

Neurological manifestations of COVID-19

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Introduction

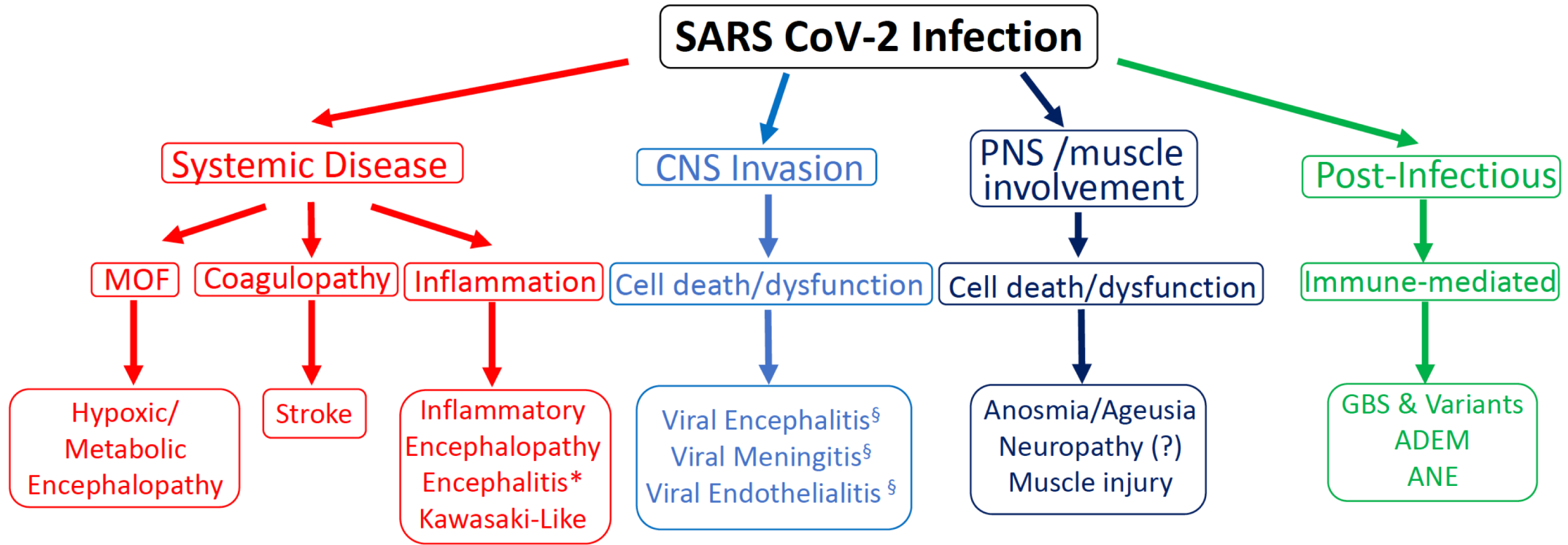
- Neurological manifestations common in COVID-19 (36% inpatients)
 - Headache 13%
 - Dizziness 18%
 - Confusion 7%
 - Paresthesia 2%
 - Myalgia 11%
 - Anosmia 5%
 - Ageusia 6%

Specific nervous system syndromes

- Central nervous system
 - **Strokes**
 - **Encephalopathy**/Encephalitis
 - **Psychosis**
 - Meningitis
 - Myelitis
- Neuromuscular system
 - **Muscle injury**/rhabdomyolysis
 - Guillain-Barre syndrome and variants
 - Cranial and peripheral neuropathies

Mao, L. JAMA Neurology; Helms, J. NEJM

Pathogenesis



* CNS inflammation with no direct evidence of viral infection

§ Direct evidence of viral invasion

Queen Square Institute of Neurology (UCL)

Cases	Main clinical features	Results of note	Treatment	Clinical outcome
Encephalopathy (n=10)	Delirium/psychosis	CSF - Normal MRI - Non-specific changes	Supportive 90% Steroids 10%	Recovery: complete 70%, partial 20%
Inflammatory CNS syndromes (para/post-infectious) (n=12)	Reduced consciousness UMN signs	CSF - Abnormal MRI - Abnormal	Corticosteroids 83% IVIG 25%	Recovery: complete 8%, partial 83%
Stroke (n=8)	Large vessel ischemic stroke	PE 50% High D-dimer 100%	Aspirin 38%,LMWH 88% apixaban 13%	Incomplete recovery 88% death 13%
GBS (n=7)	Cranial + peripheral neuropathy		IVIG 100%	Incomplete recovery 71%

Paterson, RW. Brain

Brain MRI

- Ischemic strokes
- Leptomeningeal enhancement
- Other patterns (n=37):
 1. Signal abnormalities in the medial temporal lobe: 43%
 2. Multifocal white matter hyperintensities on FLAIR with variable enhancement, hemorrhagic lesions: 30%
 3. Extensive and isolated white matter microhemorrhages: 24%

CSF SARS-CoV-2 PCR

- Sensitive to detect RNA in CSF (1-10 copies/reaction)

BUT:

- Few positive cases reported
- Of 578 CSF samples screened (confirmed COVID-19 = 23): 2 positive
- ? Timing of sample ? Method suboptimal- Antibody index

Perchetti, GA. J Clin Virol; Destras, G. Lancet Microbe

Neuropathology

Solomon (n=18)

- Acute hypoxic brain injury in all
- No vasculitis/thrombi
- No olfactory bulb damage
- RT-PCR + 6/52 sections but: negative immunohistochemical analysis

von Weyhern (n=6)

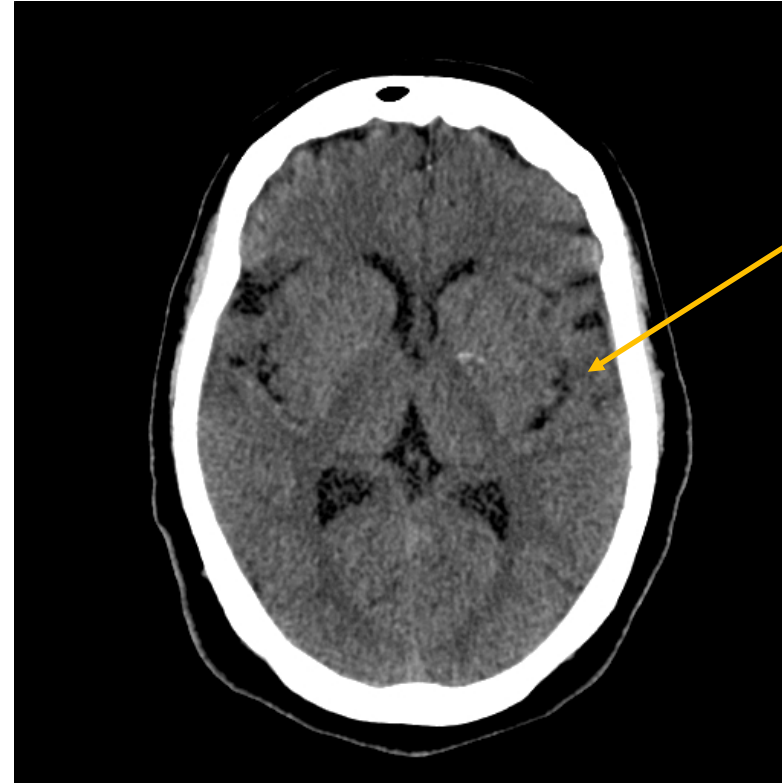
- Lymphocytic panencephalitis and meningitis
- Brainstem perivascular and interstitial inflammatory changes
- No endothelialitis

Solomon, IH. NEJM; von Weyhern, CH. Lancet

Case discussions

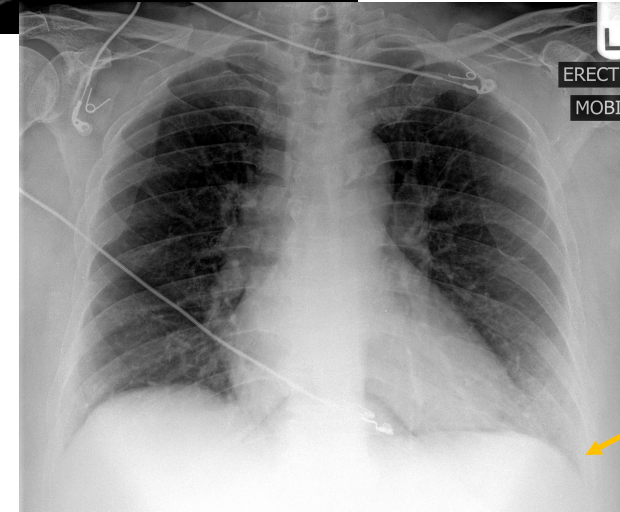
62 yo W

- DM type 2
 - Hypertensive
 - Chronic Kidney disease (Cr 76)
 - Ex-smoker
-
- Acute onset R weakness and dysarthria
 - Left LACS (NIHSS 6)
 - IV rtPA commenced at 190 minutes from onset sx



Hb	14.2
Tchol	8.44
Plts	308
INR	0.99
D-dimers	0.24
Cr	72
CRP	15
HbA1c	12.5

- Cough for 3/7 prior to weakness
- O2 sats 98% on RA, RR **30**, p76 bpm
- CXR: L LL infiltrate
- NP swab SARS-CoV-2 **pos**
- HIV, TPHA neg
- CTB: L basal ganglia infarct
- Able to mobilise independently on discharge

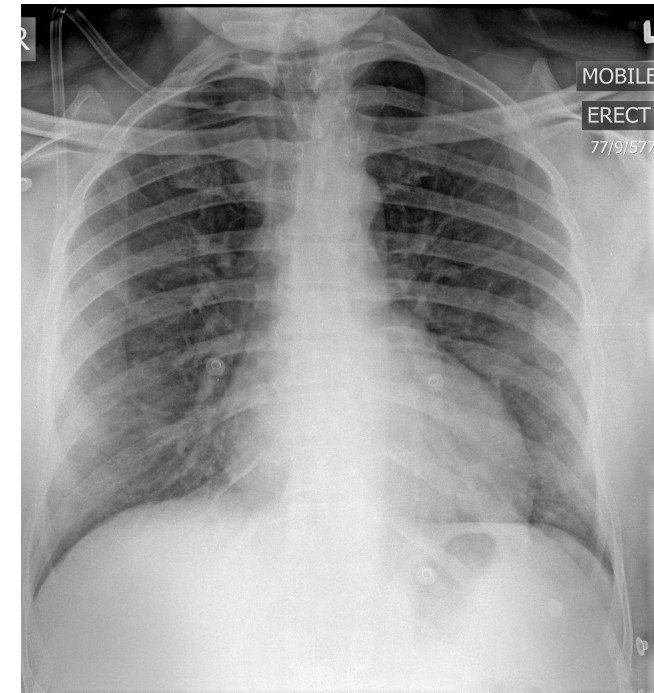


Keypoints: stroke & Covid-19

- Prognosis may be good!
- Pre-existing stroke treatment protocols should be followed
- Hyperacute treatment: IV thrombolysis and MT recommended
- Post-acute treatment:
 - Antiplatelet therapies
 - Prophylactic enoxaparin
 - Therapeutic enoxaparin decided on individual case basis
 - Preferably >10-14 days after large infarct

36 yo M

- healthy baseline
- HIV negative
- Confirmed covid pneumonia
- Neurologically normal on admission
- Treatment:
 - O₂
 - prednisone
 - prophylactic enoxaparin

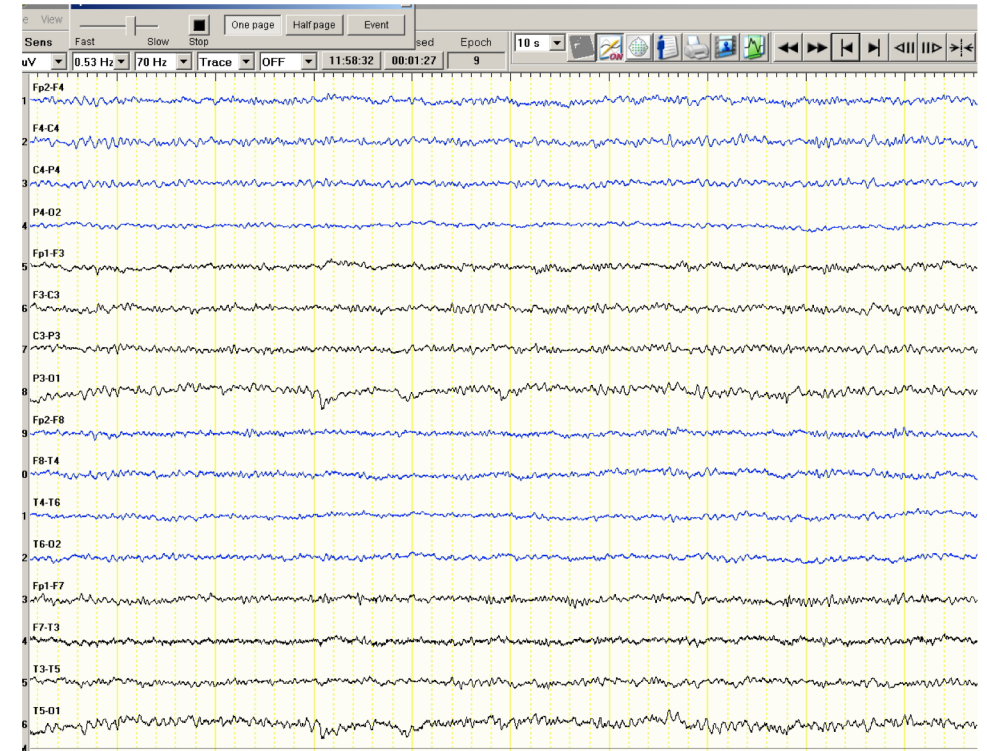


WCC	12.6
Lymph	0.76
D-dimers	0.39
Na	128
Cr	78
CRP	93
HbA1c	6.4

- Day 2: agitation/disorientation
 - O2 sats 93% RA
 - marked improvement in mental state after IV diazepam
- Assessed as subclinical epileptic seizures or covid encephalopathy
- CTB normal
- LP: mild pleocytosis

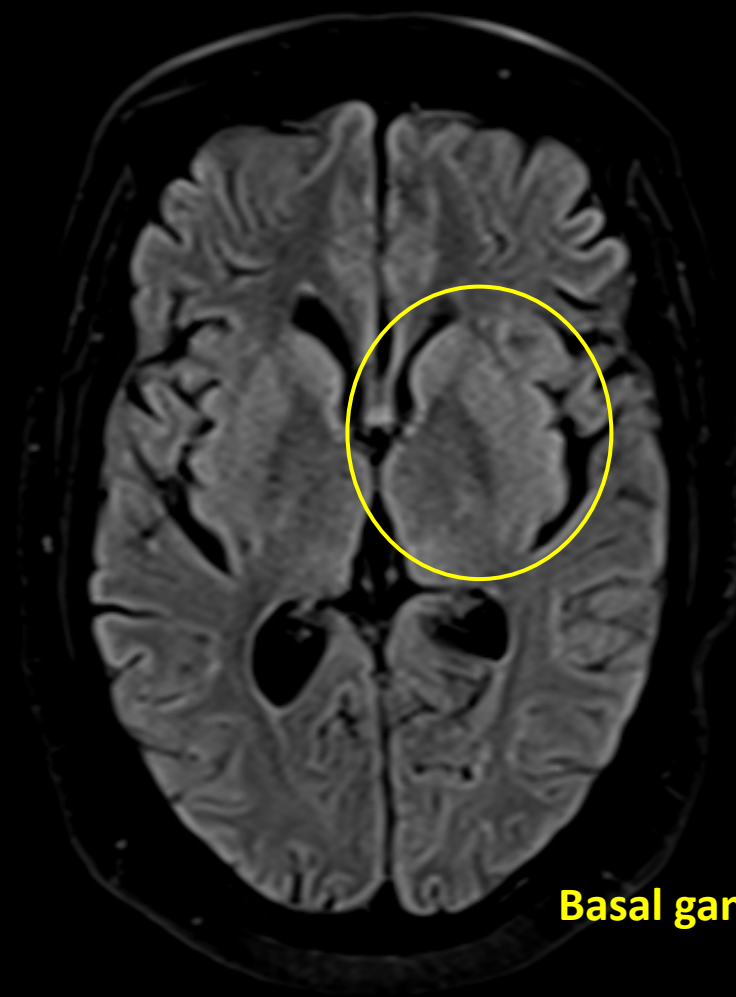
CSF	
Protein	0.37
Gluc	5.5
Polys	8
Lymphs	5
IgG index	N
FTA	neg
HSV1/2, VZV, CMV pcr	neg
CLAT, GXPT	neg
AFB culture	neg
SARS-CoV-2 pcr	neg
NMDAR ab	awaited

- Day 3: GTC seizure witnessed
 - Ongoing agitation, confusion, visual hallucinations, echolalia, repetitive movements, catatonic
 - Initial management:
 - phenytoin, sodium valproate, ceftriaxone, haloperidol
 - Stopped steroids
- EEG normal
- MRI brain normal
- Acyclovir, olanzepine
- Day 9: worsening condition
 - Commenced IVMP 1g x 5/7
- 5 days later, catatonia resolved
- Discharged fully recovered





Medial temporal lobe



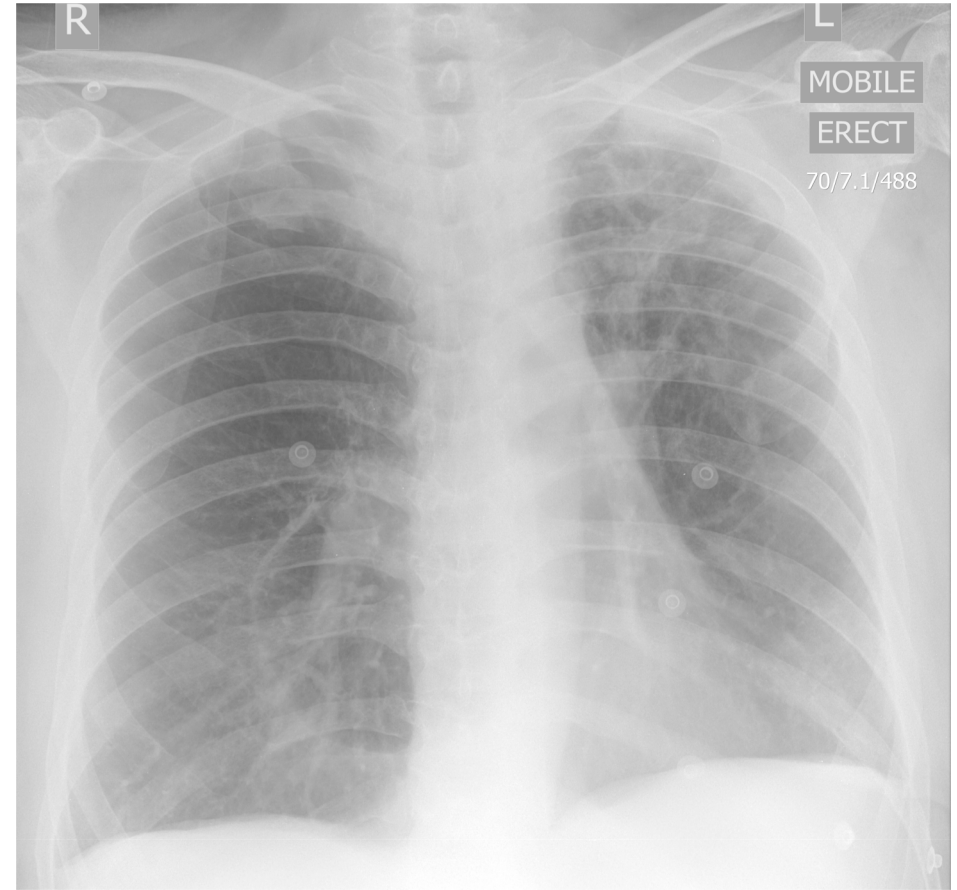
Basal ganglia

Encephalopathy/encephalitis

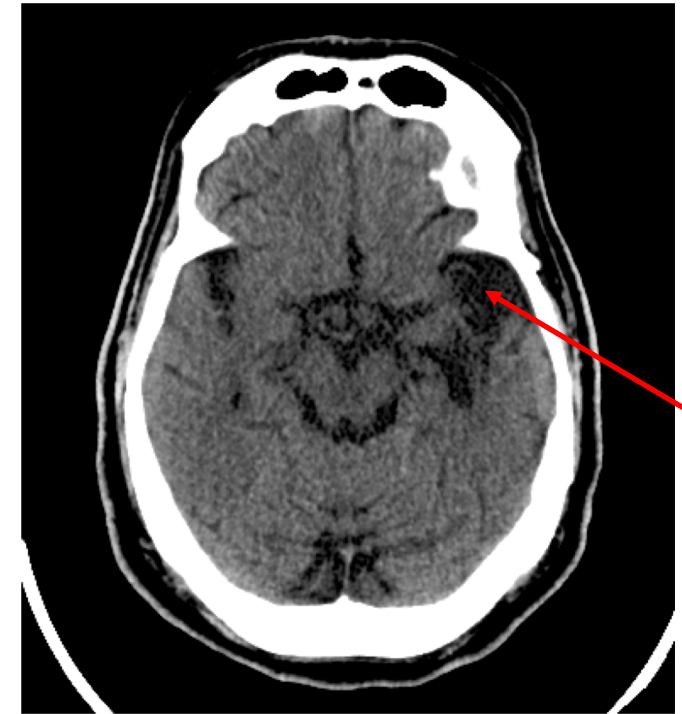
- Case of covid-19-associated encephalitis:
 - altered mental state, seizure, catatonia, csf pleocytosis
- Encephalopathy more common but encephalitis in presence of suggestive features:
 - Clinical: new onset seizures/focal deficit/movt disorder/fever/focal EEG abn
 - Compatible brain imaging, CSF pleocytosis
 - Brain inflammation on histology (gold std)
- Rapid improvement on steroids may support immune-mediated/inflammatory pathogenesis

77 yo M

- Hpt
- DM
- IHD – prev STEMI
- PTB – dx Mar 2020
- COPD
- Family: hx suggestive of dementia
- Admitted confirmed covid-19 pneumonia requiring O2
- Days later: confusion, agitation despite adequate O2 sats



- CTB: old left temporal encephalomalacia
- No metabolic cause found
- No Lp/EEG
- Pneumonia improved but ongoing agitation
- Settled over weeks back to baseline

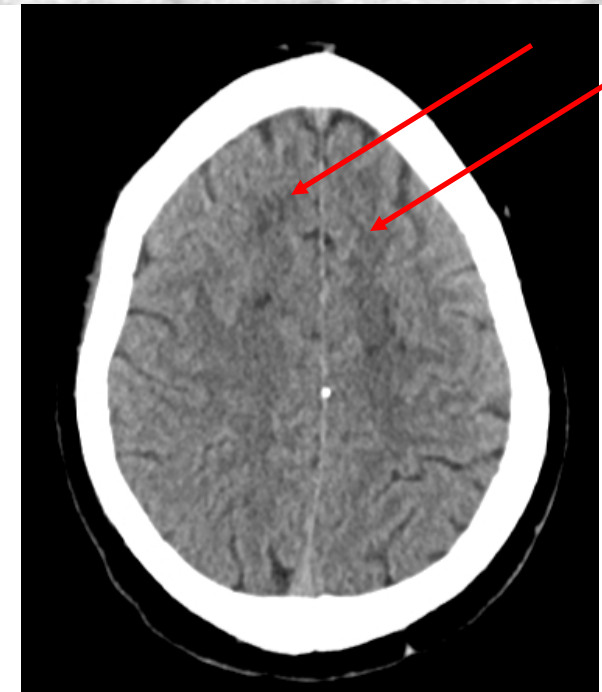
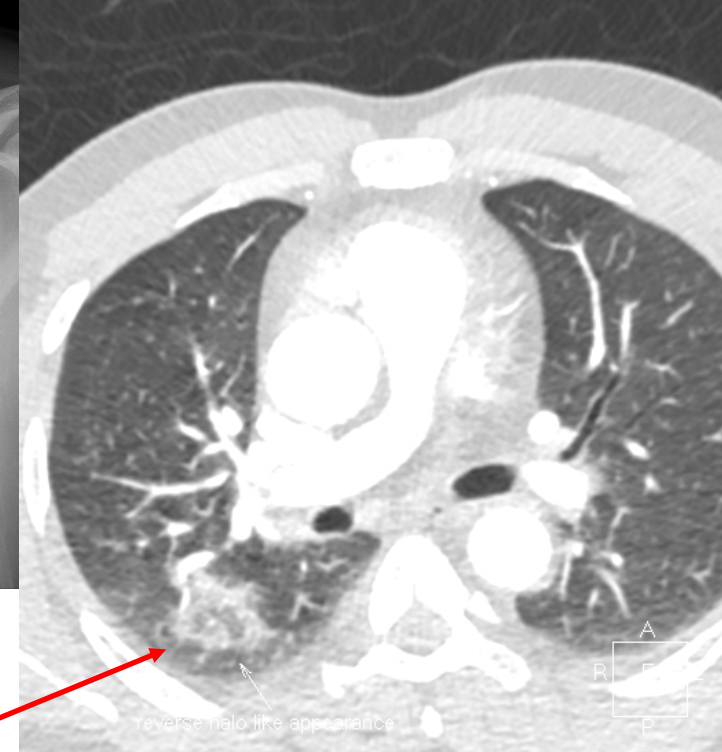
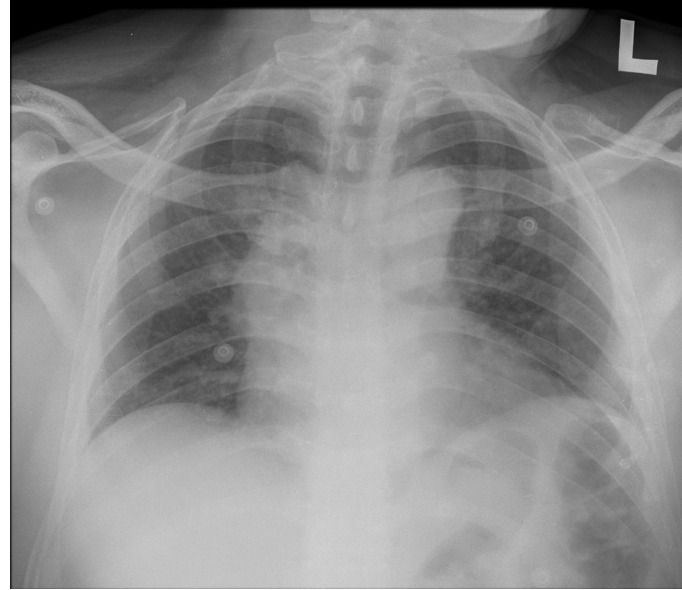


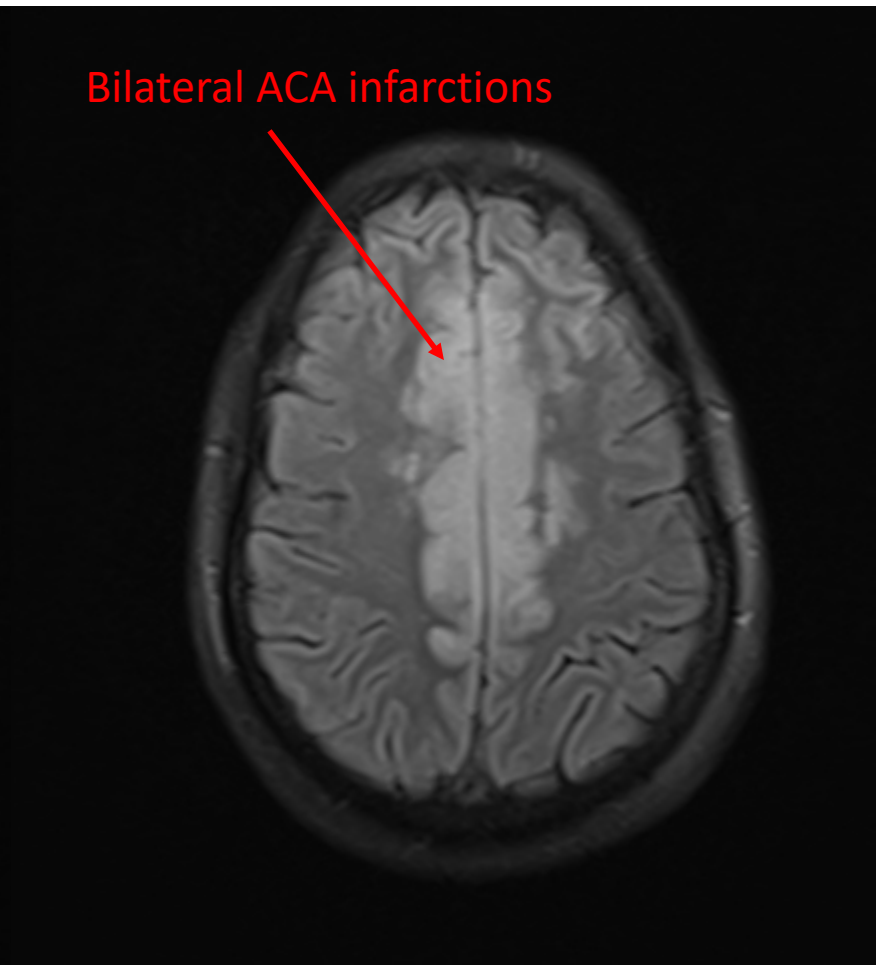
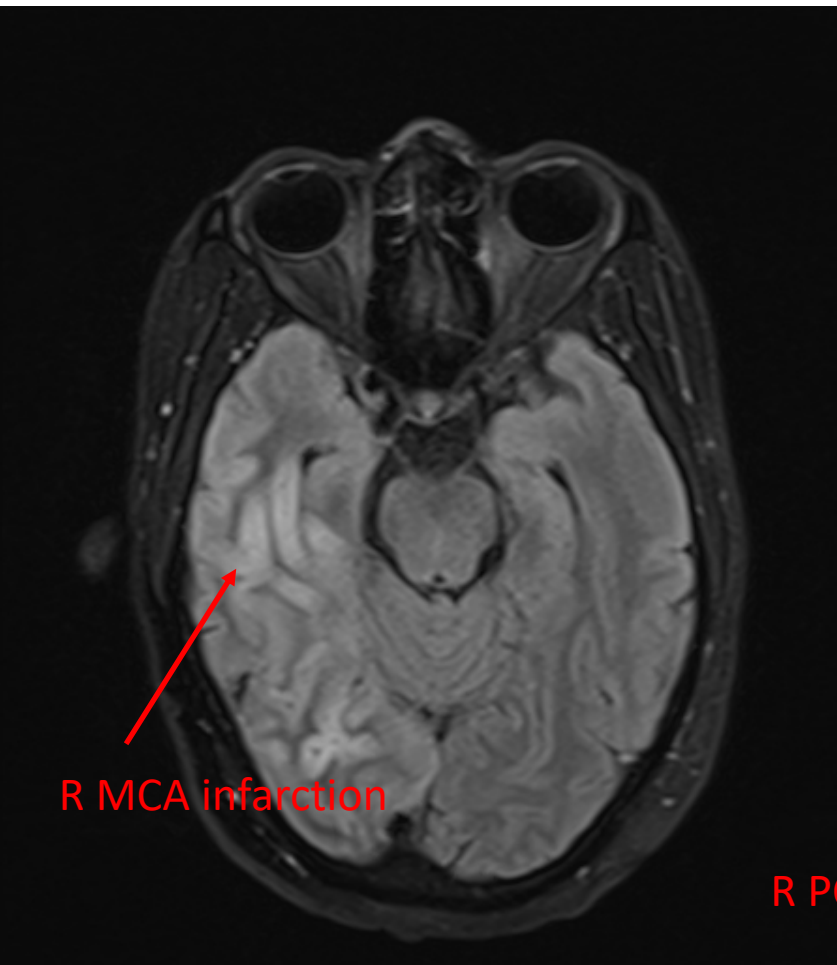
L temporal
encephalo
malacia

- Keypoint:
 - underlying dementia may only present with functional decline unrelated to pneumonia in covid-19

52 yo M

- Hypertension, on 4 agents
 - Defaulted Rx for 6 mon
- 1/7 headache, confusion, ataxia, leg weakness
- Bp 219/132 treated with IV labetalol
- CTB: old lacunar infarcts, new bifrontal hypodensities
- CXR ?widened mediastinum →
- CT angio chest 'reverse halo' suspicious for covid-19 pneumonia
 - Day 3 NP swab SARS-CoV-2 pos





- Lp normal
- Remained confused, leg weakness
- Demised prior to work-up completed

Multiterritorial cerebral infarcts and hypertensive crisis in context of Covid-19 pneumonia, b/g untreated hpt

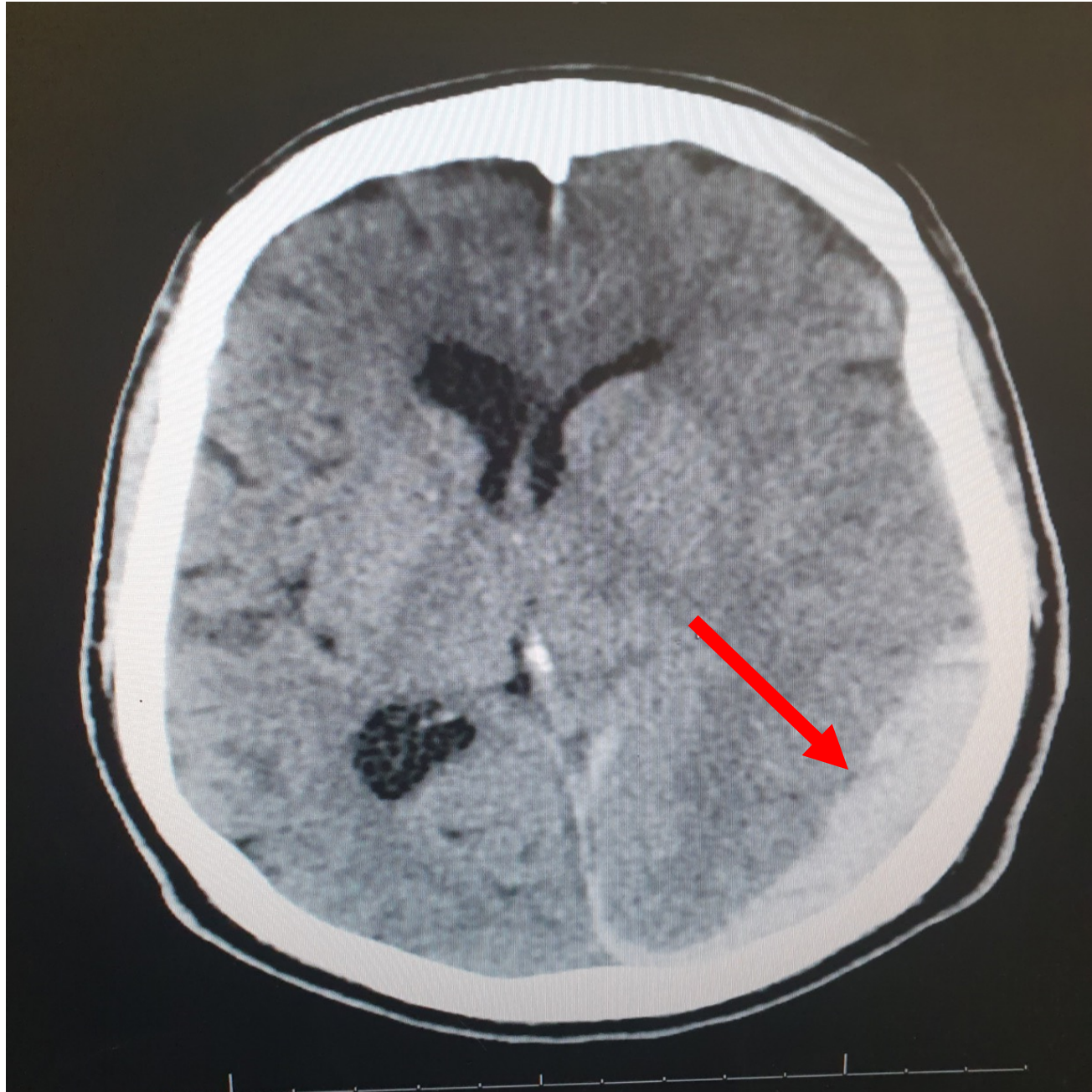
53 Yr M

- No known vascular risk factors
- Previous TB (completed treatment)
- Presented with severe confirmed COVID-19 pneumonia req HFNO₂
- HIV-, No AF, D-dimer: 0.56
- Therapeutic enoxaparin (80 mg bd)
- Day 4 of admission:
 - Severely painful distal lower limbs
 - Cold, pulseless
 - Power 0/5 ankles/toes
 - Decreased light touch: mid thigh R, knee L
 - No sphincter involvement



79 Yr M

- Independent all ADLs
- Bowel Ca 2018- completely resected
- Presented with severe confirmed COVID-19 pneumonia req double O₂
- Prednisone and therapeutic enoxaparin (80 mg bd) commenced
- Day 4 of admission- features of acute stroke:
 - Severe headache and vomiting
 - Dysphasia
 - R hemiparesis and hemisensory disturbance
 - Small laceration above left eyebrow - fall 3 days prior to admission



69 Yr F

- Background: HPT, Dyslipidemia
- Independent ADLs
- Admitted with confirmed COVID-19 pneumonia req O₂
- Increased BMI
- Newly diagnosed DM (HBA1C=8)
- Transferred to stepdown facility after 2 weeks –received oral steroids
- Readmitted 1 week later after 2/7 symptoms:
 - Increased shortness of breath and O₂ requirements
 - Paresthesia of hands and feet
 - Difficulty standing and holding objects

- Exam:
 - RR: 30 bpm, O₂ sats: 96% NRB
 - Mild neck flexion weakness
 - Areflexic quadriparesis: Distal > proximal (progressive)
 - Stocking/glove sensory disturbance
- CXR: improved
- CSF: acellular, glucose: 5.4, prot: 0.66, IgG index: 0.69
- NCS: deferred
- Diagnosis: Guillain-Barre syndrome
- Management: IVIG and therapeutic enoxaparin, Intubated
- Complication: sepsis

Thank you!