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Neuroimaging in patients with COVID-19: a neuroradiology expert group consensus

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Abstract

Neurological and neuroradiological manifestations in patients with COVID-19 have been extensively reported. Available imaging data are, however, very heterogeneous. Hence, there is a growing need to standardise clinical indications for neuroimaging, MRI acquisition protocols, and necessity of follow-up examinations. A NeuroCovid working group with experts in the field of neuroimaging in COVID-19 has been constituted under the aegis of the Subspecialty Committee on Diagnostic Neuroradiology of the European Society of Neuroradiology (ESNR). The initial objectives of this NeuroCovid working group are to address the standardisation of the imaging in patients with neurological manifestations of COVID-19 and to give advice based on expert opinion with the aim of improving the quality of patient care and ensure high quality of any future clinical studies.

Key Points

- *In patients with COVID-19 and neurological manifestations, neuroimaging should be performed in order to detect underlying causal pathology.*
- *The basic MRI recommended protocol includes T2-weighted, FLAIR (preferably 3D), and diffusion-weighted images, as well as haemorrhage-sensitive sequence (preferably SWI), and at least for the initial investigation pre and post-contrast T1 weighted-images.*
- *3D FLAIR should be acquired after gadolinium administration in order to optimise the detection of leptomeningeal contrast enhancement.*

Keywords COVID-19 · MRI · CT · Neuroimaging

Abbreviations

ACA	Anterior cerebral artery
ARDS	Acute respiratory distress syndrome
CMB	Cerebral microbleeds
CT	Computed tomography

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CTA	CT angiogram
CTP	CT perfusion
CTV	CT venogram
CVT	Cerebral venous thrombosis
FCA	Focal cerebral arteriopathy
FLAIR	Fluid-attenuated inversion recovery
ICH	Intracranial haemorrhage
MCA	Middle cerebral artery
MRA	MR angiography
OB	Olfactory bulb
OC	Olfactory cleft
SOFL	Self-reported olfactory function loss
SWI	Susceptibility weighted imaging
VITT	Vaccine-induced immune thrombotic thrombocytopenia

Introduction

Neurological manifestations in patients with COVID-19 were first reported by Mao Ling et al. at the beginning of the outbreak in China [1]. Since then, the spectrum of neurological manifestations in SARS-CoV-2 infection has been enlarged and has been widely described [2]. It ranges from central nervous system manifestations (most prominently dizziness, headache, impaired consciousness, acute stroke), peripheral nervous system manifestations (most frequently anosmia, dysgeusia, Guillain-Barré syndrome) to skeletal muscle manifestations [2]. During the current COVID-19 pandemic, vascular complications associated with SARS-CoV-2 infection have been detected early on, and they have been mostly classified as thrombotic events [3].

The most relevant neurological thrombotic event is stroke, in particular ischaemic stroke [4]. The association between SARS-CoV-2 infection and stroke appears clear, and from a chronological point of view, it seems to occur close to the time of infection: median delay of stroke from COVID-19 symptoms onset is 8.8 (6.3–11.6) days [4].

The exact incidence of neurological manifestations is very difficult to establish as patients' inclusion criteria in the different studies are highly variable [2]. Furthermore, available evidence so far consists mostly of case reports, small case series, and some retrospective observational studies, and the frequency of symptoms may vary worldwide.

However, neurological manifestations seem to be more frequent in severe COVID-19 infection, in the presence of comorbidities, and in patients with multi-organ failure [5, 6]. They also seem associated with a worse prognosis with higher mortality [7, 8].

Available imaging data are very heterogeneous across institutions, countries, and clinical settings, which makes it difficult to draw generalizable conclusions regarding the neuroimaging manifestations in COVID-19. For future research and clinical practice, standardisation of image acquisition and reporting would be very beneficial.

A NeuroCovid working group constituted of experts in the field of imaging in COVID-19 infections, inflammatory disorders, or stroke has been constituted under the aegis of the Subspecialty Committee on Diagnostic Neuroradiology of the European Society of Neuroradiology (ESNR).

The current NeuroCovid working group's objectives are to address the standardisation of the imaging, follow-up, and reporting of neuro-imaging (of the brain, spine, as well as peripheral nervous system) in patients who have COVID-19 and neurological manifestations and to issue neuroimaging recommendations. Below we present the experts' opinions based on the best currently evidence.

Neuro-imaging indications (diagnosis and follow-up, MRI and CT) in patients with COVID-19

Since the first report by Poyiadji N et al. of acute necrotizing encephalopathy lesions in a patient with COVID-19 [9], many other neuroradiological abnormalities have been reported [10–13]. There is little doubt about the usefulness of neuroimaging in patients with acute symptoms, but true incidence of neuroradiological findings is difficult to assess because of studies' methodological heterogeneity.

Raman et al. demonstrated that patients with initially moderate to severe COVID-19 requiring hospitalisation, at 2-3 months from disease onset exhibited impaired cognitive performance, specifically in the executive and visuospatial domains [15].

Some patients referred as having "long COVID" have ongoing clinical symptoms at least 1 month after SARS-CoV-2 infection, including neurological manifestations such as cognitive dysfunction or headache [16–21]. Cognitive dysfunction is reported in 85%, and memory impairments in 73% of "long COVID patients." In these cases structural MRI does frequently not demonstrate any significant COVID-related abnormalities [22]. At present the role of neuroimaging in long COVID patients is therefore mainly the exclusion of other, potentially treatable, coexisting conditions. Neuroimaging correlates of long COVID in studies using advanced and functional imaging are presently uncertain, and are subject of ongoing research.

As symptoms can evolve, and new symptoms can arise over time, it is difficult to be certain about the exact incidence of "long COVID," and the underlying pathophysiology remains largely unknown. Different hypotheses have been evoked like virus persistence, reinfection, immune

dysregulation and systemic inflammation, or post-traumatic stress [23, 24].

R. In patients with COVID-19 and neurological manifestations, neuroimaging, either CT or MRI, may be performed at least once during the acute phase in order to detect underlying causal pathology.
If an initial CT does not provide an explanation for the neurological symptoms, an MRI may be performed before concluding that neuroimaging is negative

R. In patients with initial abnormal neuroimaging findings, a follow-up MRI may be advised between 3 and 6 months following initial neurological manifestations in order to document any residual lesions as well as resolution or progression of initial lesions.

R. In patients with long COVID, neuroimaging, either CT or MRI, can be performed in order to exclude any other conditions that may coexist of gross sequelae of COVID-infection.

Position of CT imaging

For acute stroke, brain CT is, in most centres, the imaging modality of choice for diagnosis and patient triage for treatment. Early diagnostic management of stroke in COVID follows the general AHA recommendations where CT in the acute phase has achieved a recommendation of Class I with an evidence of Level A [25].

This is mainly related to the ability of CT to rule out intracranial haemorrhage (ICH), which is less frequent than ischaemic stroke in COVID-19 patients [26], but more often lobar and multifocal than in non-COVID-related ICH [27]. In severe cases of patients presenting complicated acute respiratory distress syndrome (ARDS) and COVID-19, brain CT has demonstrated the presence of cortical and subarachnoid haemorrhages possibly related to distal endothelial capillary stress and vascular fragility [28].

Studies of COVID-19 stroke patients report the presence of extensive thrombi in the supra-aortic vessels on CT-angiograms (CTAs), while involvement of small vessels is less frequent [4]. The most frequent COVID-related stroke pattern is large vessel occlusion often involving multiple arterial territories [4]. It is, however, noteworthy that the prevalence of small vessel (lacunar) infarcts is likely to be underestimated in studies using (or including CT) compared with those using MRI with diffusion weighted imaging.

A CT venogram (CTV) is indicated if there is a suspicion of cerebral venous thrombosis (CVT), either clinically or on non-enhanced CT [29].

Shahjouei et al. [30] showed a prevalence of CVT in 6/156 (4%) COVID-19 patients with a stroke presentation in a multicentre study.

A recent study of 13,500 patients [31] showed that the incidence of CVT in patients with COVID-19 is around 8.8 per 10,000, which is rare but higher than expected in the general population.

As for non COVID stroke, the role of CTP is established with a Class I level A evidence for selecting candidates for mechanical thrombectomy between 6 and 24 h [25].

Findings of non-stroke brain lesions on CT in neurologically compromised COVID-19 patients have been less frequently reported. Nevertheless, COVID-related posterior reversible encephalopathy syndrome (PRES) cases have been detected with CT and CTA [32], and COVID-related encephalopathies also were diagnosed using brain CT imaging, prompting more detailed MRI studies [33].

R. In patients with COVID-19 and clinical stroke symptoms, brain CT may be the first modality of choice to rule out haemorrhage. CT, together with CTA, helps clinicians to make an appropriate triage for endovascular treatment. In selected cases where extension of the time window for treatment is considered or where the time of onset of symptoms is uncertain, CT perfusion (CTP) is recommended.

R. In cases of acute neurological complications during hospitalisation for COVID-19, CT can represent the first diagnostic step to rule out potentially treatable lesions and/or address the need for further brain imaging with MRI.

R. CTV should be considered in patients with symptoms of cerebral venous thrombosis or with stroke symptoms but without signs of arterial ischaemia on CT/CTA.

Recommended MRI protocol in order to investigate patients with COVID-19 and neurological manifestations

We can suggest a basic protocol, with a minimum required sequences to explore the brain of patients with COVID-19 and neurological symptoms.

Multimodality MRI in the exploration of patients with acute and chronic neurological manifestations and COVID-19: Perfusion weighted Imaging, particularly Arterial Spin Labelling, Diffusion Tensor Imaging, spectroscopy, functional MRI, in particular, resting-state fMRI, are part of research investigations in patients with

COVID-19. However, their contribution in routine clinical examination has not been proven yet.

Recommended MRI protocol	Aims
Diffusion-weighted imaging	*Detection of acute ischaemic lesions*
SWI (rather than T2 GRE)*	*Detection of:* *- cerebral microbleeds* *- hemosiderin depositions* *- cortical vein thrombosis*
3D TOF MRA	*Detection of arterial occlusion or stenosis*
T1 before gadolinium injection	
Post-gadolinium 3D FLAIR (rather than 2D)	*Detection of leptomeningeal contrast enhancement*
Post-gadolinium 3D GE T1 (rather than 2D)	*Detection of intracerebral contrast enhancement and to exclude cerebral venous thrombosis*
Optional sequences	
3D-CISS T2WI	*Olfactory bulb exploration*
Coronal 3D T2 STIR	*Plexus exploration*
Sagittal T2 STIR and post-gadolinium T1	*Spinal cord exploration*
Black blood imaging sequences	*Vessel wall exploration*

More detailed consideration regarding specific sequences is now given in the subsequent paragraphs.

SWI: microbleeds

Focal areas of susceptibility artifact on SWI or T2* weighted images, largely assumed to represent cerebral microbleeds (CMB), are a common finding on brain MRI studies of critically ill patients with COVID-19 on ventilator support, with long and pronounced respiratory failure, with higher peak D-dimer levels, and disturbance of consciousness and confusion [34–37].

These SWI lesions can be punctate, ovoid, or non-spherical (linear) in shape and vary in number from few to uncountable and have a predilection for involving the corpus callosum (particularly the splenium), juxtacortical U-fibres, and main white matter tracts, such as the internal capsules and middle cerebellar peduncles. It is important to note that CT in these patients, even retrospectively, did not reveal any punctate microhaemorrhages. When a high number of microbleeds are present, they can be associated with focal reduced diffusion and/or confluent T2/FLAIR hyperintensities.

There are various possible explanations for these findings including true microbleeds, as well as intravascular microthrombi and stagnant flow of deoxyhaemoglobin-rich blood in small arteries and veins, especially if their shape is more linear. Several pathophysiological mechanisms have been evoked for these lesions, including hypoxia, ischaemia, inflammation, thrombosis, endothelial injury, or a combination of these [38–40].

These lesions are also associated with increased mortality and worse functional outcome in patients with COVID-19, so probably these SWI lesions are late complications of critically ill patients with COVID-19 and likely related to hypoxemia [41].

R. MR with SWI should be performed in critically ill COVID-19 patients with neurological symptoms. Presence of micro bleeds may predict worse outcome in these patients. SWI is preferable to T2-weighted images which are less sensitive to CMB detection.*

R. CT is not useful for the detection of microhaemorrhages.

Post gadolinium 3D FLAIR: leptomeningeal contrast enhancement

Leptomeningeal contrast enhancement has been described at the beginning of the outbreak in patients with severe COVID-19 and neurological symptoms and has since been confirmed in larger series of patients [11, 36, 37, 42].

Leptomeningeal contrast enhancement can be either limited and localised or diffuse.

The exact incidence in COVID-19 is unknown (up to 17% in the study by Kremer et al.) [43] but is greatly dependent on the MRI protocol. Indeed, the detection requires contrast media administration and is most optimally seen on post-gadolinium FLAIR images. Like in other leptomeningeal pathologies (tumoural, infectious, or inflammatory), post gadolinium FLAIR images are more sensitive than post gadolinium T1-weighted images to detect leptomeningeal contrast enhancement, particularly if the acquisition is delayed after gadolinium injection [44–47].

Leptomeningeal contrast enhancement seems to correspond to an inflammatory process with lymphohistiocytic infiltration rather than a direct infectious process, as demonstrated in neuropathological studies [48, 49].

R. Contrast-enhanced 3D FLAIR acquisition may be suggested in imaging of COVID-19 patients because it may be more sensitive than contrast-enhanced T1-weighted imaging for detection of leptomeningeal enhancement.

Vascular imaging: vessel wall imaging and MR angiographic studies

COVID-19-associated vasculitis and vasculopathy have been described as one of the defining features of virus-induced systemic disease with multi-organ involvement, based on post-mortem studies [50]. In the context of

COVID-19, there have so far been only very few reports describing MR angiography (MRA) findings and vessel wall enhancement, indicative of vasculitis or post-viral vasculopathy. The true prevalence of vasculitis in this condition remains unknown, as high resolution in MRA and dedicated vessel wall imaging are not routinely performed in COVID-19 patients with neurological symptoms.

Dixon et al. [51] described a case of a 64-year-old patient with COVID-19 pneumonia on mechanical ventilation, inotropic support, and haemofiltration, who failed to be responsive following sedation hold. MRI showed multi-territory arterial infarcts, and a postcontrast T1 SPACE MRI sequence demonstrated pathological concentric vessel wall enhancement of both middle cerebral (MCA), anterior cerebral (ACA), vertebral arteries, and the basilar arteries, which responded to immunosuppressive treatment with resolution of the vessel wall enhancement in the MCA and ACA and reduced vertebrobasilar enhancement.

Lersy et al. [52] found arterial vessel wall thickening and concentric enhancement, suggestive of vasculitis, in 11/ 69 patients (16%) in a consecutive cohort of COVID-19 patients on the intensive care unit, undergoing a brain MRI, most commonly involving the middle cerebral, basilar, and posterior cerebral arteries.

Subsequently, Uginet et al. [53] used MRA and high-resolution vascular black blood sequences in 34 patients with COVID-19 encephalopathy. They detected circular enhancement and thickening of the basilar and vertebral arteries in 85% of cases without any evidence of associated arterial narrowing on MRI angiography and any infarcts in the corresponding arterial territories.

Further evidence of a vasculitic processes in COVID-19 patients comes from a recent nuclear medicine study by Sollini et al. [54], who used [^{18}F]FDG-PET/CT in patients with "long COVID" and detected a mild to moderate [^{18}F]FDG uptake in vessels for 61% of their patients.

From the above studies, it is clear that vasculitis in COVID-19 may be more frequent than suspected initially. It is of note that vessel wall enhancement is not necessarily associated with the luminal narrowing on MRA. A normal-appearing MRA does, therefore, not exclude COVID-19-associated vasculitis.

However, care has to be taken to use dedicated "black blood" vessel wall imaging sequences with complete saturation flowing spins, as ordinary post-contrast T1 weighted spin-echo sequences may give false-positive results due to the enhancement of slow intraluminal flow. Furthermore, one has to be aware of the pitfall of physiological enhancement of the vasa vasorum in proximal intracranial vessels.

It remains at present an open question in which clinical scenarios dedicated black blood vessel imaging sequences, in addition to MRA should be recommended. Otherwise, unexplained arterial infarcts may represent such an indication.

If there is a suspicion of cerebral venous thrombosis, an MR venogram (MRV) can be performed instead of a CTV (see discussion above). Most cases of acute/subacute venous sinus thrombosis also show "blooming artifact" on SWI sequences.

It is currently emerging that venous thrombosis can also be a complication of vaccine-induced immune thrombotic thrombocytopenia (VITT) [55]. This is likely to prompt an increased use of CT and MR venograms.

R. Intracranial MRA should routinely be performed in stroke patients in whom MR is the initial imaging modality (which is the minority of cases), and in whom a vasculitic process is suspected. A normal vessel calibre on MRA does, however, not exclude a vasculitis.

R. Black blood vessel wall imaging should only be performed in selected patients with COVID-19 in whom there is a strong clinical or radiological suspicion that lesions could be secondary to a vasculitic rather than thrombotic/embolic process.

R. In many centres, CTV is the first-line investigation in patients with suspected CVT, but MRV represents an alternative and SWI may be more sensitive in detecting isolated cortical vein thrombosis.

Peripheral nervous system: olfactory bulb, plexus

Isolated anosmia/hyposmia is reported as a typical symptom of COVID-19 infection [56]. The prevalence of self-reported olfactory function loss (SOFL) among SARS-CoV-2–infected patients is around 52.7% [57]. However, a quantitative olfactory deficit is observed in a greater proportion of patients using objective olfactory function tests [58]. Most cases experience a quick recovery of olfactory disorders [59]. Long-lasting impairment of smell is, however, possible [60].

The link between olfactory disorders and viral damage to the neurosensory tract is still debated. A recent work [61] demonstrated that SARS-CoV-2 can enter the nervous system by crossing the neural–mucosal interface in olfactory mucosa, exploiting the close vicinity of olfactory mucosal, endothelial, and nervous tissue, including delicate olfactory and sensory nerve endings.

Although olfactory impairment in COVID-19 patients has been largely documented, only a few reports of olfactory bulbs (OB) imaging abnormalities are available, most of them focusing on the acute disease stage [62, 63].

Bilateral inflammatory obstruction of the olfactory clefts (OC) was observed on MR imaging of the nasal cavity of a

COVID-19 patient, but no anomalies of the olfactory bulbs and tracts [56]. Another study reported a case with anosmia evaluated with 3D-CISS T2WI, which demonstrated severe enlargement and abnormal high signal intensity on T2, being interpreted as bilateral olfactory bulb oedema and also olfactory cleft mild oedema. The follow-up MR imaging (D24) showed a reduction in the volume of the bulbs [64].

As pointed out by Shor et al. [65], signal intensity of olfactory bulbs can vary with field strength, the MR vendor and the acquisition parameters of T2-FLAIR sequences. Furthermore, it has previously been reported that OBs could appear hyperintense on T2-FLAIR in healthy subjects [66]. For these reasons, T2-FLAIR signal intensity should be compared with the surrounding structures, such as the cortex or the optic nerves, and possibly quantified.

Enhancement of olfactory bulbs following gadolinium injection has been described in a few cases [67]. Case reports of olfactory bulb atrophy in COVID-19 patients with persistent anosmia have been described [68, 69]. It should be noted that in all the literature the intensity of olfactory bulbs has been defined as normal when the bulbs had the same intensity as cortex, as typically seen in healthy controls. Abnormal olfactory bulb intensity is defined when the bulbs are more hyperintense than the cortex on T1WI and/or STIR. After gadolinium injection on T1WI, and more easily on T1 W Fat Sat, enhancement of the olfactory bulbs is defined when they become more hyperintense in comparison with their intensity on pre-gadolinium T1WI. However, when there is only the post-gadolinium T1WI and the bulb is more hyperintense than the normal cortex, this represents olfactory bulb intensity abnormality and maybe an enhancement or microbleeding (methaemoglobin); for this reason, acquiring a post contrast 3D FLAIR can give a more reliable interpretation of the presence/absence of focal enhancement of the OB.

Some degree of degeneration of the OB has been confirmed in a small cohort of anosmic COVID-19 patients studied with both paranasal CT and MRI [70]. Future studies may evaluate changes in olfactory bulb volume in larger cohorts of COVID-19 patients at multiple timepoints with supplementary objective psychophysical olfactory function testing.

It is not so clear if the loss of the sense of smell related to COVID-19 is reversible or irreversible. It appears to last between 8 and 9 days on average, but can go on for several weeks for some patients, and in some studies last for many months. Some authors demonstrated that olfactory training (repeat and deliberate sniffing of a set of odorants) demonstrated improved olfaction. Others used oral and intranasal corticosteroids to exclude an inflammatory component in patients with postinfectious OD. However, corticosteroids are not currently recommended for individuals treatments. Other medications that have shown promise in postinfectious olfactory dysfunction include intranasal sodium citrate, which is thought to modulate olfactory receptor transduction cascades; intranasal vitamin A, which may act to promote olfactory neurogenesis; and systemic omega-3, which may act through neuroregenerative or anti-inflammatory means [71, 72]. However, to date, there is no evidence that these therapies are effective in patients with OD related to COVID-19.

There is an increased incidence of Guillain-Barré syndrome during the COVID-19 outbreak; this has been published first as case reports then as case series, for example in Italy [73]. It is not easy to demonstrate a causal relationship but recent papers seem to support a pathogenic link and or a familial occurrence of Guillain-Barré syndrome after COVID-19 infection.

There is a growing evidence of brachial plexus involvement during COVID-19 infection [74]. Peripheral nerve injuries may be associated with prone positioning on intensive care units, although other mechanisms, such as those of a neuroinflammatory nature, cannot be excluded, like true Parsonage Turner Syndrome [75], although literature is still poor. Gadolinium injection can be helpful in the differential diagnosis of brachial plexopathy, as it can show denervation enhancement more or less associated with muscular oedema [76]. Patients with lesion of the brachial plexus had severe weakness and numbness with axonometic electrodiagnostic findings.

R. Consider performing MR imaging of OB and OC in all COVID-19 patients with SOFL.

R. To obtain OB volume segmentation, 3D-T2 coronal images with high resolution (CISS and similar) may be suggested. Coronal FLAIR images may be used to detect signal abnormalities.

Spinal cord

Acute transverse myelitis cases have been reported in the literature [76], mostly as single case reports. Due to the heterogeneity of published data, underlying causality is difficult to be easily inferred.

There was a slight male predominance (60%) with a median age of 56 years [77]. Neurological symptoms first manifested after a mean of 10.3 days from the respiratory symptoms [77]. MRI demonstrated mainly longitudinally extensive lesions who spanned 9.8 vertebral segments, or less frequently short-segment lesions [76, 77]. Necrotic-haemorrhagic transformation was rare [77]. CSF was infrequently positive for SARS-CoV-2 but demonstrated in 3/4 of cases inflammatory abnormalities [76, 77].

The underlying pathophysiological mechanism remains unknown, but a para-infectious or post-infectious immune-mediated aetiology seems possible [78].

However, cases of spinal cord ischaemia have also been reported during COVID-19 infection, but the causal relationship remains unknown [79].

R. Consider performing MR imaging of the spinal cord in patients with spinal cord main clinical presentation but also in patients with brain demyelinating lesions.

Proposal of structured reporting of MRI

(1) State what sequences and specifically whether SWI (of T2*) and post-contrast sequences were performed.
(2) If the study is normal: "Normal study with no evidence of acute or chronic infarcts, microbleeds or white matter lesions."
(3) If abnormal, start with the predominant abnormality (stroke/haemorrhage/white or grey matter lesions) and then go systematically through the remainder of the checklist below:

	Presence (yes/no)	If yes—describe further
√	Infarct	Acute, subacute, chronic Cortical, subcortical, small vessel, single/multiple, single/multiple territories
√	Macrohaemorrhage	parenchymal, subdural, subarachnoid, single/multiple, central/peripheral
√	Cerebral microbleeds (CMB)	1–4; 5–10; > 10 (numerous) central/peripheral; involving (yes/no): corpus callosum, internal capsules, middle cerebellar peduncles
√	White matter hyperintensities	well defined/ill-defined/confluent/location restricted/non-restricted diffusion enhancing/non-enhancing haemorrhagic/non-haemorrhagic further specify if possible: e.g. likely to be incidental SVD, ADEM like/CLOCC like
√	Grey matter lesions	Cortical/deep nuclei Hippocampal/extra-hippocampal swelling/no swelling restricted/ non-restricted diffusion haemorrhagic/non-haemorrhagic
√	Leptomeningeal involvement	Enhancement/FLAIR hyperintensity Focal (less than 3 sulci)/ diffuse (more than 3 sulci)/
√	Cranial nerve involvement	Enhancement/FLAIR hyperintensity Olfactory nerve/ other cranial nerves
√	Intracranial vessels	arterial stenosis/thrombosis venous thrombosis vessel wall enhancement
√	Other relevant findings	

Conclusion

Summarise main findings and state likely aetiology.
Examples of conclusions:

(1) The multiple well-defined white matter hyperintensities are likely to represent ADEM in the context of COVID-19 infection.
(2) The multiple peripheral microbleeds, sparing the corpus callosum and internal capsules, could be due to cerebral amyloid angiopathy and are not necessarily related to COVID-19 infection.

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Informed consent Written informed consent was not required for this study because it is a recommendation article.

Ethical approval Institutional Review Board approval was not required because it is a recommendation article.

Methodology
- Retrospective
- Observational
- Multicentre study

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