НЕЙРОВИЗУАЛИЗАЦИЯ ПРИ ВИЧ-ИНФЕКЦИИ

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NEUROIMAGING IN HIV

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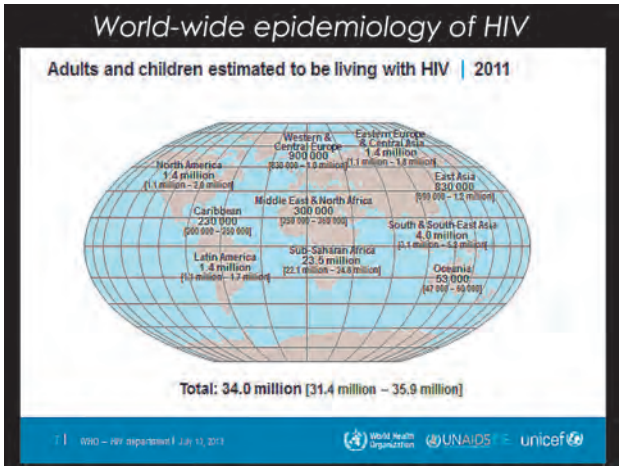
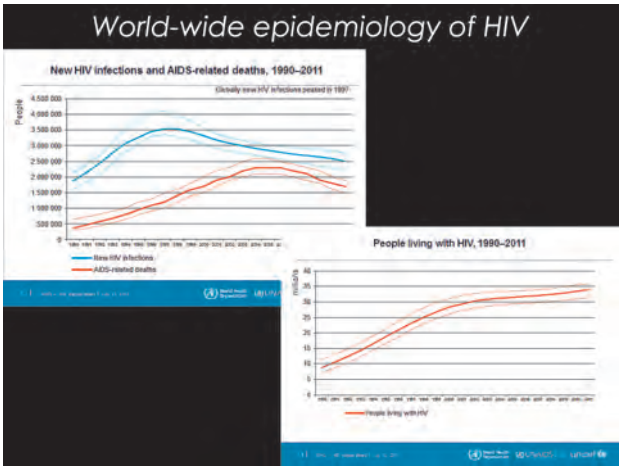
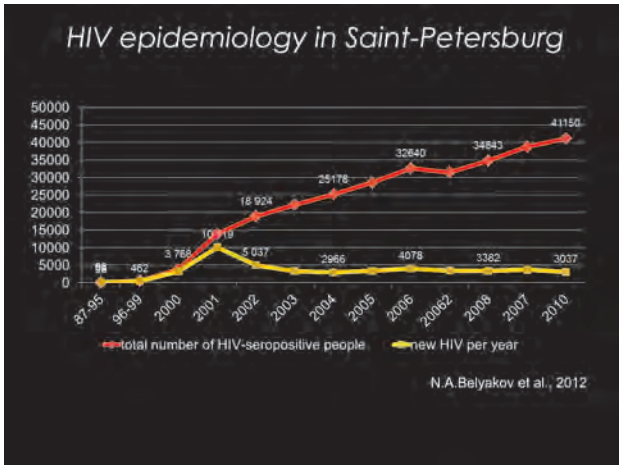
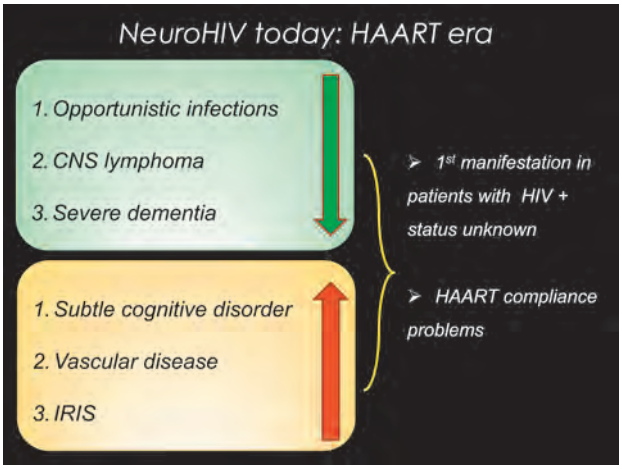
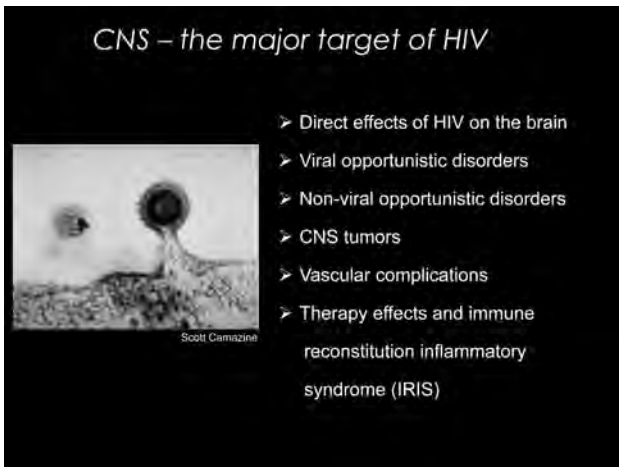
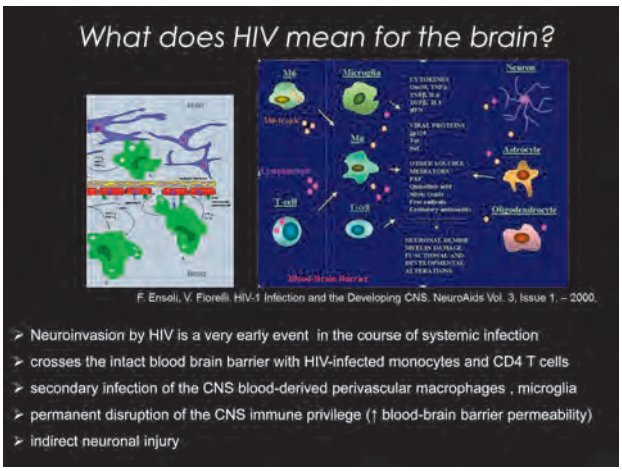






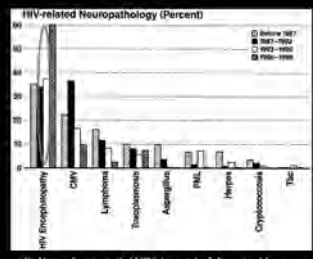






What does HIV mean for the brain?

1. Chronic viral infection
2. Long term immunoactivation in CNS
3. CNS compartmentalisation – viral reservoir
4. CSF viral load underestimates brain viral replication
5. Major viral target in the brain – basal ganglia
6. HAART cannot prevent HIVE, but decreases it`s severity



J.K. Neuenburg et al. JAIDS Journal of Acquired Immune Deficiency Syndromes. - 2002.- Vol.31.-P.171–177

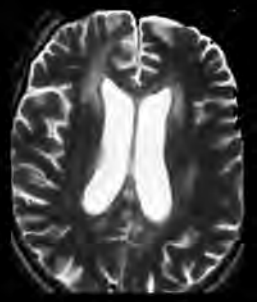
Clinical manifestations of HIV

1. Cognitive decline (84%)
2. Headache
3. Seizures
4. Intracranial hypertension
5. Vertigo
6. Focal neurologic deficit
7. Cranial nerves involvement
8. Myelopathy
9. Inflammatory demyelinating polyradiculopathy

No correlation with disease duration, blood viral load, CD4 lymphocyte level, HIV genotype

HIV Encephalopathy: atrophy

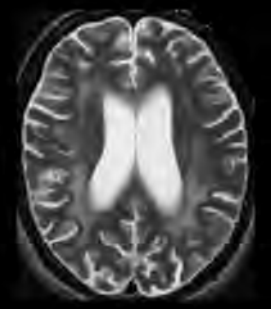
- Most common finding
- Could be the only finding
- Regional pattern of atrophy with predominant involvement of basal ganglia and white matter
- HAART slows down the progression rate but doesn't change its pattern



HIV Encephalopathy: white matter changes

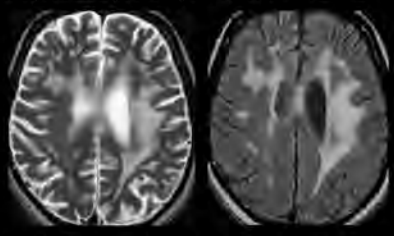
Typical features:

- T2 WI, FLAIR: hyperintense
- T1 WI: isointense
- CT: hypodense
- (-) contrast enhancement
- (-) mass effect
- (-) U-fibers



Large confluent bilateral symmetrical areas in the white matter

HIV Encephalopathy: white matter changes



Large confluent asymmetrical areas in the white matter

- T2 WI, FLAIR: hyperintense
- T1 WI: isointense
- CT: hypodense
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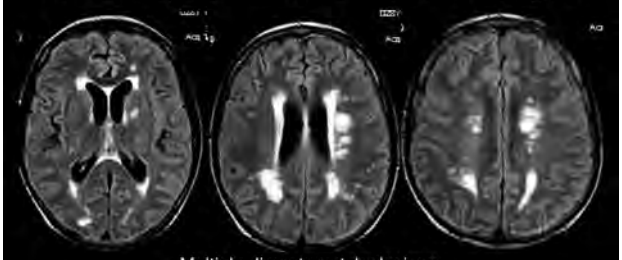
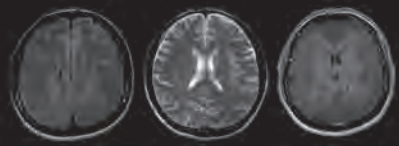
HIV Encephalitis: white matter changes

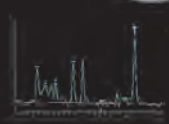


Multiple discrete patchy lesions

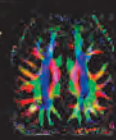
- T2 WI, FLAIR: hyperintense
- T1 WI: isointense
- CT: hypodense
- (-) contrast enhancement
- (-) mass effect
- (-) U-fibers

HIV Encephalopathy: early changes





MTR

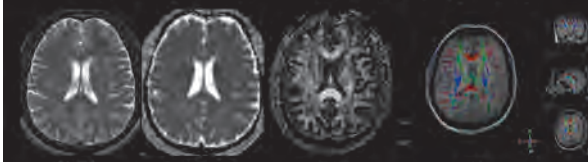


- Subcortical white matter
- ⇩ Naa (neuronal loss)
- ⇧Cho (astrocytosis, microglial proliferation)

- Slightly ⇩ in white matter lesions
- Diffuse involvement of normal appearing white matter

⇩ Fractional anisotropy

DTI in early HIV encephalopathy



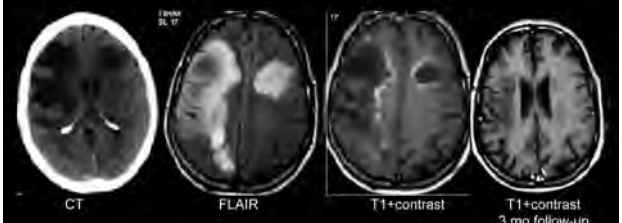
T2-ВИ ADC FA FA

- ⇧ of ADC, MD, progressive ⇩ of FA
- ⇩ FA: injury/loss of highly aligned structures (axons); replacement of axons with less ordered cells (glial cells)
- ⇧ MD: is associated with inflammation, elevation of inflammatory chemokines
- Localization: subcortical frontal white matter, genu > splenium of corpus callosum, inferior and superior longitudinal fasciculus

Microstructural white matter desorganization

- DTI changes imply microscopic damage to fiber tracts despite their normal appearance on macroscopic MR images of the brain
- Whole-brain FA measures the cumulative injury induced in the brain by HIV
- Changes of MD and FA in subcortical regions are associated with cognitive impairment in HIV patients
- FA measures more prognostic of dementia status than ADC measures
- Patients who receive HAART have healthier white matter

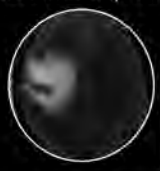
Rare manifestations: Tumefactive demyelination



1. Cause - primary HIV infection
2. More often in HAART-naïve with preserved CD4 cell counts
3. Can mimic MS/intracranial neoplasms
4. incomplete arc of serpiginous ring enhancement more pronounced on the medial aspect of the lesions
5. MR-spectroscopy: high Cho/Cr, Lac/Cr and normal/low NAA/Cr ratio

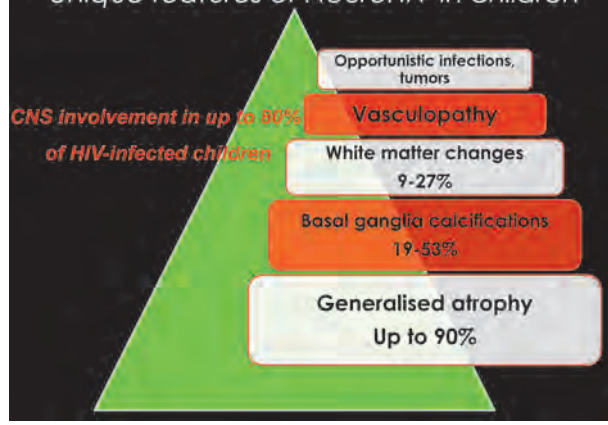
Saravanan M, Turnbull IW. Brain: non-infective and non-neoplastic manifestations of HIV. Br J Radiol. 2009 Nov;82(983):956-65.

Focal brain syndrome with unusual «ring enhancement»



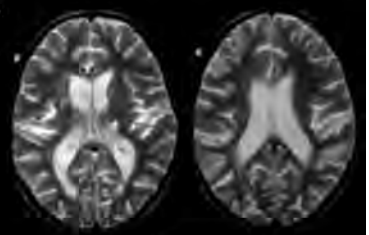
No steroids prior to brain biopsy

Unique features of NeuroHIV in children



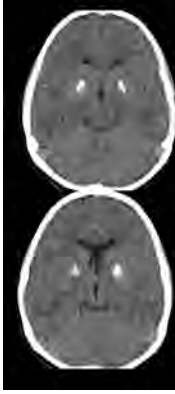
NeuroHIV in children: generalised atrophy

- In up to 90% of HIV- positive children
- Central atrophy > cortical atrophy (usually frontal lobes)
- Ventriculomegaly disproportional to the degree of cortical atrophy



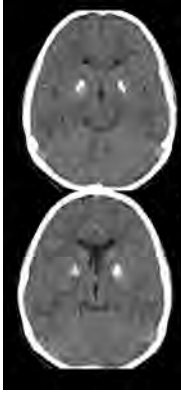
10 y.o. HIV-seropositive girl

NeuroHIV in children: basal ganglia calcifications



- unique to vertically infected children
- prevalence varies from 19-53%
- never seen before the age of 1 year
- calcifications before 2 months - most likely due to other congenital infections e.g. toxoplasmosis or rubella)
- associated with abnormal neurological examination
- the degree of calcifications is thought to be directly roportional to the viral load and severity of encephalopathy

NeuroHIV in children: basal ganglia calcifications



Typical:
- CT: bilateral, symmetric hyperdensities involving globus pallidus and putamen

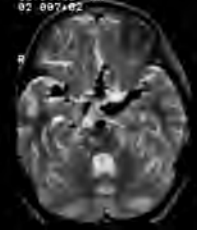
- Less common:
  - White matter (predominantly frontal)
  - Cerebellar calcifications

Only in assocaiation with basal ganglia calcifications

- CT remains the investigation of choice

NeuroHIV in children: vasculopathy

- Diffuse fusiform dilatation of the major arteries of the circle of Willis
- Pathogenesis is unclear
- Signifies a grave prognosis
- Rare pathologic entity
- Usually 8-13 years old
- Advanced HIV
- Most frequent presentation with stroke or intracranial hemorrhage
- Pathology: medial fibrosis with loss of muscularis, destruction of the internal elastic membrane, intimal hyperplasia
- Latency period after onset of HIV infection 2 to 11 years

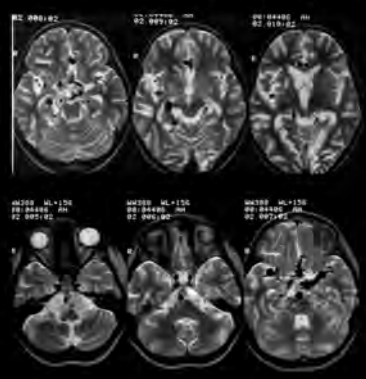


NeuroHIV in children: vasculopathy

- Patients with HIV have a thinner the media to wall thickness ratio than unaffected control subjects within the same age group
- Thinning of the media could be a preclinical stage of HIV vasculopathy
- The smooth muscle cells in the media can be directly infected with HIV with progressive damage

Gutierrez J, Glenn M, Isaacson RS, Marr AD, Mash D, Petito C. Thinning of the arterial media layer as a possible preclinical stage in HIV vasculopathy: a pilot study. Stroke. 2012 Apr;43(4):1156-8.

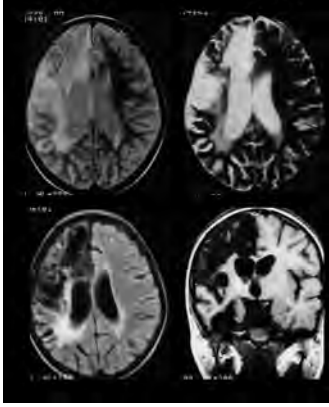
NeuroHIV in children: Vasculopathy



Initial examination 11 y.o.

Follow-up 2 years later: progression of fusiform arterial dilatation

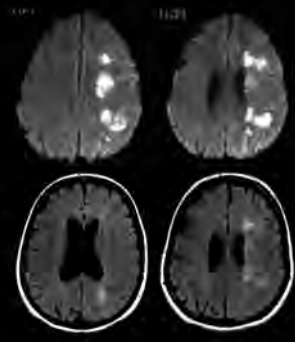
NeuroHIV in children: Vasculopathy



Follow-up 4 years later after the initial exam: stroke with almost total involvement of the right hemisphere

Stroke in HIV

- More common than in general population
- Risk factors:
  - Hyperlipidemia in HIV
  - Hypercoagulable state
  - Endocarditis, valve vegetations
  - Vasculitis
  - HIV-vasculopathy in children
  - Carotid, vertebral arteries dissection
  - HAART, illegal drugs



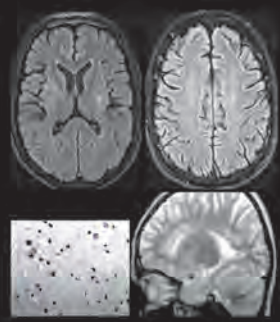
Acute stroke in 25 y.o. female

Meningitis in HIV

Meningeal involvement in HIV: viral, bacterial, mycobacterial , fungal, meningeal carcinomatosis in PCNSL, chemical meningitis

Early stage: primary HIV meningitis
Late stages: predominantly herpesvirus meningoencephalitis, including CMV

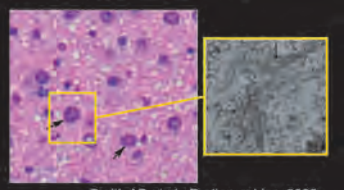
Most common opportunistic encephalitis: M. tuberculosis and Cryptococcus neoformans



HIV-meningitis
MRI/CT: no meningeal abnormality
CSF analysis

Opportunistic infections: progressive multifocal leucoencephalopathy

- ✓ 80% in HIV
- ✓ 20% non-HIV:
  - 13% hematologic and oncology condition
  - 5% organ transplantation
  - 3% rheumatologic treatment, antibody therapy, idiopathic immune deficiency syndrome

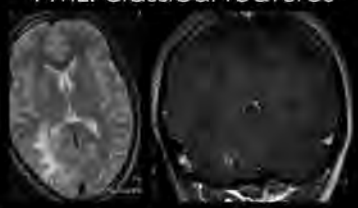


Smith AB et al. Radiographics. 2008 Nov-Dec 28(7):2033-58

Prevalence JCV antibodies in healthy individuals - 85% with the highest rates of initial infection before 20 years.

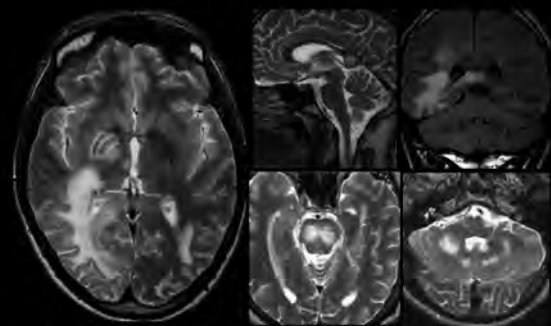
The principal histopathological feature is demyelination

PML: classical features



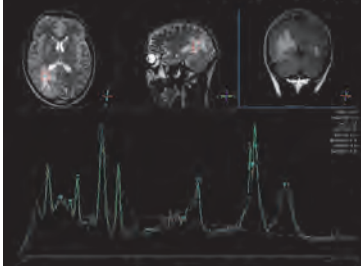
- ✓ Confluent bilateral asymmetric white matter lesions
- ✓ Starts in the subcortical U-fibers then moves into deeper white matter
- ✓ CT: hypodensities, less sensitive than MRI in early stage
- ✓ T1: hypointense, less commonly – isointense
- ✓ T2, FLAIR: hyperintense, margin from the adjacent gray matter
- ✓ Central area may become necrotic
- ✓ DWI: new lesion may have incomplete rim of diffusion restriction; old lesion after therapy/center of large lesion – facilitated diffusion
- ✓ «-» mass-effect
- ✓ «-» C
- ✓ «-» surrounding edema

PML: location



1. Parietal lobe > 2. Frontal lobe > 3. White matter of the posterior fossa: middle cerebellar peduncle, pons, cerebellum > 4. internal and external capsule, corpus callosum >5. thalamus > 6. basal ganglia

PML: MRS, PET

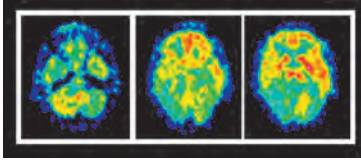


H^1-MR spectroscopy:

⇩ NAA - neuronal loss

⇧ choline - myelin destruction

⇧ ml - local glial proliferation secondary to inflammation



CMV encephalitis

Most people are infected with CMV by the time of late adulthood

Particularly susceptible to CMV: intrauterine infection and immunocompromised (HIV, solid organ, bone marrow recipients)

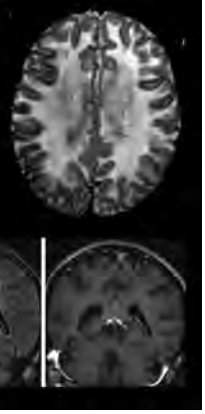
CMV is neurotropic, replicates in ependyma, germinal matrix, capillary endothelium

www.wikipedia.com

- ✓ Meningoencephalitis – most common manifestation;
- ✓ Ventriculoencephalitis - advanced HIV infection, may rapidly decline to coma or death
- ✓ Enhancing mass lesions - only in patients with advanced AIDS
- ✓ Polyradiculopathy is more common in adults, and is rare in children

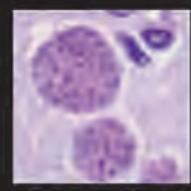
CMV encephalitis

- ✓ May be normal
- ✓ Diffuse/multifocal lesions in white matter
- ✓ Cortical/subcortical, periventricular areas
- ✓ T1 hypo-, T2, FLAIR hyperintense
- ✓ «-» surrounding edema
- ✓ «+» meningeal enhancement
- ✓ «+» periventricular enhancement
- ✓ «+» cranial nerve enhancement
- ✓ Ventriculomegaly/hydrocephalus



Toxoplasmosis

- ✓ The most common cause of focal brain lesion in HIV, bone marrow and peripheral stem cell transplantation
- ✓ 20-70%of population seropositive for *T. gondii* in USA
- ✓ Dx:
  - ✓ Clinical features
  - ✓ Neuroimaging
  - ✓ Antitoxoplasma antibody titers in CSF
  - ✓ Direct detection in the brain tissue, blood, CSF by staining, PCR
  - ✓ Clinical and radiologic improvement with specific treatment



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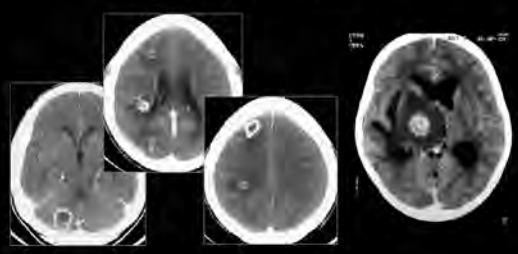
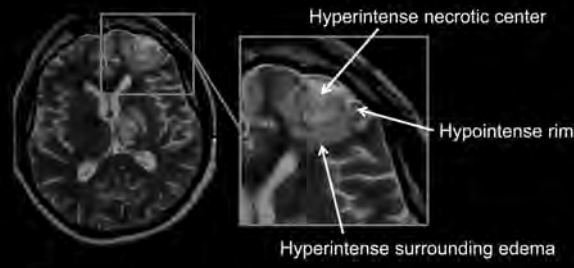
Toxoplasmosis



CT:

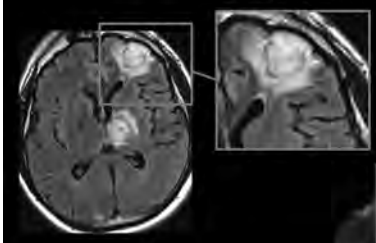
- ➢ usually multiple ill-defined hypodense lesions
- ➢ surrounding edema and mass effect
- ➢ follow up: complete resolution, residual lucencies or calcifications
- ➢ thin, smooth rim/ solid nodular/ «target» enhancement
- ➢ Basal ganglia, corticomedullary junction, thalamus, cerebellum

Toxoplasmosis

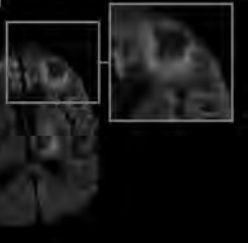


- ➢ MRI – most sensitive imaging modality
- ➢ T2WI - multiple hypointense lesions, with hyperintense necrotic center and surrounding edema, mass effect

Toxoplasmosis



FLAIR: hypointense rim with hyperintense necrotic center and surrounding edema



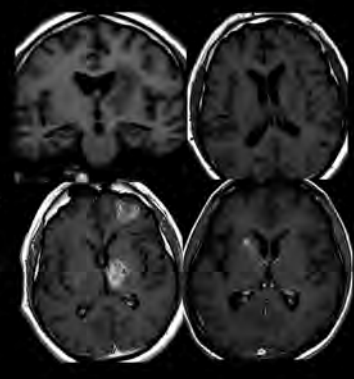
DWI: hyperintense rim with hypointense necrotic center (facilitated diffusion)

Toxoplasmosis

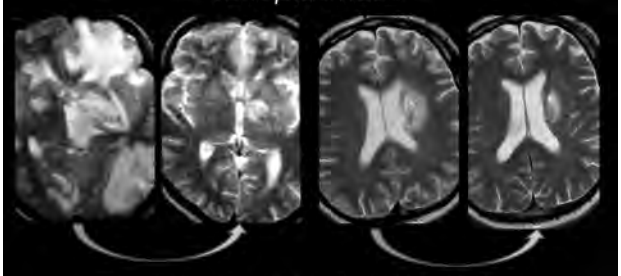
- ➢ T1 WI: ill-defined hypointense lesion

could be hyperintense (necrotic/proteins?)

- ➢ T1 WI +C : rim, nodular punctate, «target» enhancement with surrounding hypointensity (edema)



Toxoplasmosis

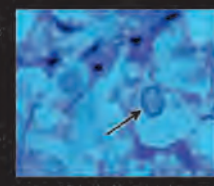


TE lesions usually resolve in 2-4 weeks; lack of resolution suggests another etiology

In at-risk patients suggest treatment should be started empirically

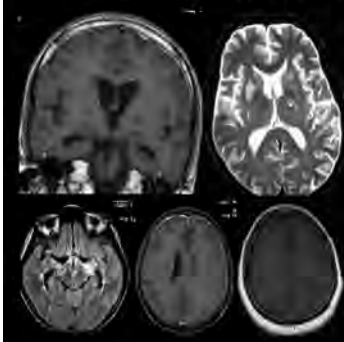
Cryptococcosis

- The 3rd most common opportunistic infection in AIDS
- Wide-spread
- Hematogenous spread from the primary infection in the lungs
- Typical: infection of the leptomeninges, spread along the perivascular spaces with involvement of the basal nuclei, thalamus, brain stem, cerebellum, white matter



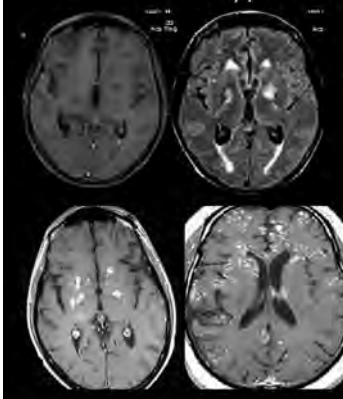
Smith AB et al. Radiographics. 2008 Nov-Dec 28(7):2033-58

Cryptococcosis



Dilated perivascular spaces:
- ➢ T2 WI: hyperintense
- ➢ FLAIR: multiple small hypointense lesions, could be hyperintense rim
- ➢ Location: basal nuclei, thalamus, brainstem, cerebellum, white matter
- ➢ Gelatinous pseudocysts: larger, confluence of dilated perivascular spaces
- ➢ T1 WI+C: variable, may be leptomeningeal enhancing
- ➢ «-» in immunocompromised

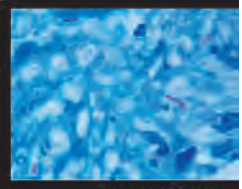
Cryptococcosis



Cryptococcoma:
- ➢ T2 WI, FLAIR: hyperintense lesion
- ➢ T1 WI: hypointense lesion
- ➢ T1 WI +C: ring-like/ solid enhancement
- ➢ Maybe milliary dissemination

Tuberculosis

CNS Infection by *Mycobacterium tuberculosis* is almost always secondary to hematogenous spread (often pulmonary)



www.wikipedia.com

Imaging:

- ✓ 50% - normal
- ✓ Tuberculous meningitis
- ✓ Localized parenchymal lesion - tuberculoma – up to 34%
- ✓ Cerebritis, abscess (rare)
- ✓ Hydrocephalus
- ✓ Stroke - 28-41% (more common bilateral, middle cerebral artery region, brain stem)

Tuberculosis: meningitis

Basal cisterns> superficial sulci

CT: may be normal (10-15%)

isodense to hyperdense exudate

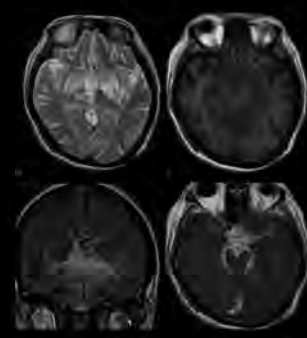
CT +C: intense enhancement

MRI:

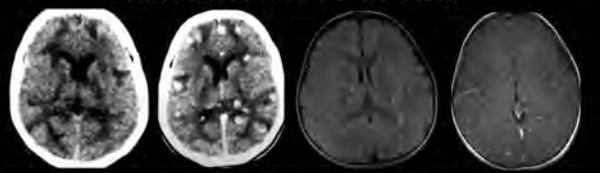
TI, T2 WI: isointense/hyperintense exudate, may be low-signal nodules

FLAIR: hyperintense signal in basal cisterns, sulci

TI WI + C: marked meningeal enhancement, nodularity



Tuberculosis: tuberculoma



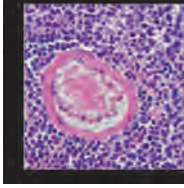
Type	CT	CT + C	MRI	T1 WI + C
noncaseating	hypodense/ isodense	homogeneous	T1WI - hypo T2WI - hyper	homogeneous
caseating with solid center	hypodense/ isodense	heterogeneous/ ring-enhancement	T1WI – hypo/iso T2WI – hypointense	ring-enhancement
caseating with necrotic center	hypodense	ring-enhancement	T1WI – hypointense T2WI – hypo rim + hyper center	ring-enhancement

Primary CNS lymphoma

1%-5% of all brain tumors primary brain tumours

The only known risk factor for PCNSL - immunodefficiency

Risk increases in:
- ✓ autoimmune diseases like Sjögren syndrome, and systemic lupus erythematosus
- ✓ viruses: Epstein-Barr virus (10-15%) and HIV/AIDS (patients on HAART in later stage of disease)
- ✓ Congenital immunodeficiency syndromes
- ✓ Severe immunosuppression (chemotherapy, long-term steroids)



- ➢ disruption of the bloodbrain barrier
- ➢ hypercellularity
- ➢ high nuclear to cytoplasmic ratio

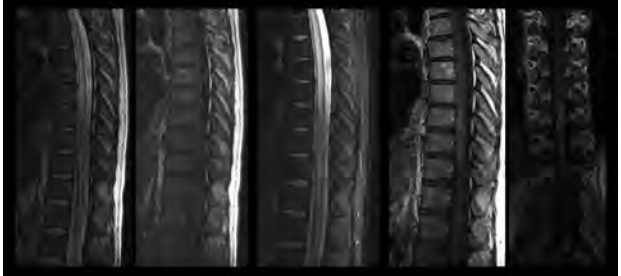
Primary CNS lymphoma

Location:

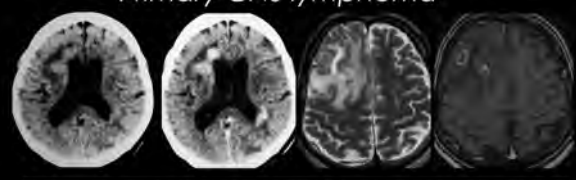
Common: supratentorial frontoparietal white matter, periventricular regions, deep gray nuclei, corpus callosum

Uncommon: posterior fossa, hypothalamus, infundibulum, pituitary gland

Rare: primary dura-based lymphomas



Primary CNS lymphoma

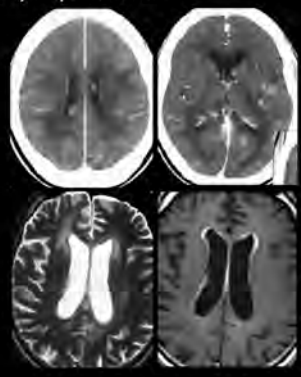


	Immunocompetent	Immunocompromised
Mean age	60	30
Multiple lesions	30-50%	Up to 80%
Necrotic changes	rare	common
CT density	hyperdense	hyperdense
T1, T2 WI	Iso-hypointense	Iso-hypointense
Contrast enhancement (CT, MRI)	homogeneous	heterogeneous
DWI	diffusion restriction	

Primary CNS lymphoma

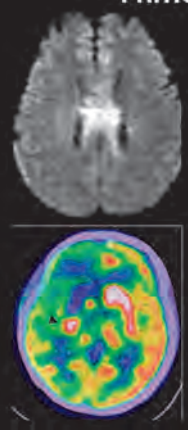
Special features of PCNSL in immunocompromised patients:

- ✓ Multiplicity
- ✓ Hemorrhage
- ✓ Lack of enhancement
- ✓ Necrosis
- ✓ Calcification
- ✓ Atypical location



PCNSL in HIV

Primary CNS lymphoma



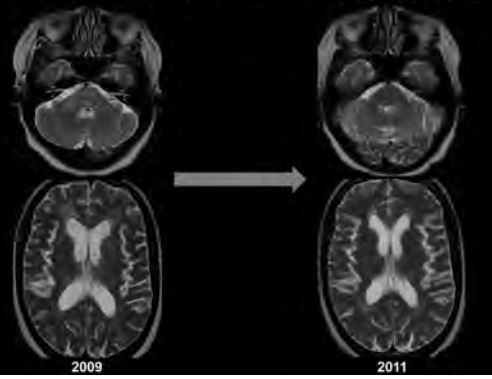
- ➢ DWI: diffusion restriction
- ➢ Perfusion: low relative cerebral blood volume (rCBV)
- ➢ MR Spectroscopy: high Cho/Cr, low Naa
- ➢ PET: increased uptake of FDG/methionine
- ➢ Thallium-201 single-photon emission CT: intense

focal Tl-201 uptake

Bathla G. The Many Faces Of Intracranial Lymphoma. Poster No.: C-0031. ECR 2012

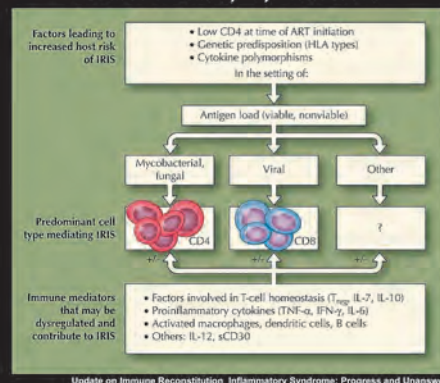
Role of the HAART in HIV

HAART: reversibility of HIV-encephalopathy



2009 2011

HAART: immune reconstitution inflammatory syndrome



Update on Immune Reconstitution Inflammatory Syndrome: Progress and Unanswered Questions. *Colleen F. Kelley, Wendy S. Armstrong.* Current Infectious Disease Reports 2009, 11:486–493

IRIS

Paradoxical

Unexpected deterioration in a patient who was successfully treated for an opportunistic infection after HAART initiation. Microbiologic analyses are negative: no signs of previous or newly acquired infection.

Unmasking

HAART reveals a subclinical previously undiagnosed opportunistic infection. Immune response against a living pathogen, which can generally be isolated by microbiological analyses.

Most common in neuroIRIS:

1. Tuberculosis
2. PML
3. Cryptococcosis
4. Herpes virus infection (herpes simplex virus, VZV, CMV, EBV)
5. HIV-encephalitis
6. Autoimmune leucoencephalopathy

PML-IRIS

- ➢ Progressive neurologic deficit;
- ➢ Mortality 50%;
- ➢ Predominantly CD8 inflammatory infiltrate
- ➢ Enlargement of the lesions
- ➢ Atypical: surrounding edema, «+» C
- ➢ regress of imaging changes in 3 -6 months

Martin-Blondel G. et al. Pathogenesis of the immune reconstitution inflammatory syndrome affecting the central nervous system in patients infected with HIV. Brain. 2011 Apr;134(Pt 4):928-46.