

Appendix E1

Methods

Indications and timing for brain MRI in patients with mechanic ventilation was decided on a protocol established by ICU teams. Patients with ventilator support in ICU were managed in accordance with the guidance of Surviving sepsis campaign (17). According to this protocol, level of sedoanalgesia was gradually decreased, as positive end-expiratory pressure (PEEP) is decreased. Sedation was stopped for PEEP levels below 6 cm H₂O, and neurologic status of patients were checked 24 hours later for level of consciousness and response to stimuli. If patients decreased level of consciousness persisted after another 24 hours, cranial MRI would be performed for further assessment of underlying CNS related changes. This protocol was followed in majority of cases; however, there was variation in MR scanner availability dedicated to COVID-19 patients across institutions which limited the number of MRI scans performed in some of the institutions. Indications for patients with noninvasive ventilator support in ICU were decided on a case-by-case basis based on pathologic neurologic signs.

MR sequences included postcontrast and susceptibility series in addition to conventional sequences. Majority of the cases had the following sequences: Axial TSE T1, TSE T2, FLAIR, SWI, 3D TOF, sagittal TSE T2, coronal fat-saturated TSE T2, postcontrast axial TSE T1, postcontrast sagittal 3D TurboFLASH T1 with multiplanar reconstructions, postcontrast sagittal 3D Flair (3D SPACE) with multiplanar reconstructions. However, in three cases, postcontrast series could not be obtained due to patient's intolerance and in two cases only limited examination (DWI and FLAIR alone) could be acquired. COVID-19 related cranial MRI findings were evaluated by consensus of reviewers for dominant pattern of involvement including leptomeningeal, cortical, subcortical white matter, deep white matter, corpus callosum, deep gray matter, brain stem and cerebellar structures. For cases with cortical signal abnormalities, particular attention was paid to presence of subtle hemorrhagic changes or leptomeningeal enhancement. Additionally, acute ancillary findings such as acute cerebrovascular disease, venous thrombosis, and chronic parenchymal changes were also reviewed.

Although CT was used in ICU patients to exclude hemorrhage and large vessel occlusion, CT studies were not included due to low sensitivity for subtle parenchymal and/or meningeal abnormalities.

Results

Full Description of MRI Findings

Twelve of 27 (44%) patients with MRI were abnormal. COVID-19 related neuroimaging findings were identified in 10/27 (37%) cases as cortical FLAIR signal abnormality (Fig 2, Figs E1–E4). Among these 10 cases; increased cortical diffusion weighted signal with corresponding low ADC values was seen in 7 cases, subtle leptomeningeal enhancement in 5 cases (out of a total of 8 cases that received contrast), and punctate cortical blooming artifact in 3 cases. In one case, leptomeningeal enhancement was seen only on postcontrast 3D FLAIR images and was not

discerned on postcontrast T1WI or TurboFlash T1WI images (Fig E4). Accompanying subcortical and deep white matter signal abnormality on FLAIR images was seen in 3 and 3 cases, respectively. No case of corpus callosum, deep gray matter or infratentorial involvement was identified. The distribution of cortical signal abnormality was not specific and involved the frontal lobe in 4 cases, parietal in 3, occipital in 4, temporal in 1, insular cortex in 3 and cingulate gyrus in 3 cases. CSF was obtained in 5 out of 10 cases with cortical signal abnormality identified on MRI. Total protein was elevated (mean 79.9 mg/dL, range 59.9–109.7 mg/dL) in 4 of these patients. The cell count, glucose levels, IgG index, albumin were within normal limits, and RT-PCR for HSV DNA and SARS-CoV-2 were negative in all 5 specimens. Oligoclonal bands were checked in 3 specimens and were negative. Acute intracranial findings in the absence of cortical FLAIR signal abnormality included a case of acute transverse sinus thrombosis with no additional findings and a case of acute infarction in right MCA territory.

In 15/27 cases (55.6%), MR did not reveal any COVID-19 related or acute intracranial findings. CSF was obtained in two of these cases which showed elevated CSF protein despite negative MRI.

Chronic parenchymal changes or non-COVID-19 related findings included chronic small vessel ischemic changes in 4 cases, infarct sequel in 4 cases, parenchymal atrophic changes in 3 cases, cavernoma in 1 case and intracranial metastatic lesion in 3 cases.

Anosmia was not a dominant symptom in this patient group and was detected in a single case (Fig E4).

Reference

17. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med* 2020;46(5):854–887.