NEUROLOGICAL NEURORADIOLOGICAL CONFERENCE

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

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BACKGROUND

- ผู้ป่วยชายไทย โสด อายุ 40 ปี
- เดิมทำกิจวัตรประจำวันได้ตามปกติ
- CC : สับสนมากขึ้น 1 วันก่อนมา รพ.

HISTORY

6 สัปดาห์ก่อนมา รพ. ผู้ป่วยมีอาการปวดตึงศีรษะ ปวดตื้อๆ บริเวณท้ายทอย ไม่ร้าวไปไหน ไม่เวียนศีรษะ ไม่มีบ้านหมุน ไม่มีคลื่นไส้อาเจียน อาการปวดศีรษะค่อยๆเป็นมากขึ้นเรื่อยๆ จาก 3 คะแนน เป็น 8 คะแนน มักปวดมากที่สุดที่ท้ายทอย บางครั้งปวดที่ขมับสองข้าง ปวดตื้อๆ กลอกตา ไอ จาม เบ่งถ่ายไม่มีอาการปวดมากขึ้น ไม่ตื่นมาปวดกลางคืน ท่านั่งและนอนปวดเท่าๆกัน อาการปวดทุเลาบางครั้งแต่ไม่หายสนิทไม่มีไข้ ญาติสังเกตว่าผู้ป่วยคิดช้า ตอบช้า แต่ยังพูดคุยรู้เรื่อง ใช้คำถูกต้อง ทำกิจวัตรประจำวันได้

HISTORY

4 สัปดาห์ก่อนมา รพ. มีอาการเดินเซ ซ้ายขวาทั้งสองข้าง รู้สึกอ่อนเพลียไม่มีแรง ยังลุกจากที่นั่งได้ ยกแขนได้ ไม่มีรองเท้าหลุด ยังสามารถเดินช้าๆ ได้ ไม่มีเวียนศีรษะ บ้านหมุน ไม่คลื่นไส้อาเจียน ไม่มีหยิบจับของไม่ถูก รู้สึกเหนื่อยง่ายมากขึ้น เดินขึ้นบันไดประมาณ 10 ขั้น ต้องหยุดพัก ไม่เจ็บหน้าอก นอนราบได้ ไม่ขาบวม ไม่มีไข้ อาการปวดศีรษะลักษณะเดิมไม่ดีขึ้นจึงไปคลินิกใกล้บ้าน ได้ยาแก้ปวดและยาแก้เวียนศีรษะมารับประทาน อาการไม่ดีขึ้น แต่ไม่แย่ลง อาการอ่อนเพลียพอๆเดิม

HISTORY

2 สัปดาห์ก่อนมา รพ อาการปวดศีรษะดีขึ้น ไม่มีอาเจียน ไม่มีตามัว ไม่รู้สึกว่ามีไข้ แต่มีอาการคิดช้า พูดช้า และสับสนมากขึ้น เช่น จับช้อนมาถือไว้ จนญาติต้องมาบอกให้ตักข้าว จึงตักข้าวกินได้ , เวลาถามจะนึกคำตอบนาน กว่าจะตอบได้ แต่สามารถตอบได้ตรงคำถาม , มีช่วงสับสนบอกจะไปเข้าห้องน้ำที่บ้านญาติ บางครั้งหาของไม่เจอ จำไม่ได้ว่าเก็บไว้ที่ไหน ญาติเห็นว่าอาการเป็นมากขึ้นจึงพามา รพ.

PAST HISTORY

- HIV infection :
  - Presented with prolong fever with weight loss 1 month (2548)
  - Anti HIV positive , CD4 12/2548 410 (34%)
  - On 3TC , TDF, EFV
  - จากนั้นกลับไปรับยาต่อที่ รพ เชียงราย ขาดยา 1 ปี จากนั้น กลับไปรับยาต่อเนื่องที่ รพ เชียงราย ตั้งแต่ ปี 2553
  - จำ CD4 ล่าสุดไม่ได้
- Chronic HCV infection
  - ไม่เคย U/S abdomen , HCV VL
- Old pulmonary tuberculosis : Sputum AFB positive ปี 2553 IRZE ครบ 6 เดือน
- Late latent syphillis : Dx 2553 ยังไม่เคยรักษา

PERSONAL HISTORY

- MSM with unsafe sex
- Deny IVDU, blood transfusion
- Social alcohol drinking
- Smoking 10 pack/year

CURRENT MEDICATION

- 3TC(150) 2 tab po hs
- TDF(300) 1 tab po hs
- EFV(600) 1 tab po hs

PHYSICAL EXAMINATION

- Thai male patient, well co-operative
- V/S: BT 38.0 ^{0}c, BP 122/80 mmHg, HR 94 bpm, RR 18/min lymph node
- HEENT: oral thrush , no OHL, no pale conjunctivae, anicteric sclerae.
- Lymph node: no palpable lymph node.
- Heart: normal S1S2, no murmur.
- Lungs: normal breath sounds, equal both lungs, no adventitious sounds.

PHYSICAL EXAMINATION

- **Abdomen:** no distension, normoactive bowel sounds, soft, not tender, liver and spleen can not be palpated
- **Extremities:** no pitting edema
- Skin : PPE both legs and arms

PHYSICAL EXAMINATION

- **Neuro:**
- Alert, psychomotor retardation, orientated to time, place, person
- Slow fluent speech with normal naming , comprehension, repetition , memory , calculation , no paraphasia
- Eye exam : no papilledema, no CMV retinitis, no HIV retinopathy
- Pupil 3 mm RTLBE, no RAPD, normal VF by confrontation, no ptosis, full EOM, no ptosis, no nystagmus, normal facial sensation, intact corneal reflex bilaterally, normal hearing , no tongue or uvula deviation, normal gag reflex,no tongue atrophy

PHYSICAL EXAMINATION

- No muscle atrophy , normal tone
	Rt	Lt
Motor power UE	V/V	V/V
Motor power LE	V/V	V/V
- BBK plantar response both side, clonus negative
- Reflex 2+ all
- Normal PPS
- Intact proprioception all extremities
- Romberg sign negative

PHYSICAL EXAMINATION

- Cerebellar : no gaze evoked nystagmus , normal finger to nose and heel to shin , no dysdiadokokinesia bilaterally ,no gait or truncal ataxia
- Stiff neck negative, kernig's sign negative

PROBLEM LIST

- Subacute progressive headache
- Rapidly progressive dementia
  - Psychomotor retardation
  - Alteration of consciousness : content
- Systemic symptom : Unrecognized fever, Fatigue
- U/D
  - HIV infection
  - Chronic HCV infection
  - Old pulmonary tuberculosis
  - Late latent syphilis

IMAGING

INVESTIGATION

- CBC Hb 14.5, Hct 43%, WBC 10340 cell/mm^3 (N 76, L12) Plt 257,000/ul
- Renal: BUN 12 Cr 0.78
- LFT: SGOT 40 SGPT 41 ALP 80 TB1.22 DB 0.57 Alb 4 Glb 5.6

- **Anti HIV positive, CD4 126 (13%), VL 2922**
- HBs Ag negative, AntiHBs negative, AntiHBc negative
- Anti HCV positive , VL 739, genotype can not be detected
- Treponemal Ab reactive, VDRL weakly reactive , TPHA reactive 145.7
  CSF FTA : non-reactive (late latent syphilis)

INVESTIGATION

- **CSF 23/9/59 : OP 16 cmH2O CP 8 cmH2O Clear**
  - **WBC 103 cell/cumm (PMN 3% Mono 97%) RBC 100 cell/cumm**
  - **Glucose 40/90 mg/dl(44%) Protein 126.9 mg/dl**
  - **G/S , AFB, mAFB, wright stain : negative**
  - **C/S negative**
  - **Cyotospin : negative**
- CSF(27/9/59)
  - WBC **55 cell/cumm (PMN 2% Mono 98%) RBC 100 cell/cumm**
  - **Glucose 59 mg/dl , Protein 165 mg/dl**

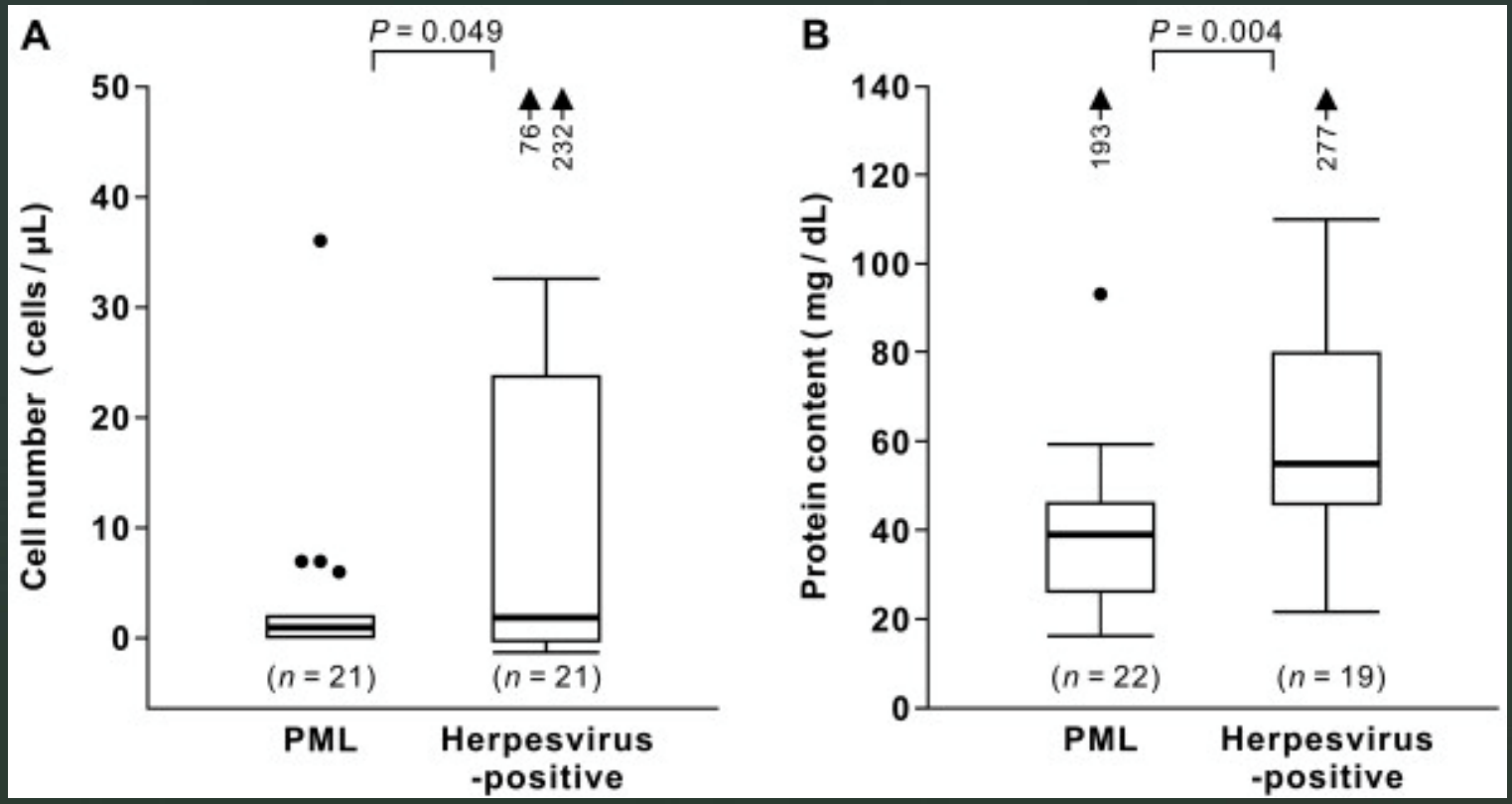
INVESTIGATION

- **CSF encephalitis virus**
  - **John cunningham virus positive (8140 copies/ml)**
  - **EBV positive (13685 copies/ml)**
  - **CMV undetectable**
- Serum cryptoAg negative, india ink negative
- Sputum AFB,mAFB, PCR for MTBC : negative
- Sputum PCR for PCP, IFA for PCP : Negative

CSF findings in patients with PML

- Cell counts : less than 20 cells/mm^3.
  - The median cell count 2 cells/mm^3 , mean was 7.7 cells/mm^3.
- 55% had an abnormally elevated CSF protein
  - mean : 66.5 mg/dL.
  - highest recorded : 208 mg/dL (2.08 g/L)

Neurology. 2013 Apr 9; 80(15): 1430–1438.



CSF cell counts (A)
total protein contents (B)
in PML and herpesvirus-positive patients.

BMC Neurol. 2013; 13: 200.

REAL TIME PCR-Epstein-Barr virus

- **CSF encephalitis virus : EBV positive (13685 copies/ml)**

> 200 copies /ml = Positive

J Clin Pathol. 2019 Jul 17. pii: jclinpath-2019-205822.

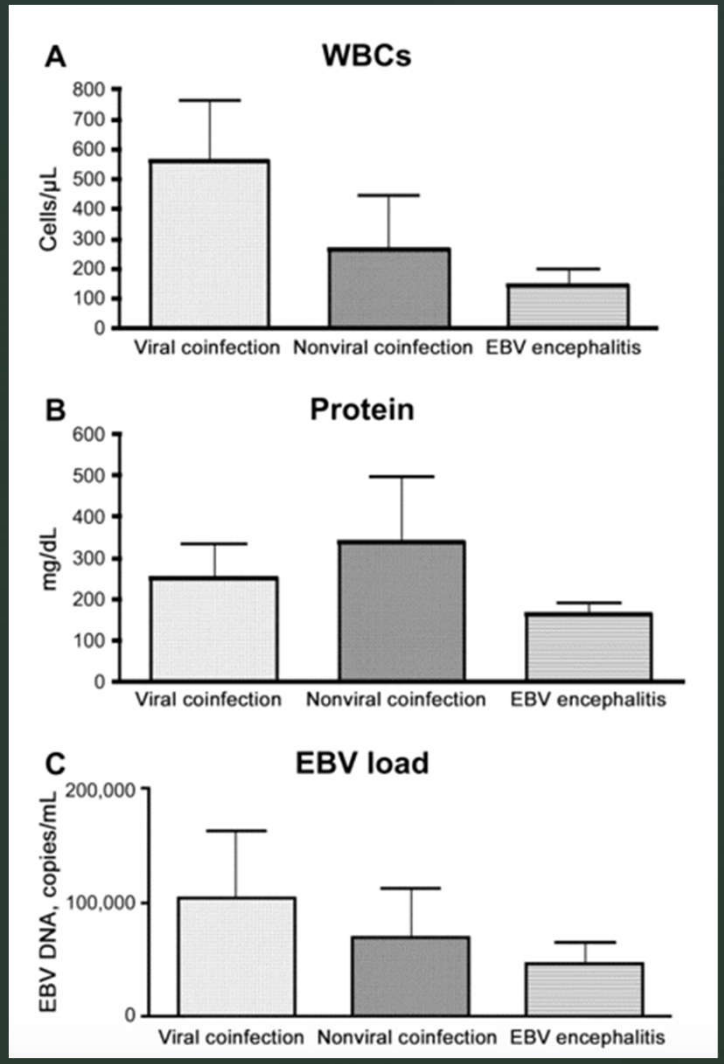
Diagnosis of EBV encephalitis

Clinical :

- Fever
- Change in level of consciousness
- Seizures
- Focal neurologic deficits
- IICP

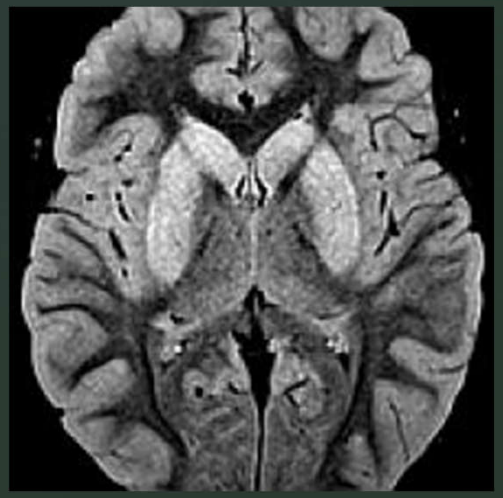
CSF

- WBC 100-1000(Lymphocyte)
- Normal or elevated protein concentration
- normal glucose (45-85mg%)



The Journal of Infectious Diseases, Volume 191, Issue 2, 15 January 2005, Pages 234–237,

Diagnosis of EBV encephalitis



Imaging

- CT : non-specific areas of decreased attenuation(low sensitivity)
- MRI :
  - bilateral and symmetric increased T2-weighted signal
  - caudate nuclei, putamina ,thalami and may also involve the cortex.
  - Involvement of the white matter, brainstem and splenium is possible, but rare.
  - Both increased and reduced ADC

AMERICAN JOURNAL OF NEURORADIOLOGY-case-collections-diagnosis/epstein-barr-encephalitis

Herpesvirus DNA	No. (%) of CSF specimens		
	Total [a] (*n* = 299)	JCV-positive (*n* = 42)	JCV-negative (*n* = 257)
HSV-1	1 (0.3)	0 (0)	1 (0.4)
HSV-2	0 (0)	0 (0)	0 (0)
VZV	8 (2.7)	1 (2.4)	7 (2.7)
CMV	5 (1.7)	0 (0)	5 (1.9)
HHV-6	0 (0)	0 (0)	0 (0)
EBV	19 (6.4)	5 (11.9)	14 (5.4)

BMC Neurol. 2013; 13: 200.

MRI patterns in the PML and EBV

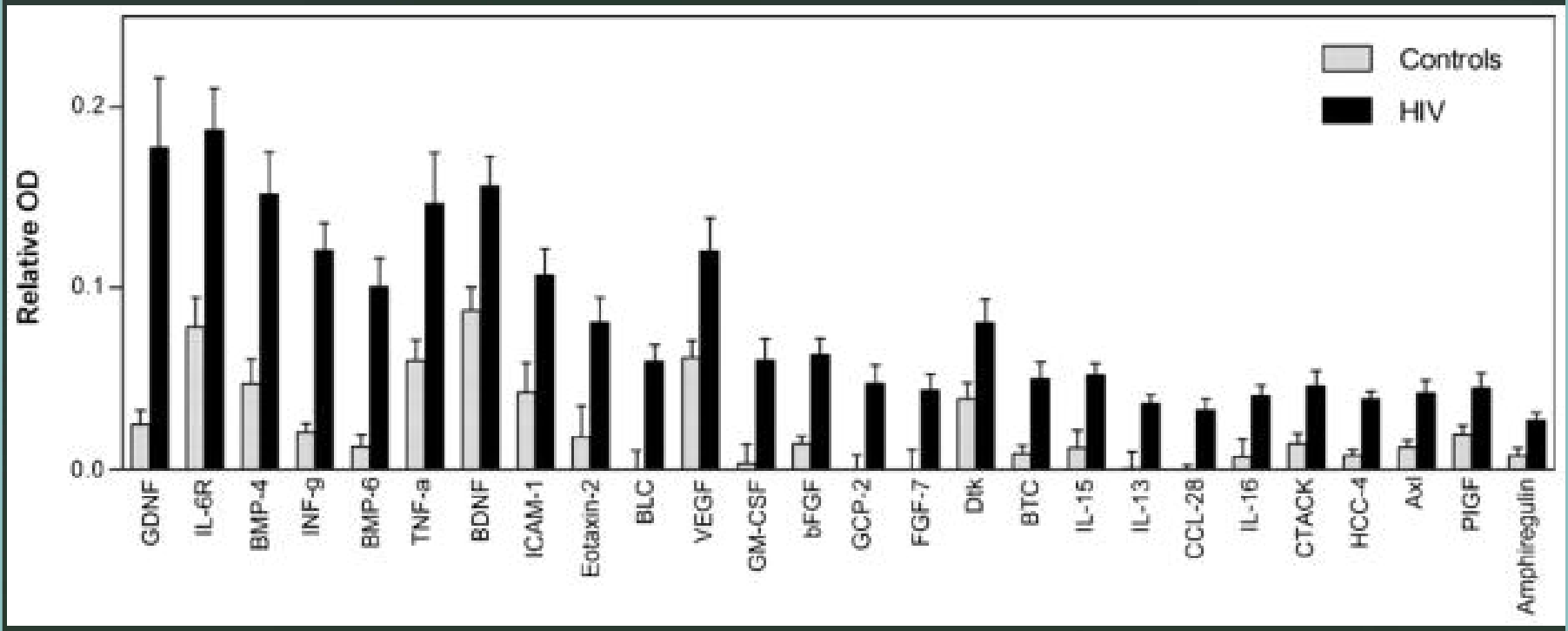
Detected Viral DNA in CSF	No. of patients	Neurologic symptom (%)	Cerebral white matter	Cerebellum	Brain stem	Other	Unknown
JCV[b]	25	25 (100)	**21 (84.0)**	4 (16.0)	**7 (28.0)**	2 (8.0)	2 (8.0)
EBV	12	9 (75.0)	**7(58.3)**	**5(41.7)**	1(8.3)	2(16.7)	0(0)

BMC Neurol. 2013; 13: 200.

Variable	Appearance	Opening Pressure (mm H_2O)	RBC	WBC	Protein (mg/dL)	Glucose (mg/dL)
Fungal meningitis	Normal or cloudy	Normal or ↑	0	Normal or ↑ (mono-nucleated)	↑	↓
Tuberculous meningitis	Normal or cloudy	↑	0	Normal or ↑ (mono-nucleated)	↑	↓
Viral encephalitis	Normal	Normal or ↑	0	Normal or ↑ (mono-nucleated)	Normal or ↑	Normal
Spinal cord block	Normal	Normal	0	Normal	Slightly ↑	Normal

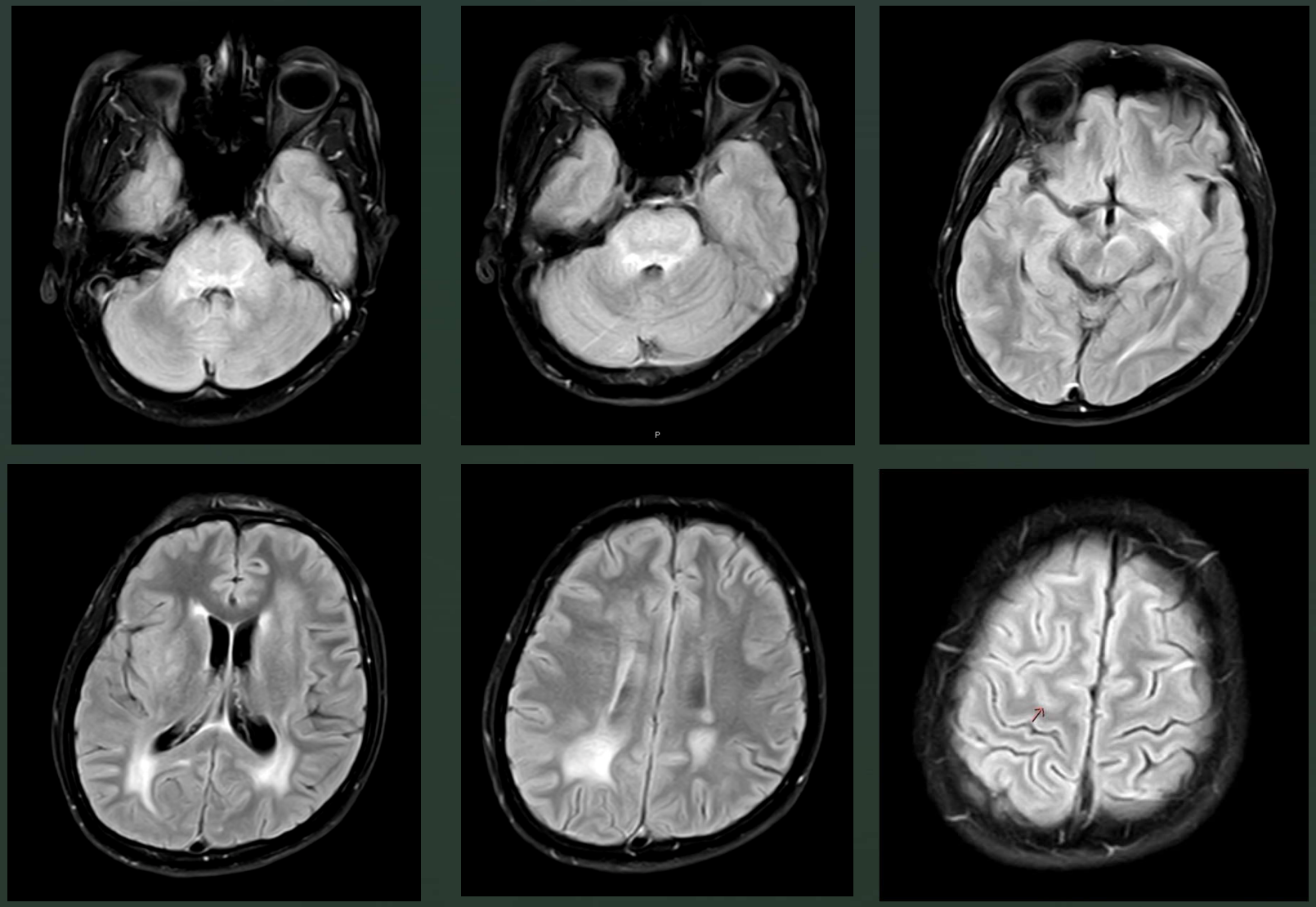
Protein changes in CSF of HIV-infected patients: evidence for loss of neuroprotection

Rick B. Meeker,[⊠] Winona Poulton, Silva Markovic-Plese, Colin Hall, and Kevin Robertson



J Neurovirol. 2011 Jun; 17(3): 258–273.

MRI

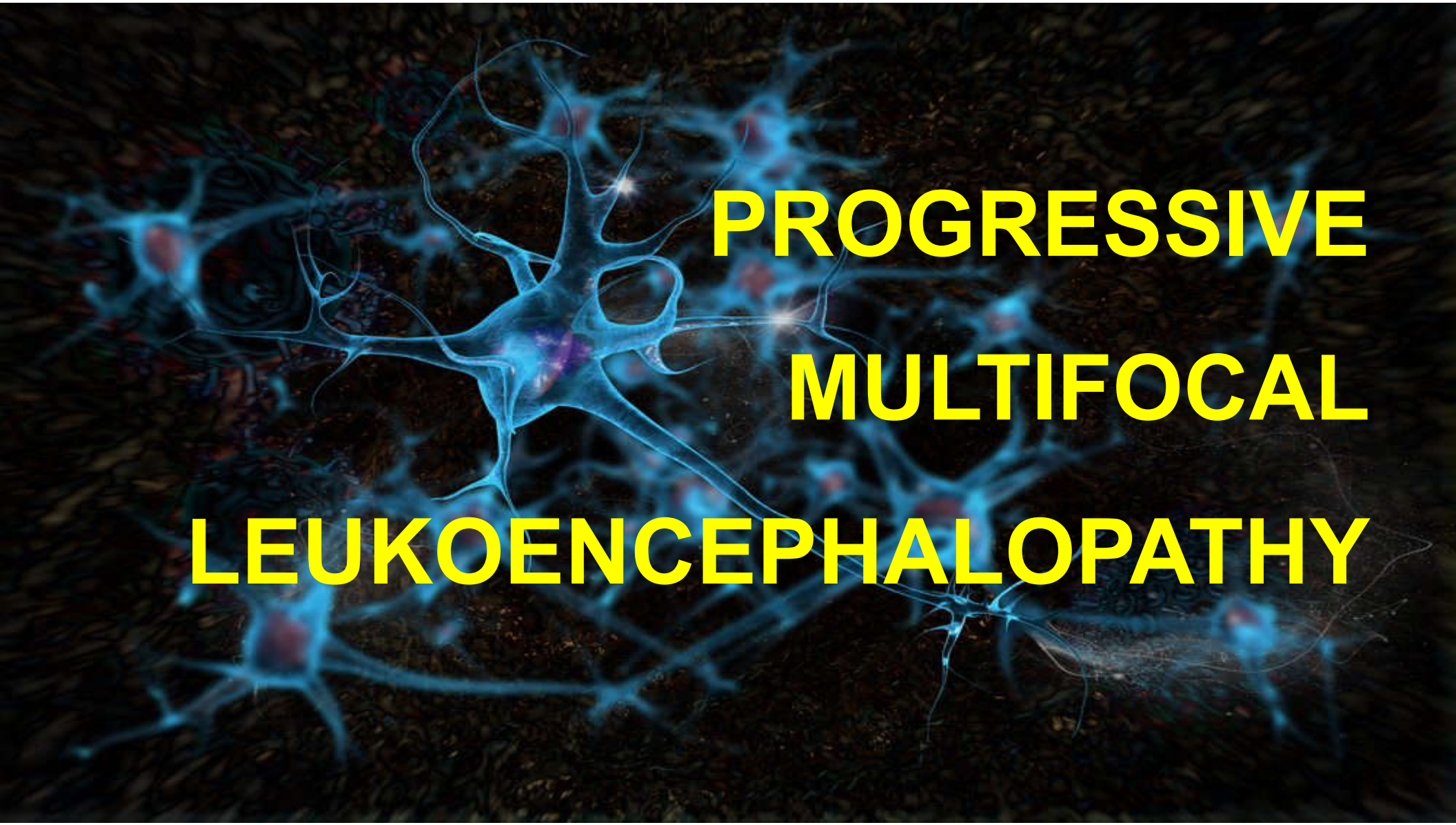


DIAGNOSIS

- Progressive multifocal leukoencephalopathy
- AIDs with chronic HCV infection , late latent syphilis

MANAGEMENT

- 3TC(150) 2 tab po hs
- TDF(300) 1 tab po hs
- EFV(600) 1 tab po hs
- Bactrim 2 tab po pc OD
- Benzatine PenG 2.4 mU IM weekly 3 dose


PROGRESSIVE
MULTIFOCAL
LEUKOENCEPHALOPATHY

Introduction

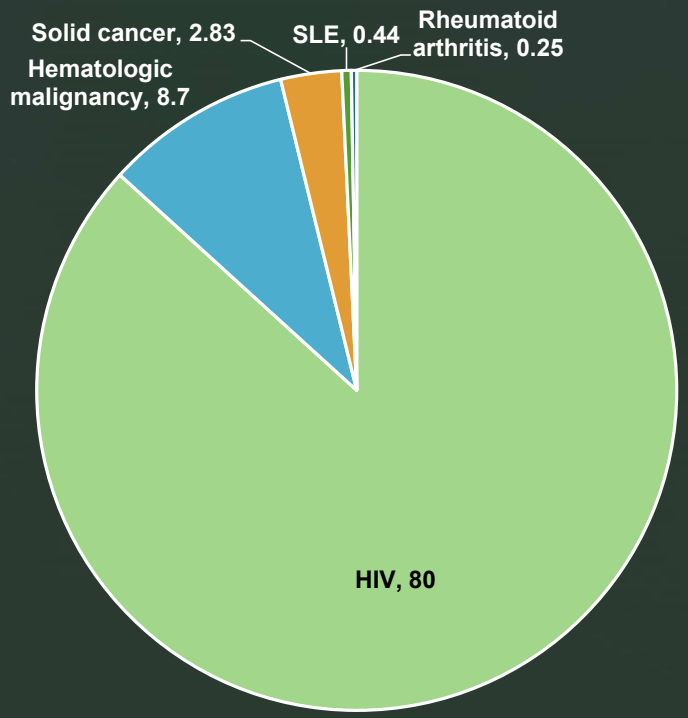
- Disease of the white matter of the brain
- Multifocal areas of demyelination
- Caused by JC virus
- Present with visual deficits, mental impairment , weakness, ataxia
- Immune disorder or receiving immunosuppressive therapy

BASIC EPIDEMIOLOGY

- **Population at risk**

  - HIV infection
  - Immunosuppression or immunomodulation
  - Hematologic and solid malignancies
  - Rheumatologic disorders ex. SLE , sarcoidosis
  - Primary immune deficiencies (idiopathic CD4 lymphopenia or SCID)
  - Therapies such as natalizumab, fingolimod, dimethyl fumarate, rituximab, alemtuzumab, efalizumab

BASIC EPIDEMIOLOGY



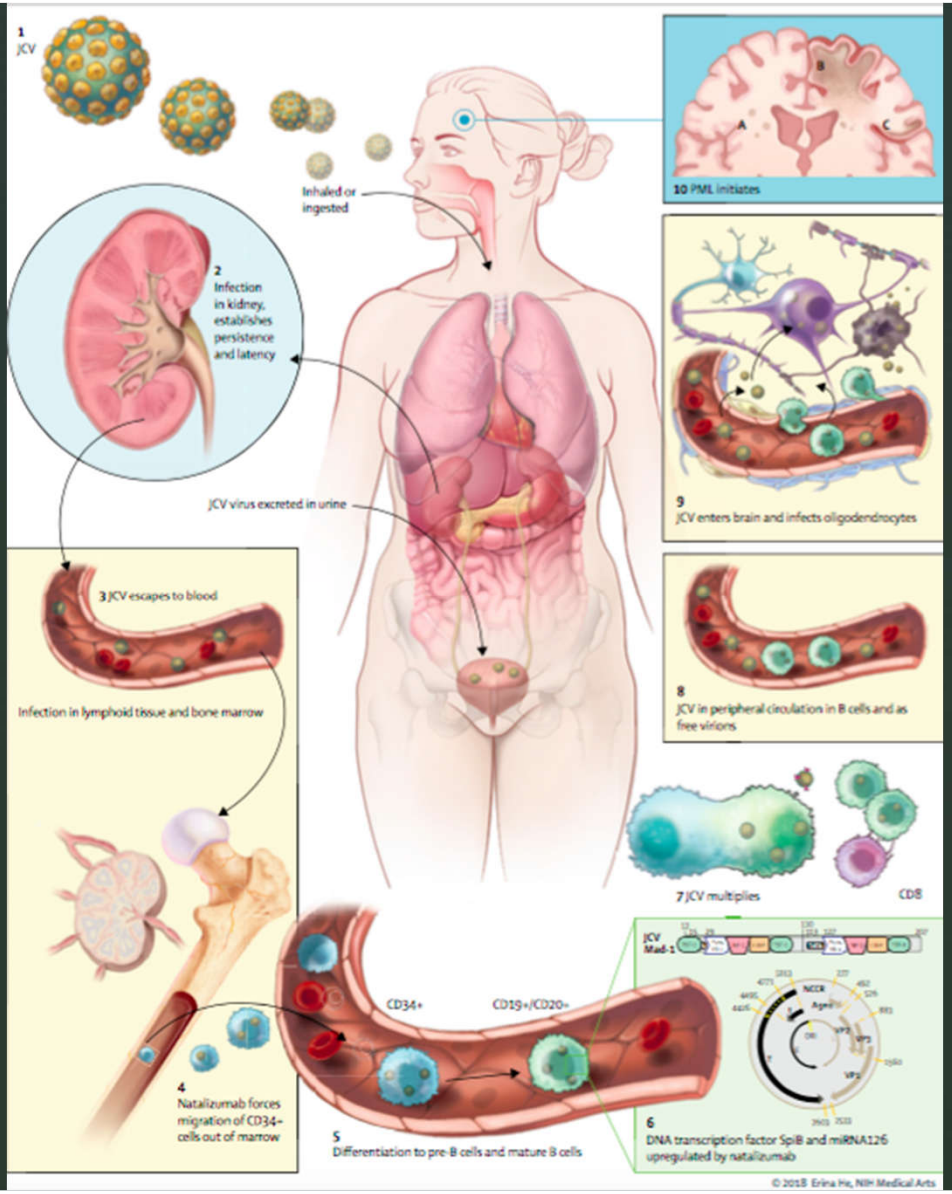
- 80% : HIV
- 8.7% : Hematologic malignancies
- 2.83% : Solid cancers
- 0.44% : SLE
- 0.25% : RA

Amend KL, Turnbull B, Foskett N, et al. Incidence of progressive multifocal leukoencephalopathy in patients without HIV. Neurology 2010;75(15):1326–32.

JC virus

- Majority of adult is infected by JC virus (75-80%)
- Half of this infection occurs during childhood.
- Primary exposure : no symptom.
- Transmission : urine to oral route or respiratory route.

Clin Microbiol Rev. 2012 Jul;25(3):471-506. doi: 10.1128/CMR.05031-11.


1
JCV
Inhaled or ingested
2
Infection in kidney, establishes persistence and latency
JCV virus excreted in urine
3 JCV escapes to blood
Infection in lymphoid tissue and bone marrow
4
Natalizumab forces migration of CD34+ cells out of marrow
CD34+
CD19+/CD20+
5
Differentiation to pre-B cells and mature B cells
6
DNA transcription factor SpiB and miRNA126 upregulated by natalizumab
JCV Mad-1
7 JCV multiplies
CD8
8
JCV in peripheral circulation in B cells and as free virions
9
JCV enters brain and infects oligodendrocytes
10 PML initiates
A
B
C
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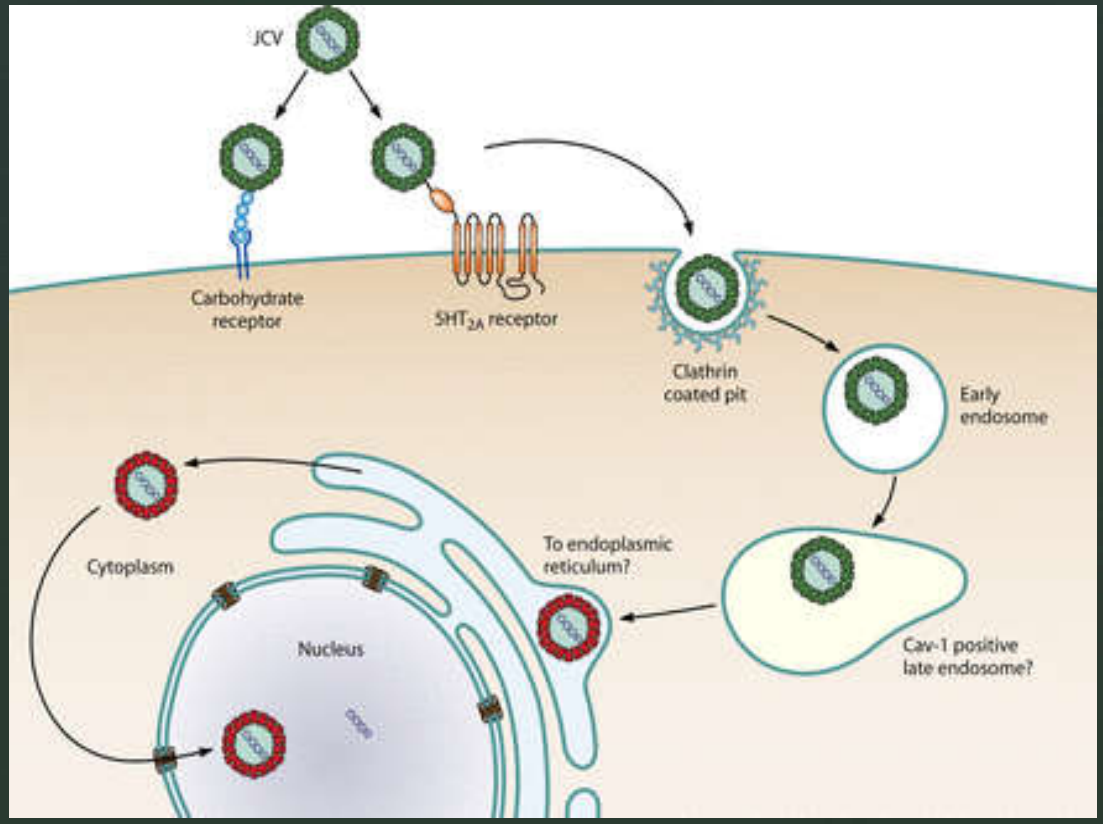
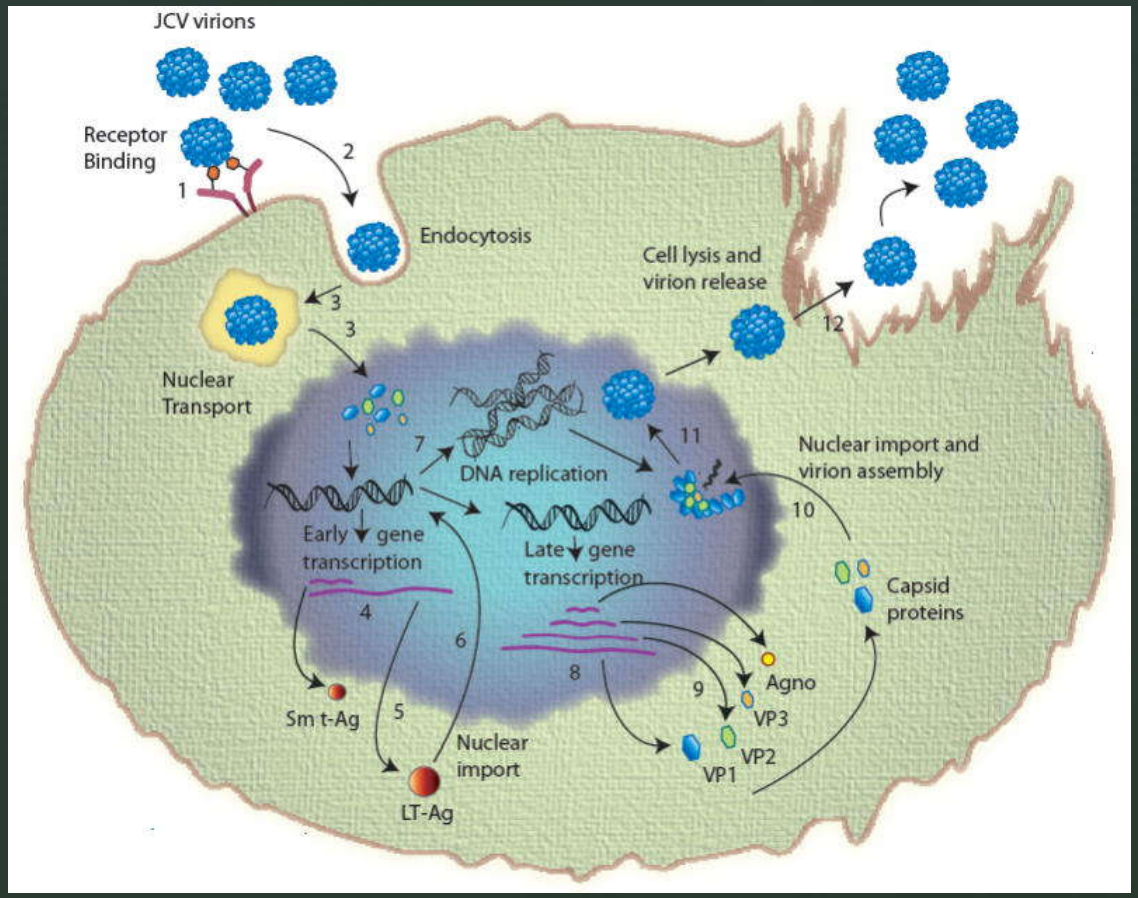
PATHOGENESIS



Clin Microbiol Rev. 2012 Jul;25(3):471-506. doi: 10.1128/CMR.05031-11.

PATHOGENESIS



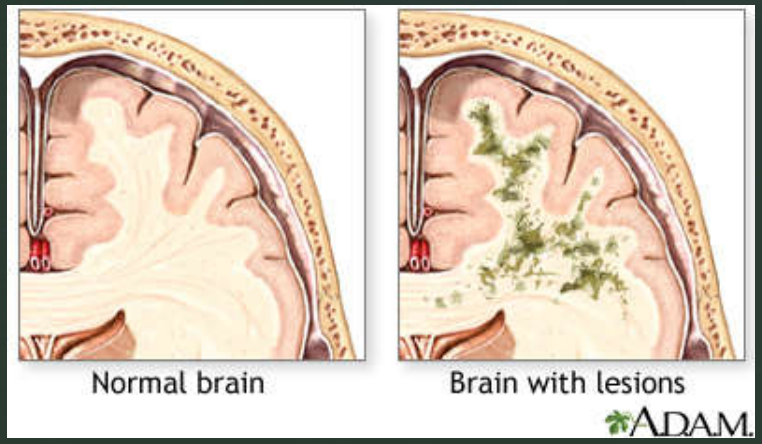
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3128336/#idm140396829694320title

PATHOGENESIS

- How JC virus cause CNS infection (PML)

1. Primary infection
2. Reactivation in immune compromise
3. Genetic rearrangement (archetype strain >>neurotropic strain)
4. Entry of the virus into the CNS
5. Infection of oligodendrocytes
6. Failure of the immune surveillance >> uncontrolled viral replication

CLINICAL PRESENTATION



- subcortical white matter disease
- Involvement in multiple regions of the brain
- Demyelination can develop in any location in the white matter including the brain stem and cerebellum

Future Virol. Author manuscript; available in PMC 2011 July 1.

CLINICAL PRESENTATION

- Visual deficit (35-40%)
- Motor weakness (25-33%)
- Cognitive deficit
- Gait impairment
- Speech disturbance
- Not affect the optic nerve, spinal cord

Future Virol. Author manuscript; available in PMC 2011 July 1.

CLINICAL PRESENTATION

Table 1 PML clinical symptoms and signs in association with different predisposing causes

PML by predisposing cause	No. of patients in each study	Cognitive and behavioral, %	Motor weakness, %	Gait abnormality and incoordination, %	Sensory loss, %	Speech or language disorder, %	Visual deficits, %	Headache, %	Seizures, %
PML in the pre-AIDS era[60]	230	36	33	13		17	34	7	5
AIDS-associated PML[23]	154	36	42	35	19	40	19	32	9
Natalizumab-associated PML[35]	42	54	45		7	24	41		14

Abbreviation: PML = progressive multifocal leukoencephalopathy.

Neurology. 2013 Apr 9; 80(15): 1430–1438.

DIAGNOSIS

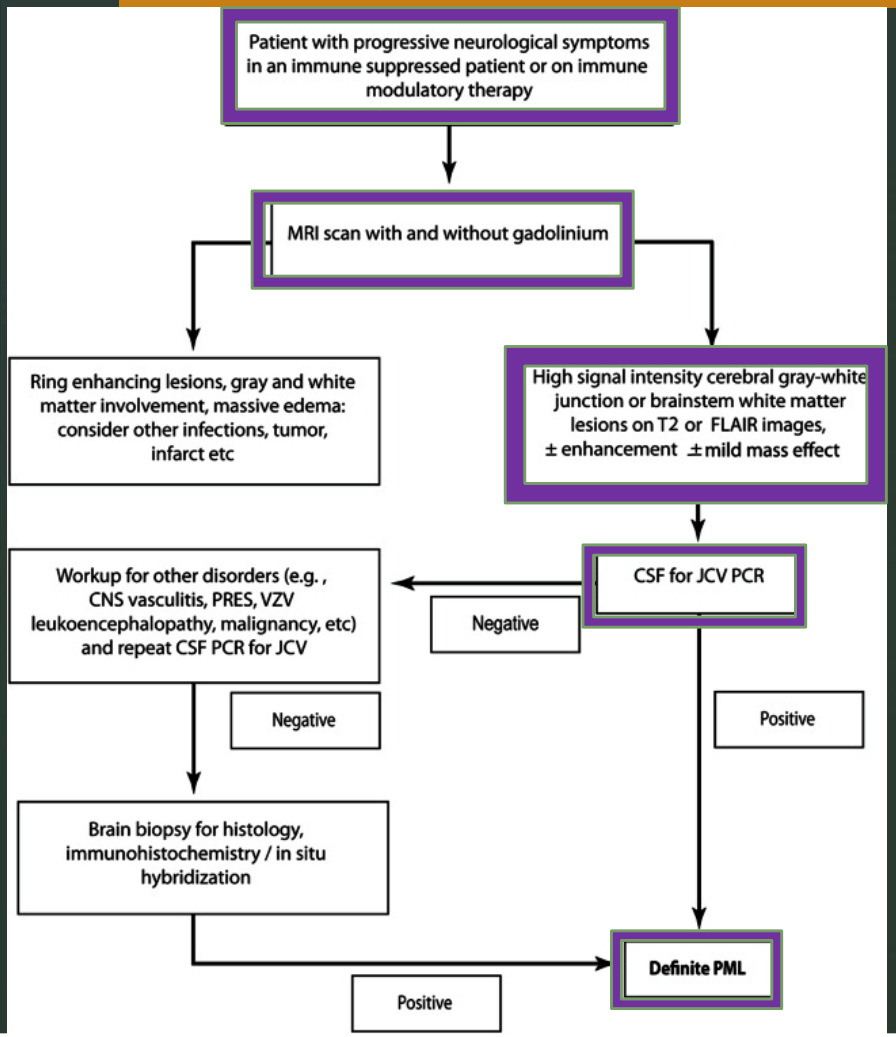


Table 2 Establishing the diagnosis with clinical, radiographic, and laboratory data[a]

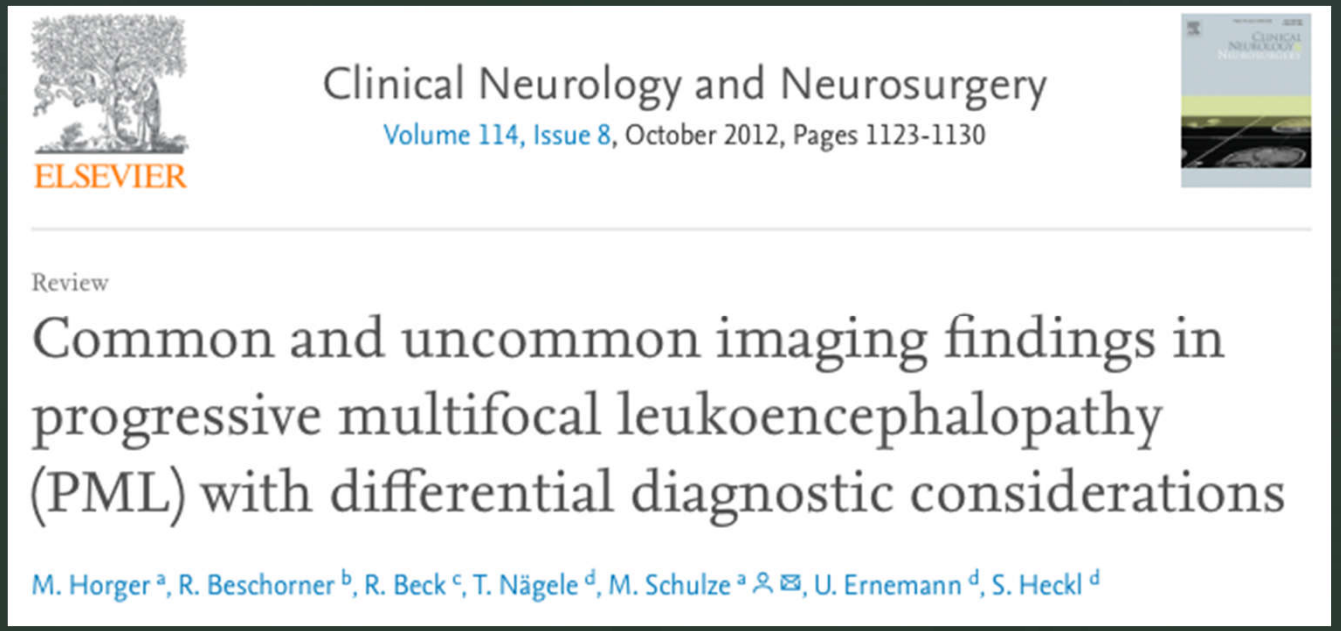
Certainty of PML diagnosis	Compatible clinical features	Compatible imaging findings	CSF PCR for JC virus
Definite	+	+	+
Probable	+	−	+
	−	+	+
Possible	+	+	−/ND
	−	−	+
Not PML	−	−	−
	+	−	−
	−	+	−

Abbreviations: ND = not done or equivocal result; PML = progressive multifocal leukoencephalopathy.
[a] + = Positive; − = negative.

Neurology. 2013 Apr 9; 80(15): 1430–1438.

RADIOLOGY

- MRI is a modality of choice : most sensitive test



ELSEVIER

Clinical Neurology and Neurosurgery
Volume 114, Issue 8, October 2012, Pages 1123-1130

Review

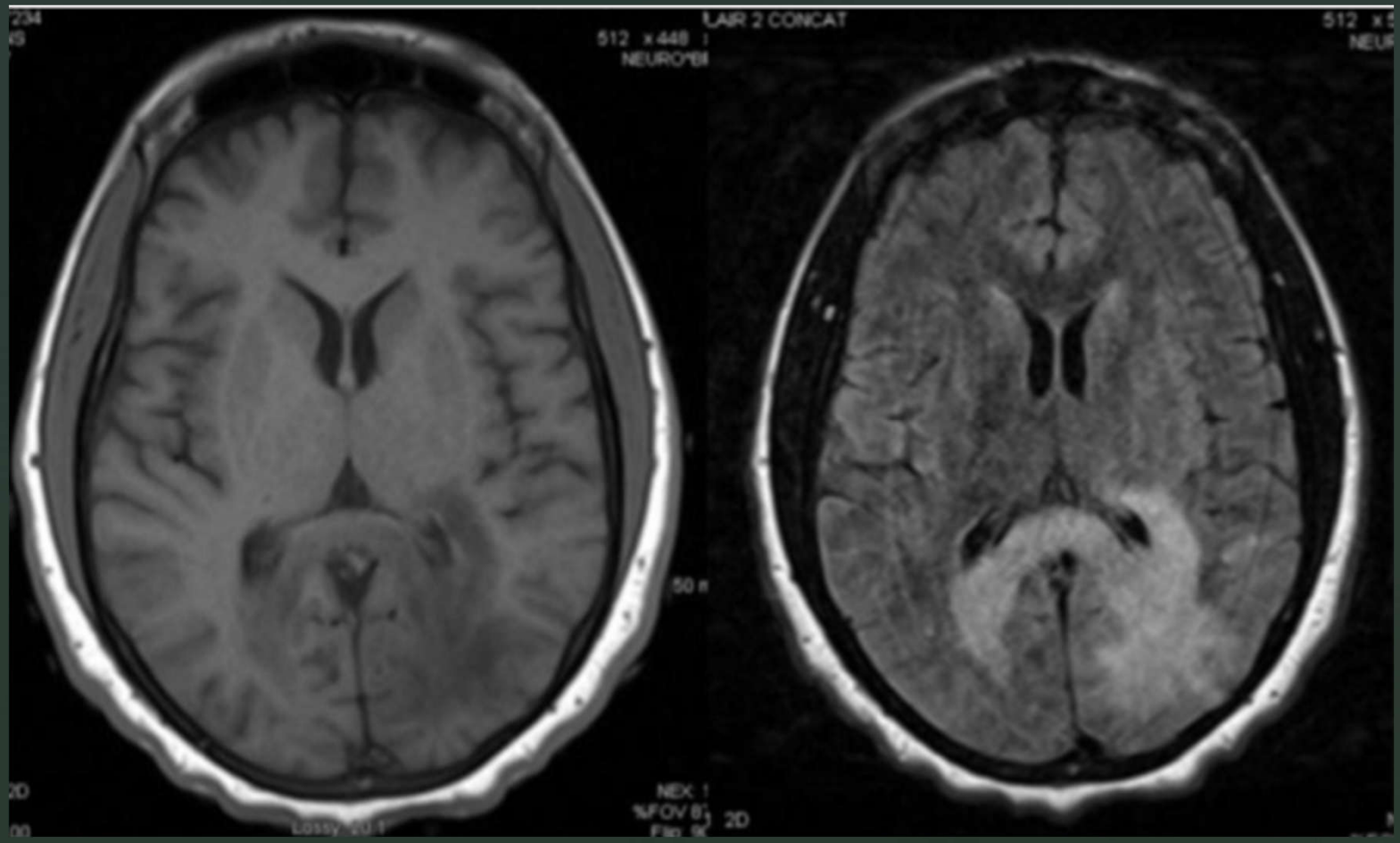
Common and uncommon imaging findings in progressive multifocal leukoencephalopathy (PML) with differential diagnostic considerations

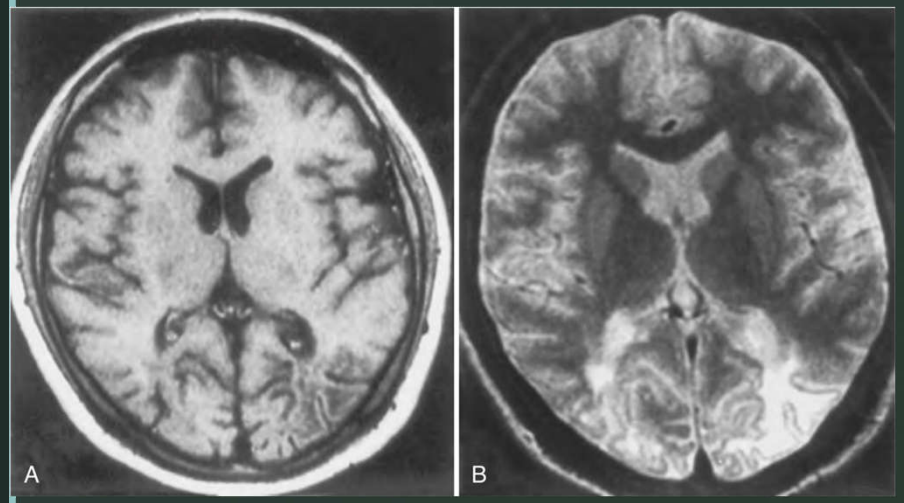
M. Horger [a], R. Beschorner [b], R. Beck [c], T. Nägele [d], M. Schulze [a] ✉, U. Ernemann [d], S. Heckl [d]

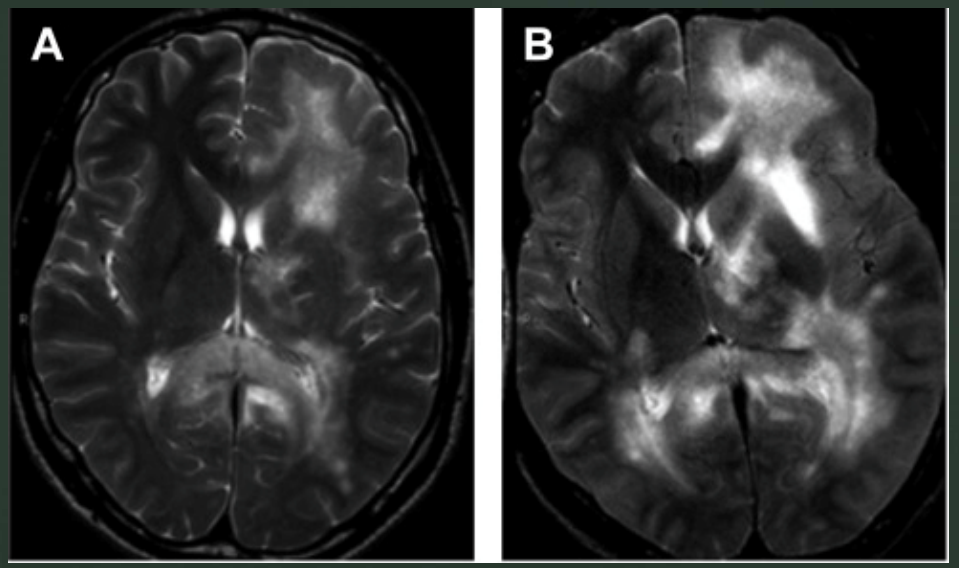
RADIOLOGY

- Multifocal asymmetric periventricular and subcortical involvement.
- Subcortical frontal and parieto-occipital regions
- Corpus callosum ,Basal ganglia, brainstem, and cerebellum can be involved.
- Subcortical-U fibers are commonly involved with a predilection for the parieto-occipital regions
- Little, or no mass effect or enhancement
- DWI : infrequently show restricted diffusion
- Chronic ischemic strokes, multiple sclerosis lesions, and low-grade gliomas can frequently mimic PML lesions
-

https://radiopaedia.org/articles/progressive-multifocal-leukoencephalopathy


FLAIR 2 CONCAT
512 x 448
NEURO*BI
NEX 1
2D


A
B

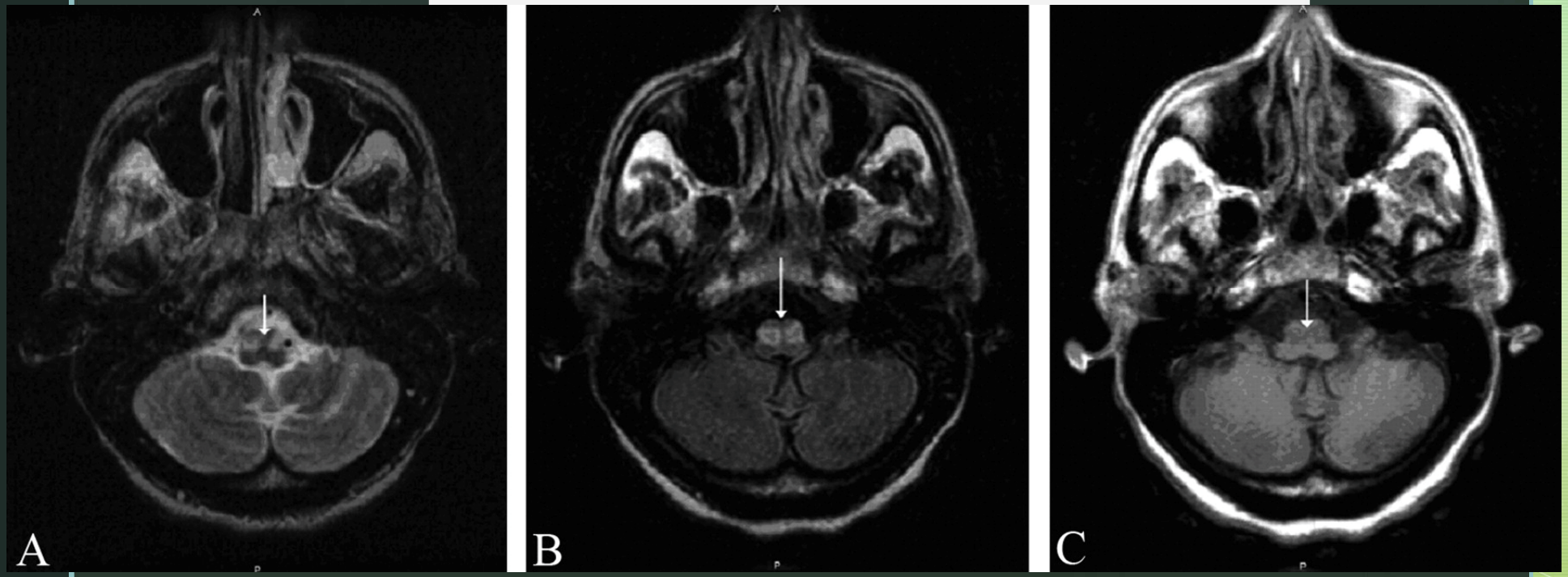

A
B

ATYPICAL MRI

December 28, 2004; 63 (12) NEUROIMAGES

MRI in PML: Bilateral medullary lesions

Rose Marie Mathew, Matthew Murnane

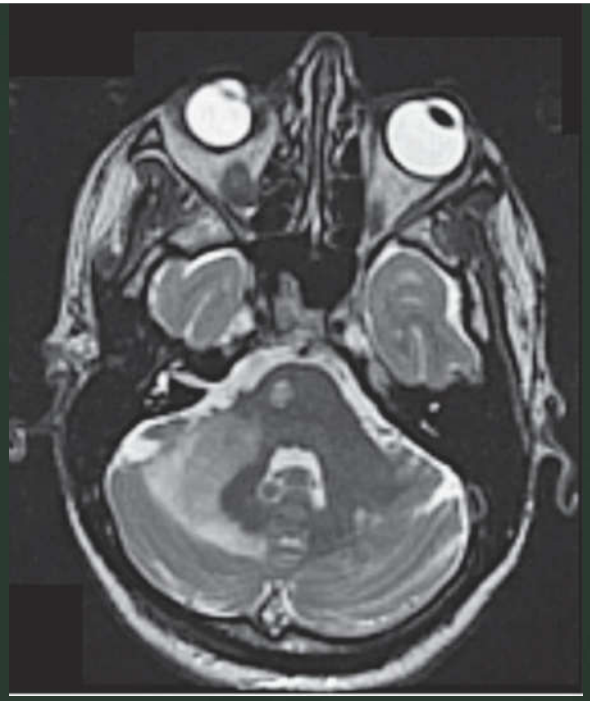


ATYPICAL MRI

Progressive Multifocal Leukoencephalopathy: a Rare Cause of Cerebellar Edema and Atypical Mass Effect

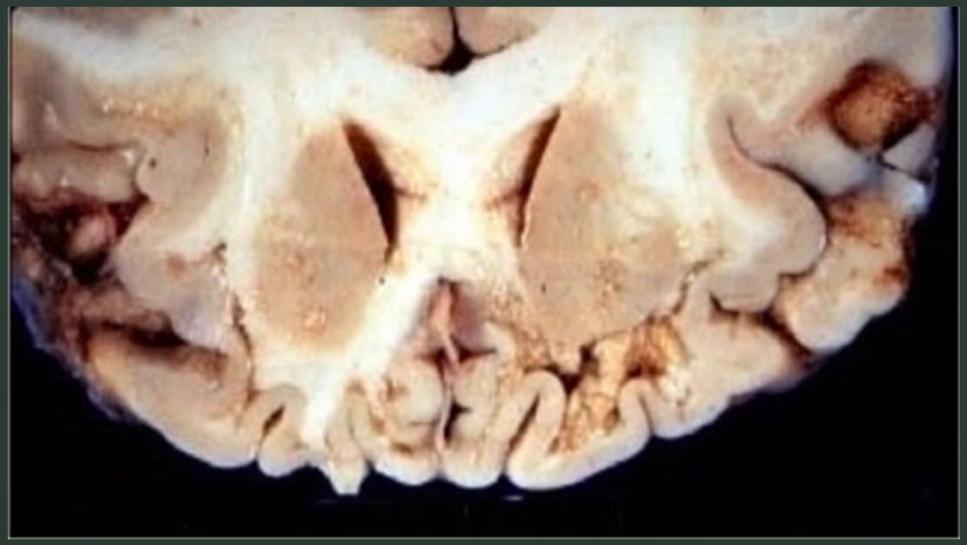
A Case Report

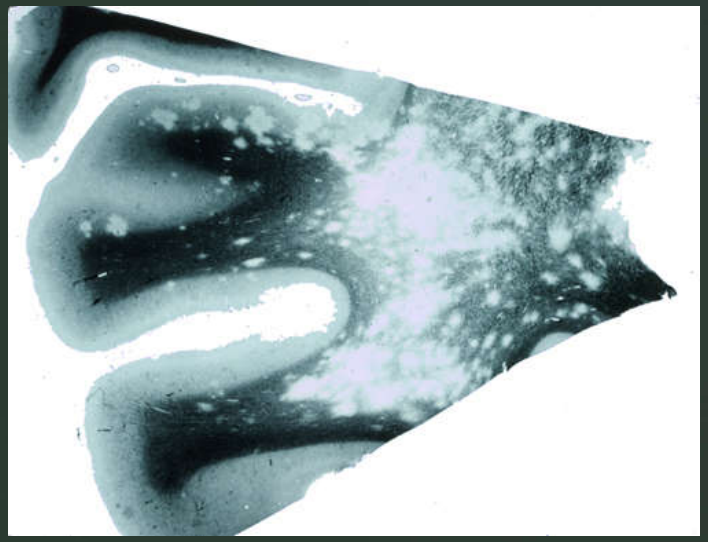
Chris Ojeda,[1] Rachid Assina,[2] Maureen Barry,[3] Ada Baisre,[4] and Chirag Gandhi[2]



BRAIN BIOPSY

Gold standard for diagnosis : when PCR for JC virus in CSF is negative

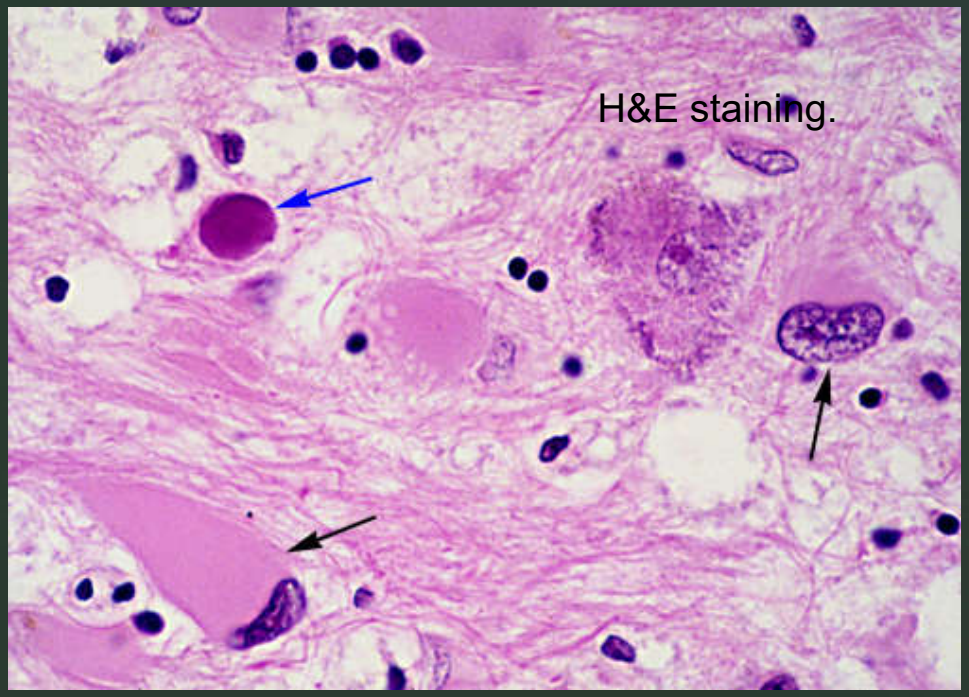




stained for myelin >>multifocal demyelination scattered throughout the subcortical white matter.

Histopathology

- Histopathological triad
  - Demyelination
  - Bizarre giant astrocytes
  - large oligodendroglial nuclei

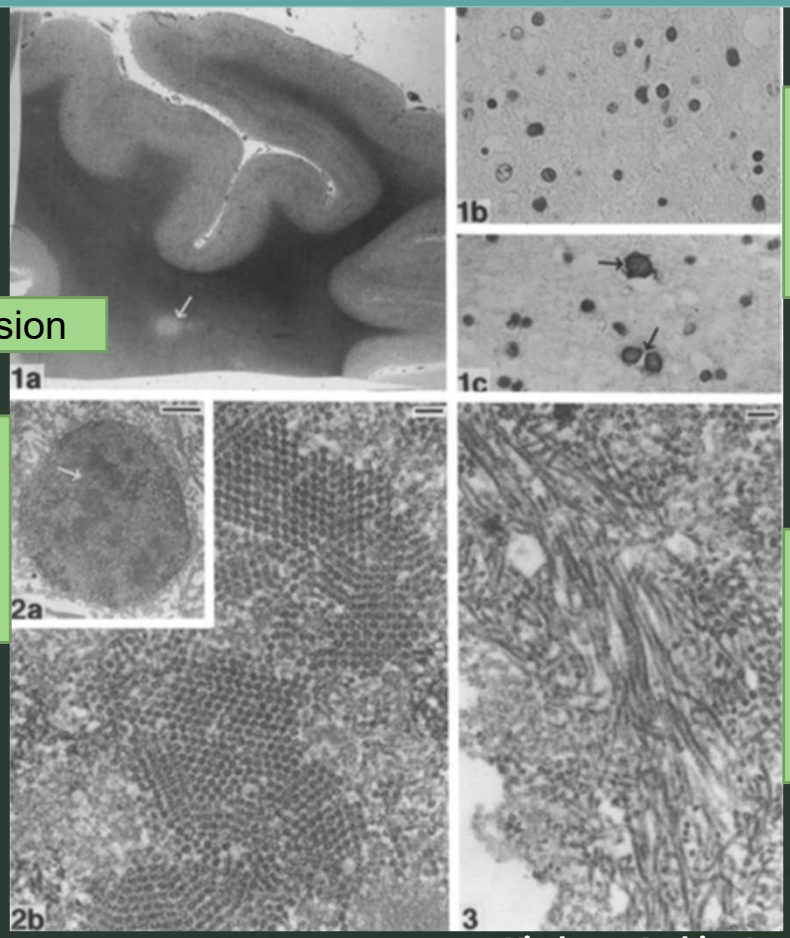


: reactive astrocytes
: oligodendrocyte nucleus

Electron microscopy

focal demyelinated lesion

A glial nucleus with a complex composite of crystals. (x 8000).



Swollen oligodendroglial cells and large astrocytes (H & E; x 400).

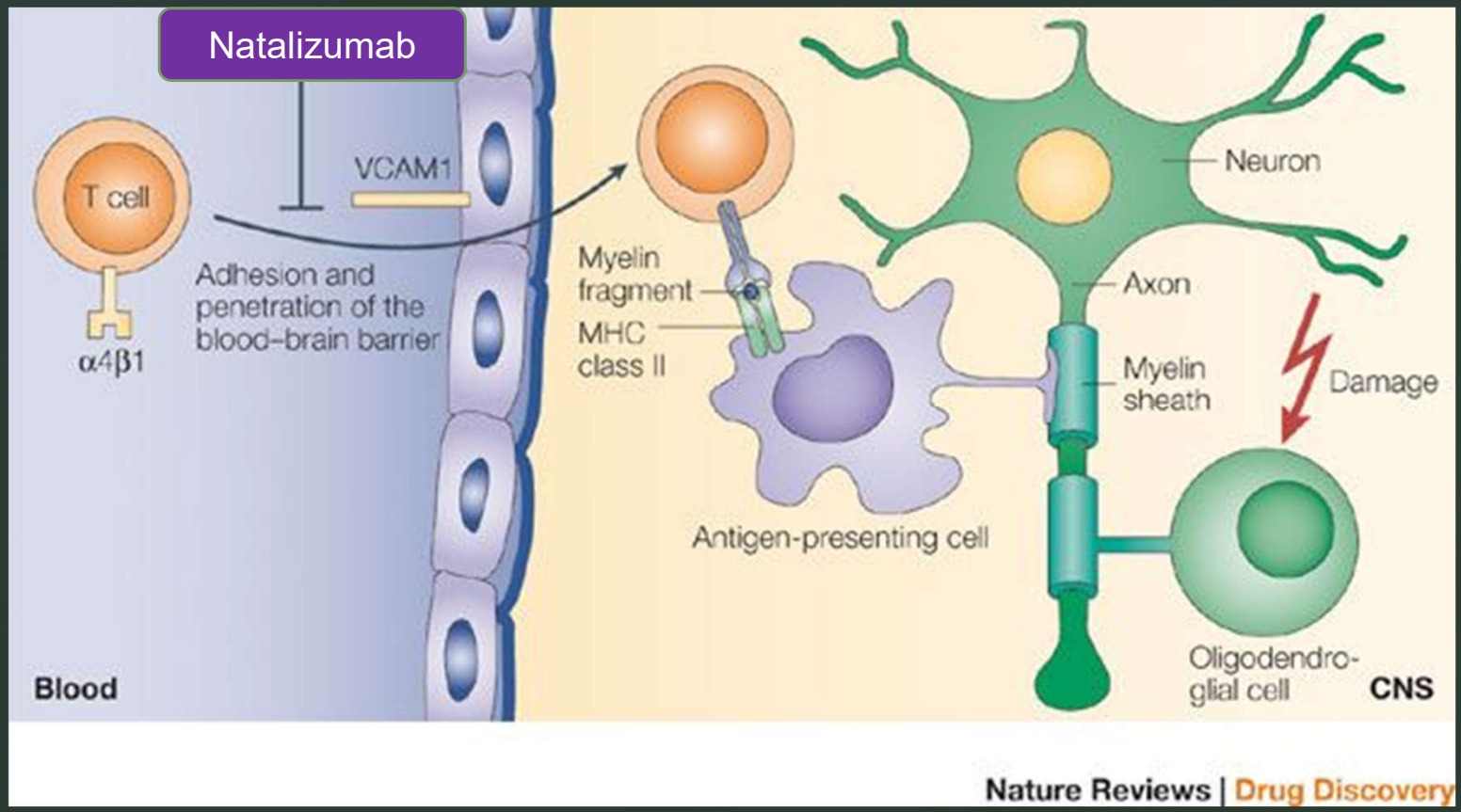
glial nucleus packed with elongated particles. (× 60000)

Virchows Archiv, June 1994, Volume 424, Issue 5, pp 569–572

NATALIZUMAB

- Target surface molecules(alfa-integrin) on B and T cells and prevent their entry to brain , skin and gut.
- PML associated with natalizumab therapy.
  - >700 confirmed cases
- Incidence at 4.2 cases of PML per 1000 patients treated with natalizumab.

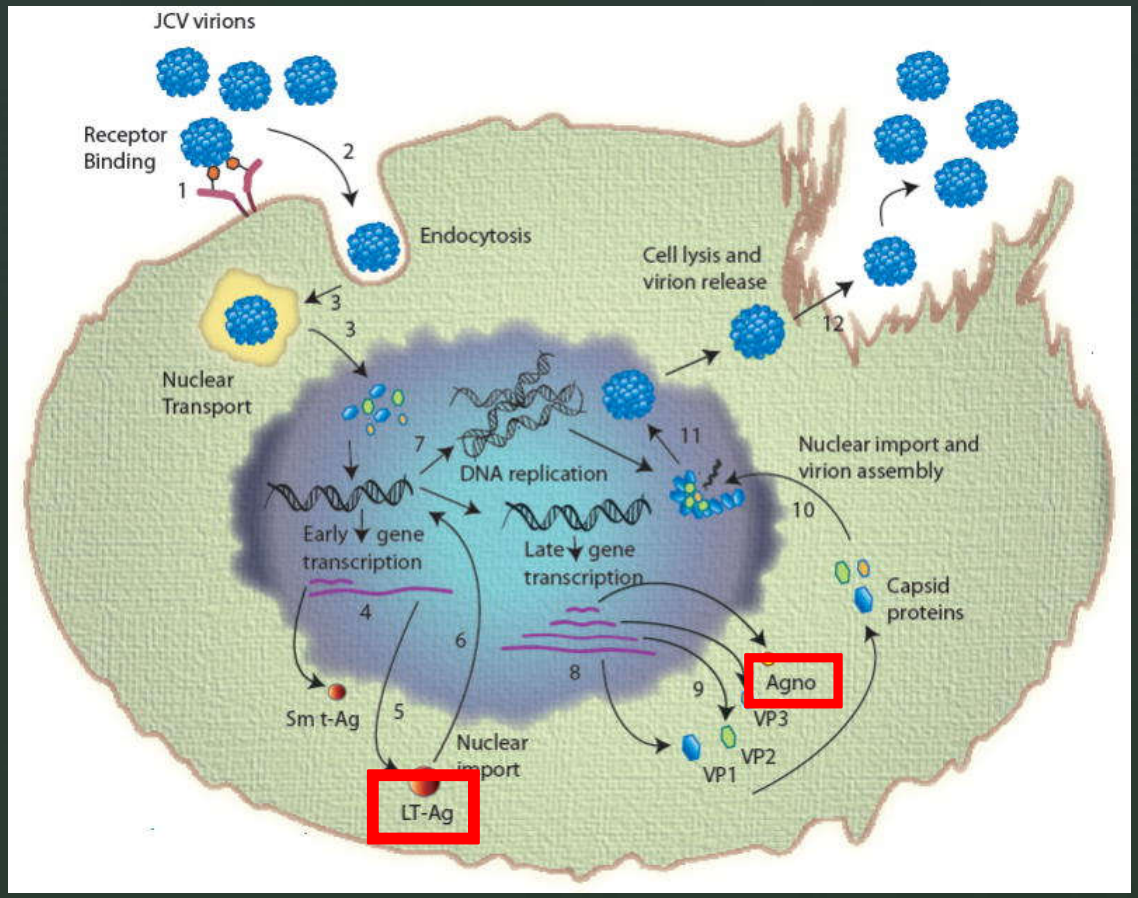
NATALIZUMAB



TREATMENT

- No specific therapy
- Mean survival in the pre-HAART era was 2-4 months
- In the HAART era
  - 50% of patients survive exceeding 12 months
  - Factor : CD4+ , VL , undetectable JC virus following HAART, contrast enhancing lesions at time of diagnosis

Development of new effective drugs



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3128336/#idm140396829694320title

HIV-associated neurocognitive disorder (HAND)

CLINICAL PRESENTATION AND RISK FACTOR

- Subcortical cognitive disorder
  - Psychomotor retardation
  - Executive dysfunction, learning impairment, memory
  - Motor symptoms : bradykinesia, incoordination, balance impairment
- Any point during HIV infection : AIDs is significant risk factor

CONTINUUM 2018;24(5, neuroinfectious disease) : 1397-1421

HIV-associated neurocognitive disorder (HAND)

DIAGNOSIS

- Screening : HIV Dementia scale(HDS), International HIV Dementia Scale(IHDS)
- Formal neuropsychological testing
- Exclude : Thyroid dysfunction, Vitamin B12 deficiency, syphilis
- CNS imaging to rule out alternative etiologies
  - Subdural hematoma , vascular dementia, PML
  - MRI : patchy or confluent symmetric subcortical T2 hyperintensities that do not enhance with gadolinium
- CSF : normal (occasionally mild lymphocytic pleocytosis or elevated protein)

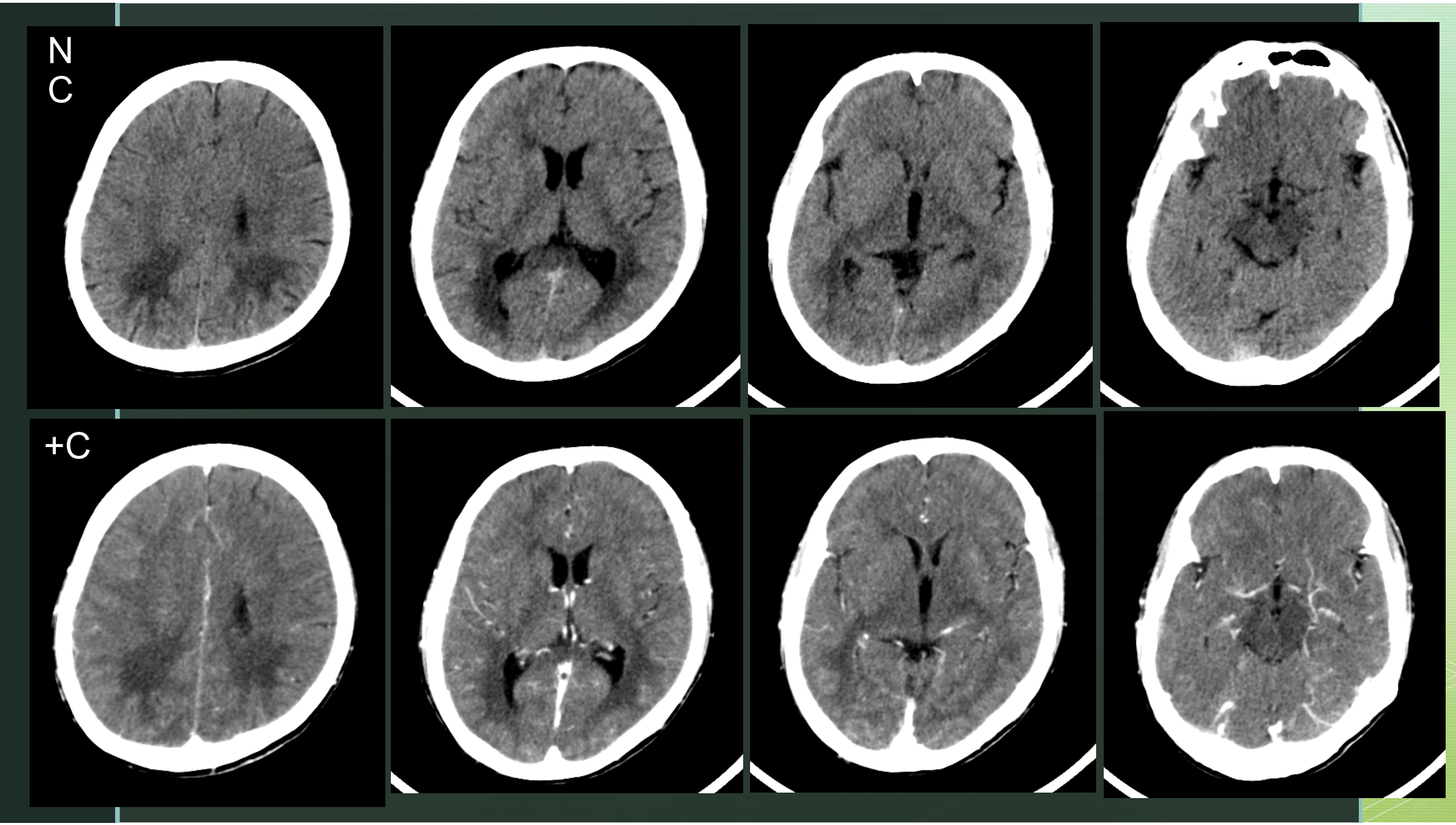
TREATMENT

No specific treatment >> ART

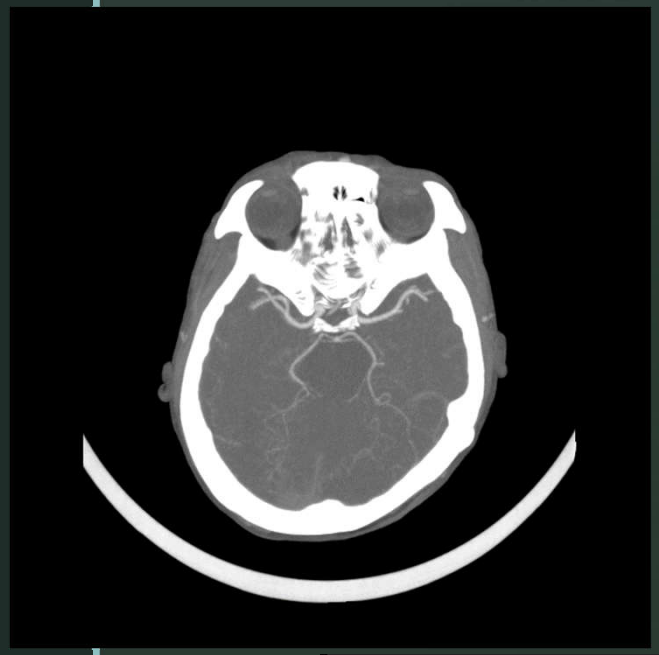
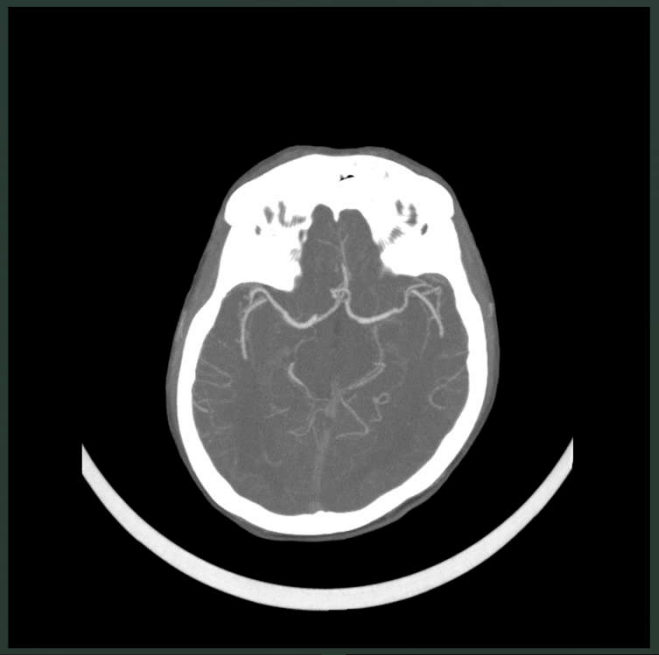
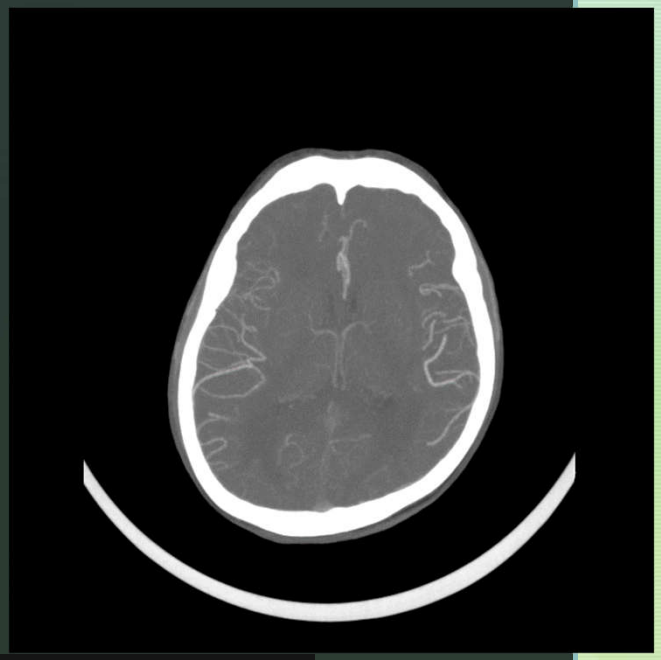
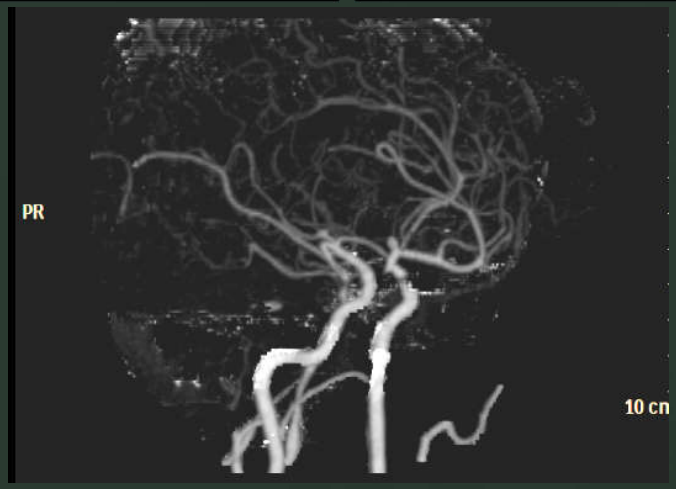
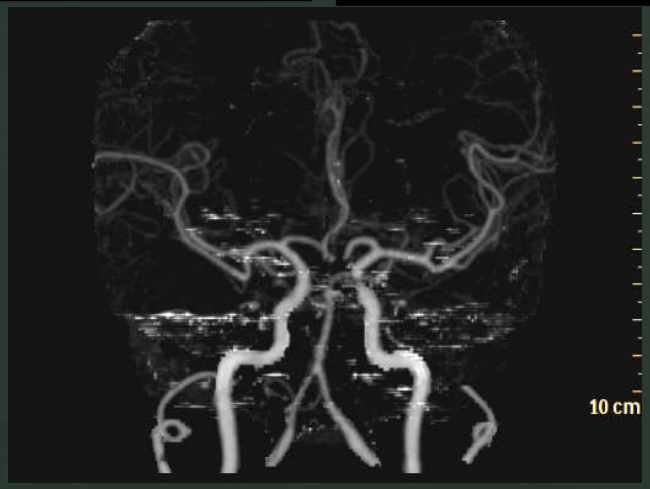
CONTINUUM 2018;24(5, neuroinfectious disease) : 1397-1421

Imaging Findings

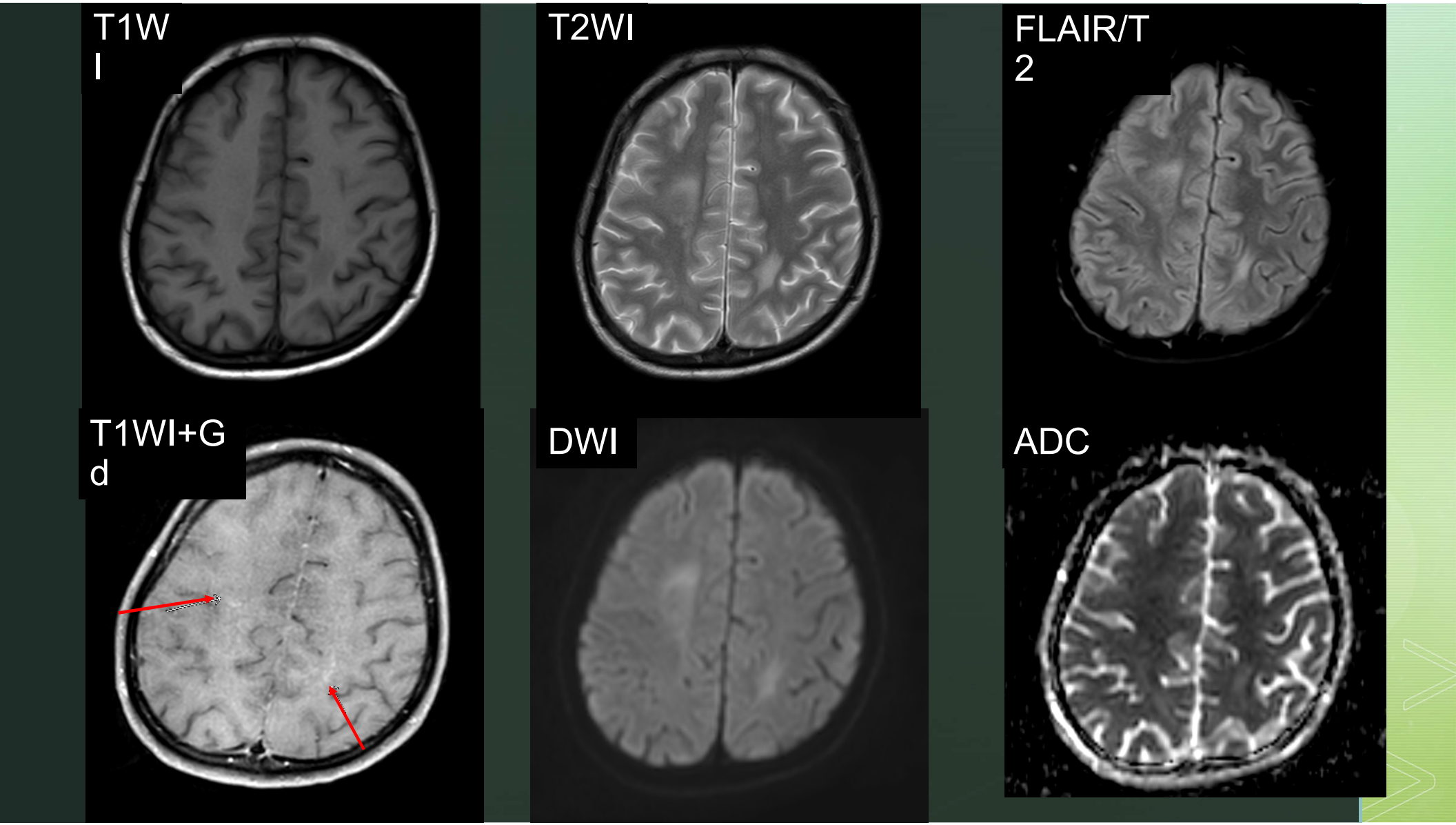
CT:Sep 22,2016

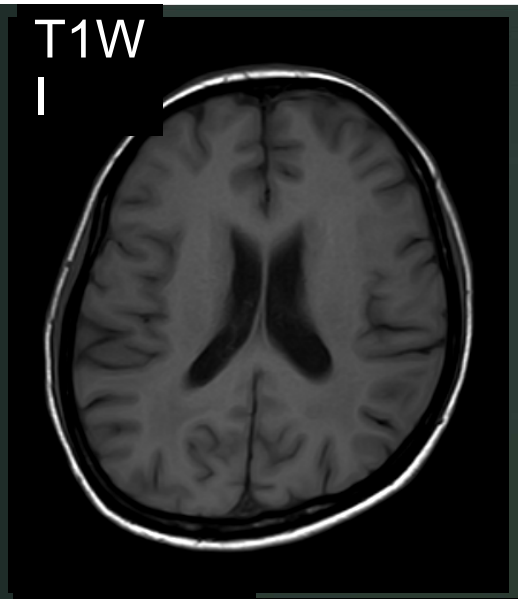

N
C
+C

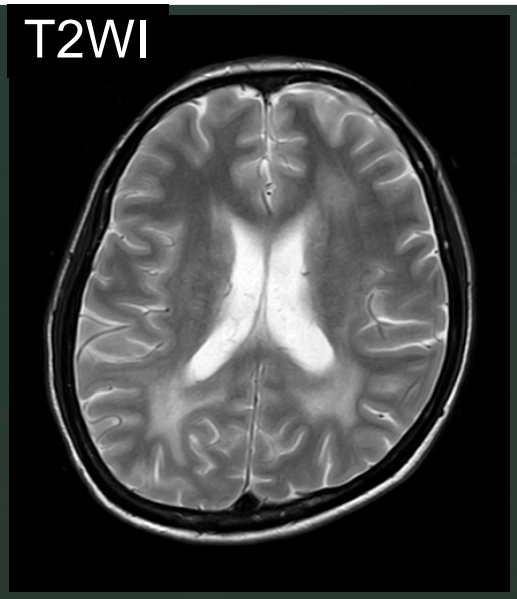
CTA:Sep 25,2016

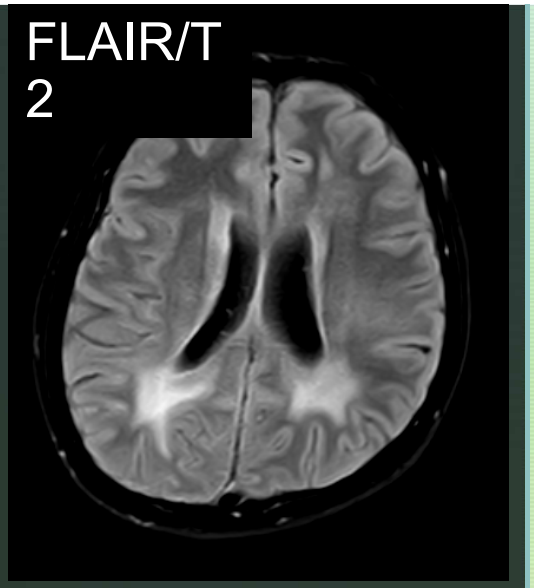




PR
10 cn

10 cm

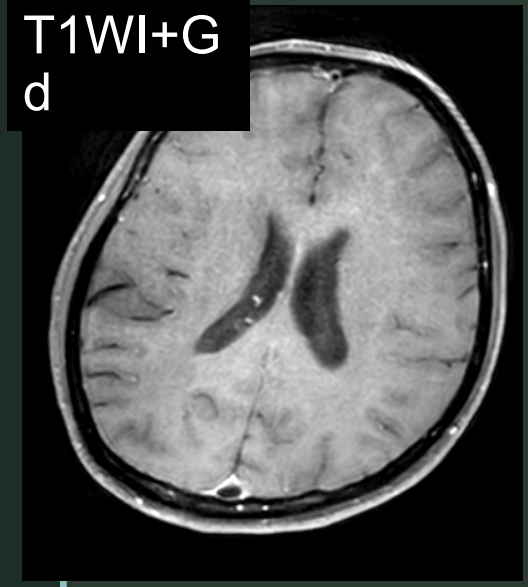
MRI:Sep 26,2016

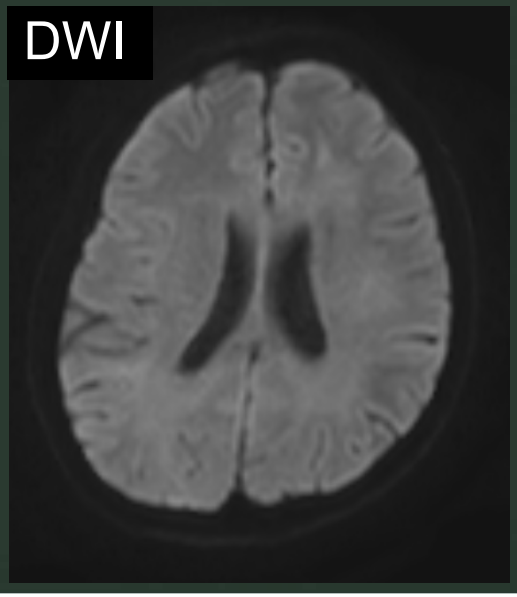

T1W
I
T2WI
FLAIR/T
2
T1WI+G
d
DWI
ADC

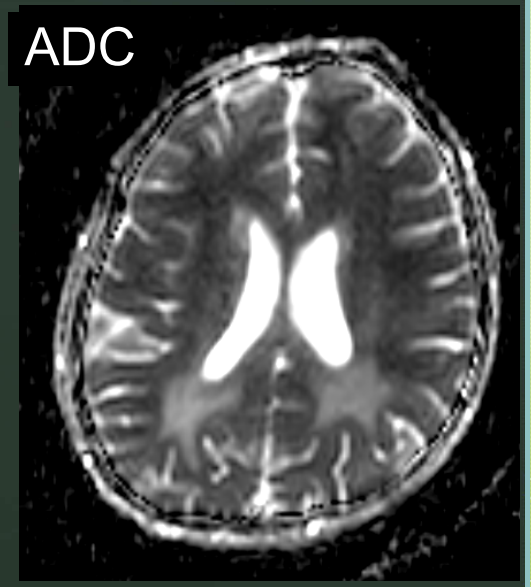

T1W
I

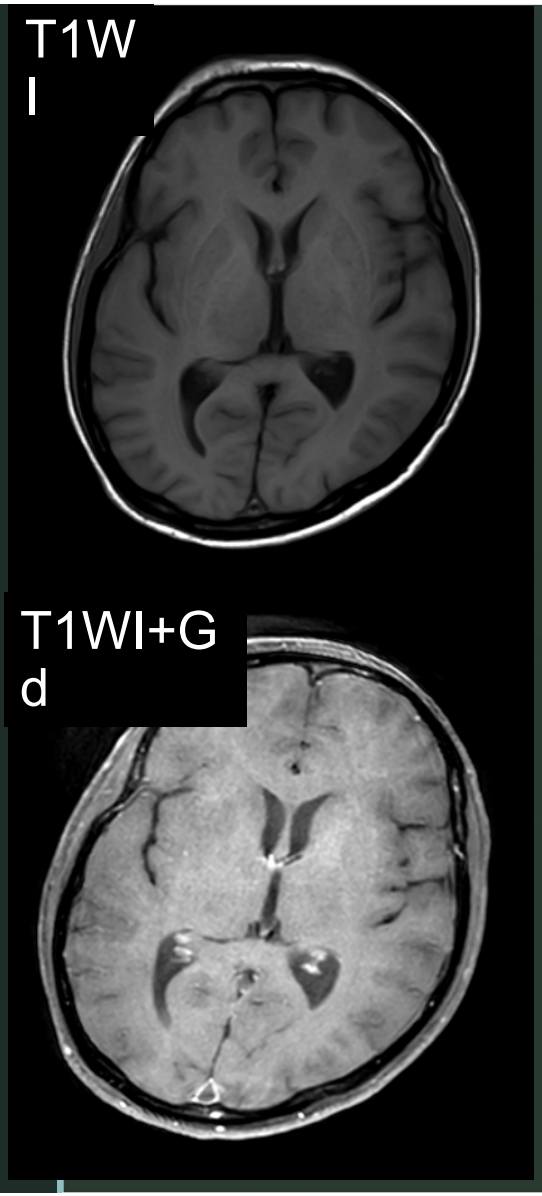

T2WI

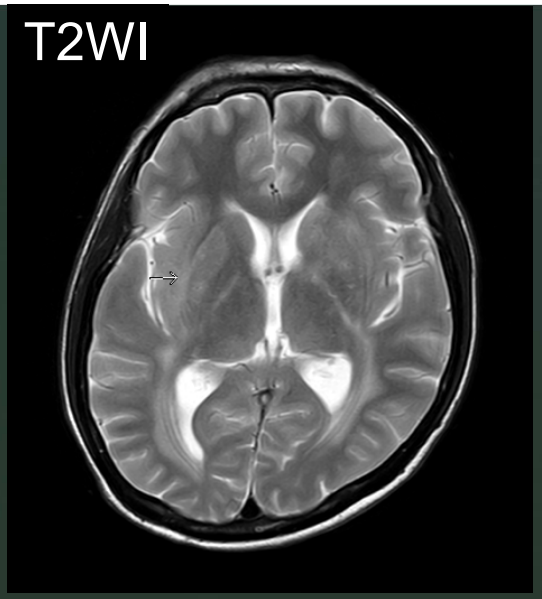

FLAIR/T
2

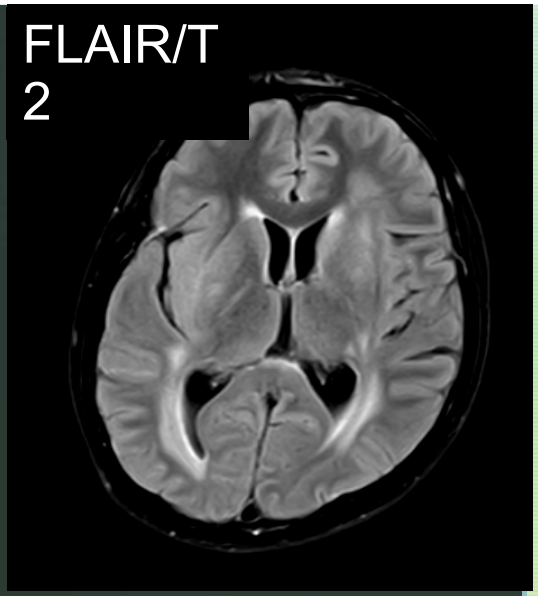

T1WI+G
d


DWI

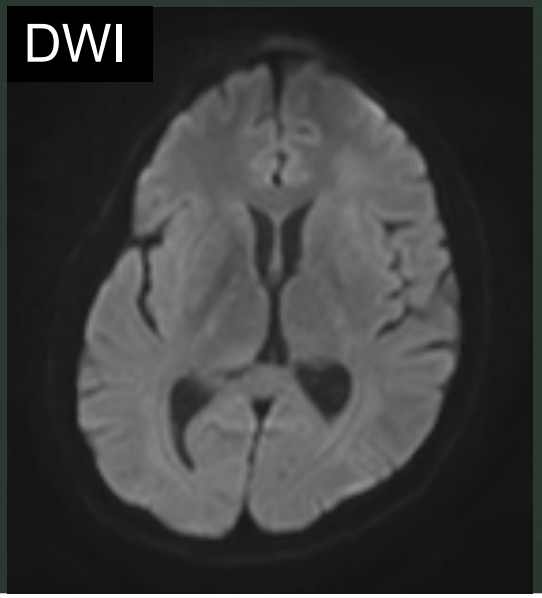

ADC

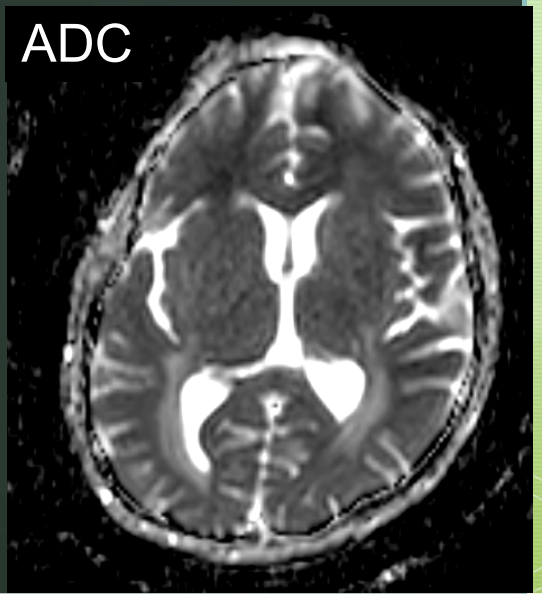

T1WI

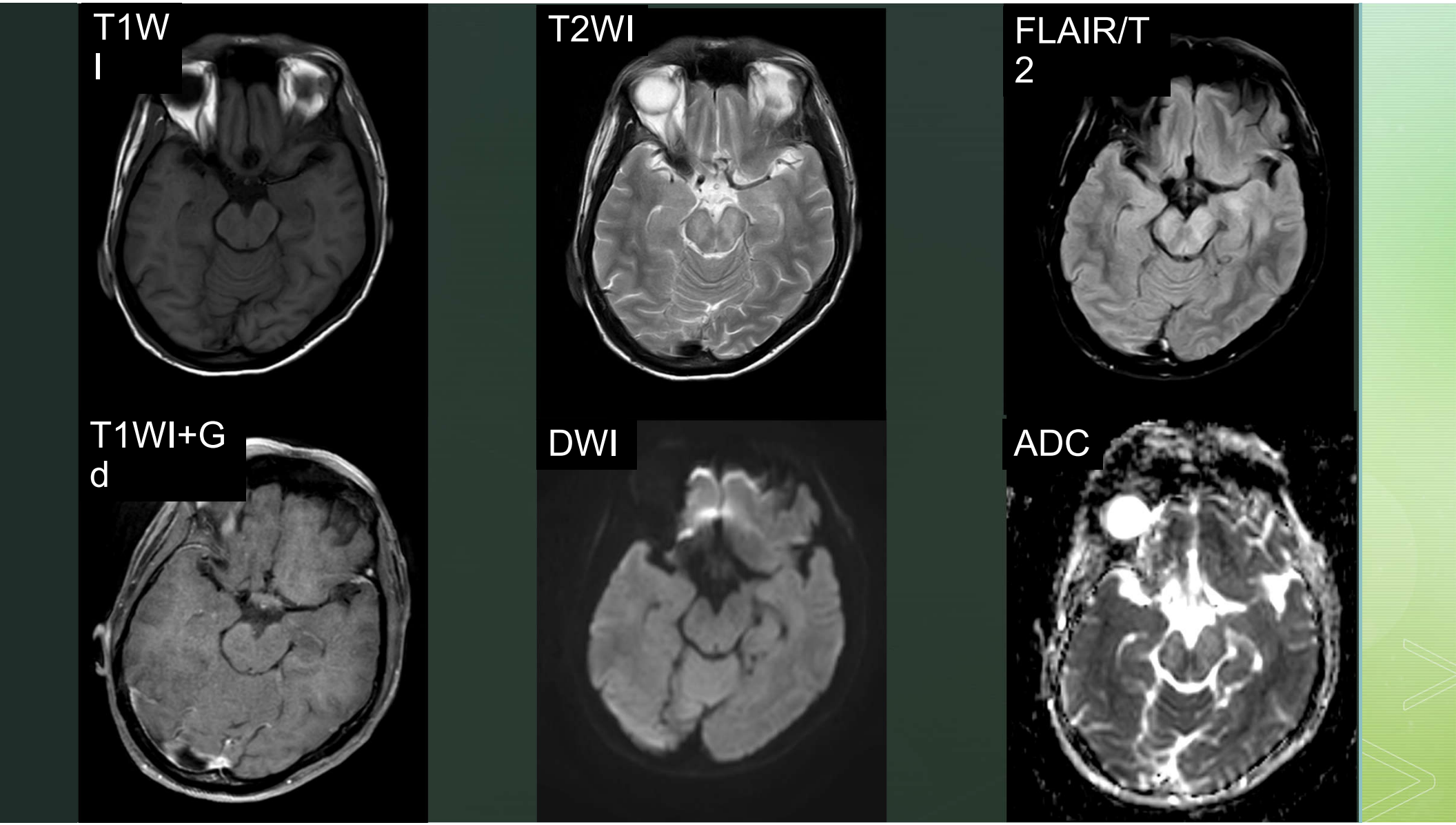

T2WI


FLAIR/T2

T1WI+Gd


DWI


ADC


T1WI
T2WI
FLAIR/T2
T1WI+Gd
DWI
ADC

Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencephalopathy

- Subacute opportunistic infection caused by DNA virus JC polyomavirus (JCV)
- JC polyomavirus infects oligodendrocytes, causes demyelination in immunocompromised patients
- Associated with immunosuppression, often AIDS, organ transplant, cancer, chemotherapy, myeloproliferative disease, and steroid treatment

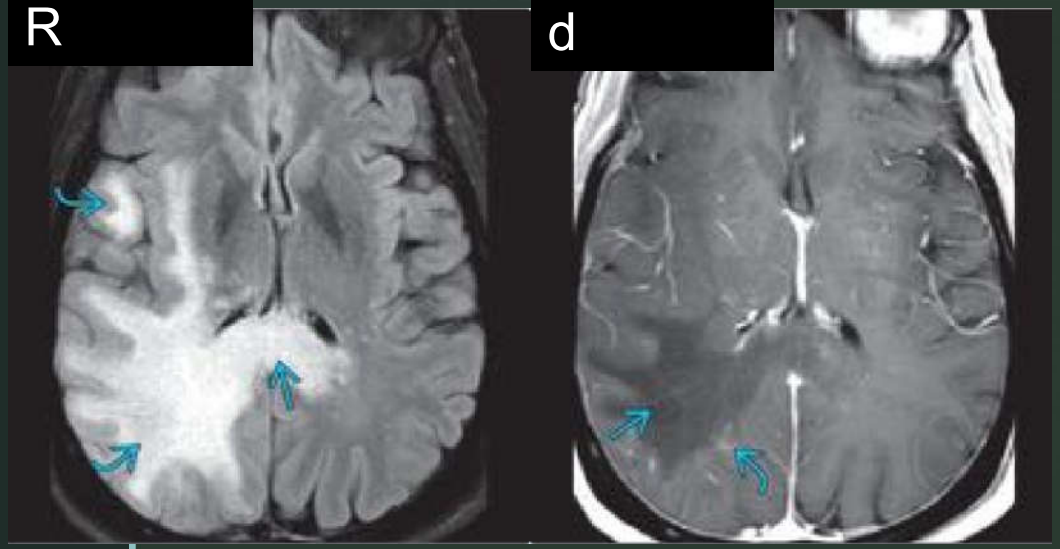
Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

Progressive multifocal leukoencephalopathy

- Best imaging tool : MR with contrast
- Location
  - Parietooccipital region, thalamus
  - Cerebellum & brainstem may be involved
- Size
  - Variable, small subcortical lesions to confluent hemispheric lesions
- Morphology
  - Solitary, multifocal, or widespread hemispheric WM lesions
- CT finding
  - Asymmetric focal zones of low attenuation involving the periventricular and subcortical white matter

Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

Progressive multifocal leukoencephalopathy

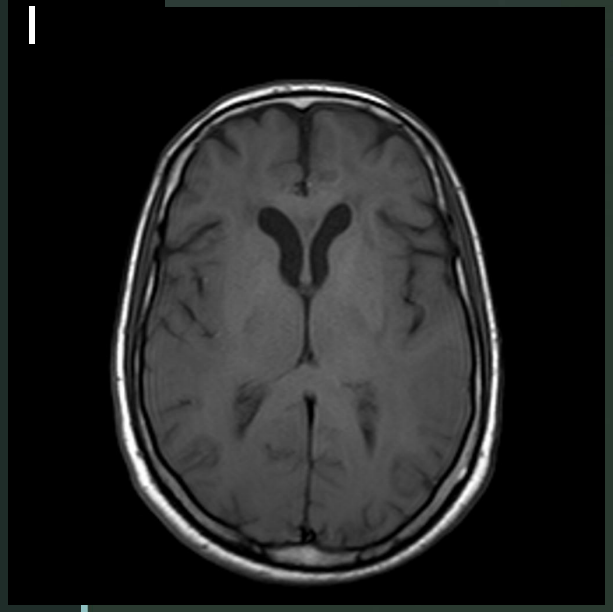


- T1WI
  - Hypointense lesions
- T2WI
  - Hyperintensity predominantly in subcortical and periventricular WM
  - Involves subcortical U-fibers
- FLAIR
  - Hyperintensity in subcortical and periventricular WM
- DWI
  - Newer lesion → slightly restricted diffusion along its margins
  - Older lesion → unrestricted
- T1WI+Gd
  - Typically no enhancement
  - Increasing enhancement attributable to immune reconstitution

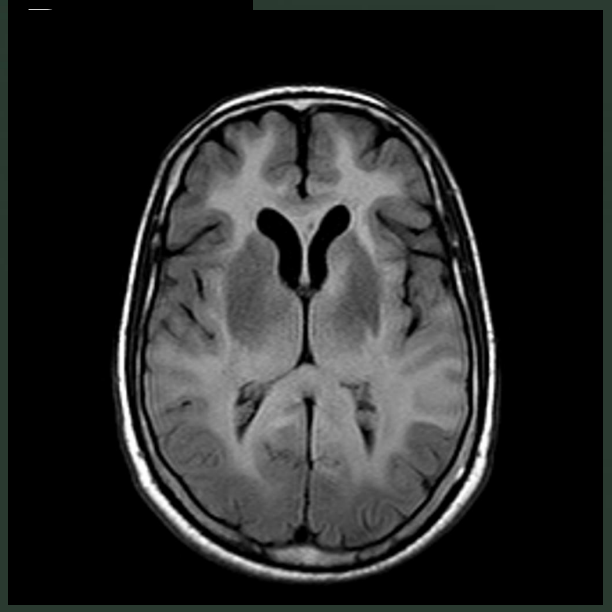
Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

Progressive multifocal leukoencephalopathy

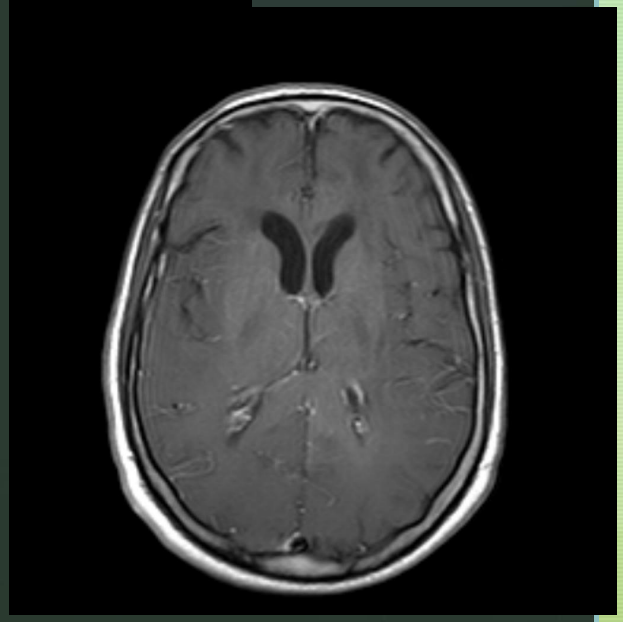
T1WI



T2/FLAIR



T1WI+G



Bilateral deep white matter altered signals that display low signal in T1, bright signal in T2 and FLAIR without significant enhancement

Case courtesy of Dr Ahmed Abdrabou, Radiopaedia.org, rID: 26

Progressive multifocal leukoencephalopathy

Progressive Multifocal Leukoencephalopathy in AIDS: Are There Any MR Findings Useful to Patient Management and Predictive of Patient Survival?

M. Judith Donovan Post, Constantin Yiannoutsos, David Simpson, John Booss, David B. Clifford, Bruce Cohen, Justin C. McArthur, Colin D. Hall, and the AIDS Clinical Trials Group, 243 Team

TABLE 1: Frequency of pretreatment MR findings in 48 HIV-positive patients with biopsy proved PML

MR Findings	Frequency (%)
Cortical atrophy	68.8
Mild	54.2
Moderate	14.6
Severe	0.0
Ventricular dilatation	50.1
Mild	43.8
Moderate	6.3
Severe	0.0
White matter lesions	100.0
Bilateral	91.7
Unilateral	8.3
Confluent	93.8
Discrete	66.7
Supratentorial	93.8
Periventricular	95.5
Centrum semiovale	93.3
Subcortical white matter	82.2
Internal capsule	35.6
External capsule	28.9
Corpus callosum	22.7
Specific lobar involvement	
Parietal	93.2
Frontal	75.6
Occipital	52.3
Temporal	33.3
Infratentorial	58.3
Brain stem	89.3
Pons	92.0
Midbrain	64.0
Medulla	36.0
Middle cerebellar peduncle	64.3
Cerebellar white matter	57.1
Gray matter lesions	56.3
Thalamus	92.6
Basal ganglia	40.7
Cortical gray	25.9
Other site	3.8
Mass effect	10.4
Minimal	100.0
Contrast enhancement (n=45)	2.2

AJNR Am J Neuroradiol 20:1896–1906, November/December 19

Progressive multifocal leukoencephalopathy -Immune reconstitution inflammatory syndrome (PML-IRIS)

PML-IRIS

- Paradoxical worsening of opportunistic infection
- After starting highly active antiretroviral therapy (HAART)
- Patients with MS treated with immunomodulatory therapy
- PML-IRIS is reported to occur in 18-45% of the HIV infected patients with PML

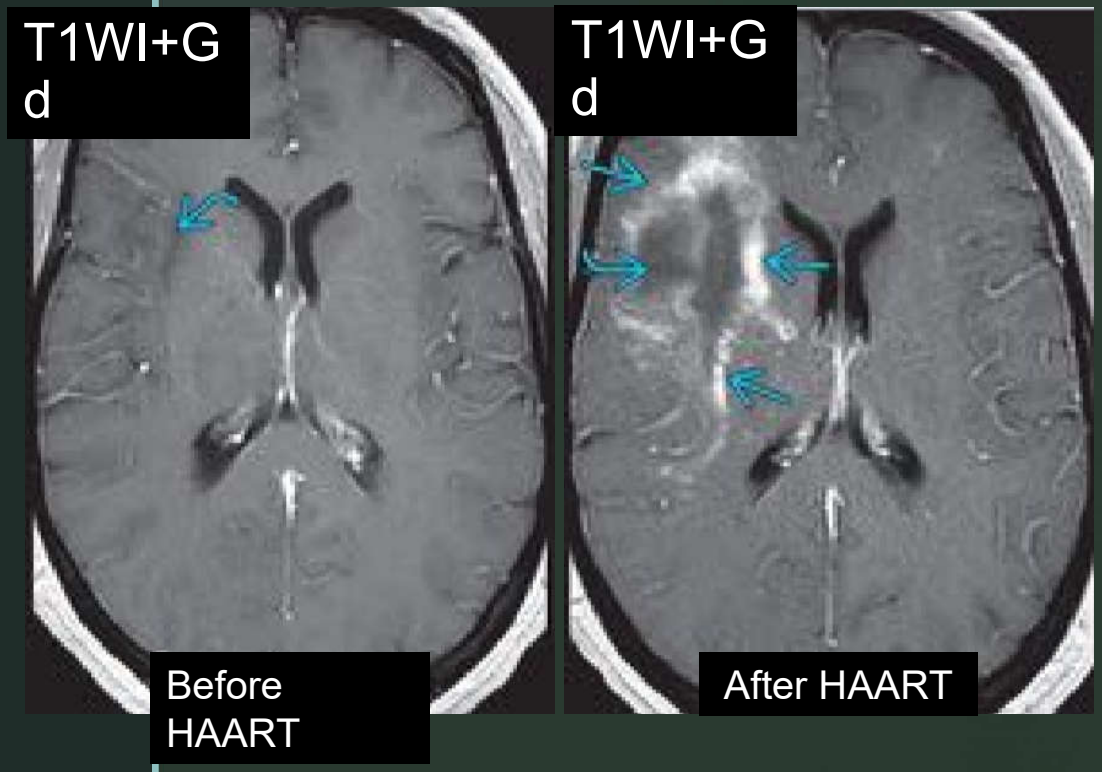
Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

PML-IRIS

- Best imaging tool : MR with contrast
- Location
  - Most common : Frontal/parietooccipital lobes
  - Less common : Posterior fossa
- Size
  - Variable, small subcortical lesions to confluent hemispheric lesions
- Morphology
  - Solitary, multifocal, or widespread hemispheric WM lesions
- CT finding
  - White matter (WM) hypodensities with increased mass effect
  - Atypical heterogeneous enhancement

Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

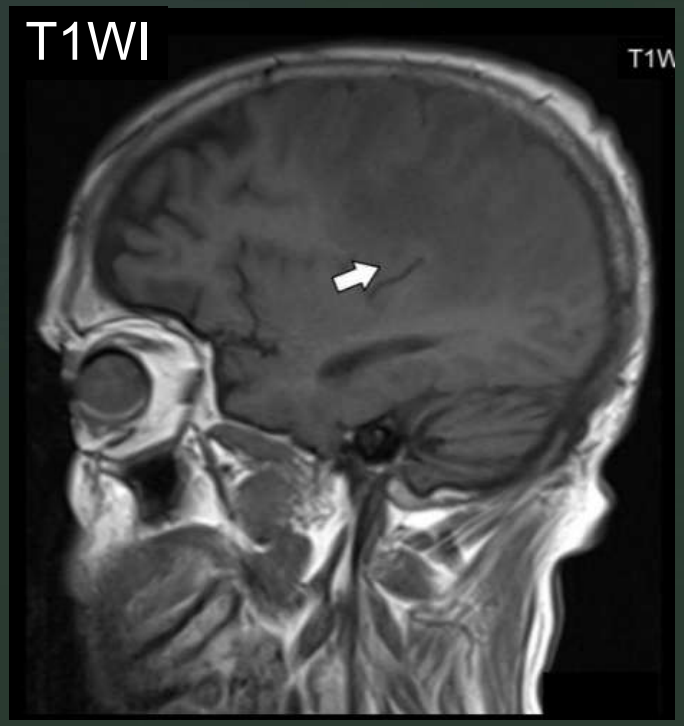
PML-IRIS

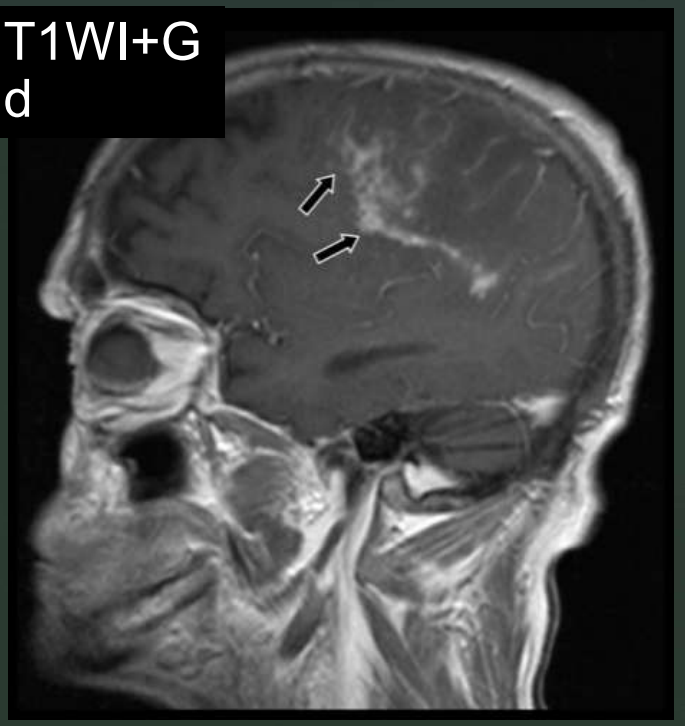


- T1WI
  - Hypointense lesions become confluent
- T2WI
  - Hyperintense WM lesions
  - Enlarge, become confluent, exert mass effect
- FLAIR
  - Hyperintensity in subcortical and periventricular WM
- T1WI+Gd
  - Patchy atypical enhancement

Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

PML-IRIS





Hypointense large lesion in the right frontal and parietal lobes, with patchy atypical enhancement.

Yousry TA, Pelletier D, Cadavid D, Gass A, Richert ND, Radue EW, Filippi M. Magnetic resonance imaging pattern in natalizumab-associated progressive multifocal leukoencephalopathy. Annals of neurology. 2012 Nov;72(5):779-87.

HIV/AIDS encephalopathy

HIV/AIDS encephalopathy

- HIV-associated neurocognitive disorders (HAND)
- Moderate cognitive impairment common despite good virologic response to therapy
- Direct HIV infection of brain
- Most frequent neurological manifestation of HIV infection

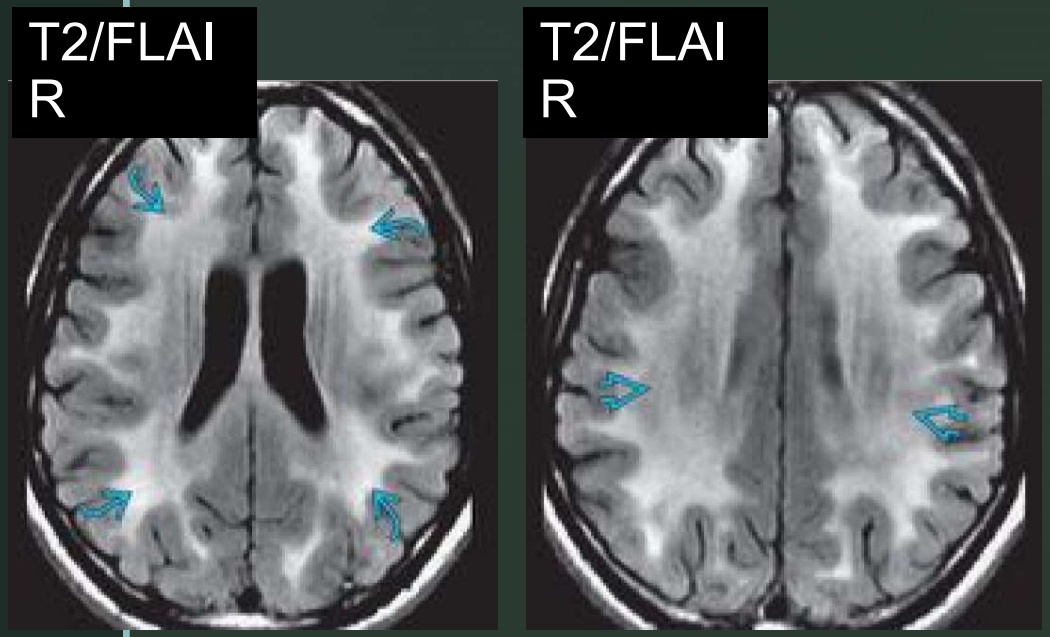
Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

HIV/AIDS encephalopathy

- Best imaging tool : MR with contrast
- Location
  - Bilateral periventricular/centrum semiovale WM, basal ganglia, cerebellum, brainstem
- Size
  - Variable, often diffuse
- Morphology
  - Extends to gray-white matter junction
- CT finding
  - Normal or mild atrophy, WM hypodensity
  - No mass effect
  - Usually no contrast enhancement

Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

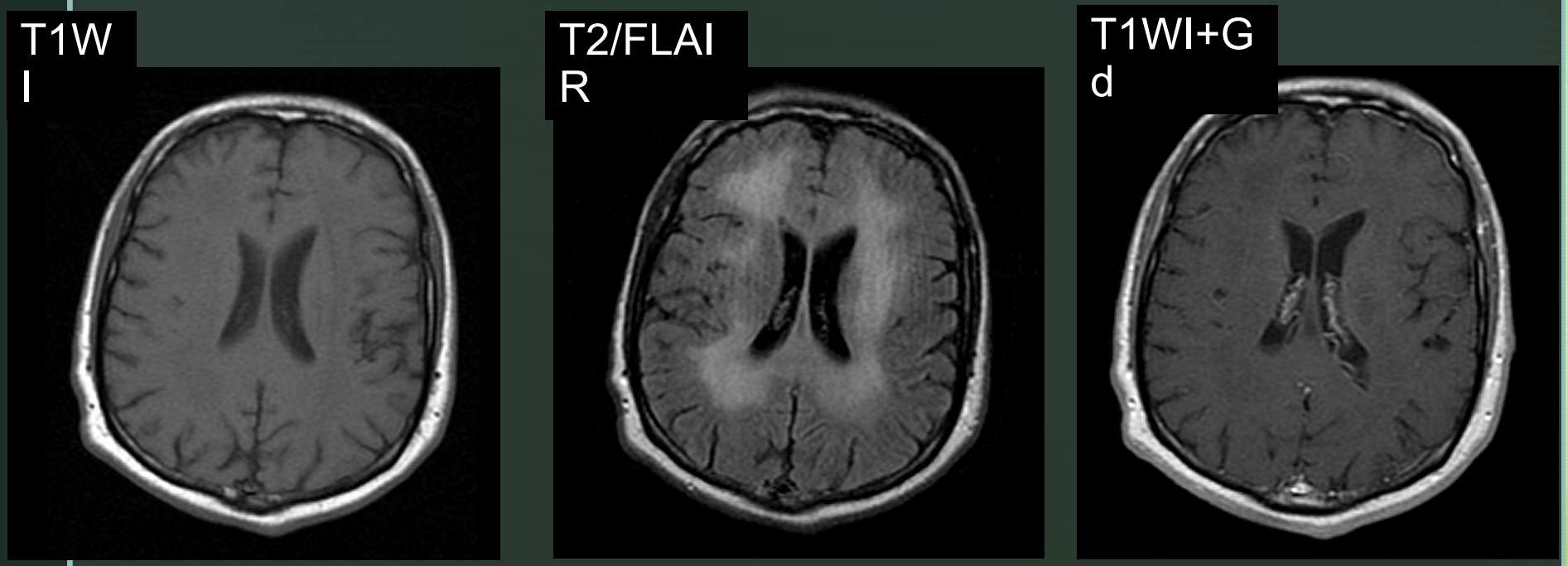
HIV/AIDS encephalopathy



- T1WI
  - WM abnormality may not be evident
- T2WI
  - 2 imaging patterns
    - Focal abnormalities of high signal intensity
    - Diffuse moderate-high signal WM changes
- FLAIR
  - Same imaging patterns as T2WI
- T1WI C+
  - No enhancement in involved regions

Osborn A, Jhaveri M, Salzman K. Brain. 3rd ed. Elsevier; 2

HIV/AIDS encephalopathy



Bilateral periventricular and deep white matter relatively symmetric T2/FLAIR hyperintensity without significant enhance

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 2