



Ischemic stroke in coronavirus disease 19 (COVID-19) positive patient: a case report

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ABSTRACT

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A new coronavirus disease called COVID-19 was declared by World Health Organization (WHO). The COVID-19 may complicated into many other conditions, including neurologic. One among this neurologic complication is stroke. This paper aimed to report a case of ischemic stroke in COVID-19 positive patient in Yogyakarta, Indonesia. A male patient, 42 years old, came to emergency department with weakness in his right arm for two days as his main complain. He also had face drop on the right side, cough, and shortness of breath. He had a history of hyperthyroid and type II diabetes mellitus. The brain CT Scan showed a lacunar infarct in the left lentiform nucleus. Patient had nasopharynx and oropharynx swab to be checked for the presence of COVID-19 and the result was positive. The pathophysiology of stroke in COVID-19 include the hyperactivation of inflammatory factors that causes a fatal inflammatory storm. It also cause a damage of coagulation system which causing the D-dimer and platelet abnormalities, hypercoagulability from critical illness and cardioembolism from virus-related cardiac injury. Moreover, COVID-19 may cause a direct role in viral infection in central nervous system. In conclusion, ischemic stroke can be present along with COVID-19.

ABSTRACT

Penyakit akibat infeksi corona virus baru yang disebut COVID-19 telah diumumkan oleh Badan Kesehatan Dunia (*World Health Organization / WHO*). COVID-19 kemungkinan dapat menyebabkan berbagai komplikasi termasuk gangguan neurologi. Salah satu komplikasi neurologi ini adalah stroke. Paper melaporkan sebuah kasus stroke iskemik pada pasien COVID-19 positif di Yogyakarta, Indonesia. Seorang pasien pria berumur 42 tahun dibawa ke instalasi gawat darurat dengan keluhan utama kelemahan di lengan kanan sejak dua hari sebelumnya. Pasien menderita wajah perot pada sisi kanan, batuk, dan sesak nafas. Pasien juga punya riwayat hipertiroid dan diabetes mellitus tipe II. Hasil CT scan kepala menunjukkan infark lakuner pada inti lentiformis sinistra. Pasien diambil apusan orofaring dan nosafaring untuk memastikan menderita COVID-19 dan hasilnya positif. Patofisiologi stroke pada COVID-19 meliputi hiperaktivasi faktor inflamasi yang menyebabkan badai inflamasi fatal. Selain itu stroke iskemik pada pasien COVID-19 dapat terjadi akibat adanya abnormalitas D-dimer dan trombosit, hiperkoagulabilitas, serta terjadinya kardioemboli karena gangguan fungsi jantung. Diperkirakan COVID-19 juga dapat menyebabkan infeksi langsung pada sistem saraf pusat. Dapat disimpulkan, stroke iskemik dapat terjadi bersamaan dengan COVID-19.

Keywords:

COVID-19;
stroke;
coronavirus;
comorbid;
neurologic;

INTRODUCTION

A new coronavirus disease called COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared by World Health Organization (WHO) on February 11th, 2020.¹ The WHO then announced that COVID-19 as a pandemic on March 11th, 2020.² The first case of confirmed COVID-19 in Indonesia was declared directly by President Joko Widodo on March 2nd 2020.³ Till May 8th, 2020, the number of positive COVID-19 patients in Indonesia was 12.776 patients, 2381 among them were recover and 930 patients were pass away.⁴ This number is expected to keep increasing.

The COVID-19 may complicated into many other conditions, such as acute respiratory distress syndrome, cardiovascular complications, septic shock, and acute kidney injury.⁵ There are also several case reports on neurologic complication among COVID-19 patients.⁶⁻⁸ One among the neurologic complication is stroke. However, the correlation between COVID-19 and stroke is not yet concluded. The pathophysiology of ischemic stroke and COVID-19 is also not yet fully understood. There is still very limited study discussing on neurologic complication and stroke in COVID-19 in Indonesia. This paper aimed to report a case of ischemic stroke in positive COVID-19 patient.

CASE REPORT

A male, 42 years old patient, came to emergency department of Panti Rapih Hospital, Yogyakarta with weakness in his right arm for 2 days as his main complain. He also had face drop on the right side, cough, and shortness of breath. His sputum has a cloudy appearance. About a week before this symptoms, he was travelling to South Sulawesi to attend an event. Other symptoms such as fever, sore throat, runny nose, skin rash, and diarrhea were denied. His weight decreased for the last 3-6 months,

from 65 kg to 49 kg. He had a history of hyperthyroid and type II diabetes mellitus. The patient and his family did not remember when the disease was first diagnosed. These diseases were not controlled routinely.

Vital signs at the admission i.e.: blood pressure (BP) was 122/85 mmHg, heart rate (HR) was 125 times per minute (tpm), respiratory rate (RR) was 26 tpm, and temperature (T) was 36.5°C. Patient's random blood glucose was 215 mg/dL. The physical examination revealed that the patient had paresis in right facial nerve. The muscle strength was 2 out of 5 on right arm while the others are normal. The breathing sound was normal.

The hematology test at the admission compared to sixth and seventh day of observation showed in TABLE 1. The results of liver function test and kidney function test showed in TABLE 2. The natrium level was 132 mmol/L and kalium level was 4.7 mmol/L. Patient had a non reactive result for HbsAg and anti Human Immunodeficiency Virus (HIV). The free T4 was increase (25.8 pmol/L) and TSHs was normal (1.095 uIU/mL).

The patient underwent inpatient care at isolation ward. Patient had nasopharynx and oropharynx swab on March 29th and 30th, 2020. Corona virus is transmitted through droplets and infects human after enter the respiratory tract. Nasopharynx and oropahrynx swab are the recommended way to detect the presence of corona virus in upper respiratory tract.¹⁴ The specimens were checked by Center for Environmental Health Engineering and Disease Control (*Balai Besar Teknik Kesehatan Lingkungan dan Pengendalian Penyakit/BBTKLPP*), as a center laboratory for COVID-19 in Yogyakarta. The result for COVID-19 was positive. This patient had a critical NLR and increase significantly from the day of admission to the seventh day of treatment (9.59 to 18.45). His ALC was also decrease gradually from 1760 at the day of admission to 690.9 at the seventh day of treatment (TABLE 1).

TABLE 1. The results of hematology test

Parameters	Admission (first day)	Sixth day	Seventh day
Hemoglobin (g%)	14.0	12.1	11.3
WBC ($\times 10^3/\mu\text{L}$)	20.0	10.6	14.1
RBC ($\times 10^3/\mu\text{L}$)	5.05	4.27	4.12
Hematocrit (%)	40.6	32.9	32.1
Platelets ($\times 10^3/\mu\text{L}$)	364	208	207
Eosinophil (%)	0.0	0.0	0.0
Basophil (%)	0.2	0.2	0.1
Neutrophil (%)	84.4	75.0	90.4
Lymphocyte (%)	8.8	8.5	4.9
Monocyte (%)	6.6	16.3	4.6
NLR	9.59	8.82	18.45
ALC	1760	901	690.9
MCV (fL)	80.4	77.0	77.9
MCH (pg)	27.7	28.3	27.4
MCHC (g/dL)	34.5	36.8	35.2
RDW-CV (%)	13.3	13.2	13.9

WBC: White blood cells, RBC: Red blood cells, NLR: Neutrophil-to-lymphocyte ratio, ALC: Absolute lymphocyte count, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW-CV: Red cell distribution width

He had a chest x-ray and brain CT scan. Radiologist conclude that his lung is normal with cardiomegaly (FIGURE 1). The

brain CT Scan showed a lacunar infarct in the left lentiform nucleus (FIGURE 2).

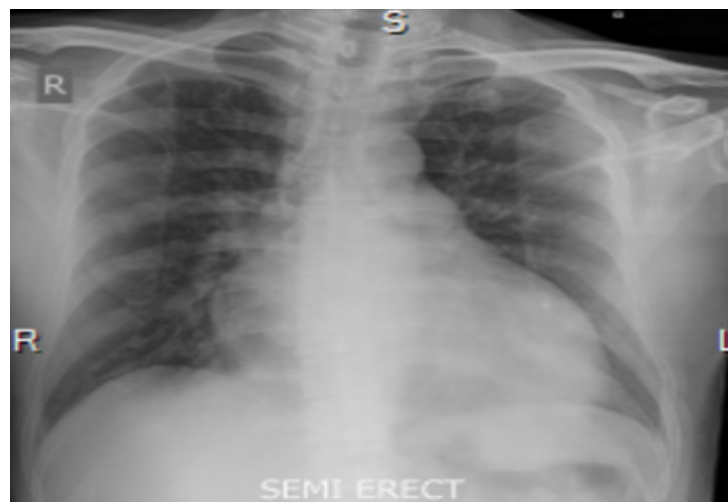


FIGURE 1. Chest X-Ray at the admission

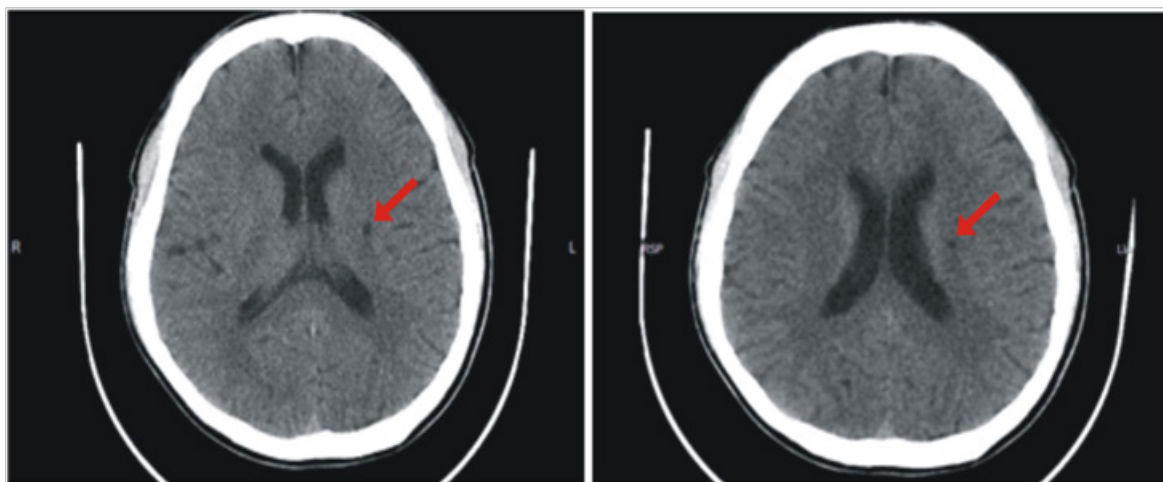


FIGURE 2. Patient's Brain CT Scan

The treatment for the patient during inpatient care were 4 L/min oxygenation with nasal cannula, levofloxacin intravenous (IV) 750 mg per 24 h, vitamin C IV 400 mg 1 times per day (s.i.d), lopinavir/ritonavir 2 tablets 2 times per

day (b.i.d), chloroquine 500 mg b.i.d, and ambroxol 3 times per day (t.i.d), codeine 10 mg t.i.d, thiamizole 10 mg s.i.d, and glicazide 80 mg s.i.d if his blood sugar > 200 mg/dL.

TABLE 2. The results of liver and kidney fuction test

Parameters	Admission (first day)	Seventh day
SGOT (U/L)	49.0	331.0
SGPT (U/L)	48.0	1268.0
Ureum (mg/dL)	58.0	246
Creatinine (mg/dL)	1.49	5.30

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase

At the second day of treatment, there was a bilateral rhonchi sound. The muscle strength was 3 on superior limbs and 4 for inferior limbs. The National Institutes of Health Stroke Scale (NIHSS) on admission was 4. Patient had a low LDL cholesterol (21 mg/dL) and normal for other lipid profile (76 mg/dL total cholesterol, 52 mg/dL LDL cholesterol, and 99 mg/dL triglyceride). Patient had an urinalysis. The results were >1.030 for specific gravity, negative for nitrit, glucose, keton, urobilinogen, and bilirubin, +2 for blood, pH 5.5, +2 for

protein, 25/μL for esterase leukocyte, 75.6/μL RBC, 6.9/μL WBC, 6.2/μL epitel cells, 3.7/μL polygonal epitel, 2.1/μL hyaline cylinder, 1.5/μL patology cylinder, 66.8/μL bacteria, 0.1/μL crystal, 0.0/μL fungi and mucous, and 12.8 mS/cm for conductivity. Patients advised to do a self-physiotherapy for his limbs at the second day.

On the third day of treatment, patient had a hypoglycemia (nocturnal blood glucose 54 mg/dL). Therefore, he was given a 2 fL of D40%. The next day, patient felt nauseous, was unable to sleep

and had a hiccup which did not stop until the next morning. Therefore we treated the patient with 4 mg ondancetron IV, 0.5 mg alprazolam tablet, 40 mg omeprazole IV and 25 mg clorpromazine tablet.

On the sixth day of treatment, patient's condition was getting worse. He had a severe dyspnea. The vital signs i.e.: BP was 110/70 mmHg, RR was 30 tpm, and SpO₂ was 97%. Patient checked for CD4 and the result was normal (435

cell/ μ L). An evaluation chest x-ray was performed. His lung showed a worse condition i.e. right bronchopneumonia with cardiomegaly. He got a nebulizer with a combination of ipratropium bromide/salbutamol and fluticasone propionate per 6 hours, furosemide 20 mg IV, methylprednisolone 62,5 mg IV, omeprazole 40 mg IV s.i.d, and hydroxychloroquin 200 mg t.i.d.

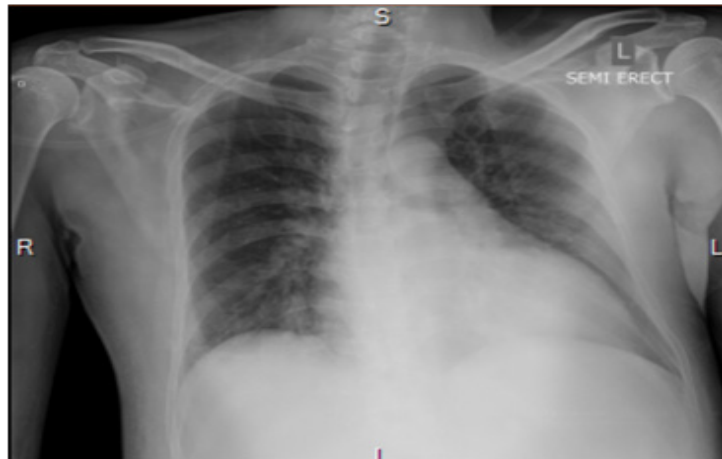


FIGURE 3. Chest X-Ray at the sixth day of treatment

On the seventh day, the patient was unresponsive. The consciousness was sopor, BP was 98/72 mmHg, HR was 76 tpm, RR was 30 tpm, T was 36.2°C, SaO₂ was 86%, and random blood glucose was 118 mg/dL. The result of hematology, liver, and kidney function tests showed a worsen condition (TABLE 1 and 2). The blood gass analysis showed a sign of acidosis (FiO₂ 95%, pH 7.338, PCO₂ 22.0 mmHg, PO₂ 66.1 mmHg, HCO₃ 12.0 mmol/L, O₂ saturation 92.2%, BE -11.8 mEq/L, TCO₂ 12.7 mmol/L, O₂-CT 11.2%, AADO₂ 568.6 mmHg, barometer pressure 736.70 mmHg). In a short period, he got cardiac and respiratory failure. The time of death was on the seventh day from admission at 07.10 am.

DISCUSSION

This is the first case report which discuss ischemic stroke in patient with

COVID-19 positive in Indonesia. As mentioned above, this patient has a history of type II diabetes mellitus. Diabetes mellitus has been known as one of a major risk factors for ischemic stroke by induce vascular endothelial dysfunction, increased early-age arterial stiffness, systemic inflammation and thickening of the capillary basal membrane.⁹ He was also had a hyperthyroid. Hyperthyroid is increasing the risk of ischemic stroke indirectly by trigerring atrial fibrillation and hypercoagulable state.¹⁰ These two conditions could be the main cause of ischemic stroke in this patient. However, the patient is also known to be positively infected with coronavirus.

Based on research by Jin *et al.*¹¹ the pathophysiology of stroke in COVID-19 include the hyperactivation of inflammatory factors that causes a fatal inflammatory storm and a damage of

coagulation system which causing the D-dimer and platelet abnormalities.¹¹

Coronaviruses are able to infect bone marrow cells, resulting in inhibition of hematopoiesis, to cause reduced lymphocyte count, decreased primary platelet formation that lead to thrombocytopenia, along with prolonged activated partial thromboplastin time, elevated D-dimer levels. COVID-19 also may increases level of autoantibodies and immune complexes, resulting in specific destruction of platelets by the immune system. The platelet consumption in COVID-19 estimated to increase due to damage in lung tissues.¹⁵ However, not all COVID-19 patients have thrombocytopenia as seen in this study and other studies. Fan, et al. report that most patients had normal platelet counts, with only 20.0% patients having mild thrombocytopenia.¹⁶ Among the 383 COVID-19 patients enrolled in retrospective study by Liu et al.,¹⁷ most patients were admitted with platelets in the normal range and a few had thrombocytopenia.

The pathophysiology of stroke in COVID-19 also could include hypercoagulability from critical illness and cardioembolism from virus-related cardiac injury.¹² Observations reflect the known biology of the virus, human angiotensin converting enzyme, as the obligate receptor for the virus spike protein, is expressed in epithelial cells throughout the body, including in the central nervous system, raising the possibility of a direct role in viral infection.¹³

Mao *et al.*⁷ explained that patients with severe infection had a higher D-dimer levels than that of patients with non-severe infection. They were more likely to develop neurologic manifestations (45.5% vs 30.2%), especially acute cerebrovascular disease (5.7% vs 0.8%).⁷ The patient in this case report also showed a sign of severe infection marked by a rapid

deterioration, the presence of liver and kidney failure (TABLE 2) despite of adequate therapy has been given. An increasing of neutrophil-to-lymphocyte ratio (NLR) and reduction of absolute lymphocyte count (ALC) are a good parameters in hematology test for COVID-19 screening and the severity of disease. This patient had a stroke in evolution due to his and respiratory distress. These may have contributed to its high mortality rate. To the best of our knowledge, this is the first case report of ischemic stroke in COVID-19 positive patient in Indonesia. This case report will give a valuable information for future research. More cases with epidemiological data are necessary to support a causal relationship.

CONCLUSION

Ischemic stroke can be present along with COVID-19. A further investigation is needed to determine the causal relationship.

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