IRIA-ICRI Guidelines and Recommendations

(INDIAN RADIOLOGICAL AND IMAGING ASSOCIATION- INDIAN COLLEGE OF RADIOLOGY AND IMAGING)

Imaging recommendations for COVID manifestations in the Central Nervous System

Indian Radiological & Imaging Association

IRIA House, C-5, Qutab Institutional Area, Behind Qutab Hotel

New Delhi-110 016,INDIA

Tel. +91-11-26965598, +91-11-41688846. Fax: +91-11-26565391

E-mail: iria37@gmail.com, Website: www.iria.org.in

Updated on 10th June 2021.

IRIA-ICRI Guidelines and Recommendations

Imaging recommendations for COVID manifestations in the Central Nervous System

Prepared by Indian College of Radiology and Imaging (Academic wing of Indian Radiological & Imaging Association) neurosub Specialty group

Introduction:

Severe Acute Respiratory Syndrome corona virus 2 (SARS-CoV-2) infection a global pandemic presenting as pulmonary infection has now been recognized as a multisystem disease with increased recognition of neurological manifestations[1].

Pathogenesis:

The neurological sequalae of Corona virus disease (COVID) can be grouped into four categories:

1) Direct effect due to neuro invasion by virus.

2) Para infectious immune response to infection manifesting as coagulopathy or cytokine storm.

3) Delayed immune response post infection.

4) Complications of prolonged illness and hospitalization[1].

Evidence of direct central nervous system (CNS) viral invasion is scanty; however retrograde transsynaptic spread from the nasal mucosa through the olfactory epithelium is suggested as anosmia and dysgeusia are symptoms in early COVID. It is uncertain if the hypercoagulability in COVID infection is a result of direct viral interaction with the endothelium or an abnormal inflammatory response initiated by the virus.

Cytokine storm refers to dysregulated immune response that causes immune mediated tissue damage.Hypercoagulable state is promoted by the proinflammatory cytokines as a result of endothelial dysfunction, vascular damage and activation of coagulation cascade. Neurological findings as a sequalae of treatment like prolonged intubation or extracorporeal membrane oxygenation include diffuse hypoxemic injury, microhemorrhage and post-hypoxic leukoencephalopathy[1].

Neurological manifestations of COVID:

Neurological manifestations may vary from non-specific symptoms such as headache, dizziness, myalgia and/or fatigue, olfactory or taste dysfunction to specific syndromes including meningitis, stroke, acute transverse myelitis and Guillain-Barre syndrome[1].

1. **Thromboembolicinfarcts**: It's the most commonly seen intracranial manifestationand pathogenesis is due to development of coagulopathy or endothelial dysfunction. Acute stroke

has strong prognostic indicator for poor outcome. Thromboembolic episodes may coincide with increased D-dimer levels and inflammatorymarkers. The commonly observed patterns of acute cerebralthromboembolic disease are large vessel occlusion with territorial infarcts, branch vesselocclusion, small vessel occlusion, small vessel infarcts, watershed infarcts, and extensivebilateral multivessel infarcts (Fig 1). Diffuse central nervous system vasculitis pattern has also been encountered. Small vessel microangiopathyhas been related to propensity of COVID- 19 to infect endothelialcells of different vascular beds. COVID 19 patients with thromboembolic complication have a higher clot burden with thrombus in other vessels like the cervical carotid, vertebral arteries, pulmonary arteries and lower extremity veins[1,2].

2. **Hemorrhage**: Patients with COVID 19 have hemorrhage in different location of the brain due to combination of factors like COVID 19 induced coagulopathy, disseminated intravascular coagulation & cytokine storm. Effects of treatment like thromboprophylaxis, dialysis and ECMO are also contributary. Critical illness associated microbleeds and virus induced thrombotic microangiopathy is responsible for microhemorrhage which is seen distributed in the region of corpus callosum and at grey white matter interphase (Fig 2). Microbleeds are suggested due to hypoxia-inducedhydrostatic or chemicaleffects on the blood–brain barrier (BBB) potentially accountingfor the extravasation of erythrocytes[23].
3. **Leukoencephalopathy**: Manifests as symmetrical confluent white matter T2 hyperintensity and diffusion restriction sparing the juxtacortical and infratentorial white matter (Fig 3). These findings are non-specific or related to delayed post hypoxic phenomenon.
4. **Global hypoxic injury**: Global hypoxic injury has been reported with predomiently involvement of the basal ganglia, thalami, hippocampi and cortex (Fig 4). Unusual pattern of isolated involvement of the globus pallidi has also been seen. Other pattern seen is delayed posthypoxic leukoencephalopathy[3].
5. **Posterior reversible encephalopathy syndrome (PRES):** The proposed mechanism for the development of PRES is disruption of the capillary endothelial lining leading to increased permeability of the BBB and loss of hemostatic regulation presenting as edema. This is caused by viral binding to the angiotensin converting enzyme 2 receptors in the capillary endothelium. Imaging findings include vasogenic or cytotoxic edema distributed in the watershed territory of the cerebral hemisphere with predominant parieto-occipital lobe predilection. They may also present with hemorrhage or microbleeds. The mechanism of microhemorrhage can be attributed to massive release of cytokines resulting in damage and breakdown of the BBB or increased coagulopathy[3].

6. **Meningitis and encephalitis:**Meningitis and encephalitis are uncommon in COVID patient. The radiological and clinical presentation of encephalitis is myriad. Acute necrotizing encephalopathy has been mainly described inthe pediatric population, but can also present in adults. The MRI features include multifocal involvement of thebrain most characteristically in the thalamus, brain stem, cerebralwhite matter, and cerebellum. The lesions show FLAIRhyperintense signal with internal hemorrhage, and post-contrastimages show ring enhancement. ADEM and acute hemorrhagic leukoencephalopathy has also been described. The changes may be related to intracranial cytokine storm and BBB breakdown[3,4].
7. **Cytotoxic lesion of the corpus callosum**: It has been described both in adults and children with COVID 19. These lesions are due to inflammatory damage from coincident cytokine storm.
8. **Olfactory bulb involvement**: Edema in the olfactory bulb and track with increased T2 signal intensity in the gyrus rectus. Olfactory bulb atrophy after COVID 19 induced anosmia has also been described.
9. **Cranial nerve enhancement**: Cranial neuropathies reported in COVID 19 include optic neuritis, oculomotor nerve enhancement and Miller Fisher syndrome. Miller Fisher variant of Guillian-Barre syndrome is an acute peripheral neuropathy characterized by triad of ophthalmoplegia, ataxia and areflexia. On imaging there is mild thickening and enhancement of the oculomotor nerve[1].
10. **Spinal manifestation**: Guillian Barre syndrome is seen in association with COVID 19 characterized by T2 hyperintensity in the distal cord and enhancement of the caudal nerve roots[3].
11. **Mucormycosis:**Amids the pandemic of COVID 19 there has been a surge of rhinocerebralMucormycosis. This is an opportunistic infection manifesting in patient with uncontrolled diabetes with prior steroid use, following COVID 19 infection. The nasal cavity and the paranasal sinuses are the once involved initially followed by spread of infection to orbit and brain. The CNS involvement is via contiguous extension through the cribriform plate or following skull base involvement and perineural spread. Imaging manifestations include skull base osteomyelitis, pachymeningeal enhancement, leptomeningeal enhancement, cerebritis progressing to abscess, cranial nerve infiltration, infarcts, cavernous sinus thrombosis, mycotic pseudoaneurysm, subarachnoid hemorrhage and intraparenchymal hemorrhage[5].

Imaging Recommendations:

- MRI is the imaging modality of choice and sequences should be tailored to the clinical indication. Sequences like SWI and post contrast FLAIR should be done in indicated cases.
- Patients presenting with acute stroke (hemorrhagic or ischemic): CT Brain with CTA brain and intracranial vessels or MRI Brain with MR angiogram can be performed.
- Spinal manifestation: MRI spine with contrast.

Conclusion:

Neurological manifestation of COVID 19 has been increasingly recognized and familiarity of the various presentations is important in their identification.

References:

1. Moonis G, Filippi CG, Kirsch CFE, et al. The Spectrum of Neuroimaging findings on CT and MRI in Adults with Coronavirus Disease (COVID-19). *Am J Roentgenol*. Published online 2020. doi:10.2214/ajr.20.24839
2. Lin E, Lantos JE, Strauss SB, et al. Brain imaging of patients with COVID-19: Findings at an academic institution during the height of the Outbreak in New York City. *Am J Neuroradiol*. 2020;41(11):2001-2008. doi:10.3174/ajnr.A6793
3. El Beltagi AH, Vattoth S, Abdelhady M, Ahmed I, Paksoy Y, Abou Kamar M, Alsoub H, Almaslamani M, Alkhal AL, Own A, Elsotouhy A. Spectrum of neuroimaging findings in COVID-19. *Br J Radiol.* 2021 Jan 1;94(1117):20200812.
4. Garg R, Paliwal V, Malhotra H, Sharma P. Neuroimaging Patterns in Patients with COVID-19-Associated Neurological Complications: A Review. *Neurol India*. 2021;69(2):260-271. doi:10.4103/0028-3886.314531
5. Mazzai L, Anglani M, Giraudo C, Martucci M, Cester G, Causin F. Imaging features of rhinocerebral mucormycosis: from onset to vascular complications. *Acta radiol*. 2021;(February). doi:10.1177/0284185120988828

FIGURES AND LEGENDS

Figure 1: Acute Infarct with right internal carotid artery(ICA) occlusion: 64 year old male presenting with right hemisphere stroke and RTPCR positive for COVID 19 infection. CT angiogram (A to E) showed occlusion of the right ICA with right middle cerebral artery filling across anterior and posterior communicating artery. CT chest (F) showed peripheral groundglass opacities with crazy paving. MRI Brain DWI (G) revealed acute lacunar infarcts in right hemisphere water shed territory

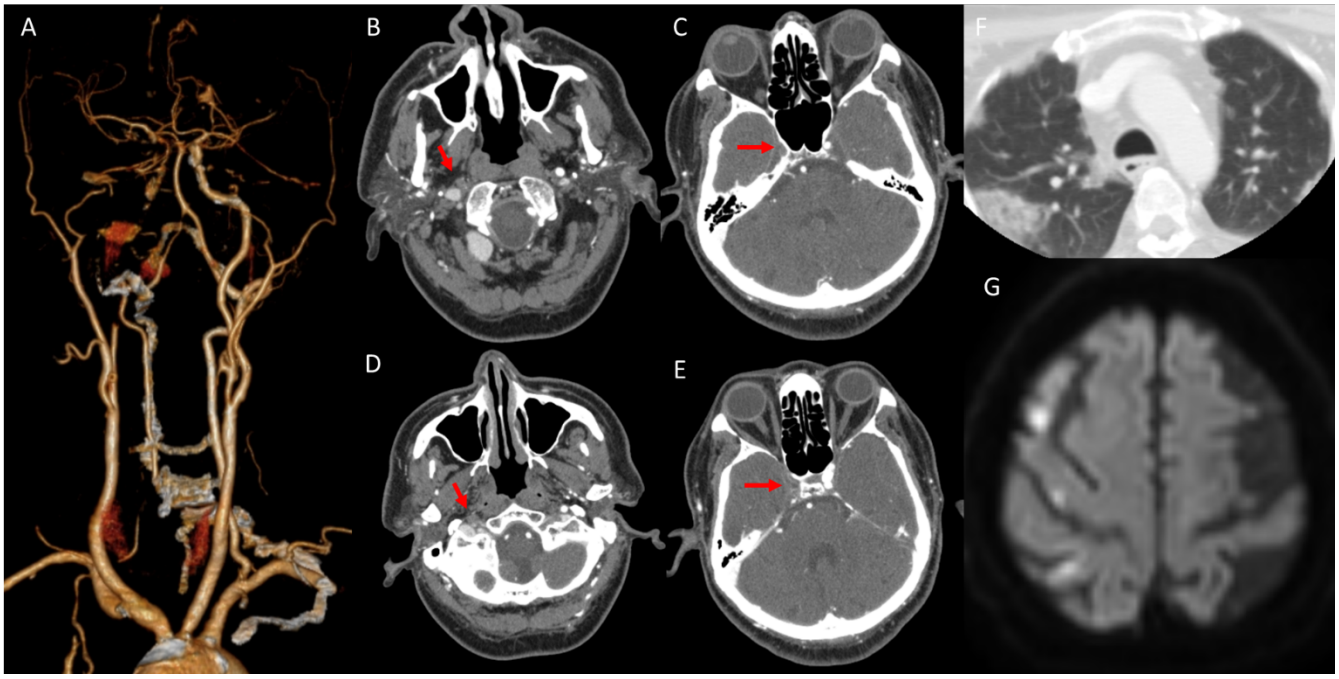


Figure 2: Critical illness induced microbleeds or Virus induced thrombotic microangiopathy: MRI Brain of 39 year old male who recovered from COVID 19 pneumonia. Axial SWI (A & C); Axial T2 (B) and Axial FLAIR (D) showedMultiple microbleed (black arrow) in bilateral cerebral hemispheres at grey-white matter interface and in the splenium of the corpus callosum with small subacute haemorrhage in left parietal lobe (white arrow)

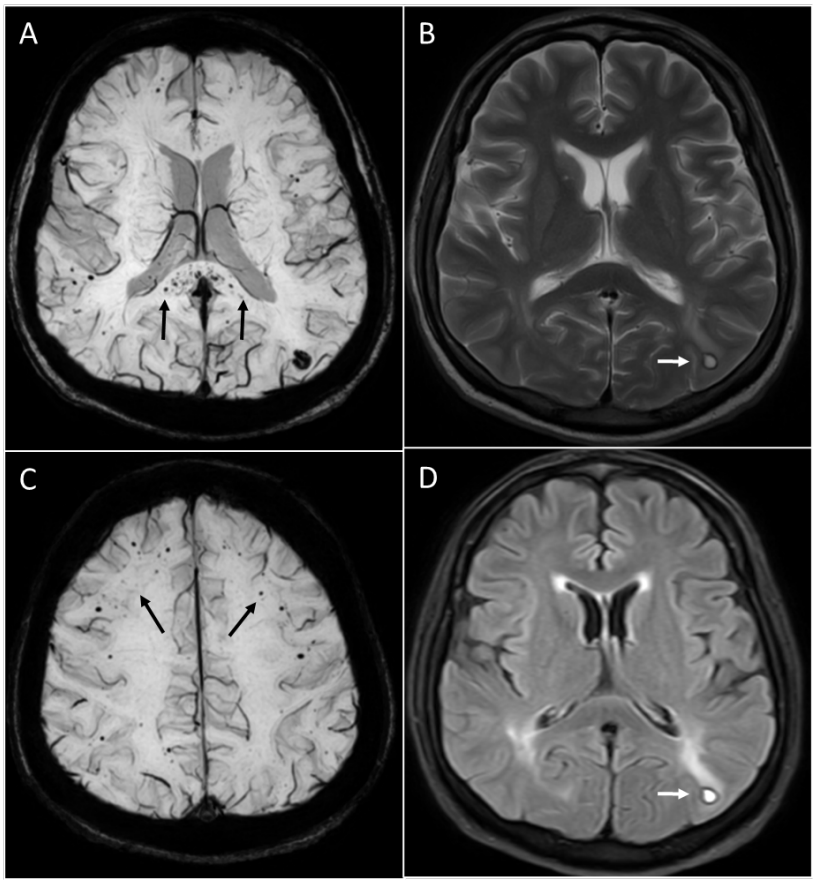


Figure 3: Leukoencephalopathy. 41 year old male with history of COVID 19 infection presented with seizures progressing to altered sensorium. MRI of the brain Axial T2 (A – D), Axial DWI (E & F),Axial GRE (G) and Coronal T1(H) revealed confluent white matter hyperintensity involving bilateral cerebral hemispheres with corresponding areas of diffusion hyperintensity. No hemorrhage or abnormal mineralization noted.

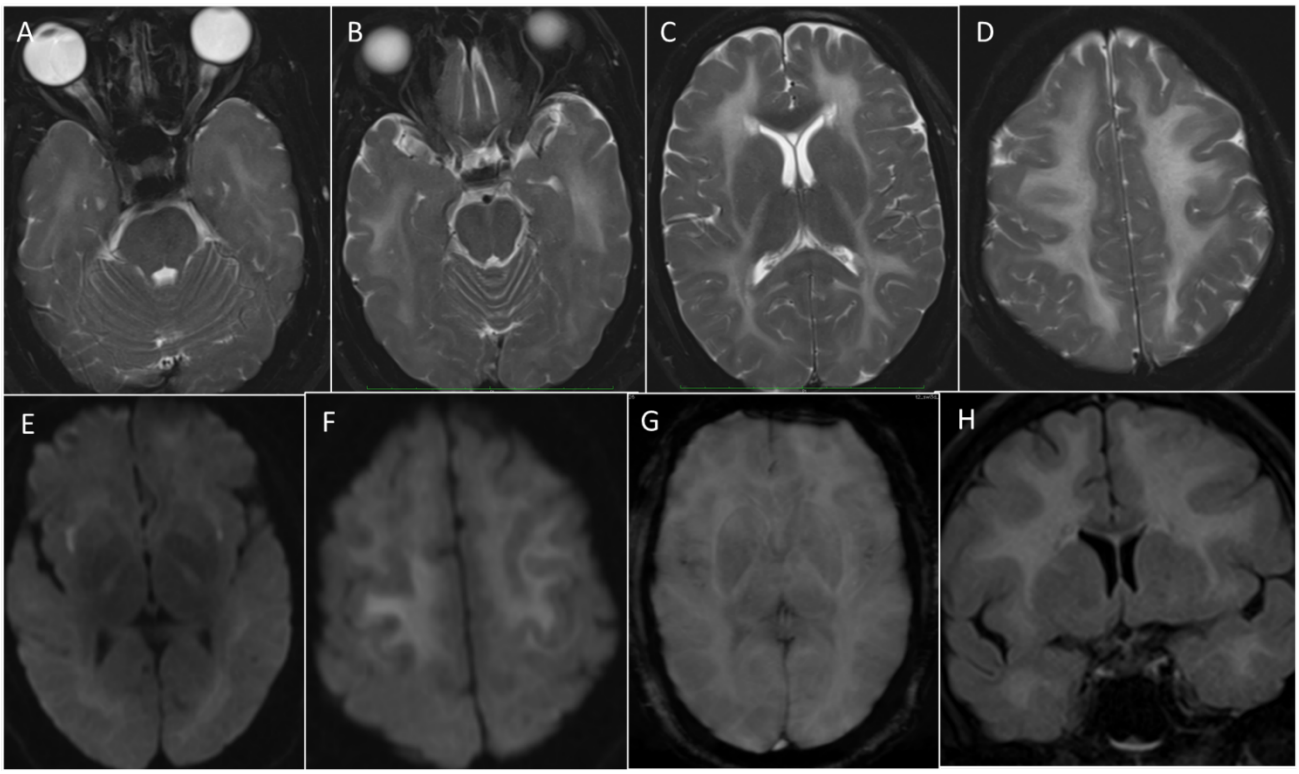


Figure 4: Hypoxic ischemic encephalopathy: 63 year old female with COVID 19 pneumonia (CT severity score of 20/25) on ventilator. CT Chest (A & E): patchy consolidation with predominant peripheral distribution. MRI Brain DWI (B & C); ADC (F & G) and FLAIR (D & H) showedgyriform diffusion restriction in bilateral temporo-occipital regions, fronto parietal regions and thalami with corresponding changes on FLAIR.

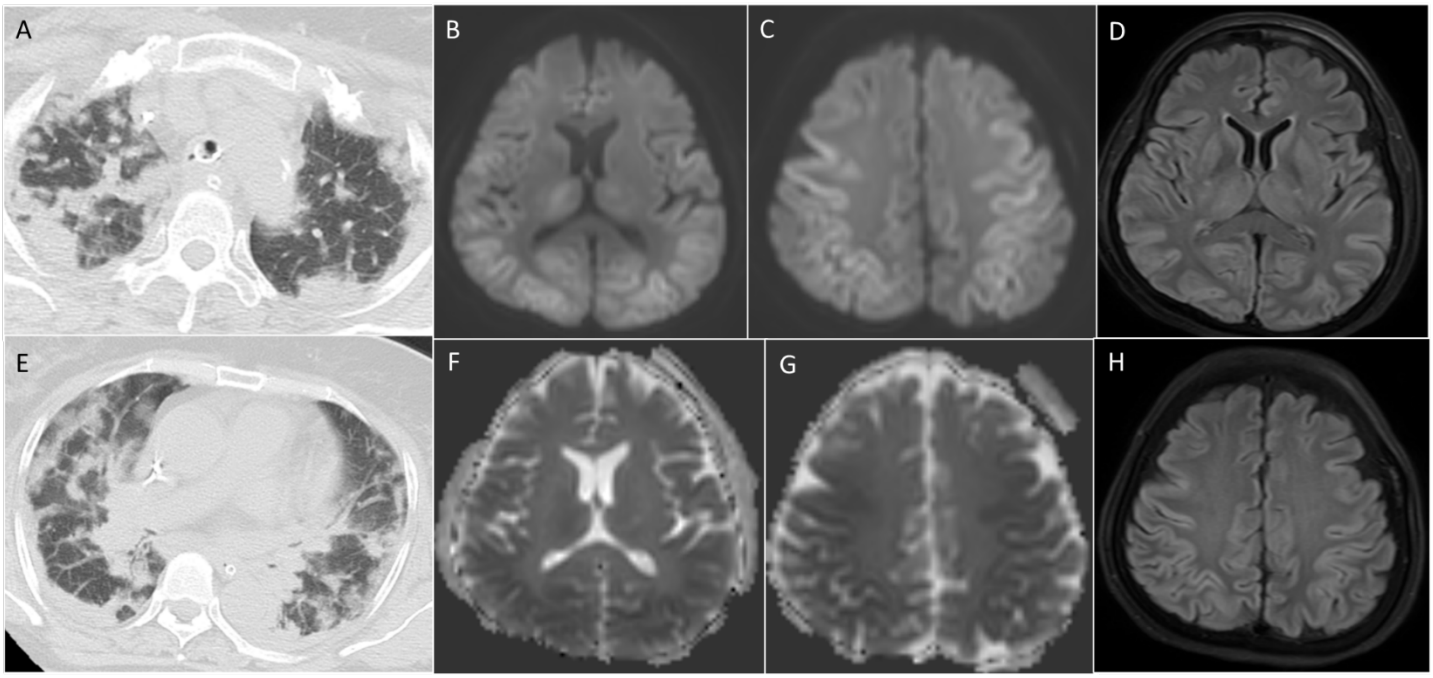
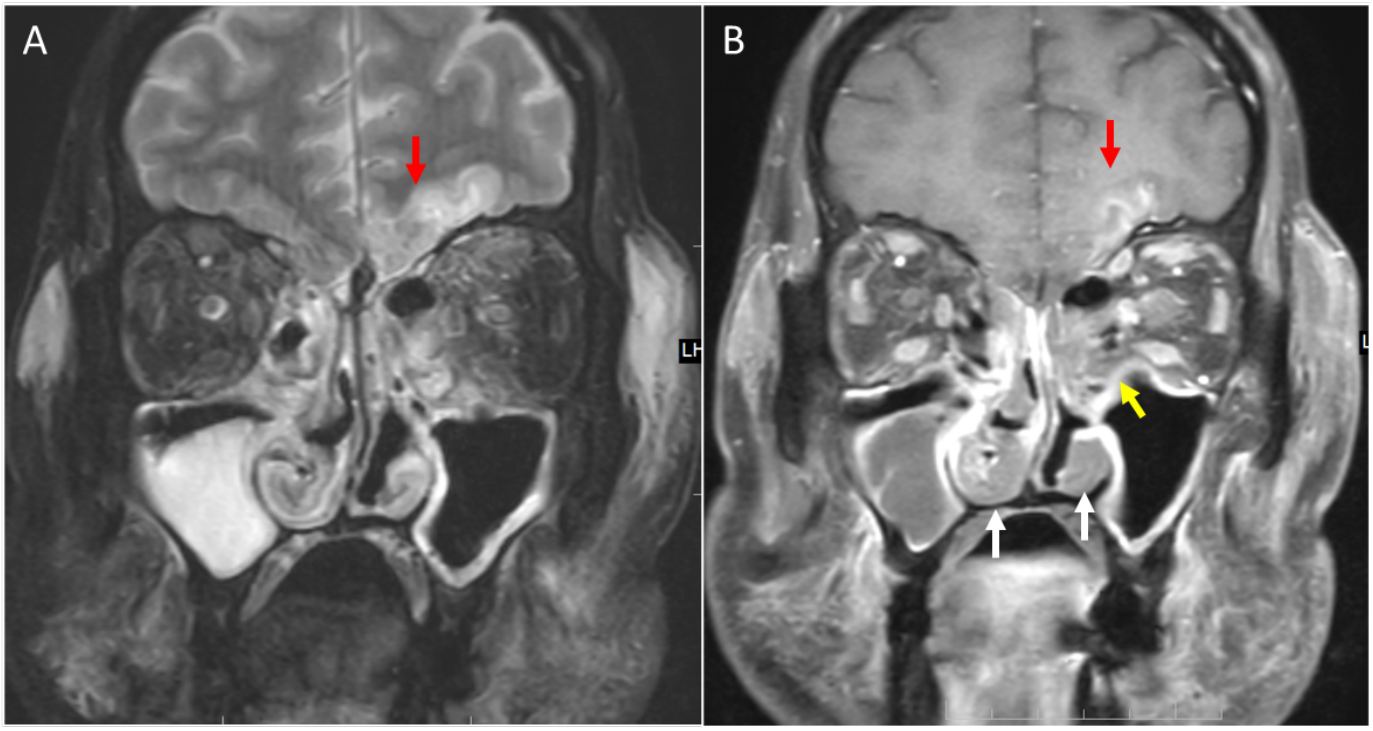


Figure 5: Invasive fungal sinusitis (Mucormycosis) with cerebritis in a 42 year old male post COVID infection.Coronal T2(A) and Post Contrast T1 (B) shows pansinusitis with lack of enhancement in bilateral inferior turbinate's (white aroow) and in left ethmoid sinus (yellow arrow). Bilateral orbital cellulitis (left > right) with cerebritis involving the left basifrontal lobe (red arrow)



Contributors : Dr.Savith Kumar, Dr. C. Kesavadas.