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Original Article

Neuroimaging findings in patients with Covid-19 in Indonesia

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Abstract

Background : Covid-19 caused by the SARS-CoV-2 virus has spread worldwide, including Indonesia. Neurological manifestations has also been reported in Covid-19 positive patients. Yet documentation of their neuroimaging findings are lacking, especially in Indonesia. The objectives of this study was to understand neuroimaging findings in Covid-19 positive patients

Methods : An observational study from medical record of Covid-19 positive patients in our hospital who developed abnormal neurologic manifestations and were followed up by neuroimaging examination from May to August 2020. Covid-19 positive diagnosis was confirmed from nasopharyngeal swab using the Real Time Polymerase Chain Reaction (RT-PCR). Neurological examination was performed by a neurologist, who then referred patients for neuroimaging examination using CT or MRI. Radiological expertise was performed by a radiologist.

Results : A total of 288 patients who are Covid-19 positive from nasopharyngeal RT-PCR swab admitted to our hospital from May to August 2020. Ten patients (3.5%) had abnormal neurologic manifestations and further neuroimaging examination follow up. Range of age 33–72 years old and slight male predominance (60%). Frequent clinical symptoms were decreased consciousness (40%), altered mental status (30%) and tremors (20%). Neuroimaging findings were large vessel occlusion (30%), vasculitis (20%), post hipoxic leucoencephalopathy (10%), basal ganglia encephalopathy (10%), non specific small vessel ischemia changes and negative findings (30%). Most patients were discharged with clinical improvement (60%), while 40% mortality rate were seen in patient with large vessel occlusion (30%) and vasculitis (10%).

Conclusion : Neuroimaging findings in Covid-19 positive patients were large vessel occlusion (LVO), vasculitis, post hipoxic leucoencephalopathy and basal ganglia encephalopathy

Keywords : Covid-19, neurological, manifestation, neuroimaging

INTRODUCTION

Covid-19 caused by the SARS-CoV-2 virus was initially found in Wuhan province, China, then spread worldwide, including Indonesia. Based on data of the Health Ministry of Indonesia until the fourth week of September 2020 there were 278.722 Covid-19 positive cases in Indonesia.[1] Despite the majority of the infected patients presented with fever and respiratory symptoms, several other manifestations such as gastrointestinal, cardiac, renal and neurologic deficits have also been reported.[2,3] One case series from hospitals in Wuhan involving 214 Covid-19 patients, showed 36.4% neurologic manifestations, including dizziness, headache, impaired consciousness and acute cerebrovascular events.[4] In several other reports, neurological manifestations has been reported as initial presentation of Covid-19 infection.[5–7]

Yet thorough documentation of neuroimaging findings are lacking, especially in Indonesia. Therefore the aim of this study was to understand neuroimaging findings in Covid-19 positive patients who admitted to our hospital.

METHODS

We retrospectively reviewed patients who are Covid-19 positive from nasopharyngeal swab using the the Real Time Polymerase Chain Reaction (RT–PCR), who showed abnormal neurologic manifestations and were followed up by neuroimaging examination, using Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) from May to August, 2020. Neurological examination was performed by our neurologist, who then referred selected patients for neuroimaging examination. Neuroimaging examination includes a-128 Multislices GE CT Scanner or a-3T Ingenia Philips MRI. Radiological expertise was performed by our Radiologist. The study was approved by the Ethics Board of our hospital.

RESULTS

A total of 288 patients with Covid-19 positive from nasopharyngeal RT–PCR swab admitted to our hospital from May to August 2020. Ten patients (3.5%) had abnormal neurologic manifestations and further neuroimaging examination follow up. Patient's gender,

TABLE 1
Clinical symptoms, neuroimaging findings and outcome in patients with Covid-19 associated neurological signs

Pts	Sex	Age	Symptoms	Imaging	Findings	Outcome
1	F	57 yrs	Decreased consciousness	CT	Brain infarcts with hyperdense BA sign (basilar artery occlusion)	Death
2	M	72 yrs	Decreased consciousness	CT	Brain infarcts with hyperdense BA sign (basilar artery occlusion)	Death
3	M	71 yrs	Decreased consciousness, left hemiparesis	CT	Brain infarcts with hyperdense MCA sign (Right M1 occlusion)	Death
4	F	59 yrs	Altered mental status, aphasia, double hemiparesis	CT/CTA	Multiple brain infarcts related to Vasculitis	Discharge, clinically improved
5	F	67 yrs	Seizure and tremors	MRI	Leucoencephalopathy at bilateral periventricle white matter	Discharge, clinically improved
6	F	56 yrs	Altered mental status, disorientation, visual hallucination	MRI	Symmetrical T2 hyperintensity at nucleus caudatus and putamen, Encephalopathy related	Discharge, clinically improved
7	M	69 yrs	Altered mental status and tremors	MRI	Small vessel ischemia at subcortex frontoparietal region	Discharge, clinically improved
8	M	45 yrs	Dysphagia and decreased gag reflex	MRI	Small vessel ischemia at subcortex frontal region	Discharge, clinically improved
9	M	66 yrs	Decreased consciousness, double hemiparesis	CT/CTA	Multiple brain infarcts related to Vasculitis	Death
10	M	33 yrs	Severe headache	MRI	Negative finding	Discharge, clinically improved

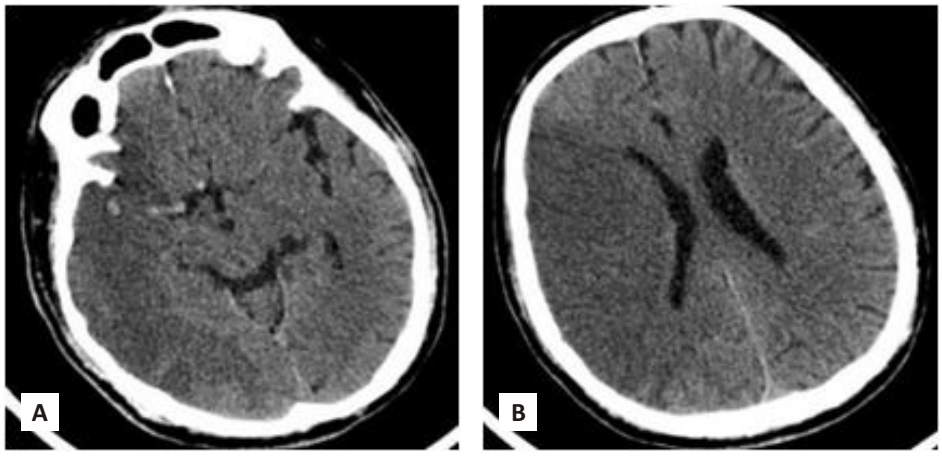

Fig. 1. Patient no. 3, a 71-year-old male with Covid-19 and right MCA stroke. **A.** Right hyperdense MCA sign (white arrow). **B.** Right MCA territory infarction. Patient died on the 4th day of hospitalization due to large infarction area and severe hipoxemia status

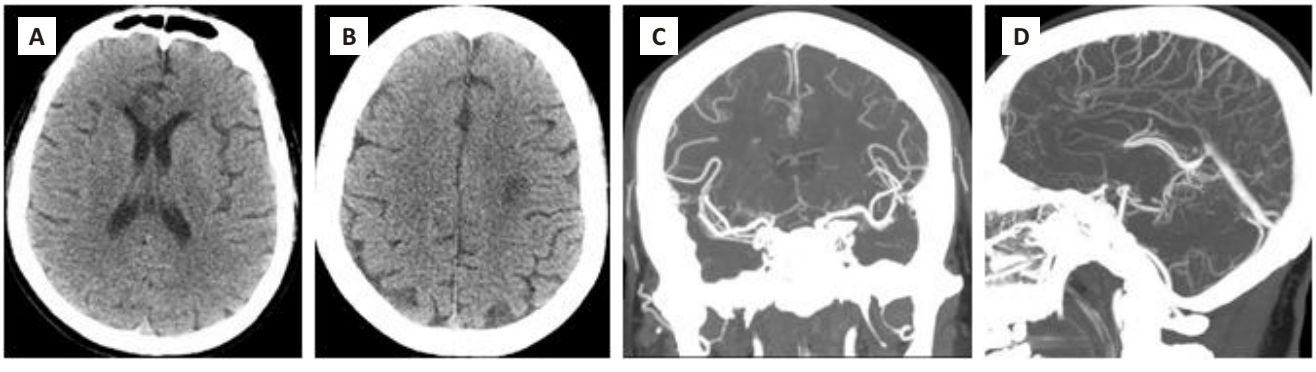

Fig. 2. Patient no. 4, a 59-years-old female with Covid-19 positive and brain infarcts related vasculitis. Non contrast CT showed multiple infarction area involving genu of bilateral corpus calosum (Fig. 2A) and left centrum semi ovale (Fig. 2B). CTA showed small caliber with vessel irregularity of bilateral anterior cerebral arteries (ACA) on coronal (Fig. 2C) and sagital maximum intensity projection (MIP) images (Fig. 2D) related to vasculitis.

age, clinical symptoms, neuroimaging findings and outcome were presented in Table 1.

Data based patients with neurological manifestations in Covid-19; a range of age 33–72 years old, female : male (40% vs 60%). Frequent clinical symptoms were decreased consciousness (40%), altered mental status (30%) and tremors (20%). Neuroimaging findings were brain infarcts related to large vessel occlusion in 30% of patients (Fig. 1), multiple brain infarcts related to vasculitis in 20% of patients (Fig. 2), post hipoxic leucoencephalopathy in 10% of patients (Fig. 3) and basal ganglia encephalopathy in 10% of patient (Fig. 4). While non specific small vessel ischemia changes and negative findings were seen in 3 patients (30%). 60% of patients were discharged with clinical improvement, while 40% mortality rate seen in large vessel occlusion (30%) and multiple brain infarcts related to vasculitis (10%).

DISCUSSION

Neurological manifestations in Covid-19 positive patients who had further neuroimaging follow up were observed in 3.5% of all positive Covid-19 cases. This was much lower than a previous study that showed that 36.4% of Covid-19 positive patients had neurological manifestations.[4] This difference might be due to small sample size and only patients with neurological manifestations and neuroimaging follow up were included in this study.

The most common neurologic clinical manifestationin our Covid-19 patients were stroke infarction (50%). This was in line with previous study that showed cerebrovascular accident (CVA) as the most common manifestation in Covid-19 in the central nervous system.[8] The mechanism of ischemic stroke in SARS-CoV-2 virus is still unclear. Patients with Covid-19 is prone to high hypercoagulability state which can cause

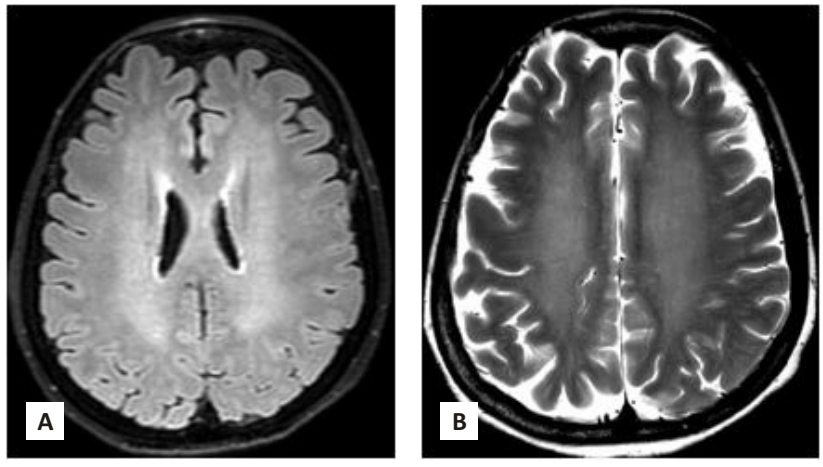

Fig. 3. Patient no. 5, a 67-years-old female with Covid-19, seizure and tremors. MRI showed Post-hipoxic Leucoencephalopathy in Fluid attenuated inversion recovery (Fig. 3A) and T2W (Fig. 3B) sequences at bilateral periventricle white matter.

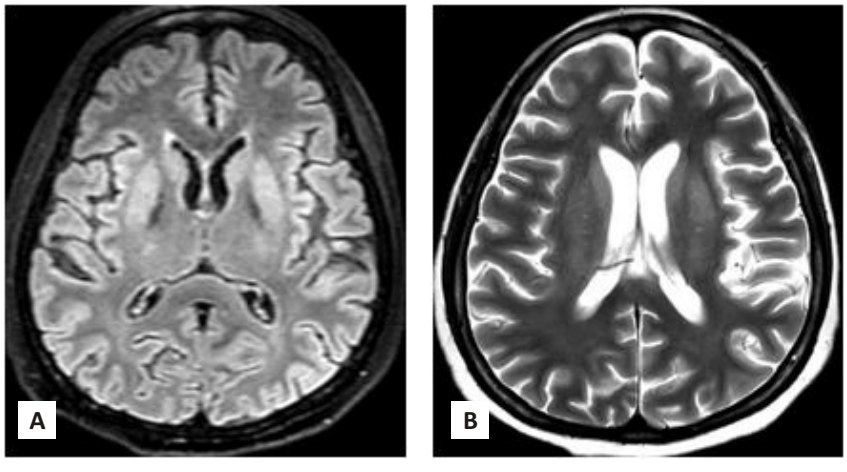

Fig. 4. Patient no. 6, a 56-years-old female with Acute Confusional Stage post Covid-19. FLAIR (Fig. 4A) and T2W (Fig. 4B) sequences showed abnormal symmetrical hyperintensity at caudate nucleus and putamen mostlikely related to encephalopathy.

clot formation in the large intracranial arteries, thus increasing risk of ischemic stroke. Other reported link to acute cerebrovascular disease in the SARS-CoV-2 virus was the cytokinesurge.[9] The hypercoagulability state and inflammatory surge that accompanies COVID-19 infection may lead to ischemic infarcts through clot formation in large intracranial vessels. High mortality rate (40%) shown in our study was seen in large infarction area related to large vessel occlusion (LVO) and severe hipoxemia status.

Ten percent of our patients who presented with seizure and tremor had bilateral periventrikel white matter Leucoencephalopathy. The mechanism underlying leukoencephalopathy in COVID-19 infection is still not clear. There are several proposed mechanism, one of them was due to neurotropism of the virus itself [10] In addition, the brain is very sensitive to oxygen deprivation, while hypoxemia is commonly seen in severe COVID-19 infection [11] In our case series, we presented evidence of white matter specific injury, which might be the sequela of COVID-19- related hypoxemia

One of our Covid-19 patients with altered mental status showed abnormal T2 hyperintensities at bilateral basal ganglia related to Encephalopathy. Basal ganglia encephalopathy in Covid-19 patients was also reported by Kaveh *et al*[12] who reported bilateral basal ganglia hemorrhage. A variety of disease may affect the basal ganglia, such as systemic disease, infections, degenerative and vascular diseases. Studies have reported that coronaviruses may first attack peripheral nerve terminals, then attain entrance to the CNS.[13,14] The average time from the first symptom to dyspnea was five

days, to hospital admittance was seven days, and to the intensive care unit was eight day according to an epidemiological Covid-19 study. Thus, the latency period maybe enough for the virus to enter the medullary neurons.[15] As a result, SARS-CoV-2 virus may enter the CNS through the hematogenous or neuronal pathway, like other respiratory viruses. The fact that some patients had hyposmia supported the later path. SARS-CoV nucleic acids has also been identified in the CSF of patients and brain tissue on autopsy.[14,16,17]

Limitations of this study were small sample size and single-center data. Larger samples and multicenter data are needed for further investigation, including research on long-term neuroimaging follow up.

CONCLUSION

Neuroimaging findings in Covid-19 positive patients were brain infarcts related to large vessel occlusion (LVO) in 30% of patients, multiple brain infarcts related to vasculitis in 20%, post hipoxic leucoencephalopathy in 10% and basal ganglia encephalopathy in 10% of patients. High mortality rate (40%) was seen in large infarction area related to LVO and severe hipoxemia status.

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