A middle aged man goes to the neurologist…

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58 y-o, caucasian, lecturer, MSM

6 months prior to presentation
Generally unwell

past 3 months
most recently a chest infection with non-productive cough
& weight loss & tired all the time

FH - Brother has sarcoidosis

?Tuberculosis
?Lung cancer
?sarcoidosis
?cardiac failure

6 months prior to presentation
Generally unwell

most recently a chest infection with non-productive cough
& weight loss & tired all the time (past 3 months)

chest x-ray, ECG, spirometry, exercise test and “blood screen - “neg”

Meds: steroids, doxycycline and salbutamol inhaler
for “chest infection”

Cognitive complaints:

*forgetful: poor short term memory, good long term memory
*problems with visual perception: reading - needs to use a finger
*occasional difficulty understanding and saying words; comprehension and retention of words written and spoken

Balance and mobility:

*walking and balance impairment - had to stop cycling, falls walking the dog even, needs one stick

Neurological examination

Brief cognitive testing: correct date and new major capitals.
He was very slow on the serial sevens test and kept making errors.

There was left-sided visual and sensory inattention.

Reflexes brisk and upgoing plantars.
Cerebellar signs predominantly on the left and more so in the left lower limb.
Joint sense was impaired at the left toes.
Gait ataxic, even using a stick.

DIFFERENTIAL DIAGNOSES:
right parietal lesion
spatial awareness and left visual field loss/inattention

?space occupying lesion (SOL) – tumour, metastasis, abscess (?TB)
?degenerative dementia - posterior variant of Alzheimer's disease

?HIV encephalopathy

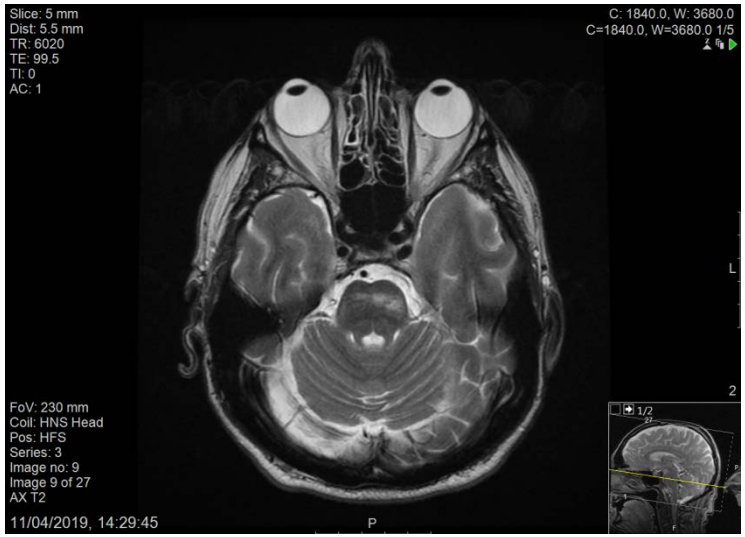
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Image 9 of 27
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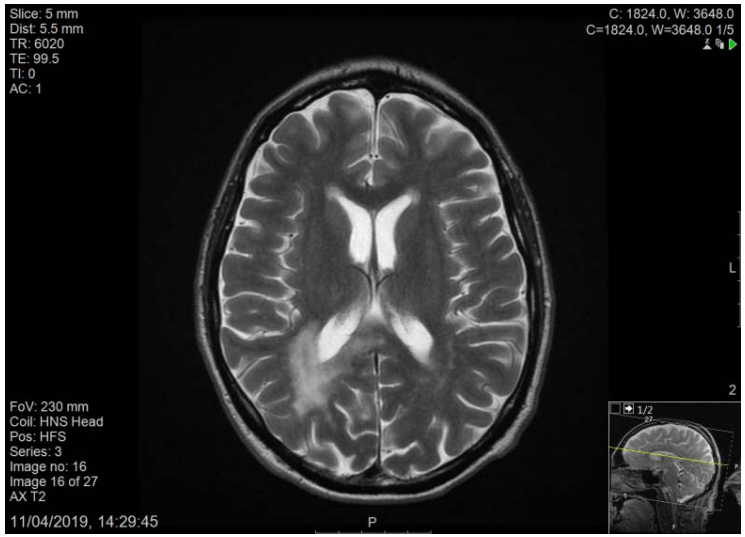
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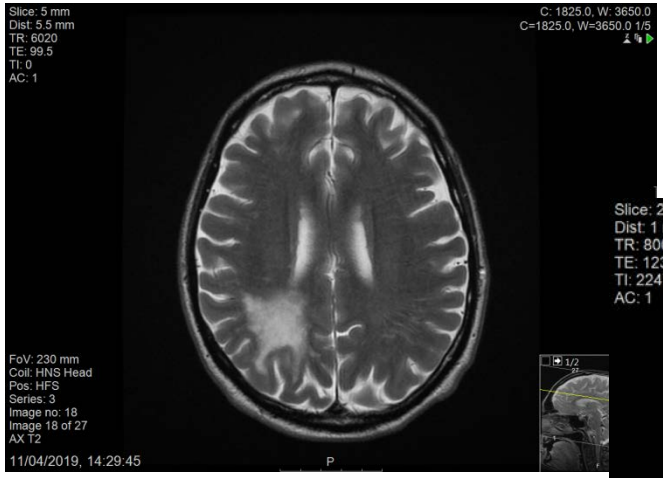
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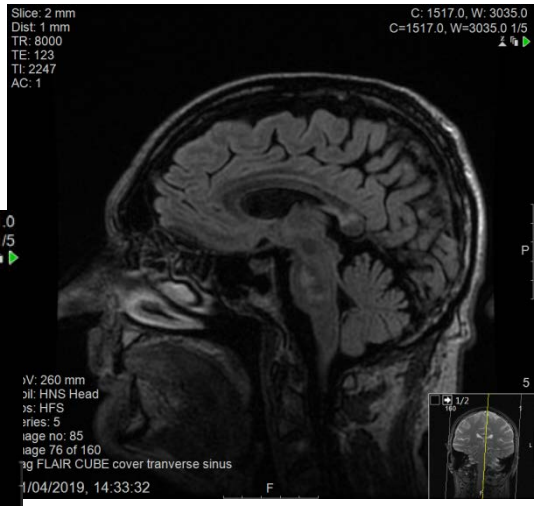
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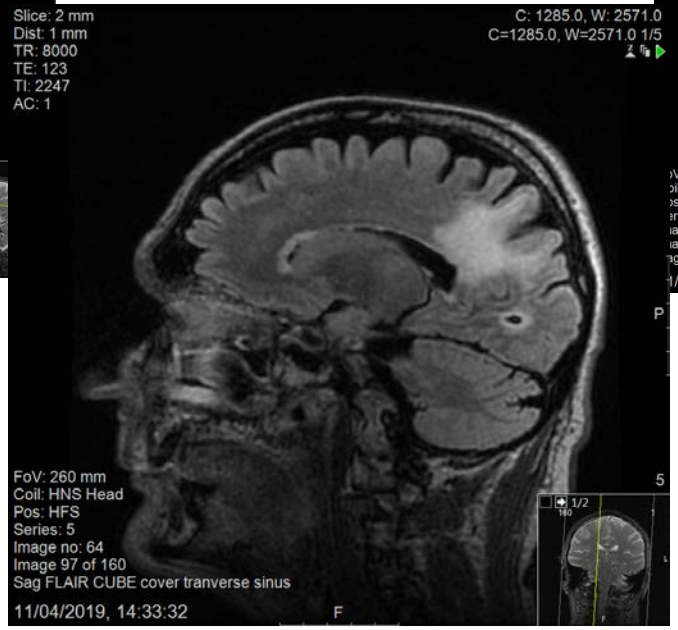
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Image 97 of 160
Sag FLAIR CUBE cover tranverse sinus
11/04/2019, 14:33:32
F
P
5
1/2

Neurological examination
Worsening attention
Worse mobility

CD4 count 80
syphilis, VZV antibody, HBV/ HCV, CRAG negative
EBV IGG +, IGM neg; CMV DNA 250
toxo and syphilis neg serum
pending: HLAB5701
no HIV VL (serum or CSF) - not sent so, no GART; No TB IGRA

CSF: HSV1-2/VZV/EBV/CMV & adenovirus neg; Crag neg;
JC virus VL 208,000,
BD glucan 456 (cut off 80)

ARVs started before CSF results

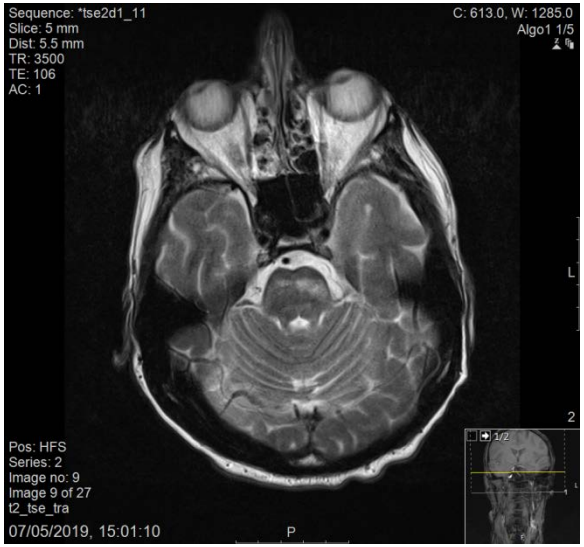
Truvada /Darunavir/ r (changed from rezolsta)

Co-trimoxazole - 120mg -> 90mg/kg (2400mg oral tds)

40mg bd prenisolone, - Current 90mg/kg

Truvada switched to Descovy due to renal function impairment;

Dolutegravir added for rapid viral load decay.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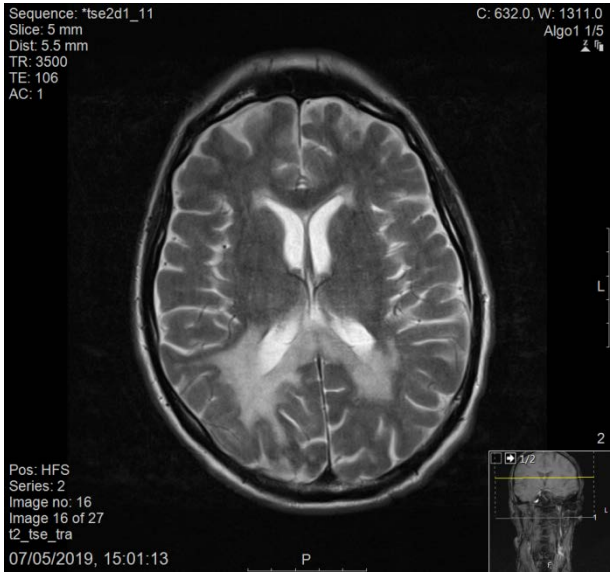
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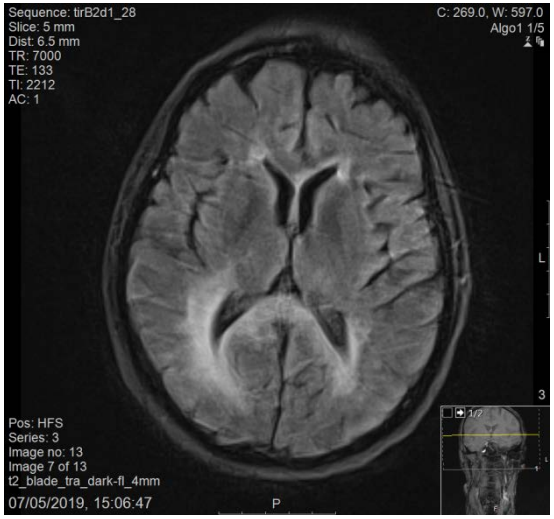
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3
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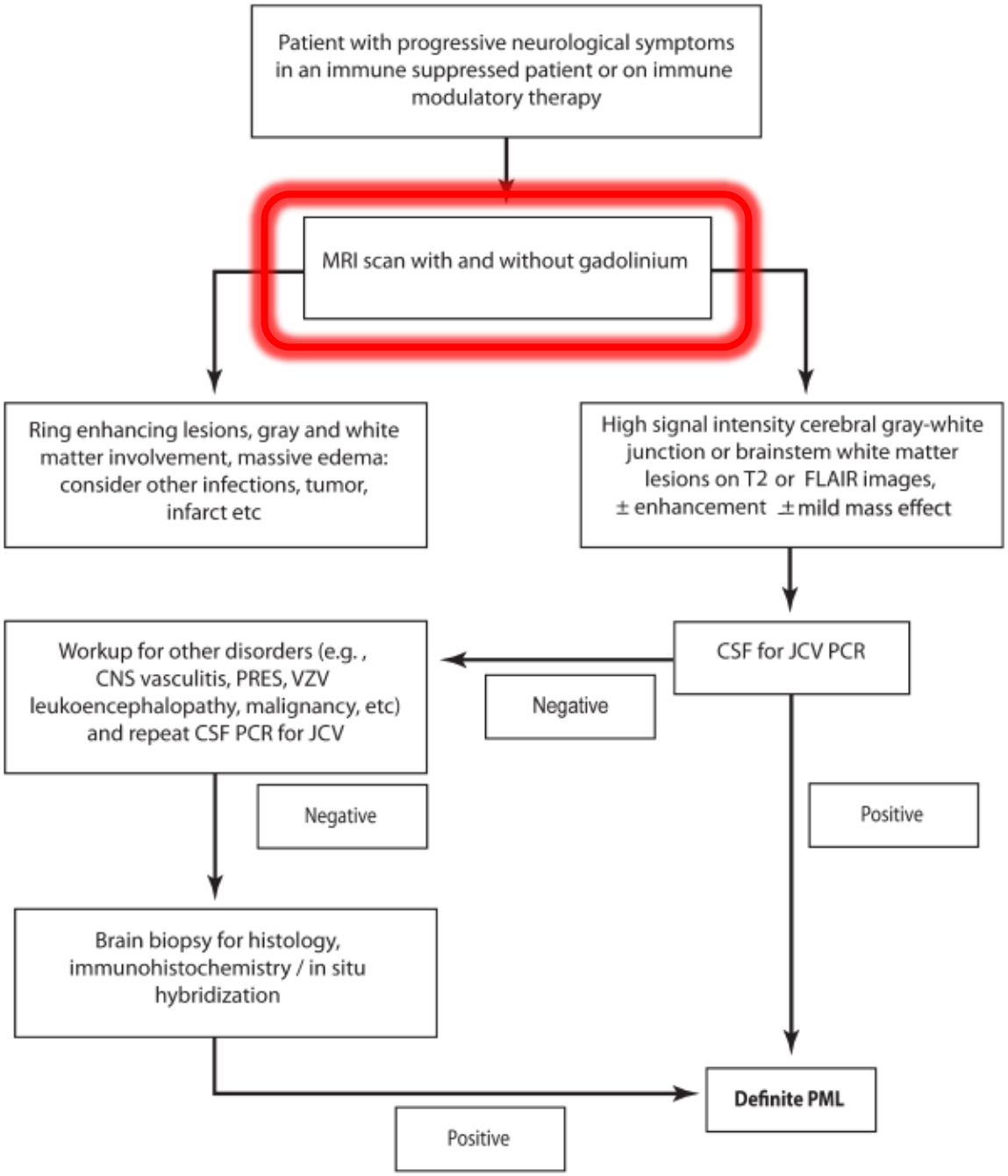
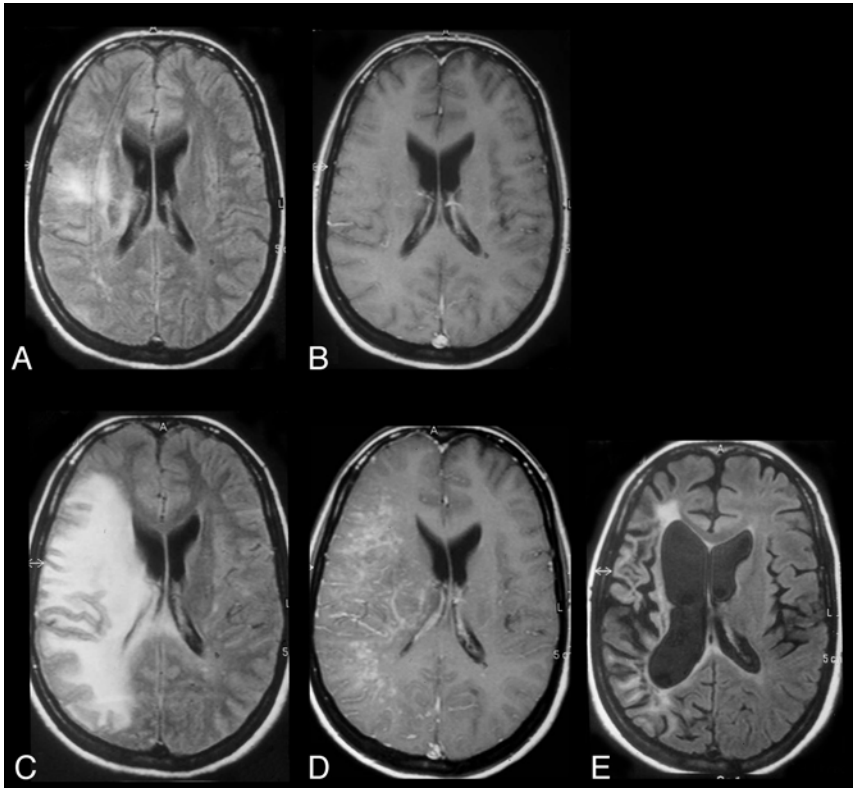

Patient with progressive neurological symptoms in an immune suppressed patient or on immune modulatory therapy
MRI scan with and without gadolinium
Ring enhancing lesions, gray and white matter involvement, massive edema: consider other infections, tumor, infarct etc
High signal intensity cerebral gray-white junction or brainstem white matter lesions on T2 or FLAIR images, ± enhancement ± mild mass effect
CSF for JCV PCR
Negative
Workup for other disorders (e.g. , CNS vasculitis, PRES, VZV leukoencephalopathy, malignancy, etc) and repeat CSF PCR for JCV
Negative
Positive
Brain biopsy for histology, immunohistochemistry / in situ hybridization
Positive
Definite PML


A
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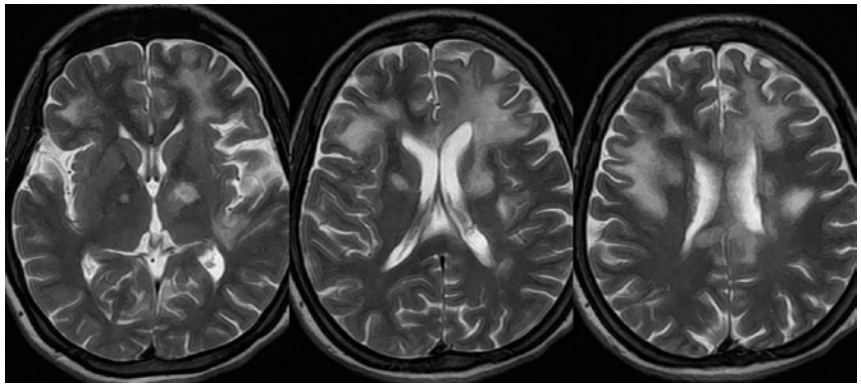
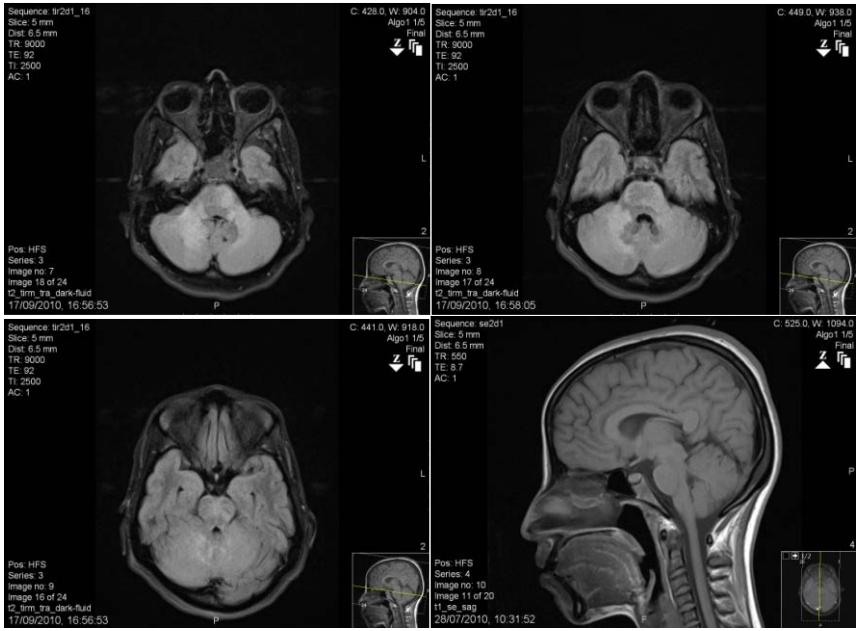
C
D
E

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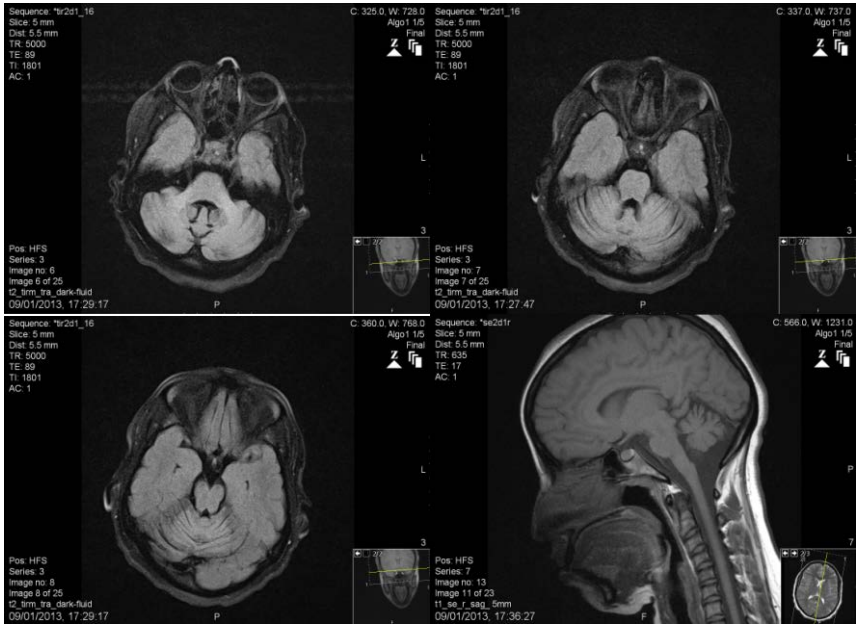
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C: 566.0, W: 1231.0
Algo1 1/5
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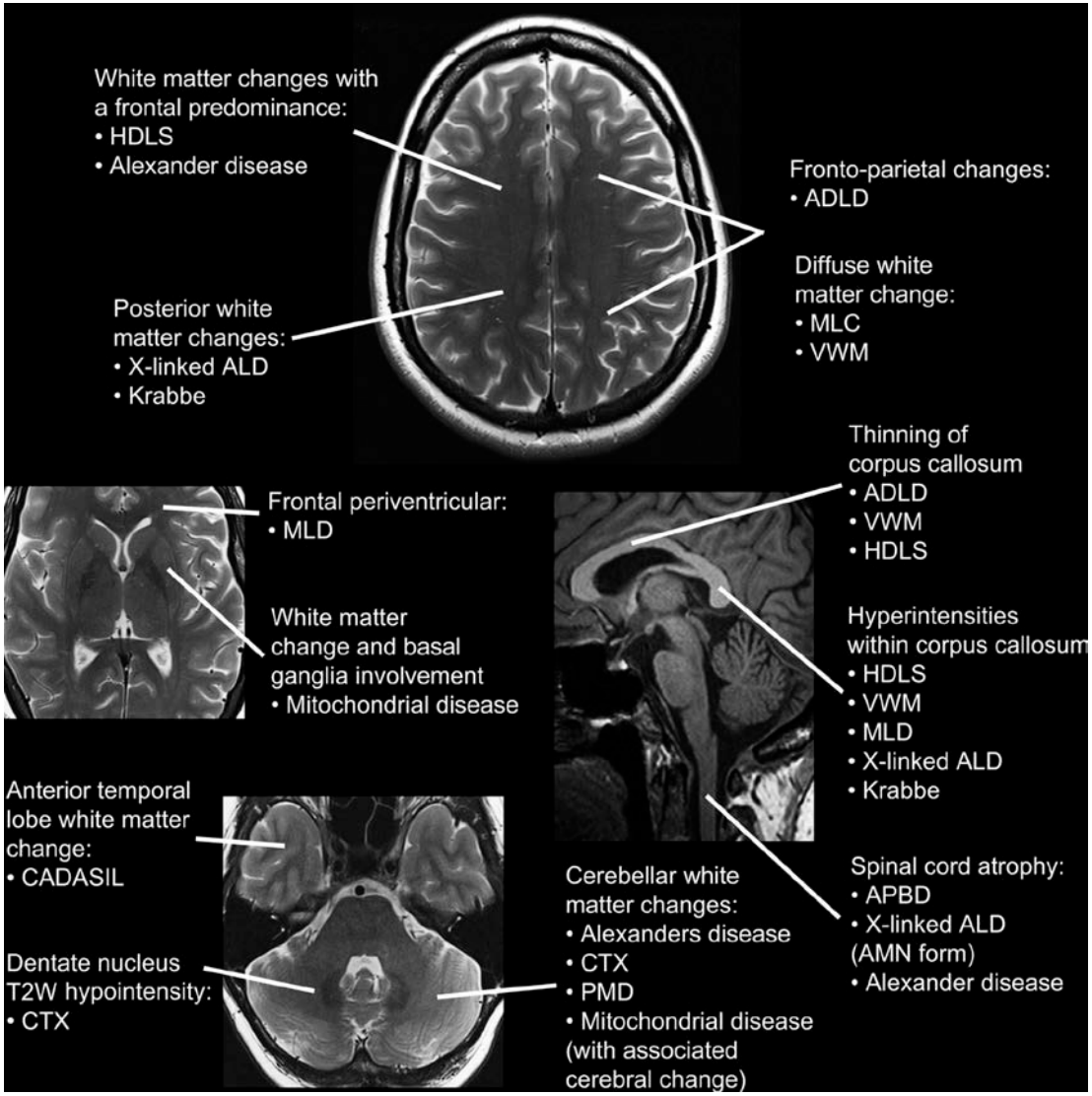
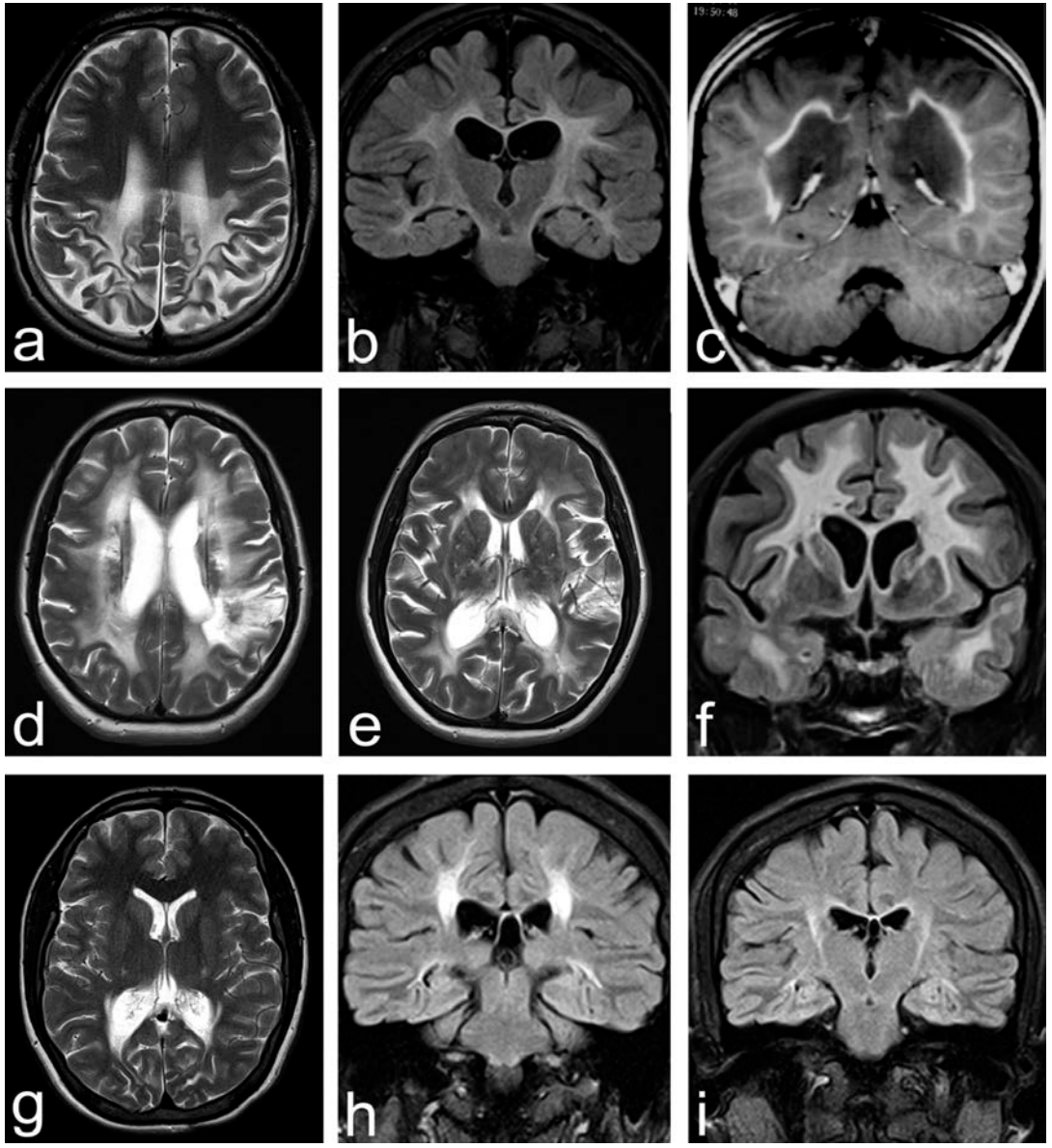
Adult onset leukodystrophies



R M Ahmed et al. JNNP 2013



X-linked adrenoleukodystrophy on axial T2-weighted (a, b, c)
CADASIL (d, e, f)
Krabbe (g, h, i)

Classic PML | JCV granular cell neuronopathy | JCV encephalopathy | JCV meningitis

	Classic PML	PML-IRIS	JC virus granule cell neuronopathy	JC virus encephalopathy	JC virus meningitis
Onset	Subacute	Immune recovery	Chronic	Subacute	Acute
Radiological findings (MRI)	Asymmetric, well demarcated, non-enhancing subcortical white matter lesions, hyperintense in T2 and FLAIR, hypointense in T1	Contrast enhancement and mass effect	Cerebellar atrophy	Cortical lesions	No defined brain lesions, ventricular dilatation
Neurological symptoms	Based on location	Based on location and inflammation	Cerebellar syndrome	Encephalopathy	Headache, stiff neck, fever
Diagnosis	JC virus detection in the CSF, brain biopsy, radiographical findings and symptoms	JC virus in the CSF, brain biopsy, radiographical findings and symptoms	Cerebellar biopsy, JC virus in the CSF, radiographical findings and symptoms	Brain biopsy, JC virus PCR in the CSF, radiographical findings and symptoms	JC virus in the CSF and exclusion of other viruses
Histology	Demyelinating lesions often at grey/white junction, JC virus detected in enlarged oligodendrocytes, bizarre astrocytes	Demyelination similar to classic PML, with addition of inflammatory infiltrates	Lytic infection of granule cell neurons in the cerebellum by JC virus	Lytic infection of cortical pyramidal neurons and cortical astrocytes by JC virus	
Treatment	cART for HIV-positive patients, discontinue or decrease immunosuppression for HIV-negative patients, plasma exchange for natalizumab-treated patients	Similar to PML, consider steroids in cases with notable neurological worsening or signs of impending brain herniation	Similar to classic PML	Similar to classic PML	Similar to classic PML

JCV granular cell neuronopathy - isolated progressive cerebellar syndrome
only cerebellar granule cell neurons are affected
preservation of the oligodendrocytes and astrocytes

JCV encephalopathy - isolated progressive cognitive deterioration and brain MRI PML
preferential infection of the cortical pyramidal neurons and astrocytes
located in the cortical grey matter and grey-white junction and
extensive infection of the pyramidal cell neurons


Grahame