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Case Report

Serial Case: Infarct Stroke In Covid 19 Patients

Retnaningsih[1], Fatiha Sri Utami Tamad[2], Dodik Tugasworo[1], Yovita Andhitara[1], Rahmi Ardhini[1], Aditya Kurnianto[1]

[1]Department of Neurology Faculty of Medicine Diponegoro University / Dr. Kariadi Hospital Semarang, Indonesia
[2]Neurology Department, Jenderal Soedirman University Purwokerto, Indonesia

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Author Affiliation:
Department of Neurology
Faculty of Medicine Diponegoro University/
Dr. Kariadi Hospital Semarang,
Indonesia

Author Correspondence:
Retnaningsih
Dr. Sutomo Street No. 16 Semarang,
Central Java 50244, Indonesia

E-mail:
retnaningsih_icu@yahoo.com

Abstract

Background : SARS-CoV-2 has been reported to cause various neurological symptoms including stroke. SARS-CoV-2 infection causes the release of cytokines, proinflammatory chemokines, immune system activation, coagulopathy, endothelium, vasculitis, hypoxia, renin-angiotensin system imbalance, and cardiovascular complications, all of which can contribute to stroke. The purpose of this study was to describe the incidence of stroke with different conditions in COVID 19.
Cases : There were two cases of stroke infarct in a COVID-19 patient who was admitted to our hospital. Both were treated with a diagnosis of stroke infarct with previous COVID-19 symptoms, the results of laboratory examinations revealed an increase in inflammatory markers in both patients and had been given appropriate treatment according to each patient's condition. But at the end of the treatment one patient died and the other patient went home with clinical improvement.
Discussion: The incidence of stroke infarct in this case is thought to be due to several factors, namely the presence of comorbidities in the patient, microvascular thrombus due to the formation of neutrophil extracellular traps (NET), activation of complement which causes thrombogenesis and vasculopathy, formation of antiphospholipid antibodies so that protein c is reduced, the formation of microparticles causes platelet hyperactivation. and increased tissue factor (TF) resulting in hypercoagulation. Adequate therapy in controlling inflammation due to COVID 19 has shown clinical improvement in stroke infarct patients.
Conclusion : There are 2 cases of stroke infarction in patients with covid 19 who have comorbidities. The first case with COVID advanced stages experienced a worsening of the condition despite being given appropriate therapy. The second case with COVID middle stages experienced an improvement in the condition after the viral inflammatory factors were controlled and the comorbidity was well controlled.

Keywords : Stroke infarction, COVID 19, SARS-CoV-2, Hypercoagulation, Vasculopathy

INTRODUCTION

Stroke is a syndrome characterized by rapidly developing clinical symptoms and/or signs in the form of focal and global brain functional disturbances lasting more than 24 hours, which are not caused by other causes other than vascular causes.[1] As a member of the coronavirus family, SARS-CoV -2 is an RNA virus that shows genetic similarity to SARS-CoV-1 and MERS-CoV.[2] In a study of 17,799 hospitalized patients with SARS-CoV-2 infection, a stroke risk of 0.9% was found with ischemic stroke occurring in 79% of patients, hemorrhagic stroke in 17%, and 4% had cerebral venous thrombosis.[3,4] Invasion of SARS-CoV-2 to the central nervous system (CNS) can be via neuronal, lymphogenous and haematogenous routes. SARS-CoV-2 infection causes the release of cytokines, proinflammatory chemokines, activation of the immune system, coagulopathy, endotheliitis, vasculitis, hypoxia, imbalance of the renin-angiotensin system, and cardiovascular complications, all of which can lead to stroke.[5,6]

Critically ill patients, those with previous co-morbidities and patients taking certain drugs such as drugs with a high risk for arrhythmias or thrombophilia will be more susceptible to stroke after SARS-CoV-2 infection.[6] Strokes in patients infected with SARS-CoV-2 are reported to have its distinctive features include occurring in young patients (mean age <55 years) without classic vascular risk factors, with a high prevalence of cryptogenic stroke and an increased incidence of large vessel stroke, even in patients with mild SARS-CoV-2 infection.[7] This case report will discuss the incidence of stroke infarction in COVID 19 patients.

CASE REPORT

Case 1

A 48 year old woman came with complaints of 3 days of SMRS fever and cough, 2 hours of SMRS the patient could not be awakened by the family, only responding with painful stimuli. While in the emergency room, the patient's consciousness improved (fully conscious), left limbs weak, could only resist light resistance, lips drooped to the right, slurred speech, headache, fever, cough and shortness of breath. She denied past medical history such as previous stroke, hypertension, diabetes mellitus, heart disease, high cholesterol. Previously denied contact history with COVID-19 sufferers, the patient had received the COVID-19 vaccination.

Physical examination revealed GCS E4M6V5, blood pressure 130/80 mmHg, pulse 80x/minute, respiratory rate 24x/minute, temperature 37.30C, SpO2 97% with O2 NRM 10 lpm. Neurologic status : central left VII and XII cranial nerve paresis, left spastic hemiparesis (strength 555/444 555/444). The results of supporting examinations were obtained:

Leukositosis	17.200/Ul,
Increase CRP level	2.07 mg/dl
Increase feritin level	1809.4 ng/ml
Increase D Dimer level	670 ug/L
Increase fibrinogen level	439mg/dl
Increase LDL level	147 mg/dl

BGA : BGA pH 7.432 pCO2 29.4 mmHg PO2 145.5 mmHg FIO2 80.0 % HCO3- 22 mmol/L SO2c 99.0 % A-aDO2 395.6 mmHg PFR 178.125 (ARDS).

Positive PCR swab, cardiomegaly (LV) chest X-ray and pneumonia brixia score 7, CT scan of the plain head of

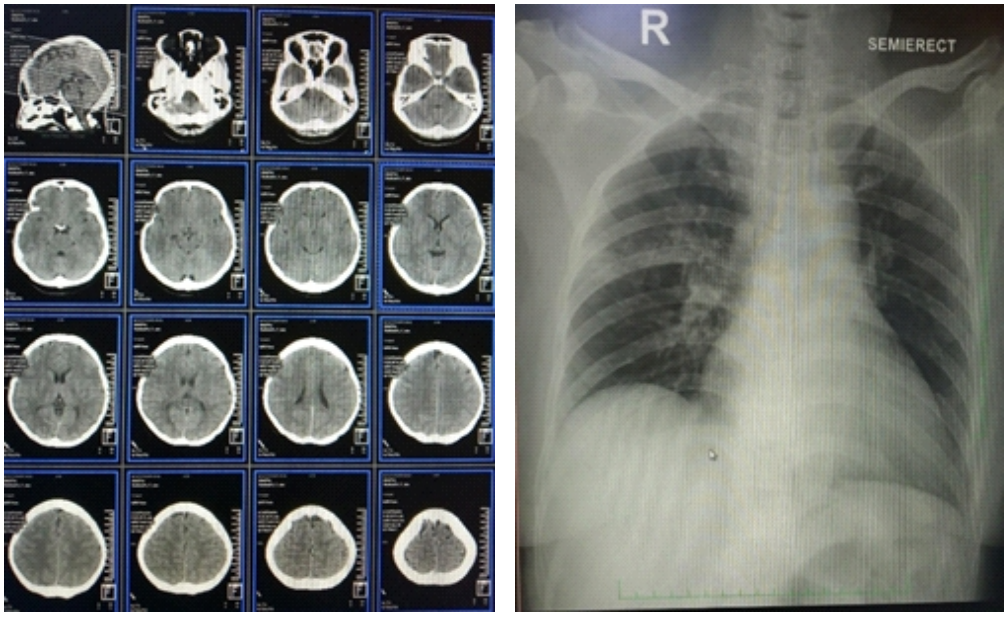

Image 1. Head CT Scan results and Ro Thorax Case 1

lacunar infarction on the posterior crus of the right internal capsule.

The patient was diagnosed with infarction stroke, confirmed covid 19 with ARDS and coagulopathy, dyslipidemia. Treated in the isolation ward with inf levofloxacin 750 mg/24 hours, inj lovenox 0.4cc/24 hours, inj omeprazole 40 mg/12 hours, inj vit B12 drip 1 ampoule/12 hours, inj vit c 1gr/12 hours, aspilet 80 mg/24 hrs, avigan 1600 mg/24 hrs (H1) then 600 mg/12 hrs (H2-H7), atorvastatin 20 mg/24 hrs, colchicine 0.5 mg/8 hrs, n-acetylcysteine 200 mg/8 hrs, paracetamol 500 mg/8 hours, cholecalciferol 1000iu/24 hours, vit B1B6 1 tab/8 hours, zinc 20 mg/12 hours.

After the fifth day of treatment the patient experienced a decrease in condition, appeared short of breath with a respiratory rate of 28x/minute, saturation 90% O2 NRM 10 lpm, BGA pH 7.439 pCO2 32.8 mmHg PO2 65.1 mmHg FIO2 80.0 % HCO3- 27.4 mmol/L SO2c 94.0 % A-aDO2 354 mmHg PFR 81.375 (ARDS), there was an increase in liver function SGOT 231 U/L SGPT 132 U/L without finding markers of viral hepatitis and increased bilirubin. So Avigan was replaced by Aluvia 2 tab/12 hours and treatment in the ICU isolation room.

Treatment in the ICU isolation of the patient has received ventilator support, treatment of COVID 19 infection with TPK 2 times and alluvia 2 tabs/12 hours, bacterial infection with inj meropenem 1gr/8 hours and inj amikacin 1 gr/24 hours, increasing the dose of lovenox 0.6 cc/12 hours, but the condition continued to worsen with inflammatory markers leukocytes 14,400/Ul, CRP 1.57 mg/dl, Ferritin 294.9 ng/ml, Quantitative D-Dimer 5610 ug/L, Fibrinogen 434 mg/dl, Ro thoracic pneumonia brixia score 12. On the 14th day of treatment the patient was declared dead.

Case 2

A 63-year-old man came with complaints of fever for 4 days. 2 days SMRS left limb weakness suddenly only able to fight light resistance, slurred speech, lips drooping to the right, and fever. History of previous illnesses such as previous stroke, hypertension, heart disease, high cholesterol was denied. History of diabetes mellitus controlled with glucodex 80 mg/24 hours. Previously denied contact history with COVID-19 sufferers, the patient had not received the COVID-19 vaccination.

Physical examination obtained GCS E4M6V5, blood pressure 170/80 mmHg, pulse 90x/minute, respiratory rate 20x/minute, temperature 37.5°C, SpO2 98%. Neurologic status: central left VII and XII cranial nerve paresis, left spastic hemiparesis (strength 555/444 555/444). Investigation results showed leukocytosis 13,400/Ul, increased CRP 6.59 mg/dl, increased ferritin 517.5 ng/ml, increased D Dimer 1010 ug/L, increased fibrinogen 534 mg/dl, GDP 158 mg/dl, HbA1c 12.9%, triglycerides 155 mg/dl, LDL 116 mg/dl.

Leukositosis	13.400/Ul
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Increase GDP level	158 mg/dl
Increase HbA1c level	12.9%,
Increase trigliserid	155 mg/dl,

Positive PCR swab, chest x-ray cor not enlarged, pneumonia brixia score 8, CT scan of plain head lacunar infarction in centrum semiovale and right corona radiata.

The patient was diagnosed with stroke, infarction, confirmed Covid 19 with coagulopathy, diabetes

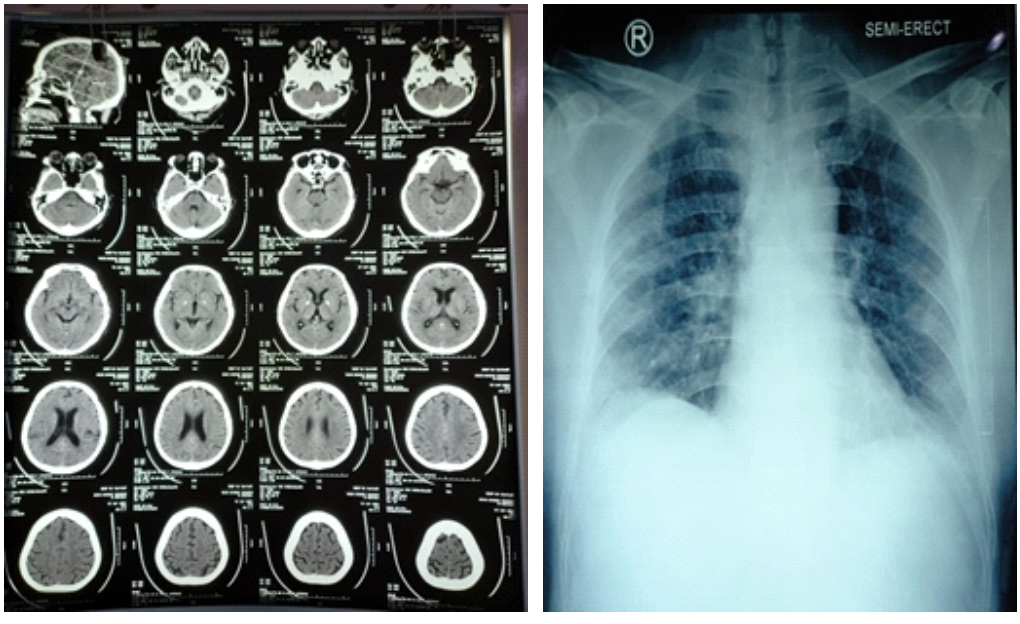

Image 2. Head CT Scan results and Ro Thorax Case 2

mellitus, hypertension and dyslipidemia. The management of this patient was treatment in the isolation ward by administering inj remdesivir 200 mg/24 hours (H1) followed by 100 mg/24 hours (D2-5), TPK 2 times, SP Heparin 750 IU/hour, then 18 IU (pk 22.00), Apidra 6-6-6 IU ac, inj ranitidine 50mg/12 hours, inj vit B12 1 ampoule/12 hours, inj vit C 500mg/12 hours, cilostazol SR 100mg/24 hours, amlodipine 10mg/24 hours, colchicine 0.5 mg/8 hours, n-acetylcysteine 200 mg/8 hours, paracetamol 500 mg/8 hours, cholecalciferol 1000iu/24 hours, zinc 20 mg/12 hours, and physiotherapy.

After 7 days of treatment the patient experienced clinical improvement and decreased inflammatory markers leukocytes 6300/UI, CRP 1.77 mg/dl, ferritin 511 ng/ml, D Dimer 770 ug/L, fibrinogen 439 mg/dl, PCR swab was still positive. Patients continued therapy at home with independent isolation.

DISCUSSION

Covid 19 infection is exacerbated by several co-morbidities such as old age, diabetes mellitus, hypertension, dyslipidemia increasing the risk of stroke infarction in the first and second cases. Endothelial dysfunction is a marker of atherosclerosis associated with vascular risk factors in the form of aging, hypercholesterolemia, hypertension, and hyperglycemia.[8] Endothelial cells are one of the main targets of SARS-CoV-2, patients with pre-existing endothelial dysfunction will be more susceptible to endotheliopathy and disease. vascular.[9]

A hypercoagulable state that causes an increase in pro-inflammatory and pro-coagulant factors, disruption of the endogenous fibrinolytic system, and platelet hyperactivity is also associated with stroke risk factors such as old age, hypertension, and diabetes. Small vessel disease due to hypertension, diabetes, and hyperlipidemia can interfere with the BBB. In addition, comorbidities such as diabetes, hypertension, and hyperlipidemia are risk factors for hypomagnesemia which ultimately increase the risk of cardiovascular disease and stroke.[6,10,11]

The incidence of lacunar infarction in this case is thought to be due to several factors, namely thrombus in the microvascular due to the formation of neutrophil extracellular traps (NETs), activation of complement which causes thrombogenesis and vasculopathy, the formation of antiphospholipid antibodies so that protein c decreases, the formation of microparticles causes platelet hyperactivation and increases tissue factor (TF). resulting in hypercoagulation.[6] The incidence of infarction stroke in cases located in the cerebral area supplied by the middle cerebral artery is in accordance with previous studies which stated that the most common occurrence of infarct stroke due to COVID 19 was in that area.[12] Different from previous studies, most infarct stroke cases were found in blood vessels big.[7,12]

In the first case, advanced stages of COVID have occurred marked by clinically decreased consciousness, ARDS with low saturation, increased inflammatory markers to the occurrence of impaired liver function. At this stage, there has been a cytokine storm that has damaged the blood brain barrier, damaged the endothelium of the blood vessels of the brain, cytokines and SARSCoV-2 have entered the brain parenchyma, thus inducing the death of neurons and the extent of the infarct area in the brain. If the injury has affected the brain stem, it will affect consciousness, breathing and heart work.[13]

The worsening clinical condition in the first case was also suspected to be due to the inflammatory factor of the COVID 19 virus which could not be controlled as seen from the high inflammatory markers despite treatment, the occurrence of ARDS and impaired liver function. This is in accordance with previous studies which stated that the mortality rate of stroke cases in COVID-19 patients was higher, especially in patients with diabetes, atrial fibrillation, impaired liver function, and congestive heart failure.[14] The treatment given was according to standards, using a mechanical ventilator, antiplatelet, anticoagulant, antiviral and anti-inflammatory. At this stage, it is necessary to consider giving double antiplatelet or TPA.[13]

The second case had middle stages of COVID with neurological deficits and increased inflammatory markers in the patient. At this stage there has been an uncontrolled cytokine storm, endothelial inflammation, platelet activation, NET formation, microparticle release, complement activation, with a hypercoagulable state that increases the risk of stroke.[13] Controlled viral inflammatory factors and good comorbid control lead to clinical improvement and reduction of inflammatory markers in these patients. The management given is in accordance with the standards, including anticoagulants, antivirals, anti-inflammatories, statins.

CONCLUSION

There were 2 cases of stroke infarction in patients with COVID 19 who had comorbidities. The first case with advanced stages of COVID experienced a worsening of the condition despite being given appropriate therapy. The second case with middle stages of COVID experienced an improvement after the viral inflammatory factors were controlled and comorbid was well controlled. The incidence of stroke in patients can be caused by various causes, one of which is COVID-19 infection.

CONFLICT OF INTEREST

In this case series there is no conflict of interest.

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