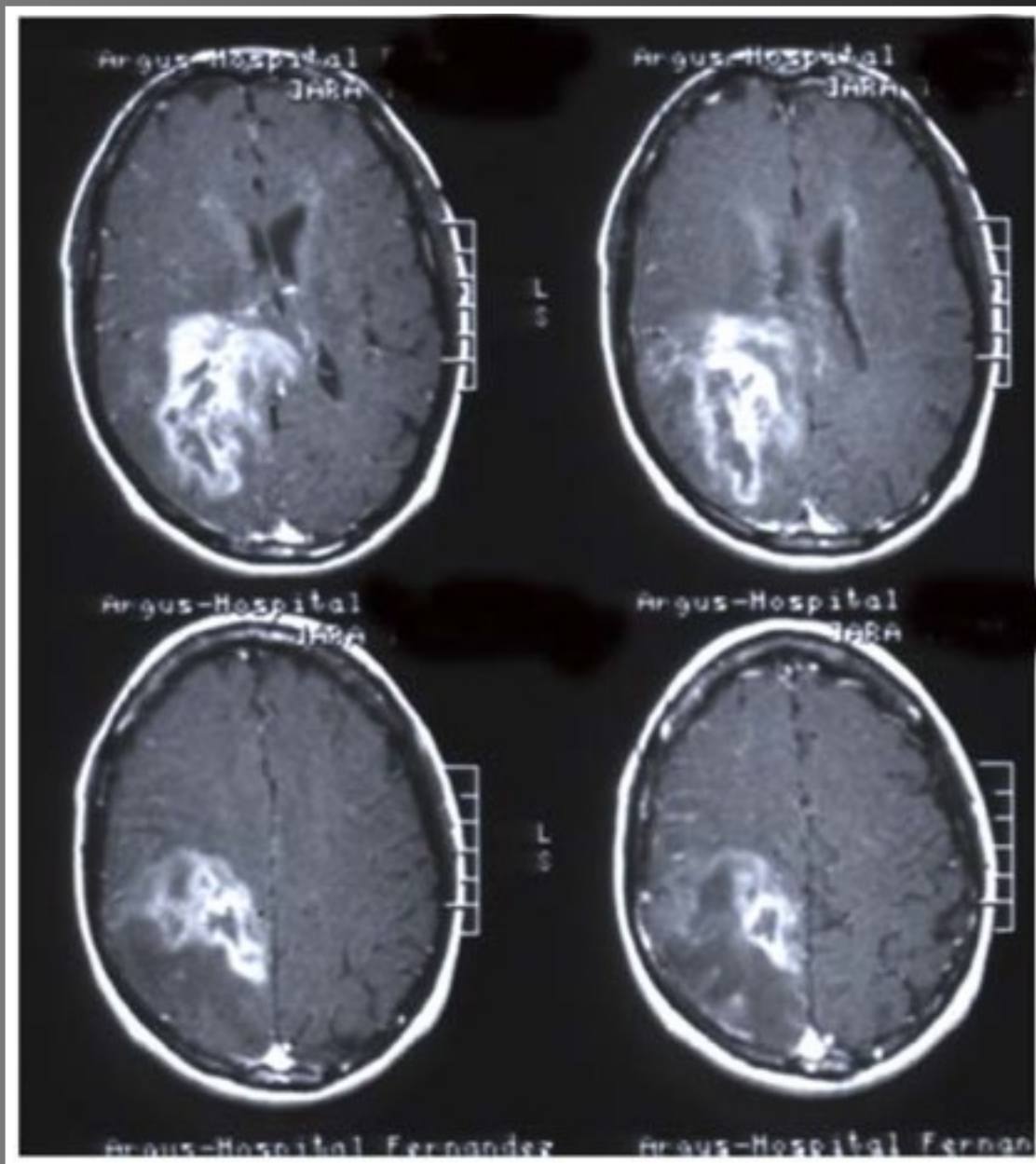


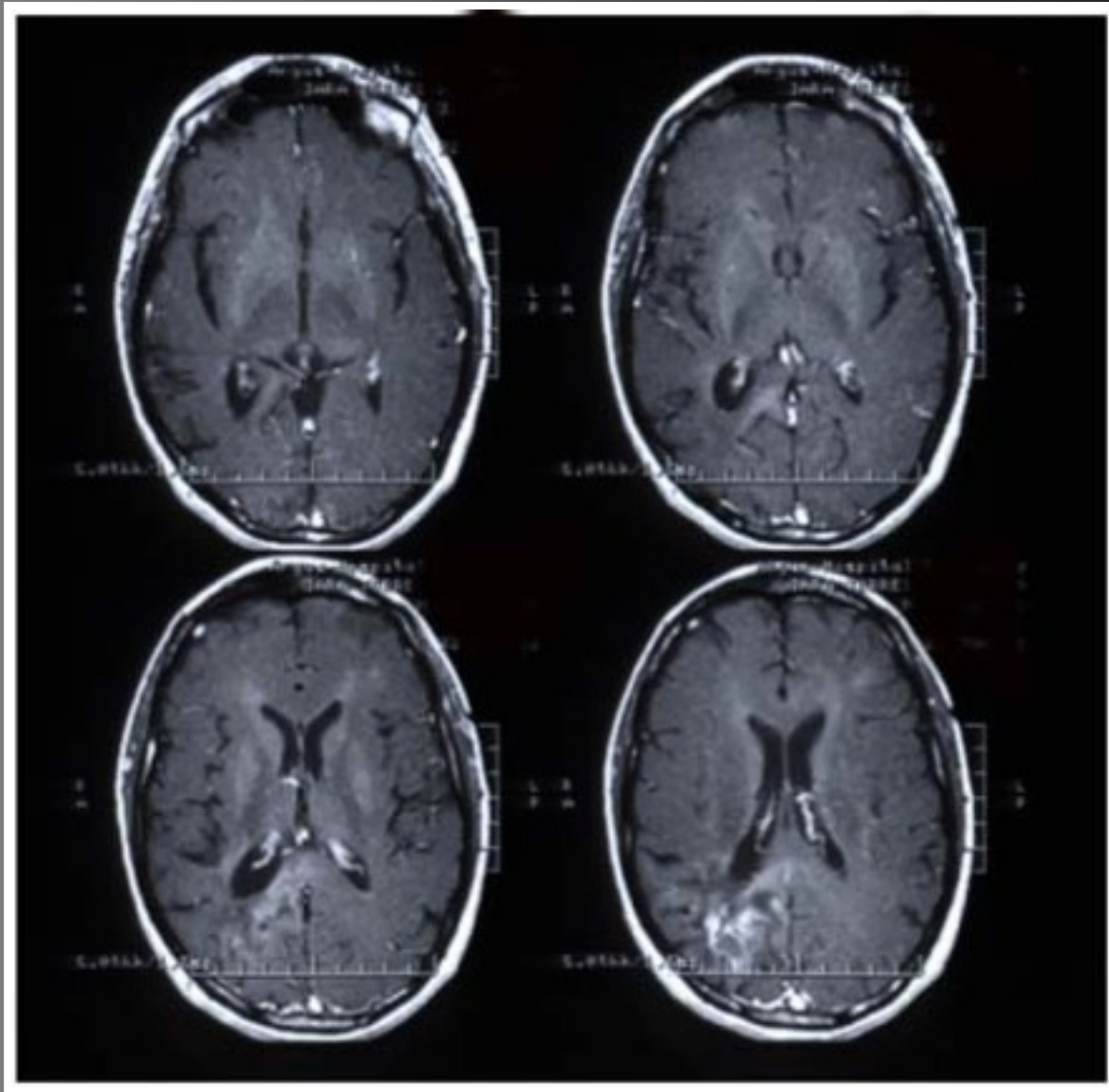
Chagas disease



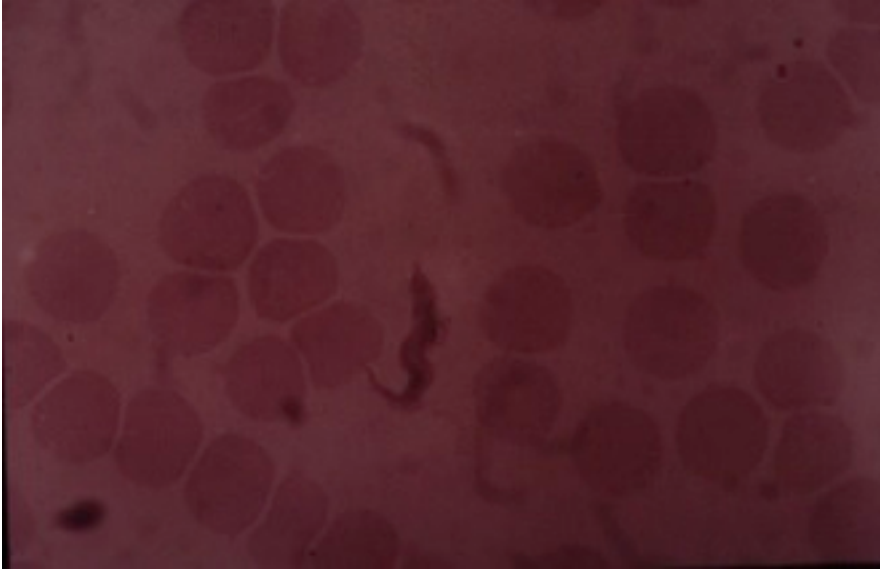
Chagas disease



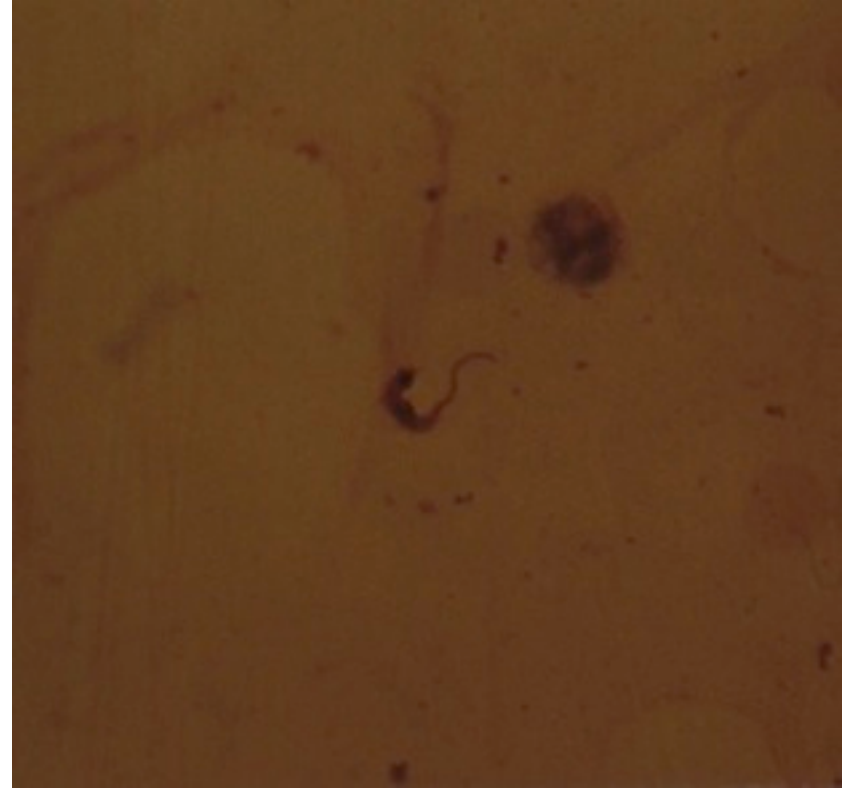




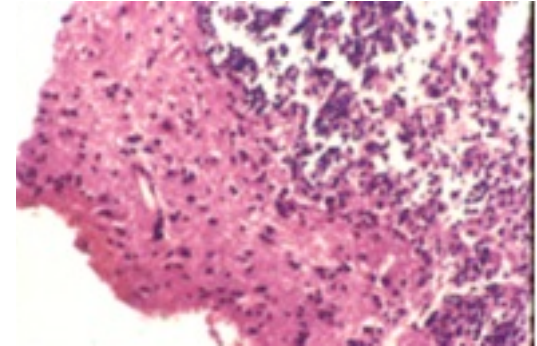
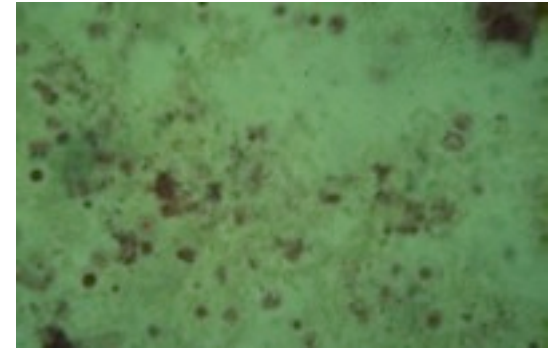
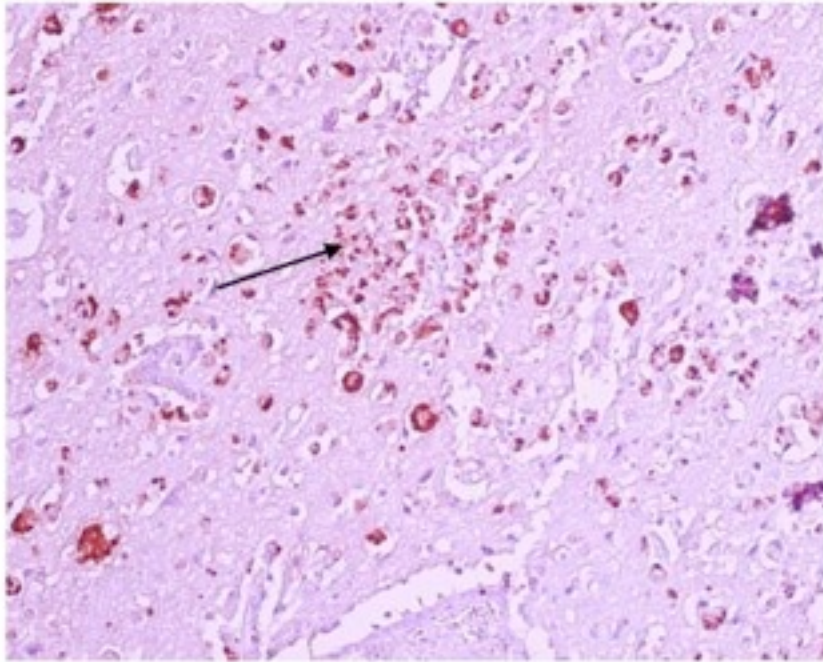
Chagas disease



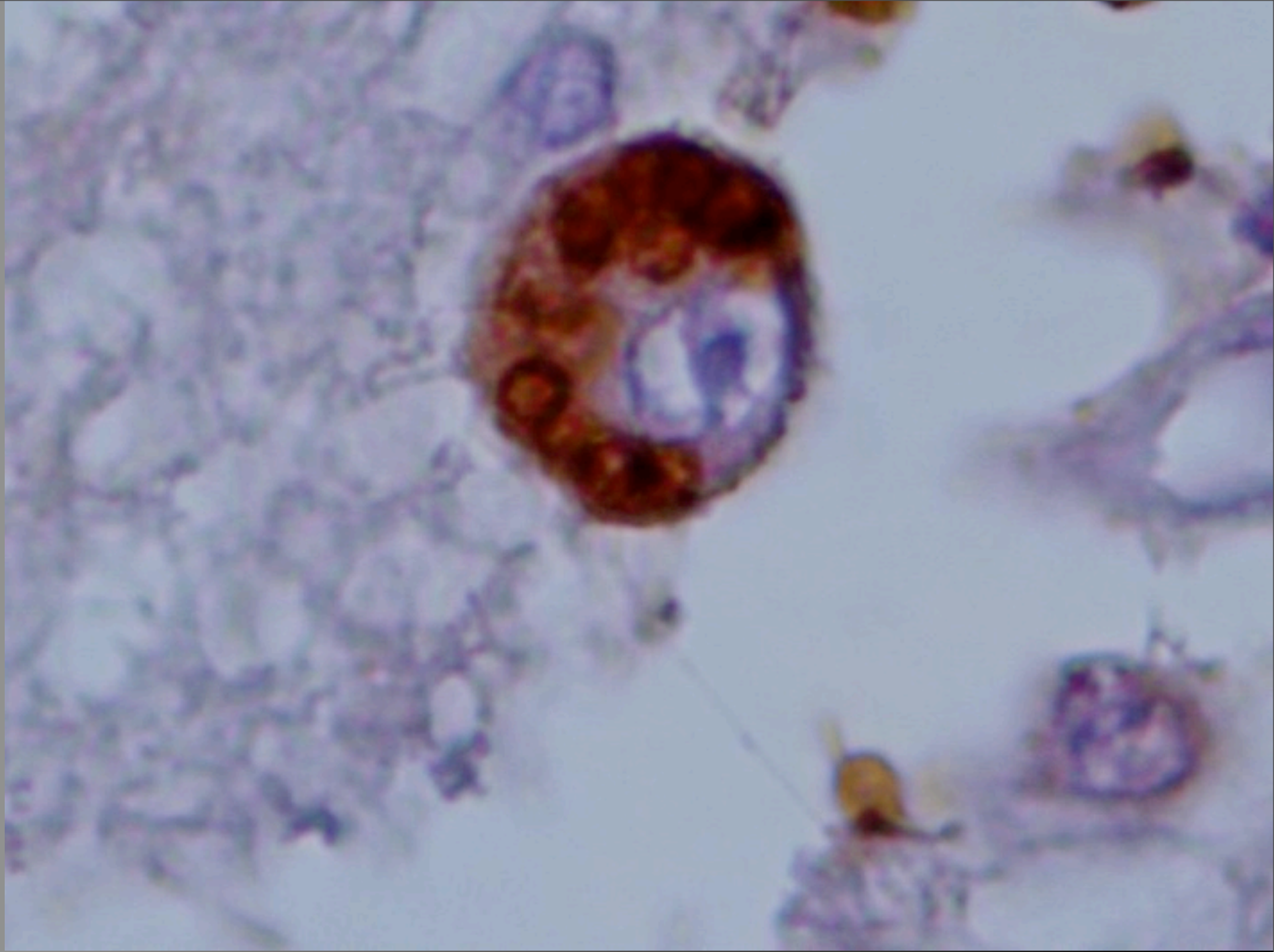
Trypanosoma in
blood and CSF
samples



Chagas disease



Meningoencephalitis with free amastigotes in brain smear,
Anti-chagas polyclonal antibody immunoreactivity. 400 X

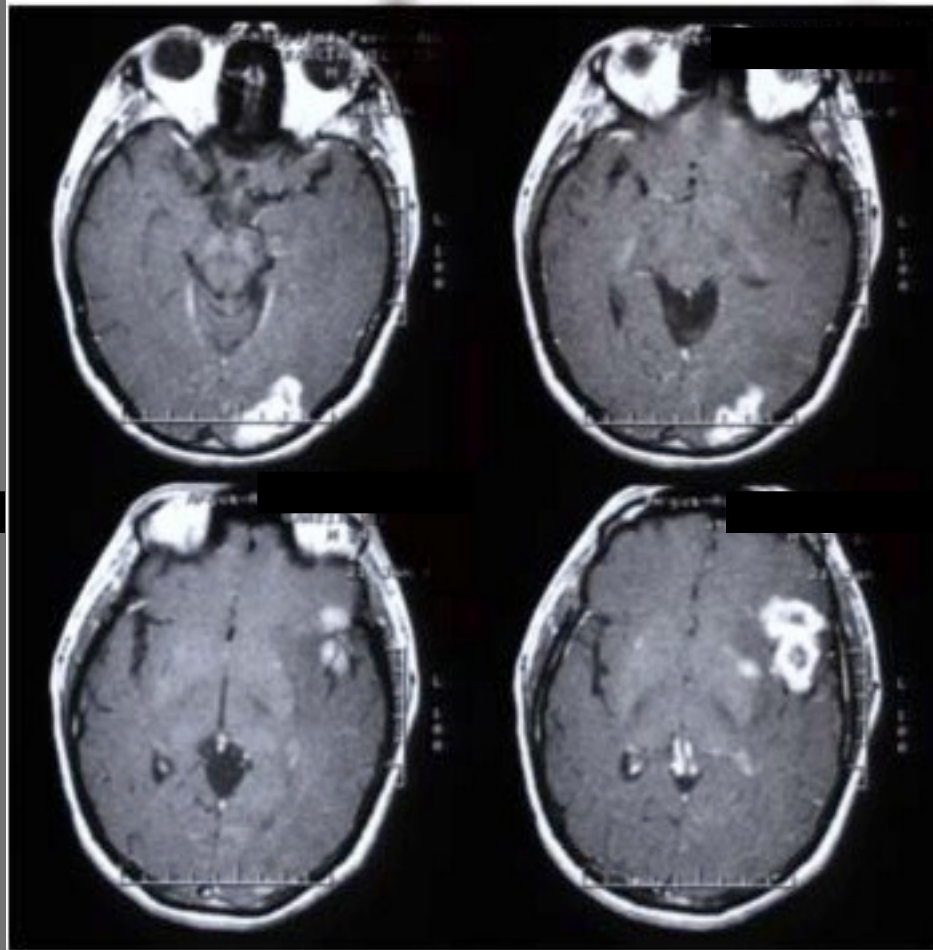


Tuberculosis

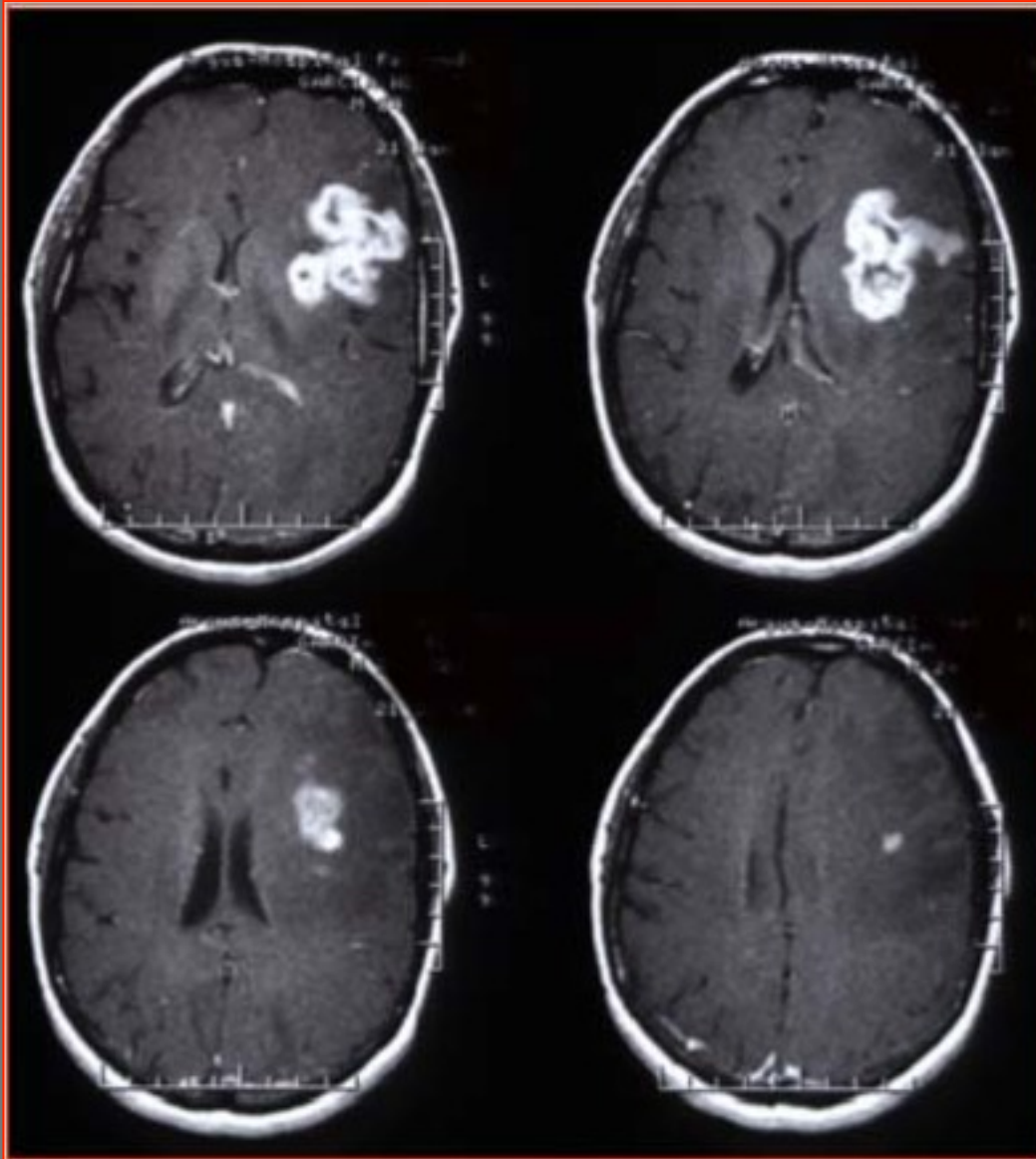
- Meningoencephalitis
- Brain Tuberculomas
- Brain Abscess
- Vasculitis

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Tuberculosis

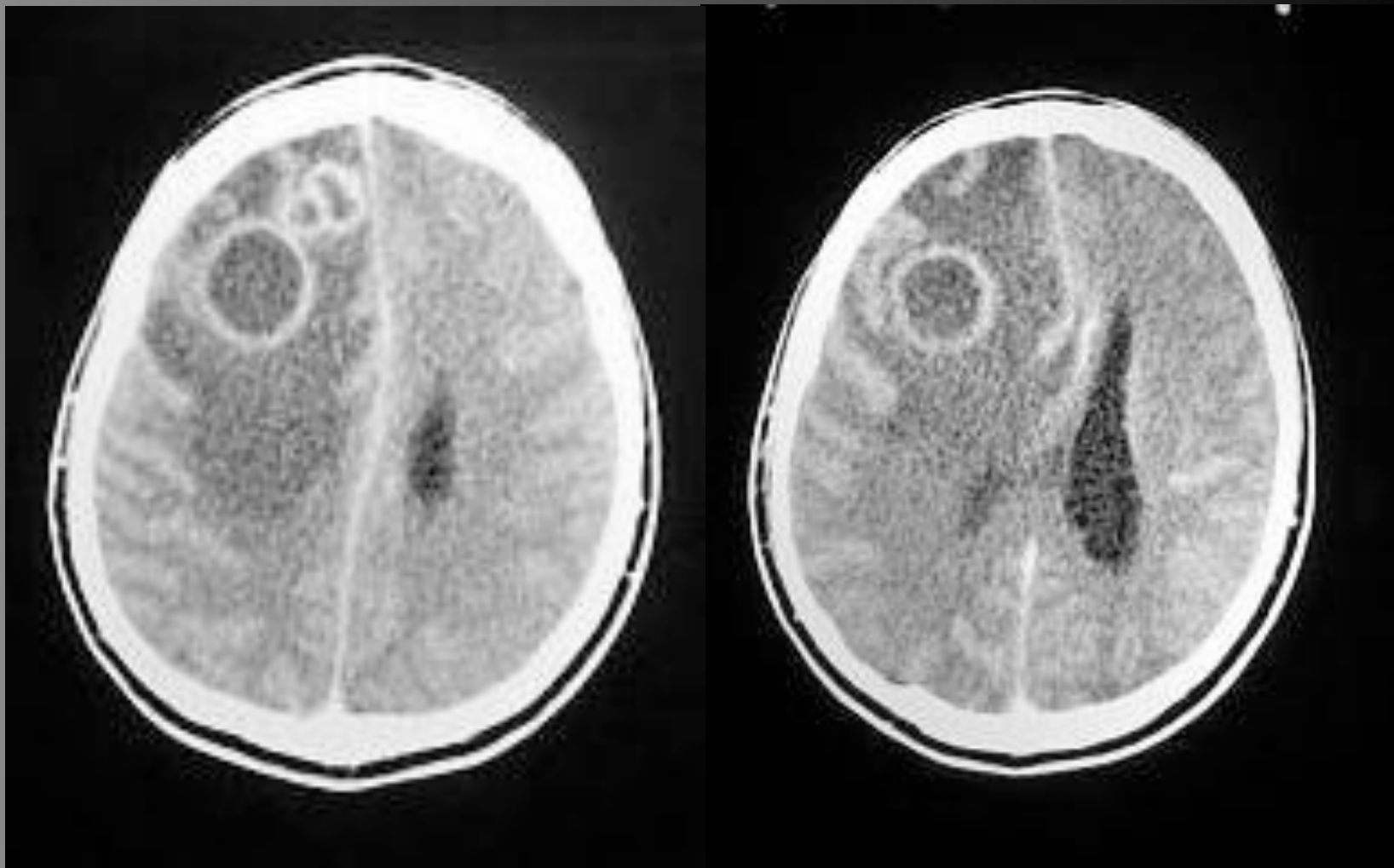


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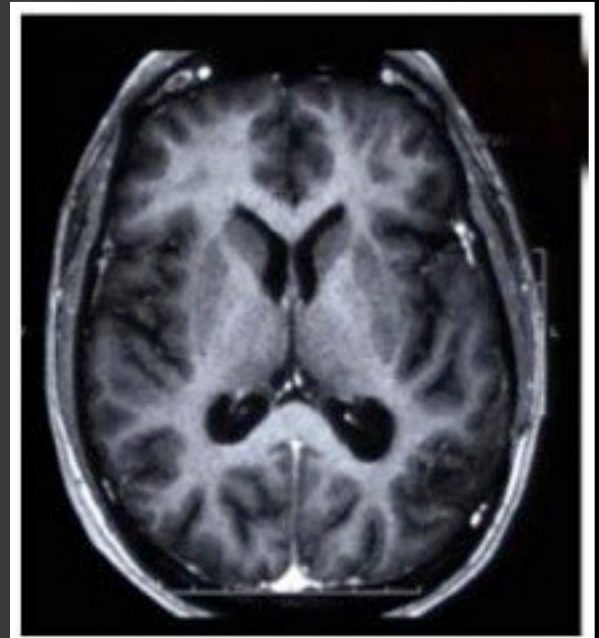
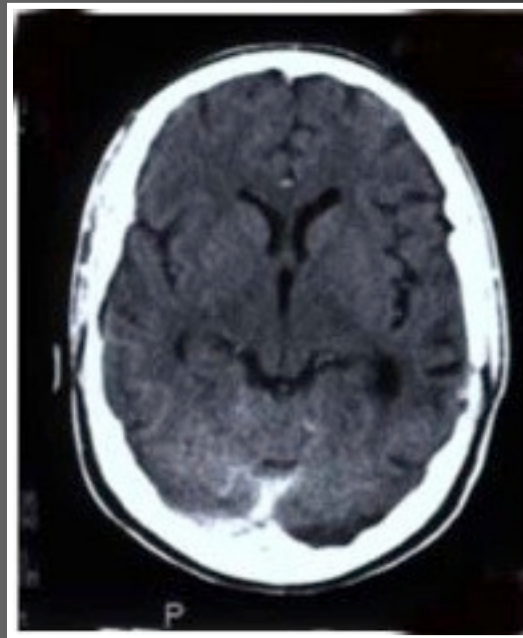
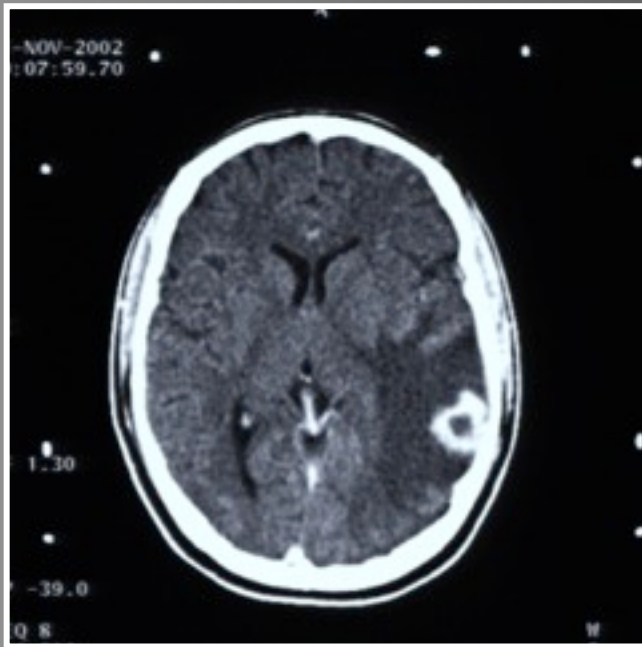
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Tuberculosis



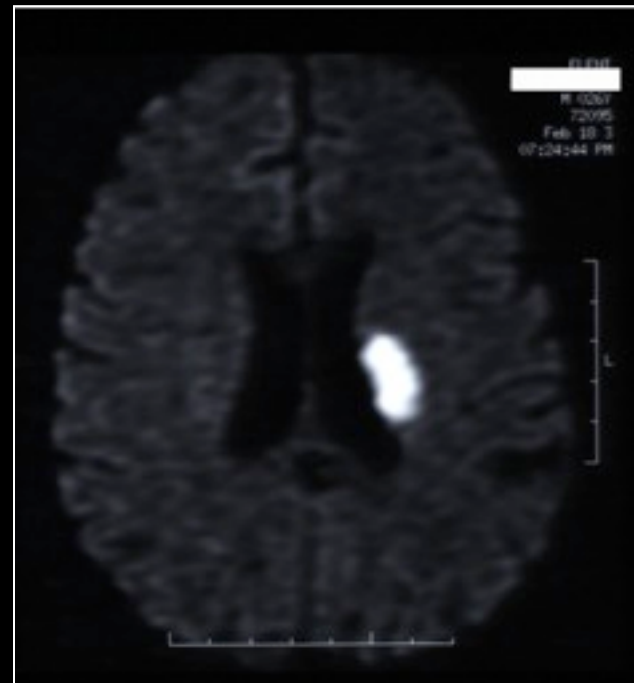
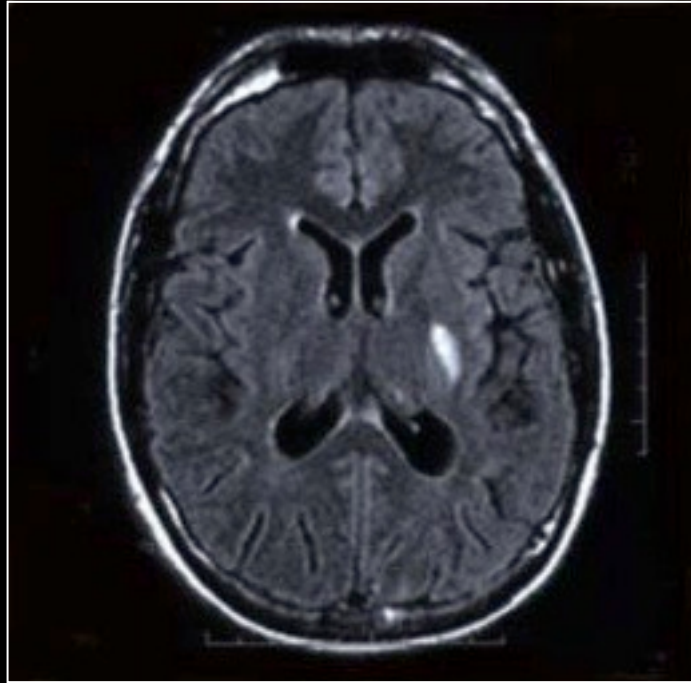
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Tuberculosis



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Tuberculosis Vasculitis



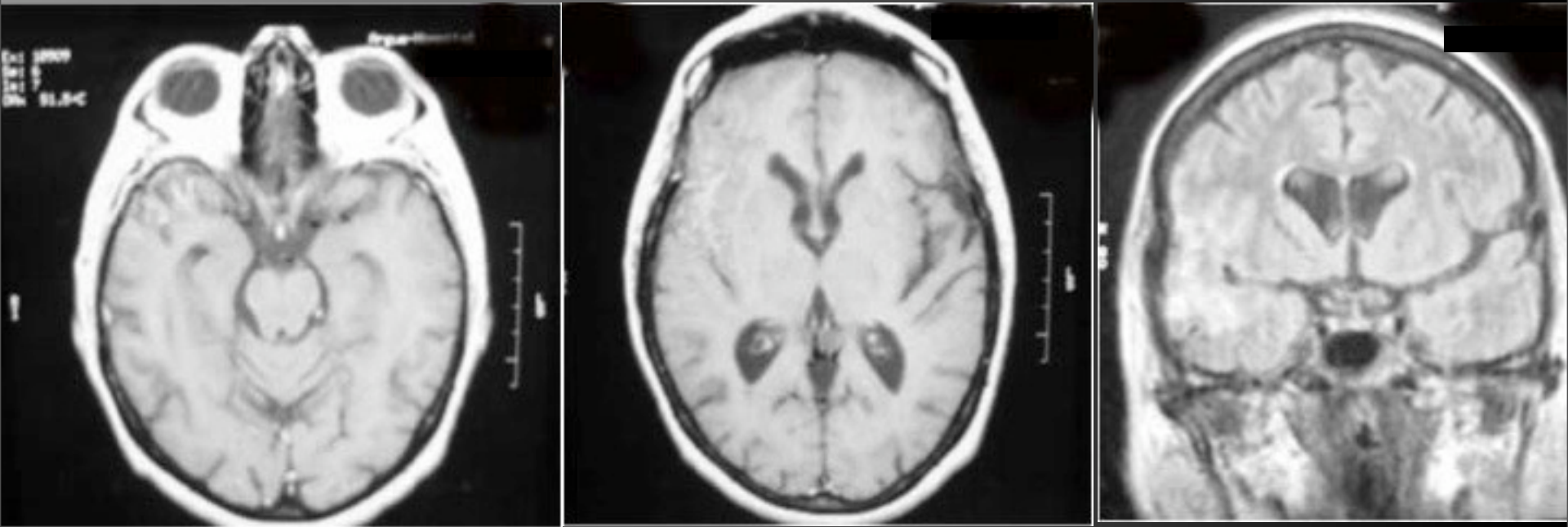
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Criptococcosis

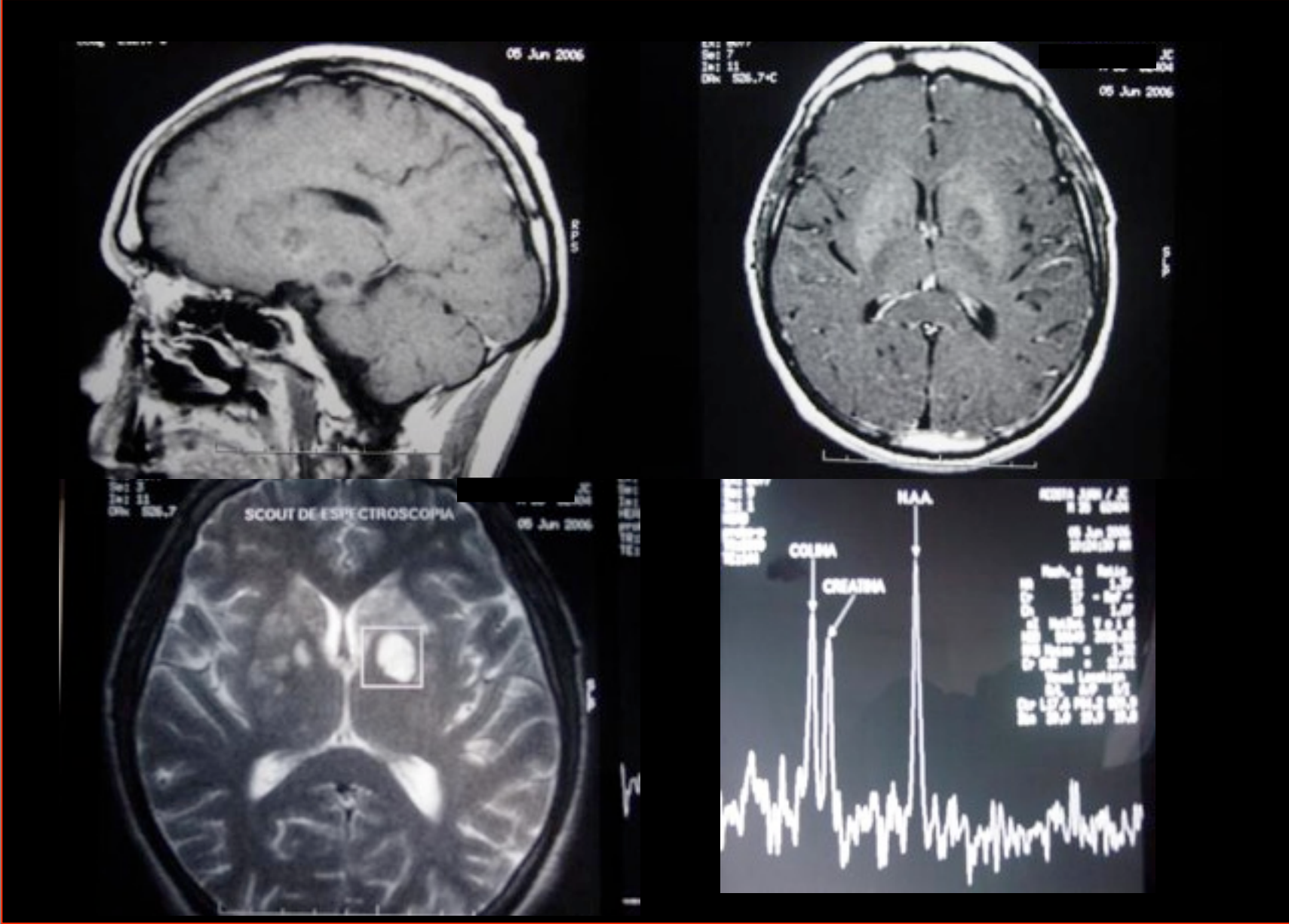
- Meningoencephalitis
- Criptococomas
- Soap bubble lesions

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Criptococcosis

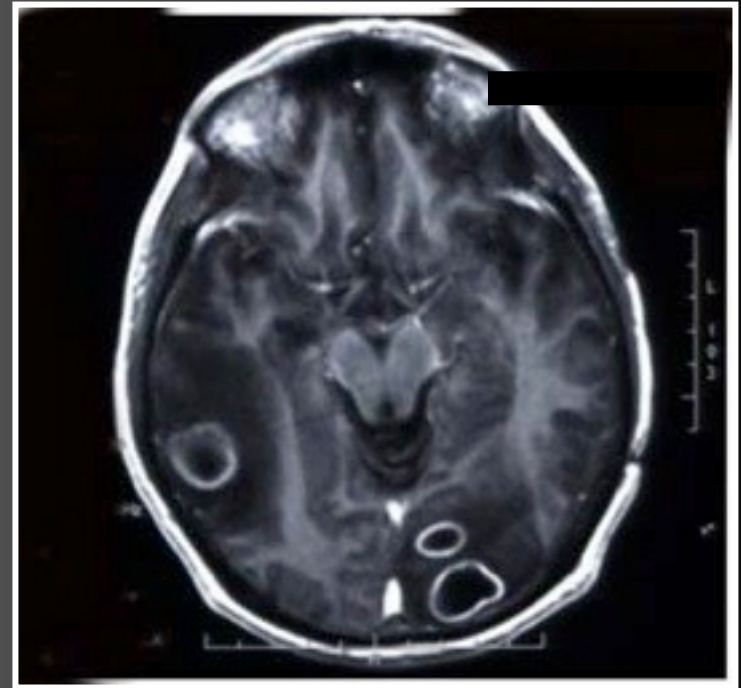
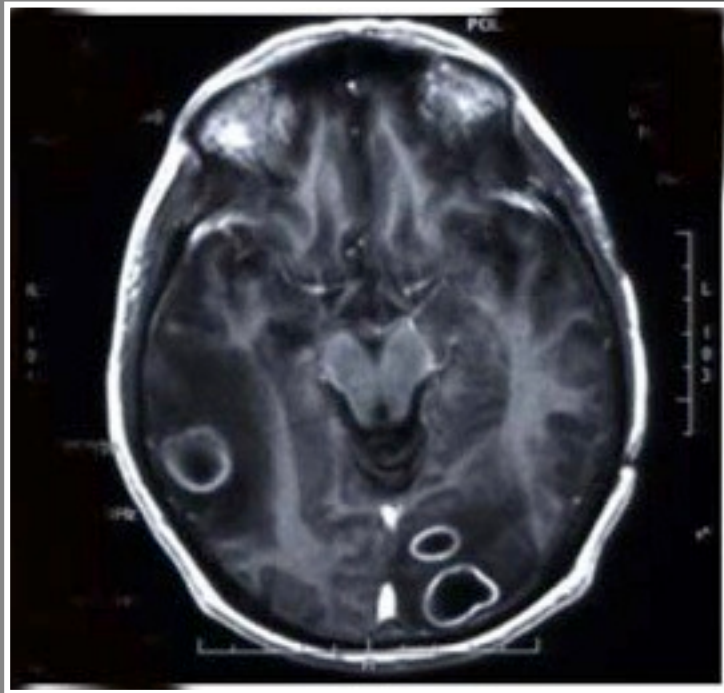


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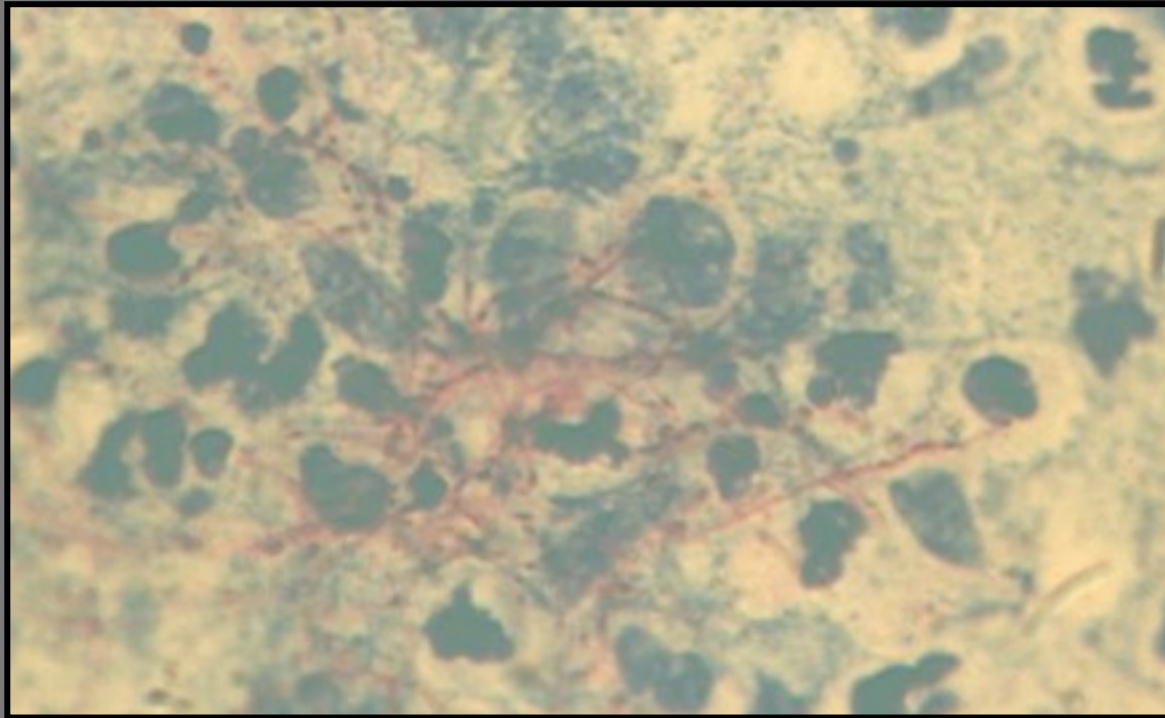
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Nocardia



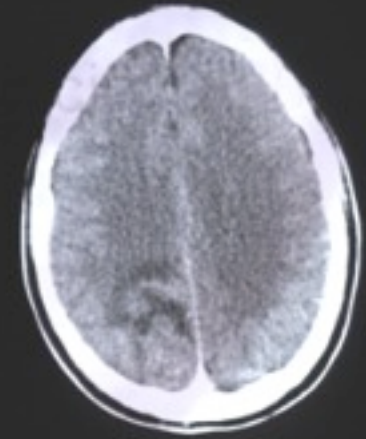
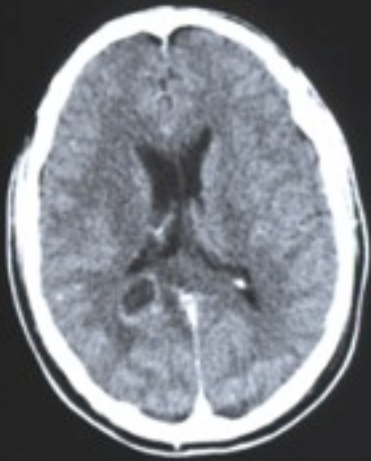
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Nocardia Abscesus

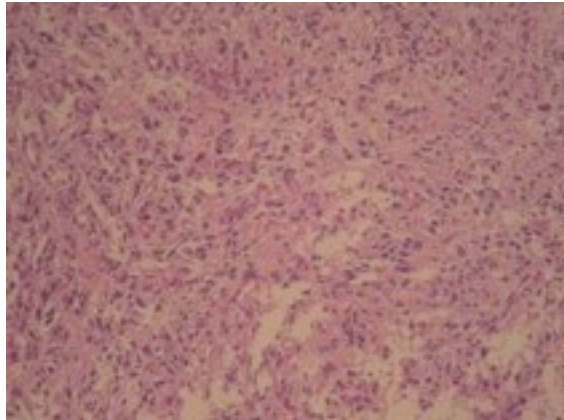


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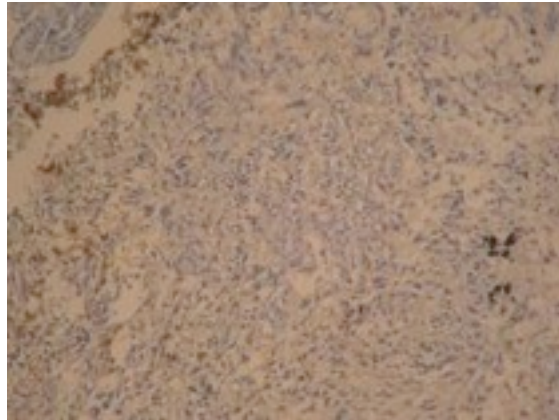
Gliosarcoma



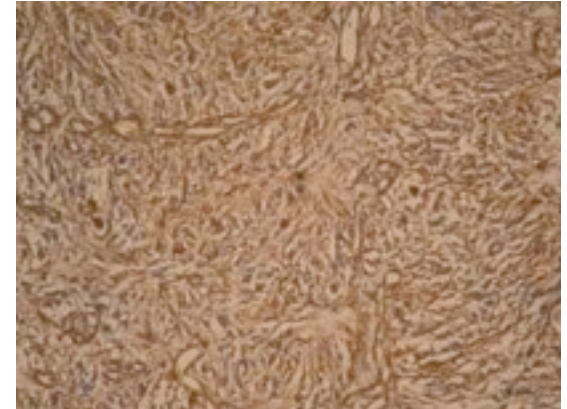
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1



2



3

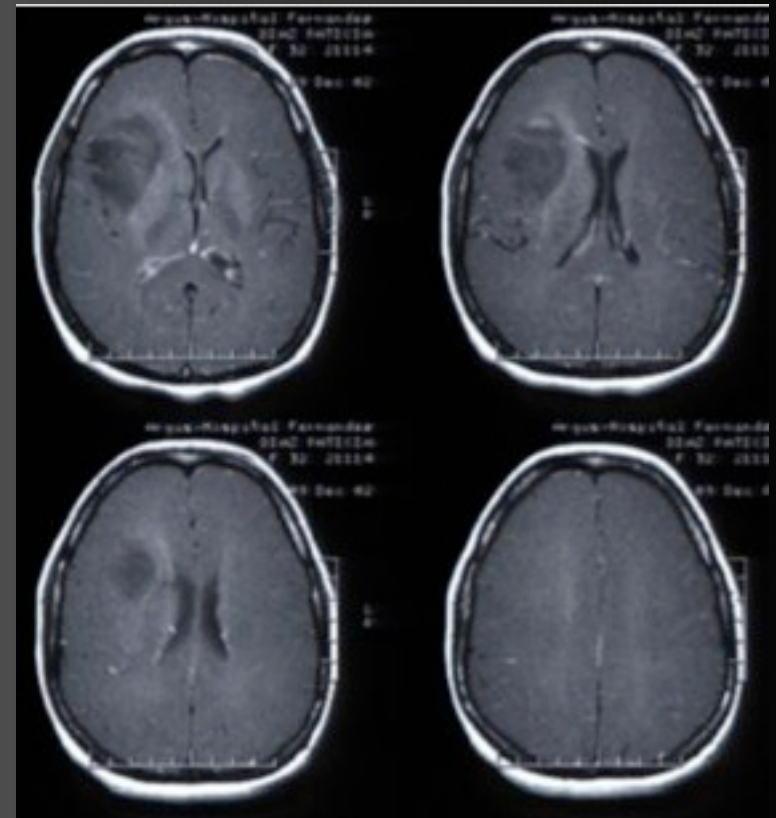
Fig. 1: Fusocellular Tumor with mitosis. HE 200 X

Fig. 2: Fusocellular Tumor, positive immunomarcation for Vimentine. 400 X

Fig. 3: Fusocellular Tumor, negative immunomarcation for GFAP. 400 X

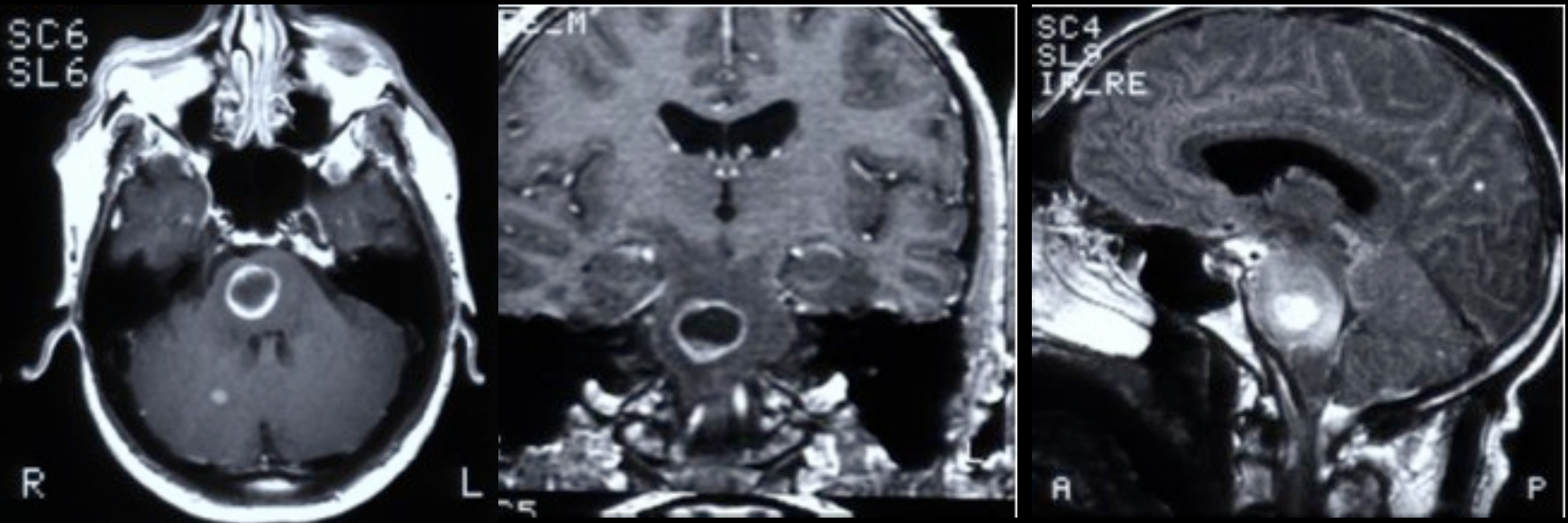
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Oligodendroglioma



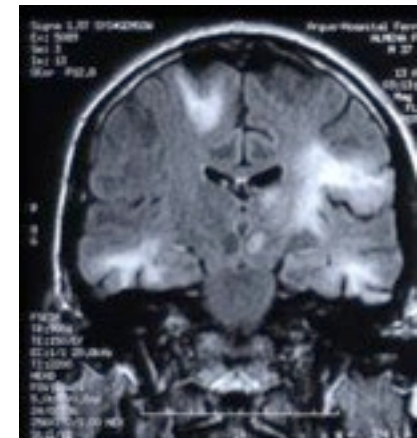
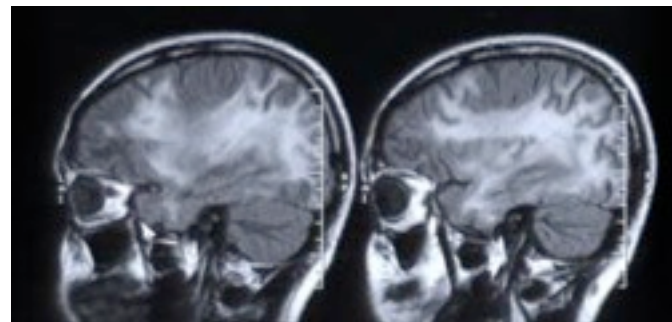
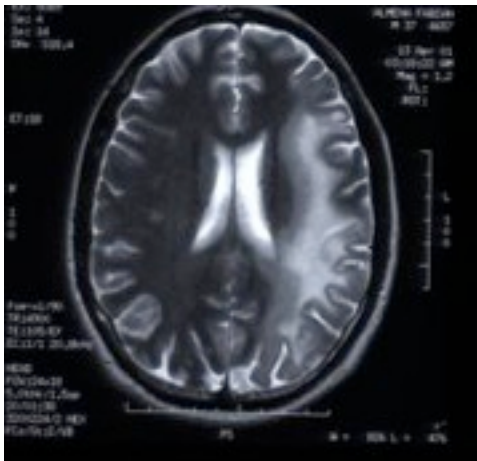
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Brain stem metastasis



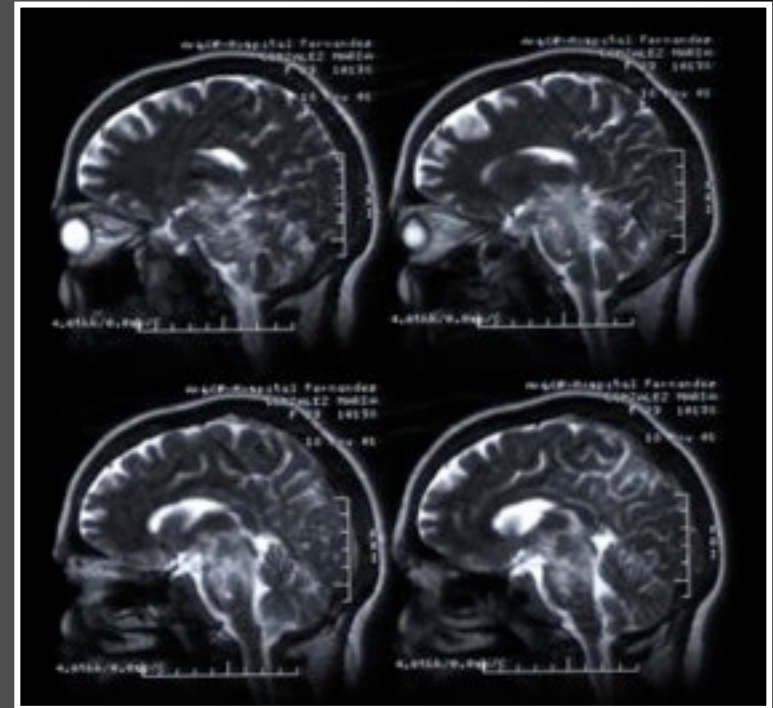
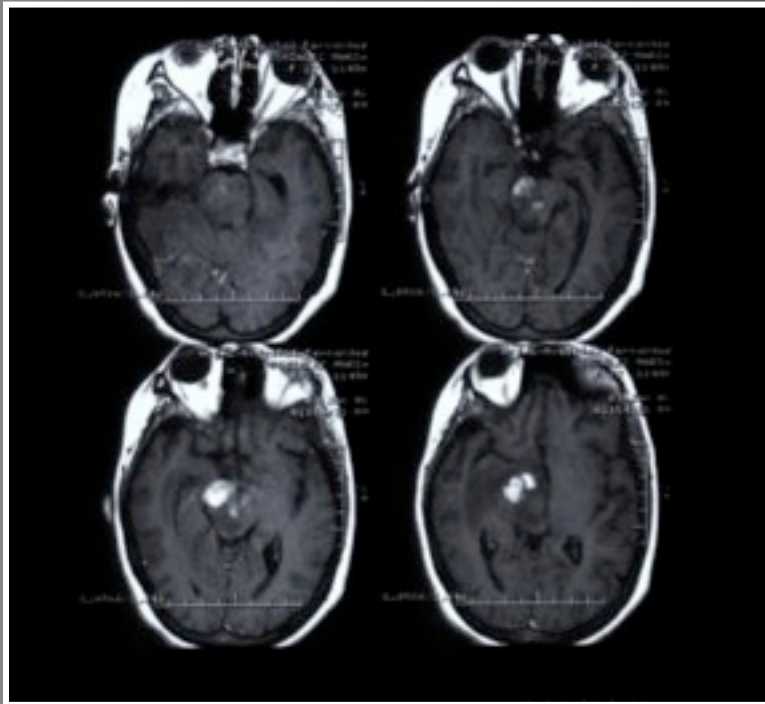
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Progressive Multifocal Leukoencephalopathy (JCV)



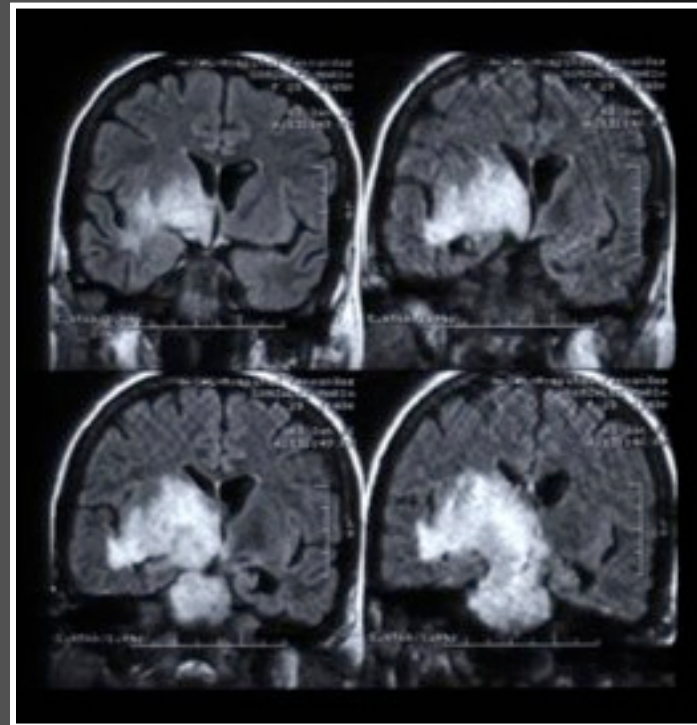
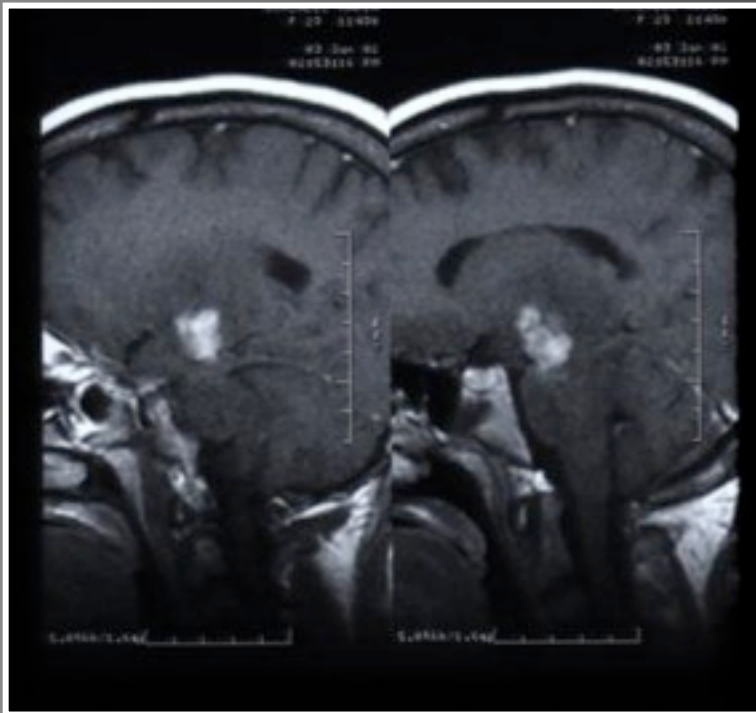
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PML

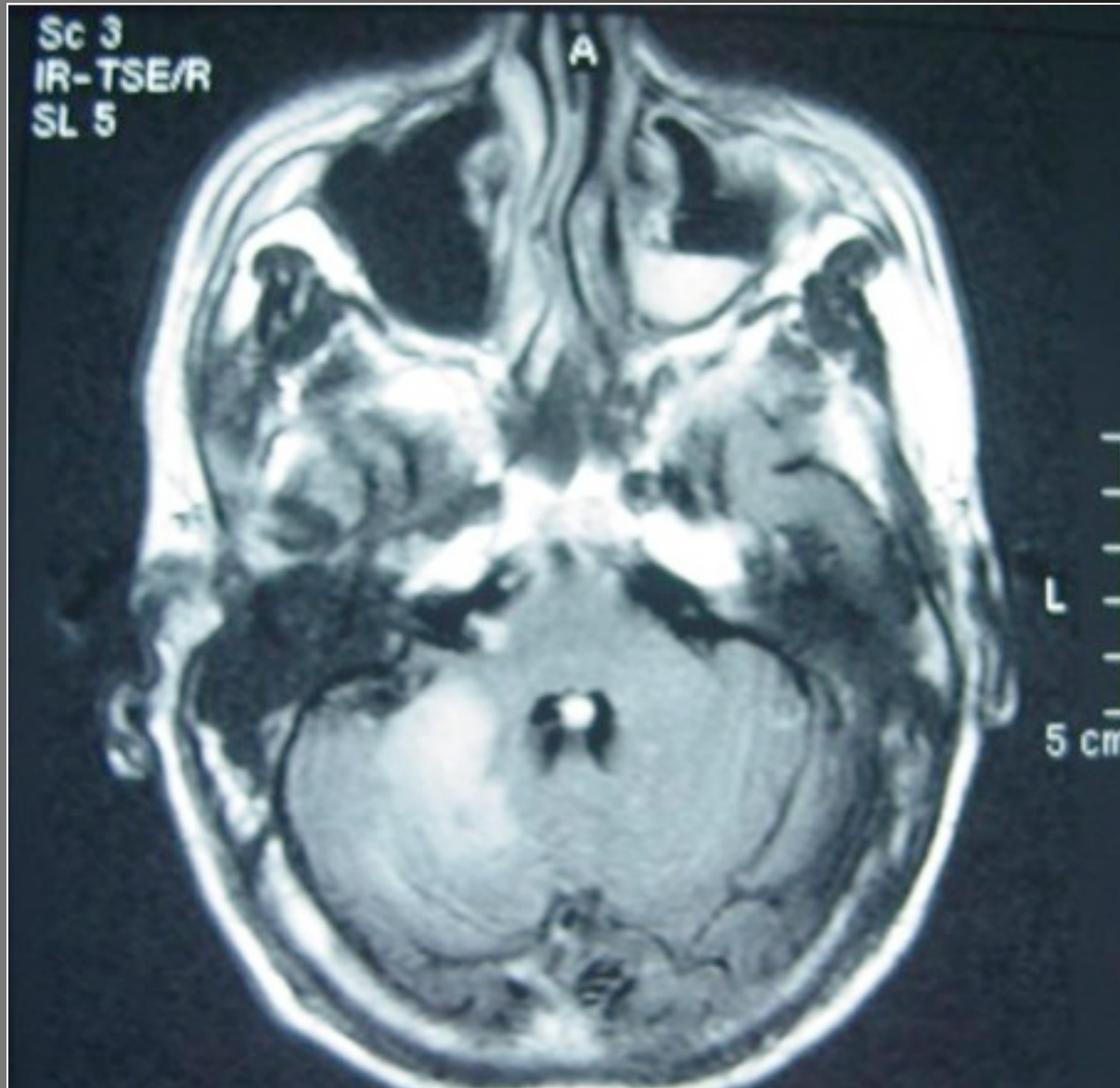


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PML

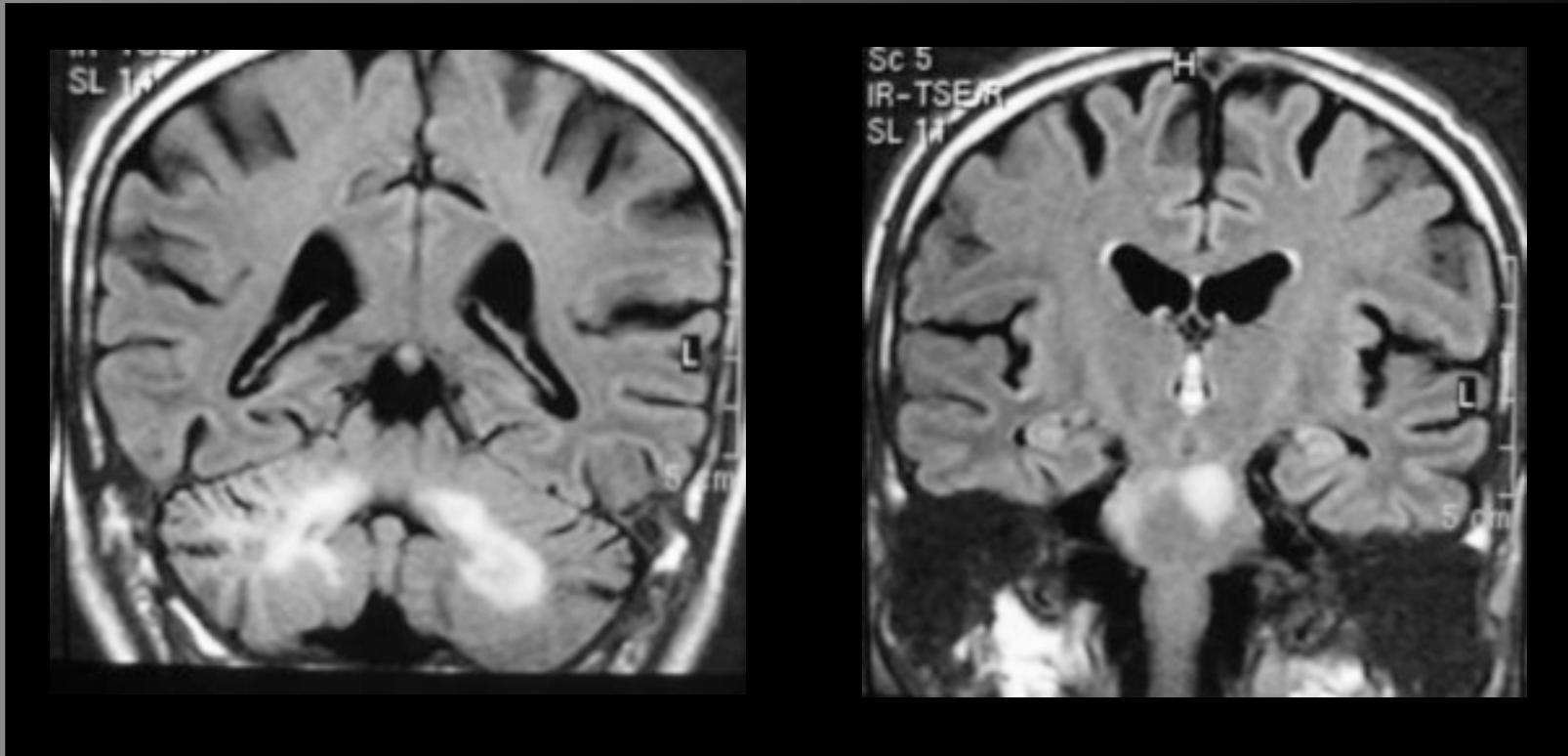


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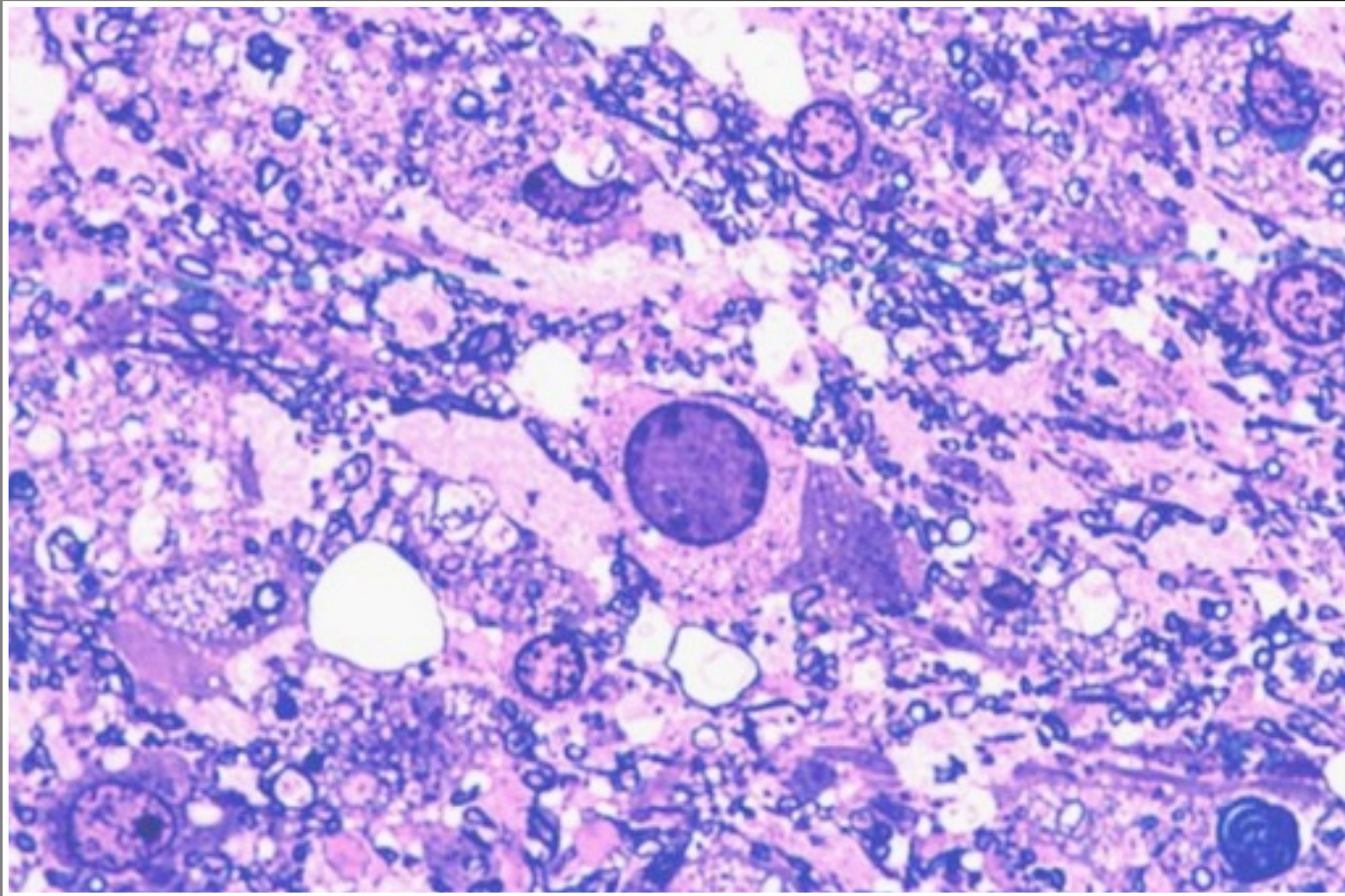
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PML



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PML :Cell with an intranuclear inclusion body.
inclusion in EPON. 1000 X



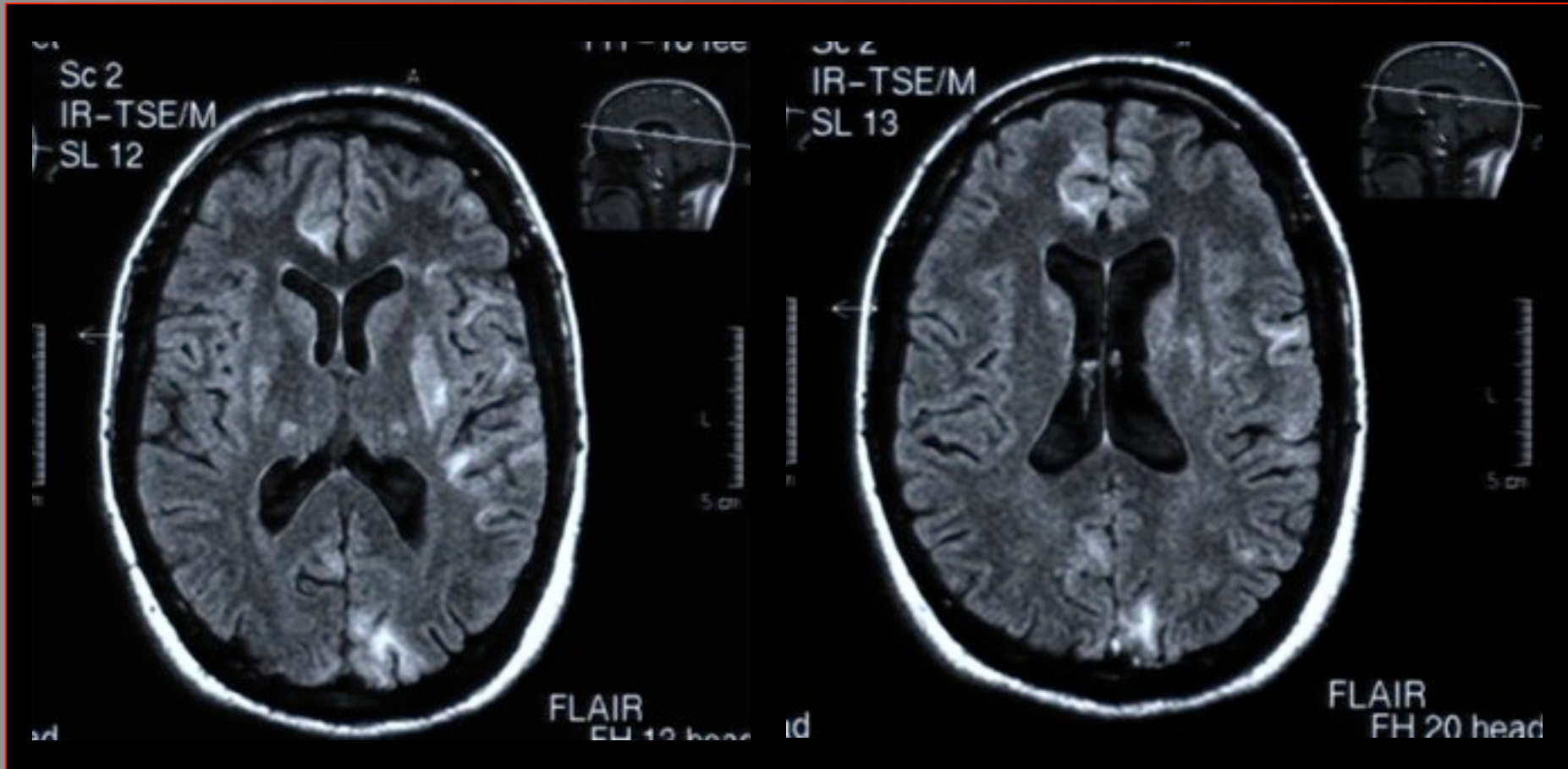
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PML (JCV + VZ)



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PML (JCV + VZ)

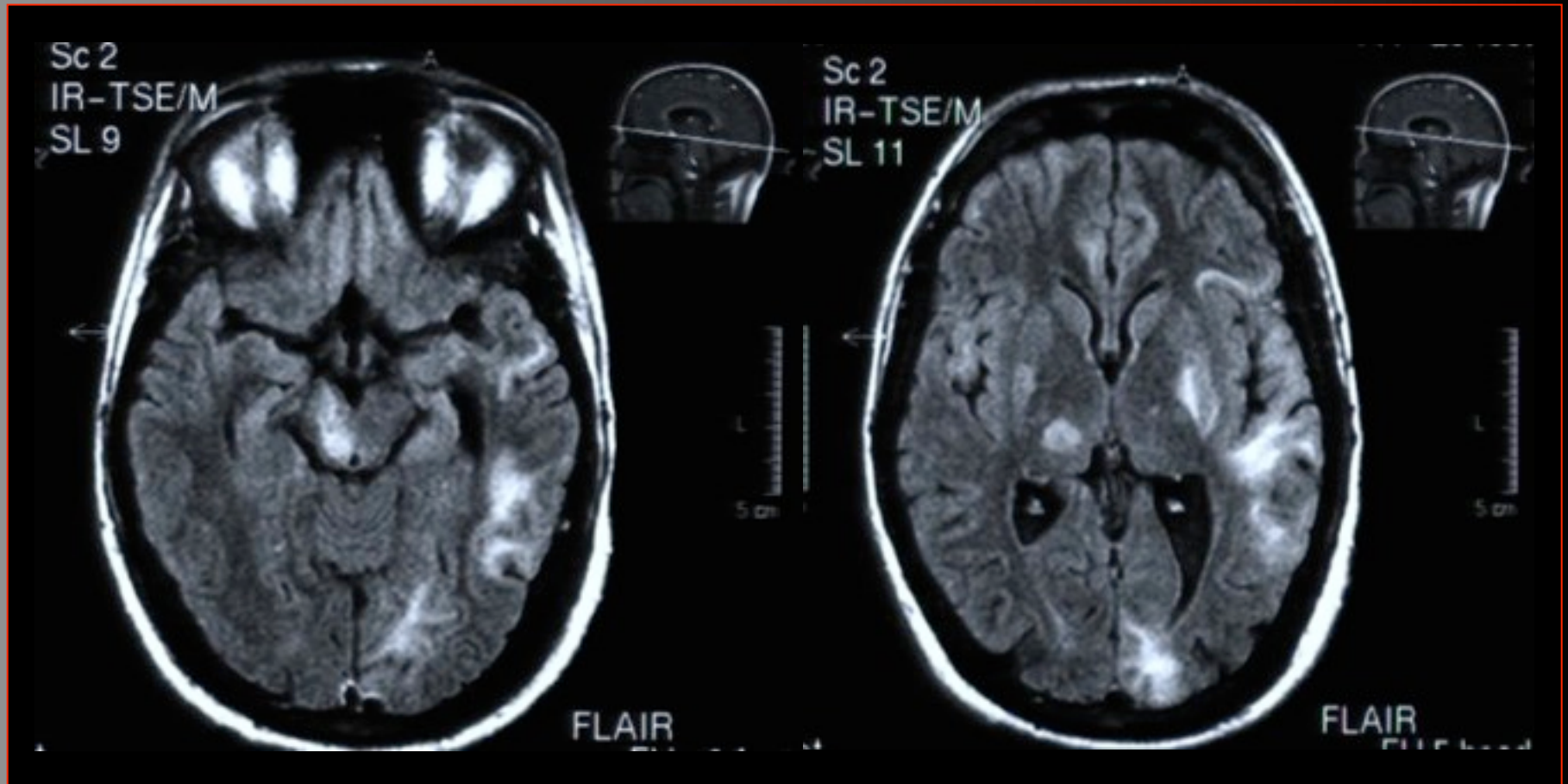


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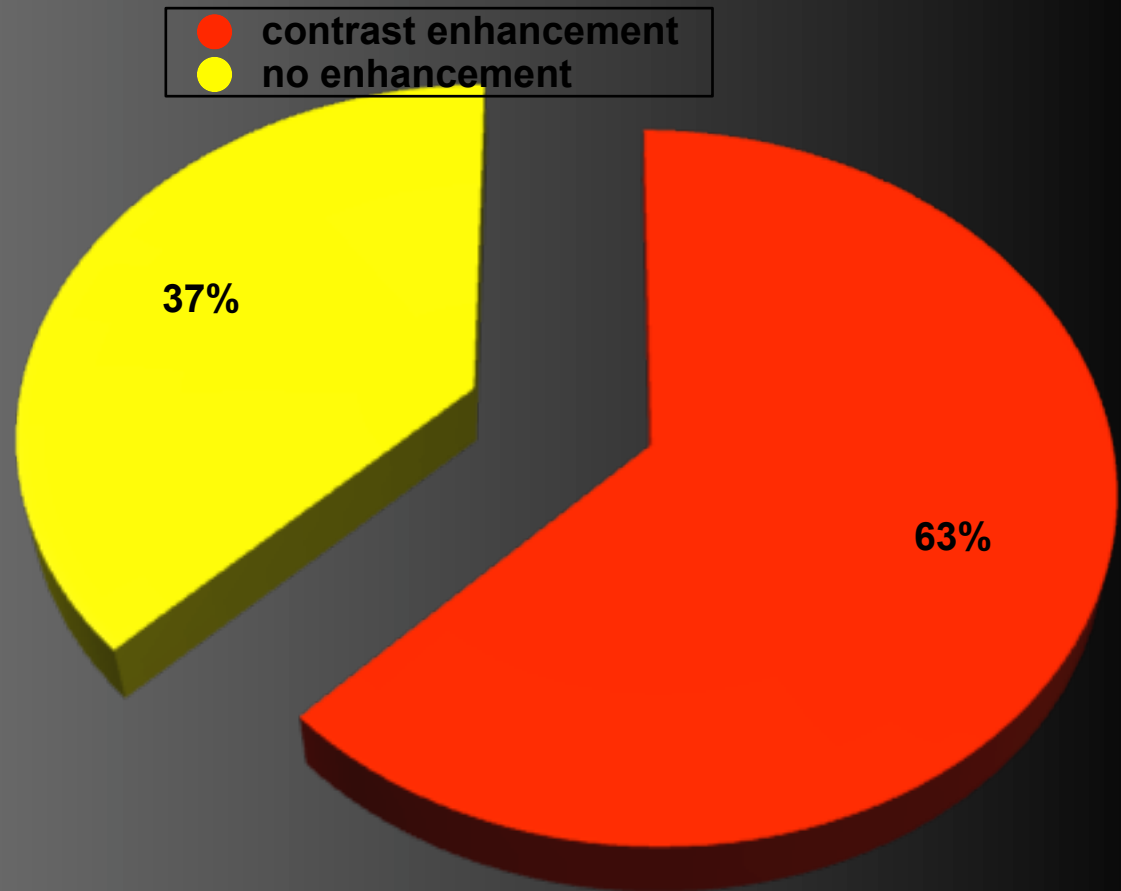
PML(JCV + VZ)



PML(JCV + VZ)

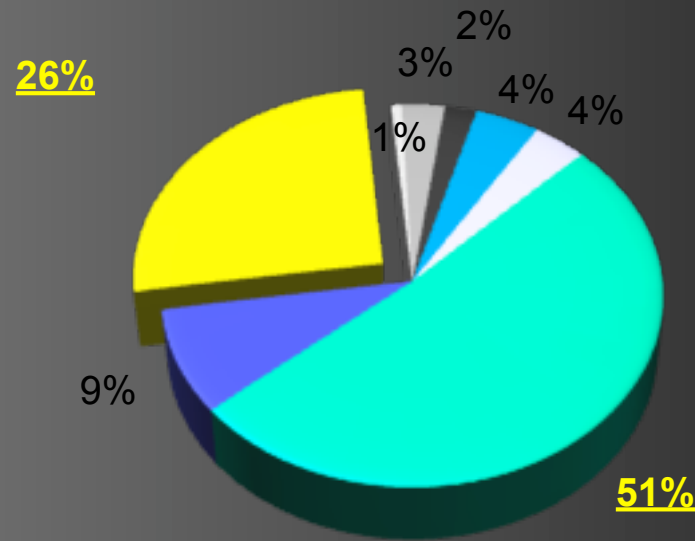


STEREOTACTIC BIOPSY IN AIDS PATIENTS (N = 300)



BIOPSIAS ESTEREOTÁCTICAS EN PACIENTES HIV + (N = 262)

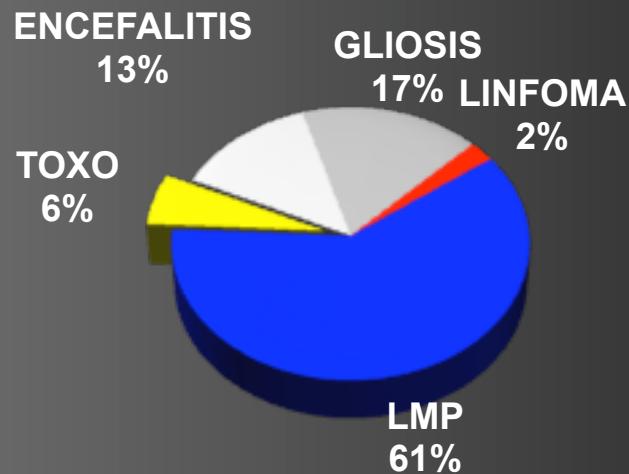
Lesiones que captan contraste (N = 161)



- Linfoma
- Chagas
- Toxoplasmosis
- Mts. Ca.
- Gliomas
- INC
- Cripto
- TBC

BIOPSIAS ESTEREOTÁCTICAS EN PACIENTES HIV + (N = 262)

Lesiones que no captan contraste (N = 101)



The Changing Pattern of HIV Neuropathology in the HAART Era

FRANÇOISE GRAY, MD, PhD, FABRICE CHRÉTIEN, MD, ANNE VALÉRIE VALLAT-DECOUVELAERE, MD, AND
FRANCESCO SCARAVILLI, MD, PhD

Abstract. Highly active antiretroviral treatment (HAART), which has been available for most AIDS patients in France since 1996, has resulted in a dramatic improvement of the progression of the disease. From the survey of our series of 343 brains with acquired immunodeficiency syndrome (AIDS) from patients who died between 1985 and 2002, we found both quantitative and qualitative changes in the pattern of human immunodeficiency virus (HIV) neuropathology. Quantitatively, despite a dramatic decrease in the number of autopsies, brain involvement remained a major cause of death. There was an overall decrease in incidence of cerebral toxoplasmosis, cytomegalovirus encephalitis (CMVE), and HIV encephalitis (HIVE), for which successful treatment is available. This contrasted with the unchanged incidence of progressive multifocal leukoencephalopathy (PML) and malignant non-Hodgkin lymphomas (MNHL). However, when looking closer at the 3 last years, the incidence of diseases affecting patients with severe immunodepression (CMVE, PML, and MNHL) decreased between 2000 and 2002, whereas infections occurring in patients with milder immunodeficiency, toxoplasmosis, varicella-zoster encephalitis (VZVE), or herpes simplex virus encephalitis (HSVE) became more frequent. In addition, we found uncommon types of brain infection such as BK virus encephalitis or general paresis. Finally, we described new variants of HIVE: severe leukoencephalopathy with intense perivascular macrophage and lymphocyte infiltration, possibly due to an exaggerated response from a newly reconstituted immune system, and chronic “burnt out” forms of HIVE as VZVE, toxoplasmosis, or PML, possibly associated with prolonged survival, in which neither inflammation nor organisms could be detected. These findings are compared with those reported in other neuropathological studies from different developed countries.

Key Words: Acquired immunodeficiency syndrome (AIDS); Central nervous system; Highly active antiretroviral treatment (HAART); Human immunodeficiency virus (HIV); Neuropathology.

Complications (N=300)

- Morbidity : 5 patients (1,7 %)
- Mortality : 2 patients (0,7%)

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Results (N=300)

Over 300 procedures we arrived to a diagnosis (histology/bacteriology/virology) in 275 patients

DIAGNOSTIC YIELD : 91,7%

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Conclusions

- Neuroradiology, as well as serologic, or csf analysis are useful but they cannot make a pathognomonic diagnosis
- Antiretroviral treatment can be started if you find demyelination in MRI with JCV in CSF (PML)
- AIDS patients with CNS lesion, atypical for toxoplasmosis or with bad response to anti toxo treatment are suitable for a stereotactic biopsy
- **Cooperation among different medical disciplines lead to a better diagnose and prognostic for those patients**

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Thank you

Claudio G. Yan





Buenos Aires 2017

**XVI World Congress of
Neurological Surgery
14-20 October 2017**

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