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PICTORIAL ESSAY

Spectrum of common and uncommon neurovascular and neurological manifestations of COVID-19 on cross-sectional imaging

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ABSTRACT

COVID-19 is an emerging and re-emerging disease that is caused by SARS CoV-2, a neurotropic virus that frequently involves the central nervous system in addition to the lungs. Findings on neuroimaging can be observed in a significant percentage of active COVID-19 and post-COVID patients, especially those who are/ have been critically ill. Accurate diagnosis of such cases on imaging aids in appropriate patient management and prevention of permanent neurological deficits. The features of CNS involvement in COVID-19 can be broadly categorized as the more common neurovascular and relatively uncommon neurological manifestations. Several pathophysiological mechanisms have been proposed for the patterns of CNS involvement and corresponding neuroimaging features in COVID-19. We have outlined the pathophysiology and indications for neuroimaging in COVID-19 and extensively discussed the neuroimaging features of the entire spectrum of neurovascular and neurological manifestations, including the rare and diagnostically challenging ones, through case-based illustrations. As new strains of COVID-19 continue to emerge, radiologists need to be aware of the imaging features of various neurological and neurovascular manifestations of CNS involvement in COVID-19 as timely diagnosis is vital in preventing or limiting permanent neurological deficits in such cases.

KEY WORDS

COVID-19, Central Nervous System, Neurovascular, Neurological, Imaging

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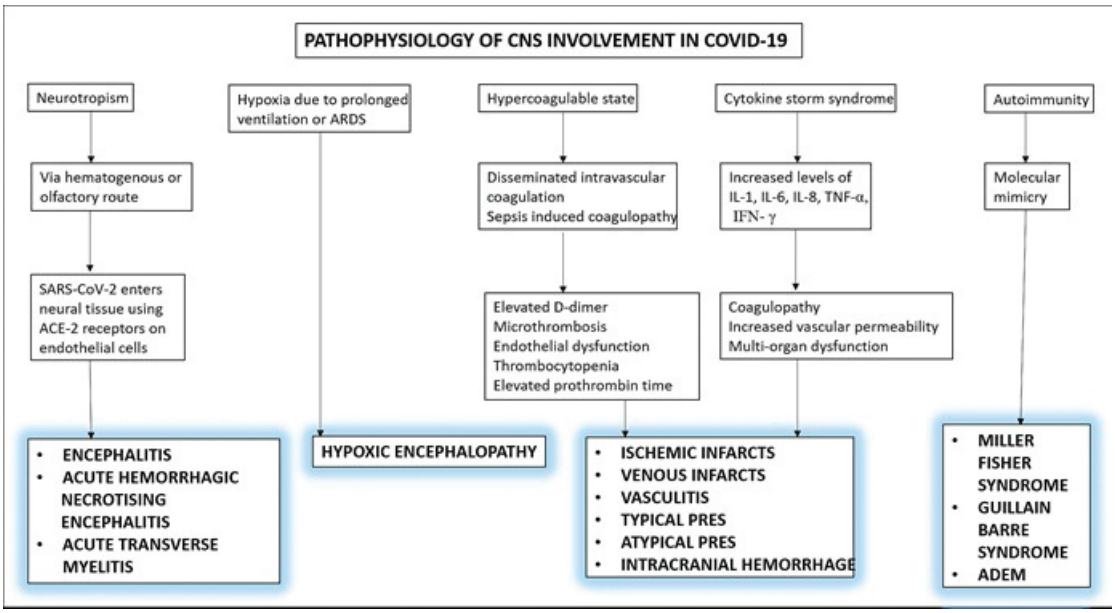

Fig. 1. *Pathophysiology of CNS involvement in SARS CoV-2; ADEM: acute disseminated encephalomyelitis, PRES: posterior reversible encephalopathy syndrome.*

Introduction

COVID-19 (corona virus disease 2019) is caused by SARS CoV-2 (severe acute respiratory syndrome coronavirus 2). Since its initial detection in late 2019, the disease has become a pandemic and spread rapidly affecting millions of people across the globe with new variants still emerging. Recent re-emergence of COVID-19 outbreaks in various parts of the world underscore the need for continued research into the novel coronavirus and its disease manifestations. Lung involvement in COVID-19 and radiological features of COVID-19 pneumonia are well scrutinized and thus well-known [1]. Less well known is the fact that SARS CoV-2 is a neurotropic virus and can affect the central nervous system (CNS) as well, causing a broad spectrum of neurological manifestations [2]. Although these manifestations are multifactorial and were routinely encountered in the pre COVID-19 era as well, presence of such neurological manifestations in the post-COVID era, especially during COVID-19 outbreaks, should alert the radiologist of the possibility of CNS involvement due to SARS CoV-2. Such involvement can lead to severe neurological sequelae. For this reason, radiologists should be aware of the imaging features of common and uncommon COVID-19 neurological manifestations and post-COVID sequelae on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). The importance of being able to suspect COVID-19 on the basis of neuroimaging patterns not consistent with the patient's demographic profile in patients without clinical suspicion of COVID-19 and in the absence of respiratory symptoms cannot be overstated. Correct diagnosis of such cases aids not only in appropriate patient management but also in prevention of permanent neurological deficits.

In this article, we have described the imaging spectrum of neurovascular and neurological manifestations of COVID-19 on CT and MRI. The pathophysiology of CNS involvement in COVID-19 and indications for neuroimaging in COVID-19 and post-COVID patients are also outlined. The neurovascular and neurological imaging abnormalities in COVID-19, including unusual manifestations, have been described in detail through various case-based illustrations.

PATHOPHYSIOLOGY OF CNS INVOLVEMENT IN COVID-19

Several mechanisms have been proposed for CNS involvement in COVID-19. These are described as follows:

- **Neurotropism:** SARS CoV-2 utilizes hematogenous or olfactory route to enter neural tissue. It gains access to neural tissue in CNS via ACE-2 (angiotensin converting enzyme 2) receptors and TMPRSS2 enzyme

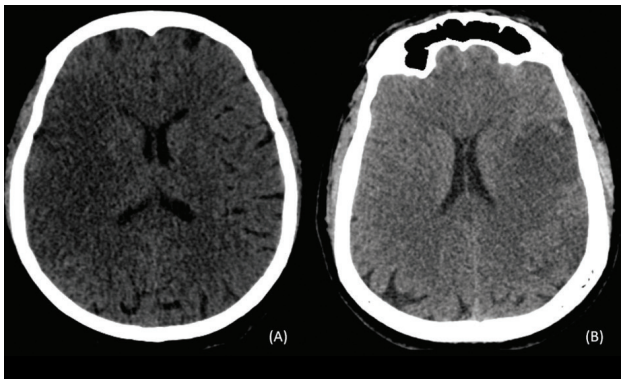

Fig. 2. *Non-contrast CT images of a RT-PCR SARS CoV-2 positive 34-year-old male and 39-year-old female show ill-defined hypodensity involving both grey and white matter in right MCA territory (A) and left MCA territory respectively (B); consistent with large vascular territorial acute ischemic infarcts.*

present on endothelial cells of cerebral vasculature [2,3,4]. This can result in encephalitis, acute haemorrhagic necrotizing encephalitis and acute transverse myelitis.

- **Hypoxia:** In patients with extensive lung parenchymal involvement due to severe COVID-19, hypoxic insult can occur due to prolonged mechanical ventilation and acute respiratory distress syndrome [5].
- **Hypercoagulable state:** SARS CoV-2 enters endothelial cells via ACE-2 receptors which can result in endotheliitis. Platelet abnormality, thrombotic microangiopathy and disseminated intravascular coagulation (DIC) can also occur in COVID-19. All these factors predispose to a hypercoagulable state and may lead to vascular thrombosis in COVID-19 [6]. Sepsis induced coagulopathy can also occur in severe cases of COVID-19 and may result in intracranial haemorrhage. It is characterized by increased prothrombin time and D-dimer levels, thrombocytopenia, endothelial cell dysfunction and microthrombosis [7].
- **Cytokine storm syndrome:** COVID-19 is associated with increased levels of various proinflammatory cytokines like interleukin-1 (IL-1), IL-6, IL-8, tumor necrosis factor-α and interferon-γ. This cytokine storm can lead to coagulopathy, increased vascular permeability and multiorgan dysfunction [2,8].
- **Autoimmune response:** Molecular mimicry can occur between the human myelin basic protein and

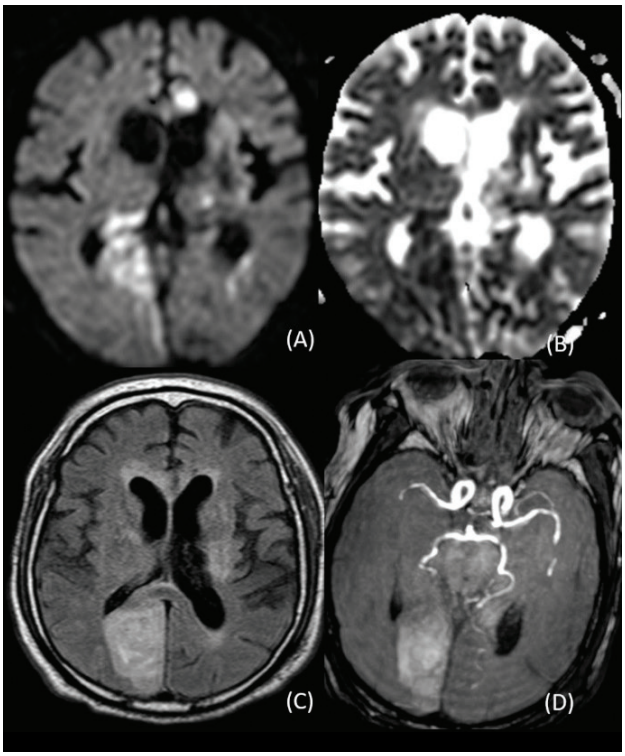

Fig. 3. *MR images of a RT-PCR SARS CoV-2 positive 62-year-old male show diffusion restriction on DWI/ADC images (A and B) and FLAIR hyperintensity (C) involving both grey and white matter in right PCA territory, on MR angiography right PCA is not visualized after P2 segment (D); consistent with large vascular territorial acute ischemic infarct.*

SARS CoV-2 epitope. As a consequence of this cross-reactivity demyelinating syndromes may occur after COVID-19 infection [2]. This includes Miller Fisher syndrome (MFS), Guillain Barre syndrome (GBS) and acute disseminated encephalomyelitis (ADEM).

The pathophysiology of CNS involvement in COVID-19 is outlined in Figure 1.

NEUROIMAGING INDICATIONS IN COVID-19 AND POST-COVID PATIENTS

To limit the spread of COVID-19, it is important to select patients requiring neuroimaging cautiously and balance the benefits of neuroimaging with the risk of disease transmission, particularly in places with high volume workflow. Dedicated COVID-19 CT and MRI scanners are preferred for reverse transcriptase polymerase chain reaction (RT-PCR) positive COVID-19 cases if available. In resource poor settings, proper precau-

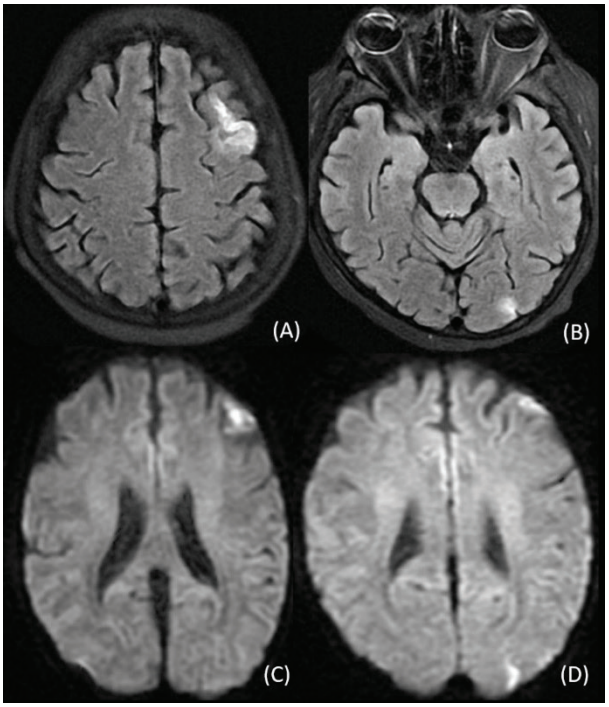

Fig. 4. *MR images of a RT-PCR SARS CoV-2 positive 56-year-old male show hyperintensity in left frontal and occipital lobe on FLAIR images (A and B) with diffusion restriction on DWI images (C and D); consistent with external border zone watershed infarcts.*

tions and post-scanning disinfection measures should be taken and unnecessary imaging should be avoided in positive cases.

Rarely in absence of pulmonary manifestations, CNS involvement may be the only indicator of disease. Such imaging findings, particularly in young patients without any predisposing factors and inconsistent with the patient's demographic profile, should alert the radiologist to the possibility of COVID-19 in the appropriate clinical setting. Early detection of such cases will not only aid in patient management but will also limit the spread of COVID-19.

Following are the neuroimaging indications in COVID-19 or post-COVID patients:

CT / MRI brain:

- Altered mental status
- Development of neurological deficit
- History of fall
- Syncopal episode
- Seizure
- Persistent severe headache [9]

MRI spine:

- Weakness of extremities unexplained by brain pathology
- Sensory loss over trunk or extremities and/or abnormal sensations like tingling, numbness, burning or coldness
- Bowel and bladder incontinence, urinary urgency, increased urinary frequency, urinary retention, constipation

NEUROVASCULAR AND NEUROLOGICAL MANIFESTATIONS OF COVID-19 ON NEUROIMAGING

As discussed above, various neurovascular and neurological manifestations detectable on neuroimaging can occur in COVID-19.

Neurovascular manifestations include [10]:

- Ischemic infarcts (large vascular, small vascular, multiterritorial, watershed and cardioembolic)
- Venous infarcts
- Intracranial haemorrhage
- Hypoxic encephalopathy
- PRES (typical and atypical)
- Vasculitis

Neurological manifestations include [10]:

- Encephalitis
- Acute haemorrhagic necrotizing encephalitis
- Acute transverse myelitis
- Miller Fisher syndrome
- Guillain Barre syndrome
- Acute disseminated encephalomyelitis

Diffuse thrombotic microangiopathy with concurrent involvement of arterial and venous circulation is a specific neurological finding in COVID-19. On imaging it is seen as multifocal cortical infarcts in arterial territories suggestive of arterial microvascular thrombosis and signal abnormality in veins indicative of sluggish flow. This diffuse microangiopathy can result in breakdown of blood-brain barrier leading to multifocal petechial bleeding and subsequently intracranial haemorrhage [11].

Studies on CSF RT-PCR for SARS CoV-2 in COVID-19 patients with neurological symptoms have shown positive results in some cases [12]. CSF analysis can show elevated proteins and WBCs in many cases, especially

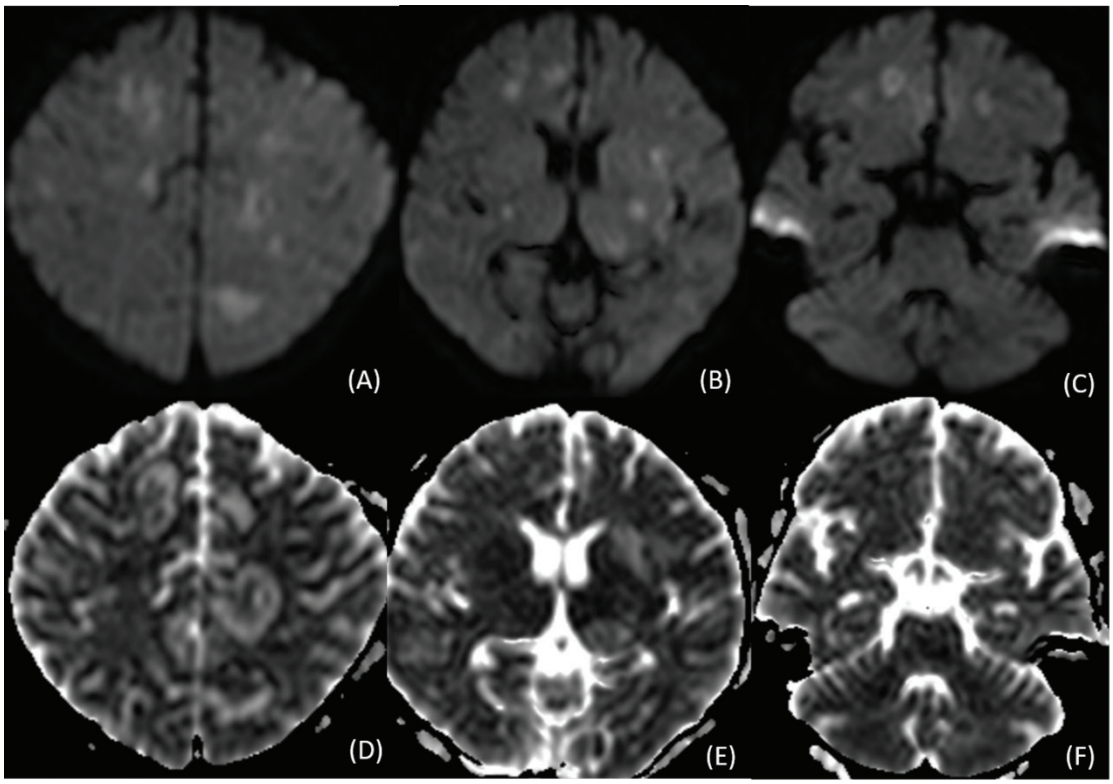

Fig. 5. *MR images of a RT-PCR SARS CoV-2 positive 49-year-old female show multiple foci of diffusion restriction on DWI (A, B and C) and corresponding ADC images (D, E and F) involving multiple vascular territories; consistent with embolic infarcts.*

those with severe COVID-19 manifestations [13]. Levels of inflammatory cytokines in CSF may also be elevated [14].

Neurovascular manifestations:

Ischemic infarcts:

Hypercoagulable state and cytokine storm increase the risk of cerebral arterial thrombosis [6]. Mahammedi et al. observed acute ischemic infarct as the most common neuroimaging finding in COVID-19 patients. Acute ischemic infarcts are due to vascular occlusion and can involve a large vessel vascular territory, small vessel vascular territories, multiple territories, watershed zones or can be embolic, with large vessel territorial infarcts being the most common [10]. Watershed infarcts can be external (cortical) or internal (subcortical). External watershed infarcts are located at junction of the territory of anterior, middle or posterior cerebral artery. Isolated external watershed infarcts are usually embolic and less frequently, are caused by haemodynamic compromise. Internal watershed infarcts are most commonly located between the territories of superficial (medullary perforators) and deep (lenticulostriate) branches of middle cerebral artery. Internal watershed infarcts are associated with haemodynamic compromise. In the presence of both external and internal watershed infarcts too, haemodynamic impairment is the most likely cause [15]. Embolic infarcts can occur because of cardiac thromboembolism or artery to artery embolization [5].

Acute ischemic infarct appears as an ill-defined or wedge shaped hypodensity involving both grey and white matter in the involved vascular territory on CT. In hyperacute infarct CT may not demonstrate any abnormality. In such cases, MRI shows diffusion restriction on DWI/ADC images. T2/ FLAIR hyperintensity in the involved vascular territory is also seen on MRI on acute infarcts. In embolic infarcts the above CT and MRI findings are seen at grey-white matter junction and in watershed infarcts these are seen at external or internal watershed zones. We encountered a number of patients with sudden onset of focal neurological deficits whose

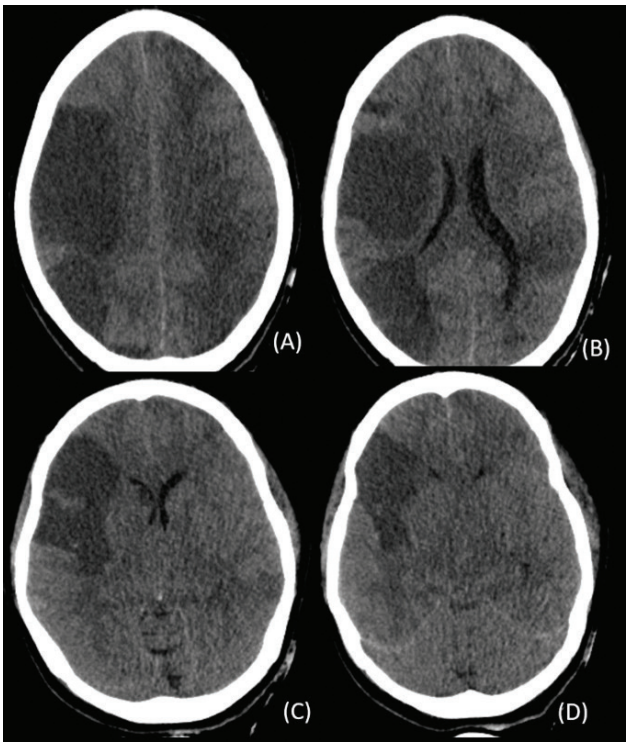

Fig. 6. *Non-contrast CT images of a RT-PCR SARS CoV-2 positive 36-year-old male show multiple wedge shaped hypodensities involving both grey and white matter in right MCA territory and bilateral external watershed zones (A, B, C and D); consistent with multi-territorial infarcts.*

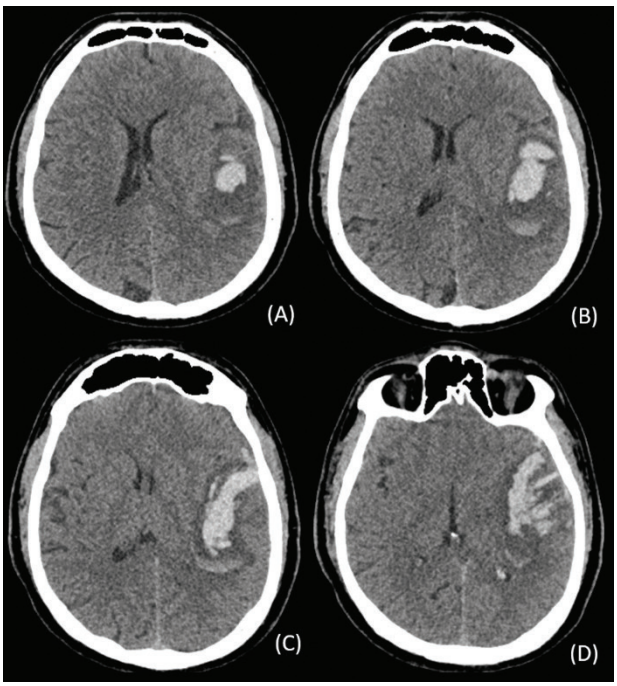

Fig. 7. *Non-contrast CT images of a RT-PCR SARS CoV-2 positive 41-year-old male show lobar bleed in left parieto-temporal region with surrounding sub-arachnoid haemorrhage (A, B, C and D); consistent with lobar intracranial haemorrhage.*

demographics and risk profile were incongruent with stroke. Some of the additional symptoms were high grade fever, headache, seizures, confusion, vomiting, diarrhoea and myalgia. Not all of them had respiratory symptoms consistent with COVID-19. Further evaluation with nasopharyngeal sampling revealed RT-PCR positive SARS CoV-2 infection. Typical imaging features of infarcts in patients with incongruent demographic profile for stroke, especially in the presence of fever, should alert the radiologist to possibility of COVID-19 as an aetiological factor. Various patterns of ischemic infarcts seen on imaging in these patients are depicted in Figures 2,3,4,5 and 6.

Intracranial haemorrhage (ICH):

Hypercoagulability and increased levels of inflammatory cytokines (cytokine storm syndrome) cause disruption of tight junctions and breakdown of blood-brain barrier leading to ICH. Mahammedi et al. found intracranial haemorrhage as the second most common finding on neuroimaging after ischemic infarct. They also found sub-arachnoid haemorrhage to be the most common pattern of ICH, others being large and small intracranial bleeds [10]. Benger et al. observed lobar bleed to be more common than basal ganglia bleed in COVID-19 patients with pre-existing hypertension [16]. Lobar bleed in a non-hypertensive patient with fever followed by sudden onset neurological symptoms, subsequently found to be COVID-19 RT-PCR positive on nasopharyngeal swab, is shown in Figure 7. Unusual occurrence of lobar haemorrhage in a patient with pyrexia led to clinical suspicion of COVID-19 in this case. Imaging picture of lobar haemorrhage in a febrile young patient without any visible vascular malformation should entail further analysis for COVID-19 infection.

Venous infarcts:

Mahammedi et al. found the incidence of cerebral venous thrombosis in COVID-19 patients to be less than that of acute ischemic infarct and intracranial haemorrhage [10]. Presence of infarcts in a non-arterial territo-

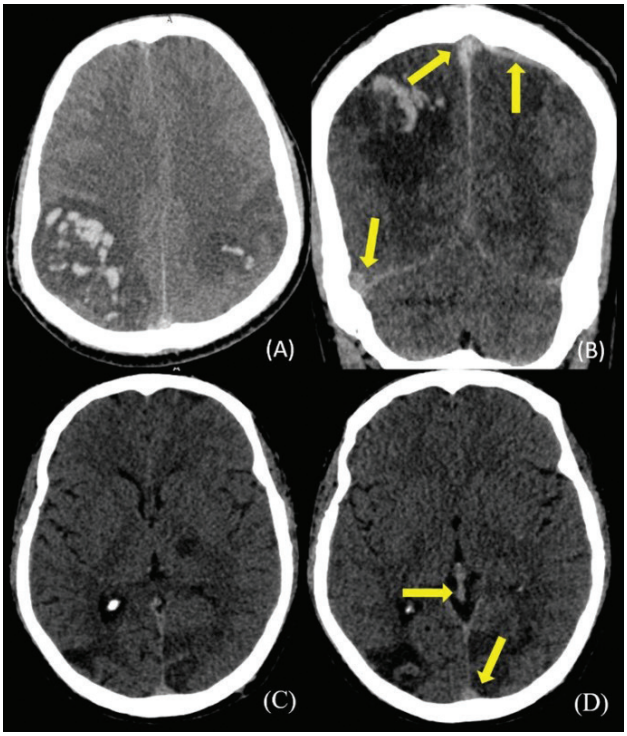

Fig. 8. *Non-contrast CT images of a RT-PCR SARS CoV-2 positive 32-year-old female show haemorrhagic infarcts in bilateral parietal region (A) with hyperdensity of superior sagittal sinus, cortical vein and right transverse sinus suggestive of thrombosis (yellow arrows in B). Non-contrast CT images of a RT-PCR SARS CoV-2 positive 35-year-old male show infarcts in left thalamus, bilateral occipital lobes (C) with hyperdensity of vein of Galen and superior sagittal sinus suggestive of thrombosis (yellow arrows in D); consistent with sinus thrombosis and venous infarcts.*

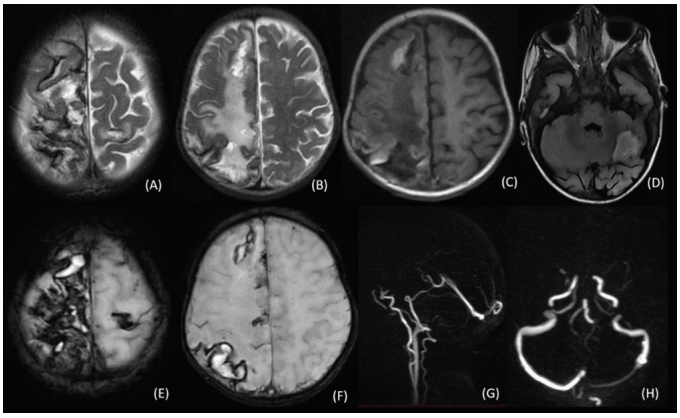

Fig. 9. *MR images of a RT-PCR SARS CoV-2 positive 15-year-old boy show altered signal intensity in bilateral frontal and right parietal lobes with hypointense gyri and sulci on T2W images (A and B), hyperintense gyri and sulci on T1W image (C) with loss of flow void in superior sagittal sinus (B and C), FLAIR image shows hyperintense area in left cerebellar hemisphere (D), multiple blooming foci are seen on T2*GRE images (E and F), MR venography shows non-opacification of superior sagittal sinus (G) and left transverse sinus (H); consistent with venous infarcts in bilateral frontal, right parietal lobe and left cerebellar hemisphere with superior sagittal and left transverse sinus thrombosis.*

ry, bilateral infarcts and infarcts with associated haemorrhage are typical for venous infarcts. Additionally, thrombosed sinuses and cerebral veins show increased attenuation (50-80 HU) on non-contrast CT in acute and subacute cases. CT venography shows filling defect in the thrombosed sinus. Empty delta sign (hypoattenuating thrombus surrounded by triangular enhancement) is seen on CT venography in subacute superior sagittal sinus thrombosis on axial images. It can also be seen in coronal and sagittal images in transverse sinus thrombosis. MRI shows absence of flow void in the thrombosed sinus on T2W and FLAIR images. MR venography shows non-visualization or attenuated calibre of the thrombosed sinus. The thrombosed sinus and cerebral veins appear hypointense on gradient echo sequences. Blooming is also seen on gradient echo sequences due to haemorrhage [17]. Haemorrhagic venous infarcts in patients with no prior history or risk factors for hypercoagulability, particularly if associated with respiratory symptoms or fever, should raise suspicion for COVID-19. Such cases with venous infarcts are illustrated on CT and MRI in Figure 8 and Figure 9 respectively.

Hypoxic encephalopathy:

Hypoxic insult occurs because of respiratory failure due to pulmonary involvement in severe COVID-19 [5]. Mild to moderate global ischemic insult causes watershed infarcts. Gray matter structures (basal ganglia, thalami, cerebral cortex, hippocampus, cerebellum), being more metabolically active than the white matter, are preferentially affected in severe ischemic injury. Earliest hypoxic injury changes are visualized as areas of diffusion restriction on DWI/ADC images with hyperintensity on T2/FLAIR images seen later (24hours – 2weeks) [18]. CT shows hypodensity in the involved areas. Severe

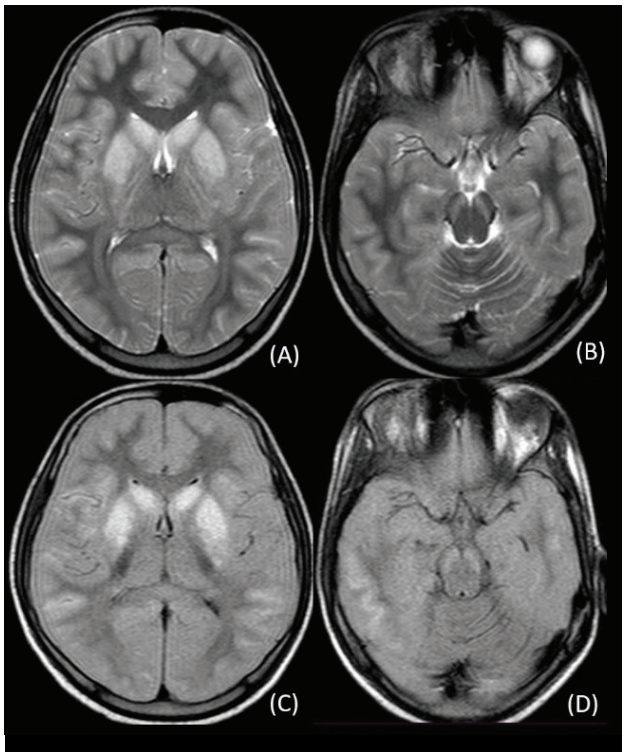

Fig. 10. *MR images of a RT-PCR SARS CoV-2 positive 40-year-old male show hyperintensities in bilateral caudate nuclei, putamina, globi pallidi, substantia nigra, parietal and temporal cortices on T2W (A and B) and FLAIR images (C and D); consistent with severe hypoxic encephalopathy.*

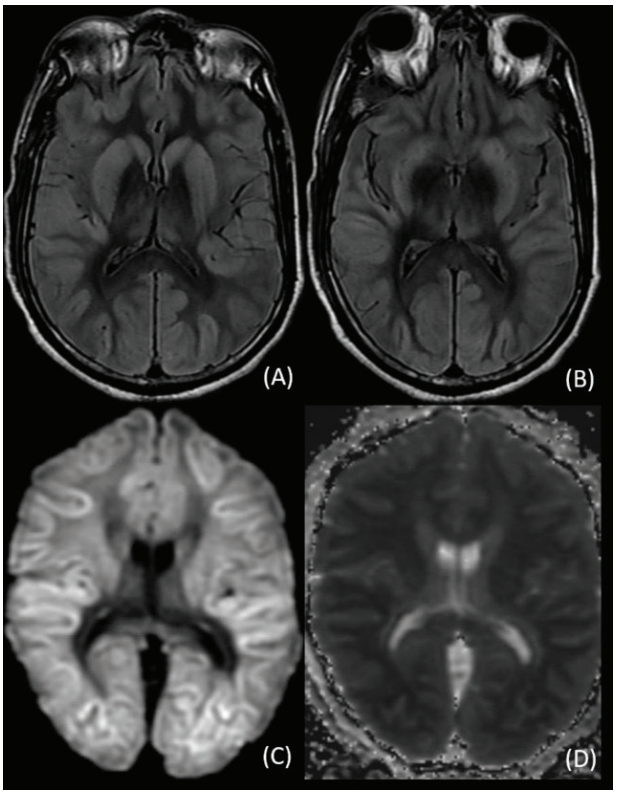

Fig. 11. *MR images of a RT-PCR SARS CoV-2 positive 47-year-old male show hyperintensity on FLAIR images (A and B) in bilateral caudate and lentiform nuclei and grey matter of frontal, temporal and occipital lobes with diffusion restriction in the involved grey matter on DWI (C) and ADC images (D); consistent with severe hypoxic encephalopathy.*

ischemic injury in COVID-19 patients with respiratory failure involving cortex and deep grey matter is illustrated in Figure 10 and Figure 11.

Typical and atypical posterior reversible encephalopathy syndrome (PRES):

Prolonged intubation, endothelial cell dysfunction and/or hypertensive encephalopathy impair cerebral autoregulation which may lead to PRES in COVID-19 patients [19]. It is a relatively uncommon neuroimaging finding in COVID-19 [10]. PRES can involve both cortex and white matter (subcortical, deep and peri-ventricular). CT shows hypodensity and MRI shows T2/FLAIR hyperintensity in the involved areas. Although there is vasogenic edema in PRES, diffusion restriction can sometimes be seen on DWI/ADC images. Also, haemorrhage can occasionally occur in the involved areas. Typical PRES involving the parietal and occipital lobes has been described in COVID-19 patients while atypical PRES can have a wide variety of imaging patterns including involvement of thalami, cerebellum and brainstem [20]. Generally, evidence of PRES in a previously non-hypertensive and non-pregnant patient should lead to suspicion of a rare cause such as COVID-19 infection in the appropriate clinical scenario. We encountered a few cases of PRES in nasopharyngeal swab RT-PCR positive SARS CoV-2 cases, without any other explainable causal factor. CT and MRI of typical and atypical PRES in COVID-19 patients is shown in Figure 12 and Figure 13 respectively.

Vasculitis:

It is an extremely rare neurovascular manifestation of COVID-19 which occurs due to endothelial inflammation and resultant occlusion of the affected cerebral vasculature. In vasculitis, due to predominant involve-

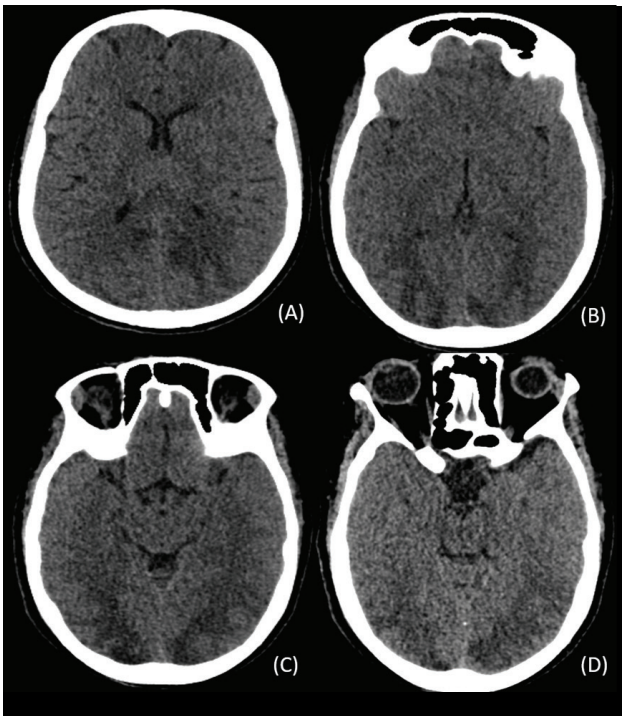

Fig. 12. *Non-contrast CT images of a RT-PCR SARS CoV-2 positive 29-year-old female show hypodensity predominantly involving the white matter in bilateral parietal and occipital region (A, B, C and D); consistent with typical posterior reversible encephalopathy syndrome.*

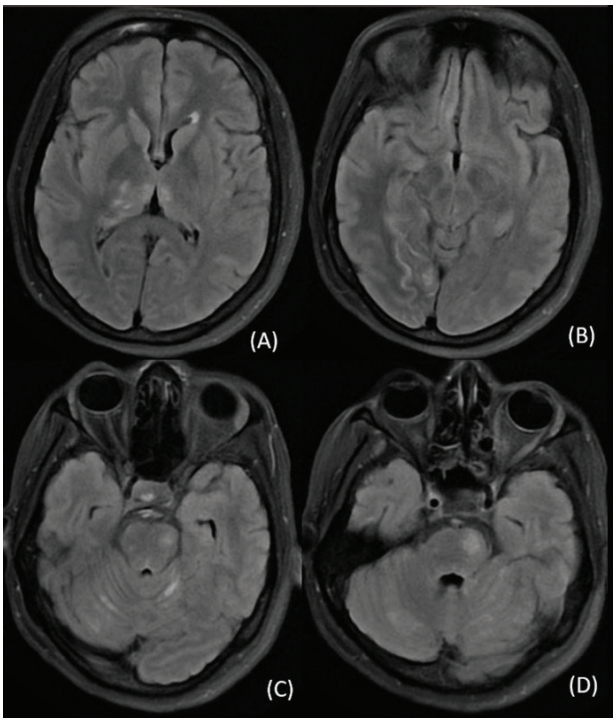

Fig. 13. *MR images of a RT-PCR SARS CoV-2 positive 52-year-old female show hyperintensities in bilateral thalami, right occipital lobe, midbrain and cerebellum on FLAIR; consistent with atypical posterior reversible encephalopathy syndrome.*

ment of distal perforating arteries, multiple small vessel ischemic infarcts are seen on neuroimaging [21]. Vasculitic infarcts may be differentiated from embolic infarcts by variable size of infarcts and infarcts in variable stages of resolution (in contrast to multiple small infarcts at the grey-white matter junction from embolic showers). A case of vasculitis in a SARS CoV-2 positive patient with variable sized infarcts and punctate post-contrast enhancement on MRI is illustrated in Figure 14. Abrupt onset of vasculitic infarcts in a patient without any prior history or other evidence of an underlying vasculitic disorder should raise suspicion for COVID-19 in the appropriate clinical scenario.

Neurological manifestations:

Encephalitis:

Encephalitis in COVID-19 occurs due to neurotropic nature of SARS Co-V2 and direct viral neuro-invasion. It is an uncommon neurological manifestation of COVID-19 and is characterized by involvement of various neural structures. T2/FLAIR hyperintensity and diffusion restriction on DWI/ADC images on MRI may be seen in the cerebral cortex, basal ganglia, splenium of corpus callosum, cerebellum and hippocampus. Involvement of cerebral white matter is suggestive of leukoencephalitis. Kihira et al. suggested that MRI findings in cases of encephalitis can be multifactorial due to concurrent features of hypoxic encephalopathy [22]. In contrast to common viral encephalitides, a specific pattern of involvement has not been described in COVID-19. Encephalitis in a patient with CSF RT-PCR positive for SARS CoV-2 is shown in Figure 15.

Acute haemorrhagic necrotizing encephalitis:

It may occur due to disruption of blood-brain barrier as a result of endotheliitis, cytokine storm syndrome or direct viral neuro-invasion. Acute haemorrhagic necrotizing encephalitis is seen primarily in paediatric population, but it may occur in adults as well. On imaging, it is characterized by multifocal T2/FLAIR hy-

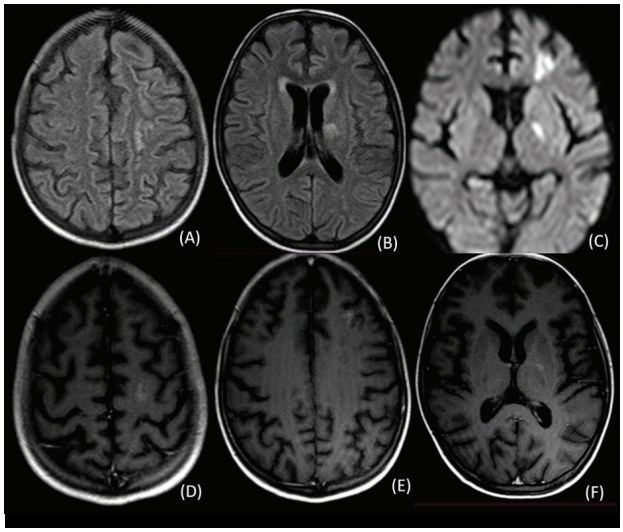

Fig. 14. *MR images of a RT-PCR SARS CoV-2 positive 63-year-old female show focal hyperintensities on FLAIR images in left centrum semiovale (A), left basal ganglia and parietal lobe (B) with diffusion restriction in left basal ganglia and anterior frontal lobe (C), suggestive of variable sized infarcts with punctate enhancement on T1W contrast enhanced images in left centrum semiovale (D), anterior frontal lobe (E) and basal ganglia (F); consistent with CNS vasculitis due to COVID-19.*

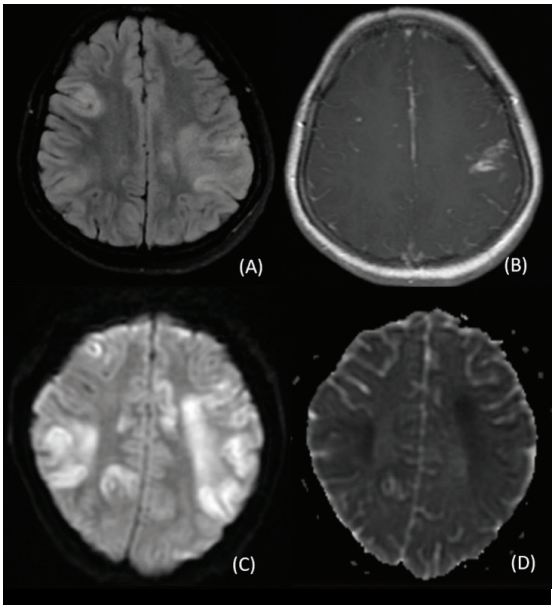

Fig. 15. *MR images of a RT-PCR SARS CoV-2 positive 12-year-old boy show hyperintensity in bilateral frontal and parietal cortices and deep white matter with gyral swelling on FLAIR image (A) with gyriform enhancement on T1 contrast-enhanced image (B) and diffusion restriction on DWI and ADC images (C and D); consistent with COVID-19 encephalitis.*

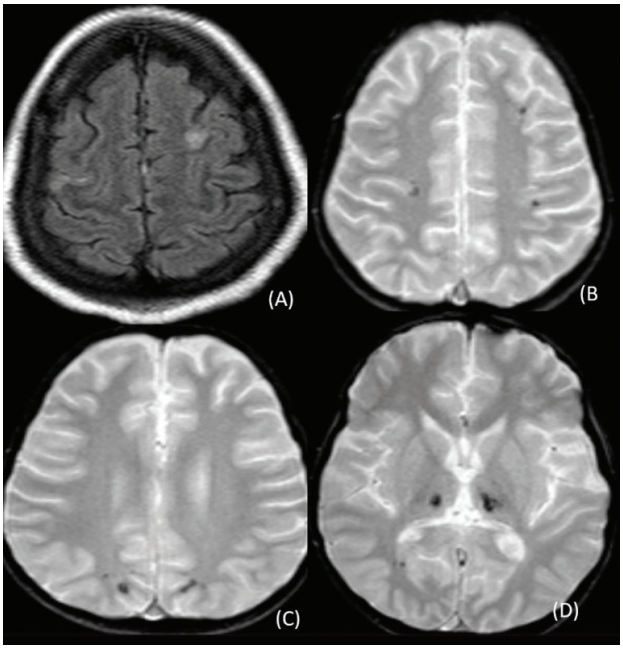

Fig. 16. *MR images of a RT-PCR SARS CoV-2 positive 10-year-old boy show hyperintensities in bilateral frontal cortices on FLAIR image (A) and multiple blooming foci in bilateral frontal, parietal cortices and thalami on T2*GRE images (B, C and D); consistent with acute haemorrhagic necrotizing encephalitis.*

perintensities involving both grey and white matter, basal ganglia and brainstem. Diffusion restriction on DWI/ADC images can be seen in the affected regions. Blooming foci suggestive of haemorrhage are seen on gradient or susceptibility weighted imaging [23]. The imaging pattern is not distinguishable from acute haemorrhagic necrotizing encephalitis secondary to influenza viruses which also causes similar respiratory symptoms and hence RT-PCR is necessary to confirm the diagnosis. Acute haemorrhagic necrotizing encephalitis with multiple focal haemorrhages is illustrated in Figure 16 and Figure 17. In one of the cases CSF RT-PCR was positive for SARS CoV-2.

Acute transverse myelitis:

It is a monophasic inflammatory process of the spinal cord [24]. Similar to ADEM it is usually associated with recent infection or vaccination. It presents with extremity weakness, horizontal level of sensory impairment and bowel, bladder complaints. Acute transverse myelitis in COVID-19 patients is a rare complication which can occur during COVID-19 (para-infectious) or

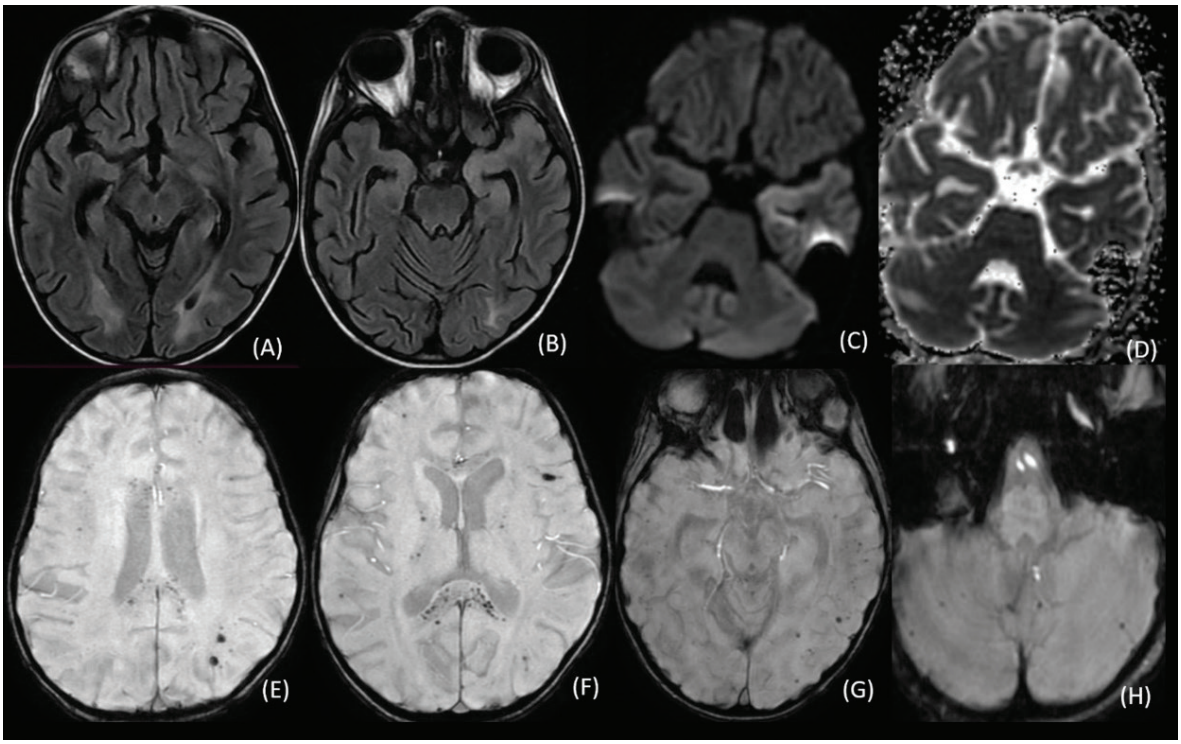

Fig. 17. *MR images of a RT-PCR SARS CoV-2 positive 62-year-old male show gyral hyperintensity, swelling and loss of grey white matter differentiation in bilateral temporal lobes on FLAIR images (A and B) with diffusion restriction in left temporal lobe on DWI/ADC images (C and D) and multiple blooming foci in bilateral cerebral and cerebellar hemispheres, genu and splenium of corpus callosum on T2*GRE images (E, F, G and H); consistent with acute haemorrhagic necrotizing encephalitis.*

after recovery from COVID-19 (post-infectious). This can happen because of the neurotropic effects of SARS Co-V2 due to presence of ACE-2 receptors on spinal cord neurons or due to inflammatory cascade associated with cytokine storm syndrome [25, 26]. MRI spine may demonstrate long segment (more than three vertebral segments) involvement of the spinal cord. T2 hyperintensity is seen in the central portion of the cord occupying greater than two-thirds of the cross-sectional area [27]. Para-infectious acute transverse myelitis in a SARS CoV-2 nasopharyngeal swab RT-PCR positive case is illustrated in Figure 18. The CSF RT-PCR was negative for SARS CoV-2.

Miller Fisher syndrome (MFS) and Guillain Barre syndrome (GBS):

Both GBS and MFS occur due to immune mediated molecular mimicry in COVID-19 patients [2]. GBS is usually a post-COVID complication in patients with severe COVID-19. However, it can also be seen after

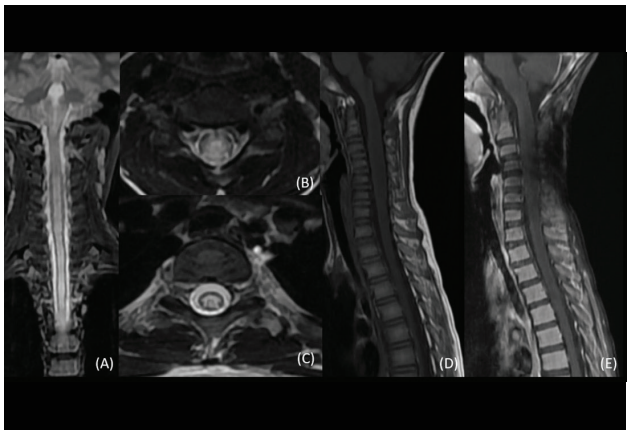

Fig. 18. *MR images of a RT-PCR SARS CoV-2 positive 49-year-old female show long segment thickening and hyperintensity in lower cervical and upper thoracic spinal cord on coronal STIR image (A), axial T2W images show hyperintensity in central cord occupying >2/3rd of the cross-sectional area (B and C), Sagittal T1W (D) and T1W contrast-enhanced (E) images show no post-contrast enhancement in the affected segment; consistent with COVID-19 para-infectious myelitis.*

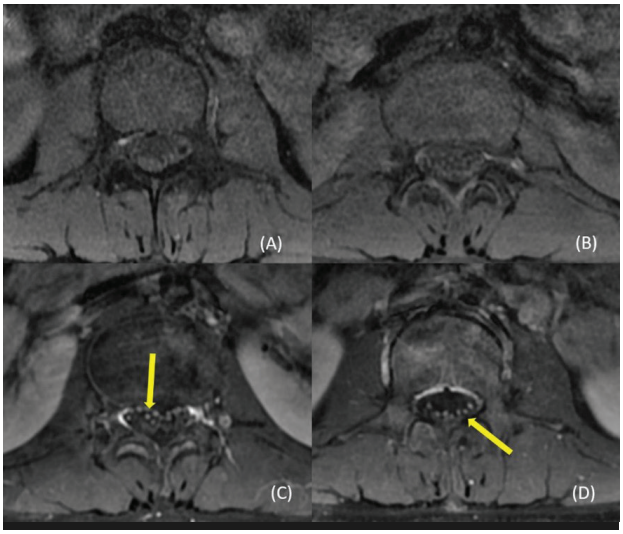

Fig. 19. *MR images of a COVID-19 recovered 24-year-old male show enhancement of both anterior and posterior nerve roots (yellow arrows) in spinal canal on axial T1-FS (A and B) and contrast-enhanced images (C and D), CSF analysis showed albumino-cytological dissociation; consistent with Guillain Barre syndrome.*

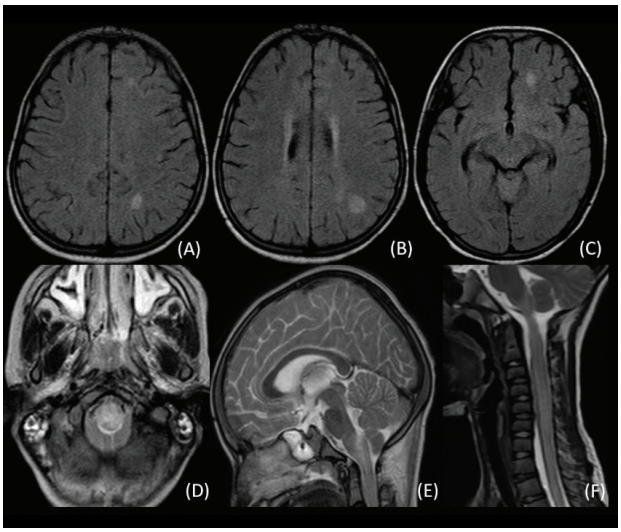

Fig. 20. *MR images of a COVID-19 recovered 41-year-old female show multifocal white matter hyperintensities in left centrum semiovale, parietal and frontal lobe on FLAIR images (A, B and C), medulla on axial (D) and sagittal (E) T2W images and long segment of cervical spinal cord on sagittal T2W image (F); consistent with acute disseminated encephalomyelitis.*

asymptomatic COVID-19 infection as well. GBS typically presents with symmetric ascending flaccid paralysis and loss of deep tendon reflexes and may have associated bowel, bladder and respiratory involvement [28]. CSF analysis shows albumino-cytological dissociation. In addition to routine MRI spine sequences, post-contrast sequence is mandatory in suspected cases of GBS for demonstrating enhancement of intrathecal nerve roots. Although both anterior and posterior nerve roots may show enhancement, isolated involvement of anterior roots is highly suggestive of GBS [28]. Thickening and enhancement of anterior and posterior nerve roots is illustrated in a COVID recovered GBS patient in Figure 19.

MFS is a variant of GBS characterized by involvement of ocular muscles (ophthalmoplegia), areflexia and ataxia. MRI brain shows enhancement and thickening of cranial nerves. CSF analysis shows albumino-cytological dissociation similar to GBS [2, 29].

Acute disseminated encephalomyelitis (ADEM):

Post-viral immune-mediated ADEM has been described as an unusual post-COVID complication. It occurs due to molecular mimicry between human myelin and SARS CoV-2. Transient anti-myelin oligodendrocyte glycoprotein antibody titre can be observed during the acute phase of the illness [30]. ADEM is a monophasic illness and presents with multi-focal neurological deficits. History of preceding infection with SARS CoV-2 one-two weeks prior is imperative for diagnosis. It is characterized by multifocal poorly marginated asymmetrical T2/FLAIR hyperintensities in supratentorial and infratentorial white matter [31]. Subcortical and deep white matter is usually affected with sparing of peri-ventricular white matter. Involvement of grey matter structures like basal ganglia and thalami can also be seen. In contrast to white matter, lesions in these areas are usually symmetrical. Brainstem and spinal cord involvement can also occur, cord involvement is long segment with associated cord edema. Acute lesions in brain and spine may show patchy enhancement [32]. ADEM in a COVID recovered patient involving supratentorial white matter, brainstem and spinal cord is illustrated in Figure 20.

Conclusion

Timely neuroimaging should be performed for specif-

ic indications in COVID-19 patients. Being aware of the pathophysiology and the common and uncommon neurovascular and neurological manifestations of COVID-19 and their imaging features, radiologists can accurately diagnose these conditions in COVID-19 and post-COVID patients and suspect COVID-19 in previously undiagnosed patients in the appropriate clinical scenario. Radiologists can thereby play a major role in prompt management and prevention of permanent neurological deficit in such cases. **R**

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NIL

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