ABSTRACT

Most of the imaging spectrums of COVID-19 are evolving day by day. Every other day, we get to know the imaging peculiarities in this novel disease. Apart from the chest involvement, neurological manifestations are well recognized in COVID-19 infection. The neurological manifestations are infarcts (ischemic or hemorrhagic), acute demyelination, acute necrotizing encephalomyelitis, micro-haemorrhages, acute demyelinating encephalomyelitis, leukoencephalopathy, global hypoxic injury, cranial nerve enhancement, cytotoxic lesions of the corpus callosum, olfactory bulb involvement and Guillain Barre Syndrome. Though the imaging findings in COVID-19 are non-specific and may not be diagnostic, proper correlation with the history and clinical spectrums can suggest the changes related to COVID-19. We have reported two severe COVID-19 cases that illustrate various neuroimaging manifestations.

Keywords
COVID-19, imaging, neuroimaging manifestations

INTRODUCTION

Coronavirus belongs to the family Coronaviridae and the order Nidovirales, a family that includes the virus ranging from the common cold to Severe Acute Respiratory Syndrome (SARS) and middle-east respiratory syndrome (MERS).1,2 The first adult case of COVID-19 was reported on 31st December 2019 in Wuhan, China. The first recorded case outside China was on 13th January 2020 in Thailand.3 World Health Organization (WHO) declared COVID-19 as a pandemic disease on 11th March, 2020.4 Globally, there have been 174,502,686 confirmed cases of COVID-19 including deaths till June 11th 2021.3 The first case of COVID-19 in Nepal is recorded on 13th January 2020, in a 32-year-old man travelling from Wuhan to Kathmandu.5 As of June 11th, there have been 601,687 confirmed cases of COVID-19 with deaths, reported to WHO from Nepal.3 Infections by COVID-19 continue to increase worldwide and Nepal is facing the second wave of the pandemic.
Most of the imaging spectrum of COVID-19 is evolving day by day. Every other day, we get to know the myriads of imaging peculiarities in this novel disease. Most of the kinds of literature have shown the involvement of the chest in COVID-19. Its multisystemic involvement is now a proven fact. With the evolving improvement of our understanding of SARS-CoV-2, an increasing number of patients with COVID-19 who exhibited neurological manifestations have been reported especially in severe admitted cases. We have compiled two cases herein that showed the neurological manifestations.

CASE 1

A 68-year-old man, known hypertensive and dyslipidemic, was admitted to Intensive Care Unit (ICU) for severe COVID pneumonia for 2 weeks duration. Reverse transcriptase Polymerase chain reaction (RT-PCR) test positive status since 2 weeks. He was dyspneic with an oxygen saturation of 84% on 10 litres of oxygen/minute. In CT, there was extensive involvement of bilateral lung fields with a CT severity Score of 23/25. During the stay in ICU, there is a history of sudden drop in the Glasgow coma scale (GCS). Cardio-pulmonary resuscitation (CPR) was performed and the patient was intubated. Blood electrolytes were within normal limits. After the vitals were stable, he was taken to the radiology department for an MRI brain to rule out intracranial cause. MRI showed bilateral symmetrical T2/FLAIR high signal intensity involving posterior limb of internal capsules and pons as well as middle cerebral peduncles (Figure 1a and 1b). The areas show restriction in diffusion-weighted images (DWI) (Figure 1c and 1d). Similar patchy discrete areas of T2 FLAIR high signal intensity are seen in the bilateral subcortical white matter of bilateral frontoparietal lobes and corpus callosum (Figure 1e and 1f). These areas show signal drop out/blooming in susceptibility-weighted images (SWI) suggestive of micro-haemorrhages (Figure 1g). On the second day after MRI, the patient deteriorated further and could not be revived.

Figure 1a. Axial T2WI shows high signal intensity within bilateral posterior limb of internal capsules (white arrows). Figure 1b. Axial T2WI shows high signal intensity within the pons in bilateral para-median location and middle cerebral peduncles (white arrows). Figure 1c. DWI shows high signal intensity within bilateral posterior limb of internal capsules (white arrows). Figure 1d. DWI shows restriction of diffusion within the pons in bilateral para-median location (white arrows). Figure 1e. Sagittal T2WI shows patchy high signal intensities within the corpus callosum (white arrows). Figure 1f. SWI shows signal drop outs/blooming in bilateral basal ganglias, corpus callosum and frontal lobes (white arrows). Figure 1g. Multiple FLAIR hyper-intense foci are seen in sub-cortical white matter of bilateral fronto-parietal lobes (white arrows).
CASE 2
A 50-year-old female presented to the fever clinic with fever (temperature 38.1°C) for 5 days duration. Nasopharyngeal swab (RT-PCR) showed a positive result for COVID-19. He was in home isolation. The patient had a history of being in contact with another confirmed COVID-19 patient in the family. He landed in an emergency with a saturation of 79% in room air after 3 days. His status further deteriorated in observation and was intubated then transferred to the Intensive Care Unit (ICU). In chest CT, there was the extensive involvement of bilateral lung fields with a CT severity Score of 23/25 suggestive of acute respiratory distress syndrome. During the stay in ICU, there is a history of a sudden drop in the Glasgow coma scale (GCS) E4M1V1 and CPR was performed. After the vitals were stable, he was taken to the radiology department for an MRI brain under strict monitoring. MRI showed subtle hyperintensities in bilateral cerebral peduncles/tectum of the midbrain (Figure 2a). Hyperintensities in the bilateral posterior limb of internal capsules showed restriction of diffusion in DWI and ADC (Figure 2b and 2c). The patient conditions deteriorated further with multiorgan dysfunction and died on 3rd day in ICU.

DISCUSSION
Coronavirus has challenged health professionals with its varying manifestations related to every human organ system. Most of the imaging manifestations are related to the chest. However, multisystemic involvement is not uncommon. The multisystemic inflammatory syndrome is a unique manifestation in the pediatric age group. Neurological manifestations of COVID-19 has been reported in many kinds of literature in children and adults. The first case report of meningitis associated with COVID-19 was a 24-year-old man with fever, and fatigue, worsening headache and sore throat. After a few days, he lost consciousness and had multiple seizure episodes. MRI revealed right lateral ventriculitis and encephalitis. The patient was RT-PCR negative from the nasopharyngeal swab but later found positive in the CSF sample.

COVID-19 have neuro-invasive capacities and may be neurovirulent by two main mechanisms: viral replication into glial or neuronal cells of the brain or autoimmune reaction with a misdirected host immune response. The probable theory is that the virus reaches the brain through retrograde transfer through the axons of the olfactory nerve. The virus in blood circulation as a direct pathway might enhance the permeability of the blood-brain barrier via cytokines produced from macrophages, which promote it to penetrate the brain. Acute necrotizing encephalopathy is a rare complication of influenza and other viral infections and has been related to intracranial cytokine storms, which result in blood-brain barrier breakdown but without direct viral invasion or para-infectious demyelination. The other possible indirect mechanism is due to hypoxia occurring due to the involvement of the respiratory system could risk patient to cerebrovascular accidents. Binding with the angiotensin-converting enzyme 2 (ACE2) receptors predisposes to stroke (hemorrhagic or ischemic). Cytokines storm also leads to a hyperimmune response which results in multisystemic inflammation. The most common neurological symptoms manifested are headache, encephalopathy, and stroke, dysfunction of taste (ageusia/hyposmia), dysfunction of smell (anosmia/hypogeusia), neuropathy and myalgia. Neurological manifestations in children with COVID-19 were identified by the ASPNR PECOBIG collaborator.
The most common imaging findings were post-infectious immune-mediated acute disseminated encephalomyelitis-like changes of the brain, myelitis and neural enhancement. Patients had splenial lesions and had myositis in children with MIS-C. Cerebrovascular complications in children were less common than in adults. Significant pre-existing comorbidities were absent and most children had favourable outcomes.9

In a retrospective, an observational study done in France including 11 hospitals, the most common neurologic manifestations were alteration of consciousness (73%), abnormal wakefulness when sedation was stopped (41%), confusion (32%), and agitation (19%).14 The most frequent MRI findings were signal abnormalities located in the medial temporal lobe (43%), non-confluent multifocal white matter hyperintense lesions with associated hemorrhagic lesions in patients (30%) and extensive and isolated white matter micro-haemorrhages (24%). A majority of patients (54%) had intracerebral hemorrhagic lesions with a more severe clinical presentation and a higher admission rate in intensive care units and development of the acute respiratory distress syndrome. Only one patient had SARS-CoV-2 RNA in the cerebrospinal fluid. The symmetric foci of white matter hyper-intensities can be correlated to post hypoxic leukoencephalopathy and focal hyperintensities in the posterior fossa or spinal cord can be explained by viral autoimmune demyelination. Because most of these patients were admitted to ICU for severe COVID-19 infection, assumptions may be considered, such as delayed post-hypoxic leukoencephalopathy, metabolic or toxic encephalopathy, and posterior reversible encephalopathy syndrome. Cytokines storm in COVID-19 can lead to thromboembolic phenomena due to hyper-coagulable state leading to microvascular thrombus and tiny microhemorrhages.15

Our first case had areas of micro-haemorrhages that may be precipitated by hypercoagulable state. The presence of micro-hemorrhages is frequent in COVID-19, and its detection is of clinical importance, as it is associated with worse respiratory, neurologic status.15 Nevertheless, the exact underlying mechanism of brain abnormalities are yet to be discovered. The areas of restriction of diffusion in the posterior limb of internal capsules and pons, hyperintensities in white matter, corpus callosum probably suggest acute demyelination. The second case also showed diffusion restriction in the posterior limb of bilateral internal capsules. Acute demyelination involving the posterior limb of the internal capsule and brainstem (showing T2/FLAIR high signal intensities showing diffusion restriction) has also been reported.13,16,18 Post-viral encephalomyelitis or acute disseminated encephalomyelitis is an immune-mediated inflammatory demyelinating disorder that occurs within days to weeks of viral infection.15 Absence of grey matter involvement and no cavitation suggest demyelination rather than necrotizing encephalomyelitis.

CONCLUSION

Multiple neurological manifestations are seen in COVID-19. Our cases involved internal capsule, corpus callosum and cerebral peduncles. The common imaging findings related to COVID-19 infections in various literature are infarcts (ischemic or hemorrhagic), acute demyelination, acute necrotizingencephalomyelitis, micro-haemorrhages, acute demyelinating encephalomyelitis, leukoencephalopathy, global hypoxic injury, cranial nerve enhancement, cytotoxic lesions of the corpus callosum, olfactory bulb involvement and Guillain Barre Syndrome (GBS). Familiarity with these neurological spectra can guide radiologists and neurologists to consider COVID-19 infections in patients who presents with primary neurological symptoms during this era of a global pandemic.

CONSENT

Written informed consent was obtained from the patients for publication of this case report and all accompanying images.

CONFLICT OF INTEREST

None declared.

REFERENCES