IMAGING OF ACUTE STROKE PATIENT WITH COVID-19: A SERIAL CASE

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ABSTRACT

Background: Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a new type of coronavirus that has never been previously identified in humans. On March 11, 2020, WHO has declared COVID-19 as a pandemic.[1] In addition to respiratory symptoms, COVID-19 is also associated with neurological manifestations, including delirium or encephalopathy, agitation, stroke, meningoencephalitis, impaired sense of smell and taste, anxiety, depression, and sleep disturbances. In many cases, these neurologic manifestations have been reported even though there are no respiratory symptoms. The type of stroke that can occur in cases of COVID-19 is generally an ischemic stroke. However, the type of hemorrhagic stroke has also been reported to occur with a smaller incidence.[3,4] The mechanism that causes stroke in COVID-19 patients is not known for certain. However, there have been several theories that could cause a stroke in COVID-19 patients. This article reports 3 cases of stroke with COVID-19 and their imaging results.

Method: Patient data was collected from the medical records of patients diagnosed with stroke with confirmed COVID-19 who were treated in the isolation room of the Saiful Anwar Hospital Malang. The patient's imaging examination data were taken from the Radiology Information System of Saiful Anwar Hospital Malang.

Keywords: Acute stroke, Covid-19.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

Case 1

A 50 years old male, comes with complaints of left hemiparesis suddenly when he woke up, accompanied by a drooping, dysarthria, and headache. The patient did not complain of fever, cough, runny nose, painful swallowing, or shortness of breath. History of contact with COVID-19 patients was denied. The patient had a history of hypertension in the last 10 years with a history of routinely taking ramipril, aspirin, and atorvastatin. The patient also has a history of diabetes mellitus for 10 years, controlled with insulin, and a history of heart ring surgery 4 month ago.

At the ER of Saiful Anwar Hospital, screening for COVID-19 was carried out with a rapid antibody test with reactive results. Then RT-PCR examination was carried out with positive results for COVID-19. CRP was

increased, D-Dimer, Procalcitonin, and ferritin were normal. Chest X-Ray results was within normal limits. No signs of pneumonia were found. A head CT scan without contrast showed sulcal effacement in the right insular lobe and right parietal lobe, dilated sulci and sylvian fissure, prominent gyri, well differentiated white and gray matter, dilated ventricular and cistern systems, no midline shift, infratentorial (pons, mesencephalon, CPA, and cerebellum) was normal, orbits and mastoid air cells were normal, and there was an isodense lesion of the left ethmoidal sinus. From the results of a CT scan of the head without contrast, it was concluded of ischemic images in the right insular lobe and right parietal lobe, senile brain atrophy, and left ethmoidal sinusitis. The patient was treated together by clinicians from the departments of neurology, pulmonology, cardiology, and internal medicine. The patient died on the 4th day of treatment.

Table 1. Laboratory Result of Patient 1

Laboratory Test	27/07/2020	31/07/2020	Normal Value
Rapid Test Antibody SARS-COV2	**Reactive**		
Nasopharyngeal swab (RT-PCR)	**Positive**		
Hb (g/dL)	13.3	13.7	13.4-17.7
Erythrocytes (10^6/uL)	4.9	5.03	4-5.5
Leucocytes (10^3/uL)	8.4	12	4.3-10.3
Hematocrit (%)	39.3	41	40-47
Platelets (10^3/uL)	250	242	142-424
Blood glucose (mg/dL)	174		
Blood gas analysis			
pH	7.4	7.33	7.35-7.45
pCO2 (mmHg)	29.5	30.3	35-45
pO2 (mmHg)	113.5	100.3	80-100
HCO3 (mmol/L)	18.2	16.2	21-28
O2 saturation (%)	98	97.4	>95
CRP (mg/dL)	**0.39**	**4.16**	<0.3
Procalcitonin (ng/mL)	<0.02	<0.02	<0.5
Total cholesterol (mg/dL)	171		60-100
Triglycerides (mg/dL)	**162**		<150
HDL (mg/dL)	45		>50
LDL (mg/dL)	75		<100
Fibrinogen (mg/dL)	301.3	396.7	154.3-397.9
D-Dimer (mg/L FEU)	0.26	0.37	<0.5

Case 2

A 60 years old female, came with complaints right hemiparesis suddenly when the patient was in the bathroom. Complaints were also accompanied by headache, vomiting more than 5 times, and decreased consciousness. When the patient is in the ER the patient tends to be sleepy. There were no complaints of dysarthria or seizures. There were no complaints of fever, painful swallowing, or shortness of breath. There were complaints of cough and cold. History of contact with COVID-19 patients was denied. The patient had a history of uncontrolled hypertension since about 4 years ago. There was no history of diabetes mellitus, heart disease, or previous stroke.

At the ER of Saiful Anwar Hospital, screening for COVID-19 was carried out with a rapid antibody test with reactive results. The results of the RT-PCR examination showed positive for COVID-19. CRP, D-dimer, and ferritin were increased, Procalcitonin was normal. Chest X-Ray results showed cardiomegaly, aortic elongation, and pulmonary congestive. The results of a CT scan of the head without contrast showed a hyperdense lesion with perifocal edema on the left thalamus with a size of 2.6cm x 1.8cm x 3.7cm. Hyperdense lesions appear to fill the right and left lateral ventricles, the third and fourth ventricles. Sulci, sylvian fissure and gyrii were normal. Good white and gray matter differentiation. Right and left lateral ventricles were dilated with rounded anterior horns and open temporal horns with VSI ±35% with interstitial edema. There was a midline shift to the right by 3 mm. Infratentorial (pons, mesencephalon, CPA and cerebellum) was normal. The orbits mastoid air cells were normal. The visualized paranasal sinuses were normal. From the CT scan of the head without contrast, it was concluded that there was an ICH in the left thalamus with an estimated volume of ±9cc, IVH filled the entire ventricular system, cerebral edema with subfalcine herniation to the right as far as ±3mm, and mild communicating hydrocephalus. CT angiography was not performed to the patient due to limited facilities. The patient was treated together by clinicians from neurology, pulmonology, neurosurgery, and internal medicine.

Table 2. Laboratory Result of Patient 2

Laboratory Test	**10/01/2021**	**11/01/2021**	**13/01/2021**	**22/01/2021**	**Normal Value**
Rapid Test Antibody SARS-COV2	**Reactive**				
Nasopharyngeal swab (RT-PCR)		**Positive**			
Hb (g/dL)	13.8		12.8	11.9	13.4-17.7
Erythrocytes (10^6/uL)	4.64		4.23	3.85	4-5.5
Leucocytes (10^3/uL)	11.91		9.36	**20.29**	4.3-10.3
Hematocrit (%)	37.80		47.1	32.9	40-47
Platelets (10^3/uL)	239		160	318	142-424
Blood glucose (mg/dL)	120		115	99	
Blood gas analysis					
pH	7.39		7.29		7.35-7.45
pCO2 (mmHg)	32		39.7		35-45
pO2 (mmHg)	70.8		140.4		80-100
HCO3 (mmol/L)	19.6		19.4		21-28
O2 saturation (%)	**94.4**		99.7		>95
CRP (mg/dL)	0.16		**0.92**	**2.15**	<0.3
Procalcitonin (ng/mL)	0.07		0.16		<0.5
Total cholesterol (mg/dL)			170		60-100
Triglycerides (mg/dL)			123		<150
HDL (mg/dL)			57		>50
LDL (mg/dL)			**112**		<100
D-Dimer (mg/L FEU)	0.38		**0.66**	**1.61**	<0.5
Ferritin (ng/mL)			**423.10**	**853.40**	13-150

Case 3

A 61 years old male, came with complaints of left hemiparesis suddenly when the patient was about to pray. Complaints are also accompanied by slurred speech and headache. There were no complaints of seizures, vomiting, fever, shortness of breath, cough, runny nose, or painful swallowing. History of contact with COVID-19 patients was denied. The patient had no history of hypertension, diabetes mellitus, heart disease, or previous stroke. Patient has been hospitalized for 14 days because of confirmed COVID-19 and had been discharged from the hospital 6 days before the current complaint occurred.

At the ER of Saiful Anwar Hospital, screening for COVID-19 was carried out with a rapid antibody test with reactive results. The results of the RT-PCR examination showed positive for COVID-19. CRP and D-Dimer were increased, Procalcitonin and ferritin were normal. Chest X-Ray results showed congestive pulmonary and aortic sclerosis. A CT scan of the head without contrast showed a hypodense lesion with ill-defined borders on the right frontotemporal lobe, right lentiform nucleus, right insular cortex with an insular ribbon sign, dense arterial sign on the right MCA. Sulci and sylvian fissure narrowed around the lesion. White and gray matter differentiation is blurred around the lesion. The right lateral ventricle is narrowed, the left lateral ventricles, 3rd ventricle, 4th ventricle, and cisterns are dilated. There was no apparent midline shift. Infratentorial (pons, mesencephalon, CPA and cerebellum) was normal. A calcification was seen in right and left internal carotid arteries. The orbits and mastoid air cells were normal. Normal paranasal sinuses. From the results of a CT scan of the head without contrast, it was concluded that there was an acute infarction in the right frontotemporal lobe, right lentiform nucleus, right insular cortex supporting MCA embolism of the M1 prelenticulostriate segment with ASPECT Score (4/10), senile brain atrophy, and arteriosclerosis bilateral internal carotid arteries. The patient was treated together by clinician from the neurology and pulmonology department. CT angiography and thrombectomy were not performed to the patient due to limited facilities.

Table 3. Laboratory Result of Patient 3

Laboratory Test	31/01/2021	01/02/2021	04/02/2021	06/02/2021	Normal Value
Rapid Test Antibody SARS-COV2	**Reactive**				
Nasopharyngeal swab (RT-PCR)		**Positive**			
Hb (g/dL)	13.7			13.1	13.4-17.7
Erythrocytes (10^6/uL)	4.36			4.13	4-5.5
Leucocytes (10^3/uL)	9.00			7.20	4.3-10.3
Hematocrit (%)	39.4			37.2	40-47
Platelets (10^3/uL)	279			299	142-424
Blood glucose (mg/dL)	128			127	
Blood gas analysis					
pH	7.43			7.36	7.35-7.45
pCO2 (mmHg)	28.9			38.8	35-45
pO2 (mmHg)	323.5			56.3	80-100
HCO3 (mmol/L)	19.3			22.2	21-28
O2 saturation (%)	99.9			87.7	>95
CRP (mg/dL)	**6.93**			**2.64**	<0.3
Procalcitonin (ng/mL)	0.06			0.03	<0.5
Total cholesterol (mg/dL)			**215**		60-100

Triglycerides (mg/dL)			152		<150
HDL (mg/dL)			**36**		>50
LDL (mg/dL)			**171**		<100
Fibrinogen (mg/dL)				**477**	154.3-397.9
D-Dimer (mg/L FEU)				**2.91**	<0.5

DISCUSSION

The type of stroke that occurs in cases of COVID-19 is generally an ischemic stroke. Hemorrhagic stroke in COVID-19 cases can occur but with a less frequent incidence. Rohit Bhatia, et al, in September 2020, stated that of 30 relevant articles of stroke in Coronavirus Disease 2019, involving 115 patients with acute or sub-acute stroke with COVID-19, 87.8% of the patients had ischemic stroke, and 5.2% were intracerebral hemorrhagic strokes.[4]

Similar to the study of Rohit Bhatia, et al, in June 2020, the study conducted by Dhamoon MS, et al published by the American Heart Association in January 2021 also stated that of the 105 stroke patients with positive COVID-19 observed, 79.1% of them was an ischemic stroke, while 15.2% was an intracerebral hemorrhage stroke.[3] In the cases we reported, case 1 and case 3 were ischemic stroke types. CT scan in case 1 showed a visible sulcal effacement in the right insular lobe and right parietal lobe, that suitable with ischemia in the right insular lobe and right parietal lobe, whereas in case 3 there was a hypodense lesion with ill-defined borders on the right frontotemporal lobe, right lentiform nucleus, right insular cortex with insular ribbon sign, dense arterial sign in the right MCA, concluded as an acute infarction in the right frontotemporal lobe, right lentiform nucleus, and right insular cortex suitable with prelenticulostriate segment I MCA embolism. Case 2 is a type of hemorrhagic stroke, the CT scan showed hyperdense lesions with perifocal edema in the left thalamus, hyperdense lesions filled the right left lateral ventricle, third ventricle, and fourth ventricle, widening of the right and left lateral ventricles rounded anterior horn and opened of temporal horn with interstitial edema, and a midline shift to the right, and concluded as ICH in the left thalamus, IVH filling the entire ventricular system, cerebral edema with subfalcine herniation to the right, and mild communicating hydrocephalus.

Dhamoon MS, et al also mentioned that in cases of stroke that occurred in positive COVID-19 patients, the most location of the ischemic stroke was the parietal lobe (43.8%), frontal lobe (34.9%), temporal lobe (28.6%). , occipital lobe (26.7%), cerebellum (20.0%), and basal ganglia (9.5%).[4] Meanwhile, in cases of COVID-19 with hemorrhagic stroke, the location is in the frontal lobe (56.3%), parietal lobe (31.2%), basal ganglia (31.2%), temporal lobe (25.0%), and occipital lobe (25.0%).[3] In the case we reported, the patient in case 1 had an ischemic stroke of the right insular lobe and parietal lobe. The patient in case 2 had ICH in the left thalamus (basal ganglia), and IVH filled the entire ventricular system. The patient in case 3 had an ischemic stroke in the right frontotemporal lobe, right lentiform nucleus, and right insular cortex. These cases are consistent with the previous study conducted by Dhamoon MS, et al.

The relationship between COVID-19 cases and the occurrence of stroke is still not certainly known, but there are several things that may be related to the occurrence of stroke in COVID-19 cases. Among them are viral neurotropism, endothelial dysfunction, coagulopathy, inflammation, and other potential mechanisms such as cardio embolism from myocardial injury related to viral infection.[5-8]

The systemic inflammatory response caused by infection can lead to endothelial dysfunction and induce procoagulants. Inflammatory response in COVID-19 patients associated with multiple pathways. Elevated levels of D-dimer in patients with acute ischemic stroke onset also support that SARS-CoV-2 can induce an acute inflammatory response in the vessel wall and trigger a hypercoagulable state.[9,10]

Atherosclerosis in patients with COVID-19 infection may increase the risk of ischemic

stroke because the infectious virus has the potential to destabilize atherosclerotic plaques through systemic inflammatory responses, cytokine storms, and changes in the specific immune cells polarization towards an unstable phenotype. In addition, COVID-19-infected patients with cardiovascular comorbidities may have a potential risk of dysrhythmias, which can lead to cardioembolism and increase the risk of ischemic stroke.[9,10]

The mechanism of hemorrhagic stroke in COVID-19 patients is not certainly known as well. Zilan Wang, et al. stated that one of the possible causes of hemorrhagic stroke in COVID-19 patients is a cytokine storm, as well as an increase in blood pressure caused by a decrease in ACE-2 expression. ACE-2 is an important enzyme in the renin-angiotensin system (RAS) which regulates blood pressure, fluid and electrolyte balance, and vascular resistance. SARS-CoV-2 that binds to the ACE-2 receptor will decrease the ability of ACE-2 to lower blood pressure. Decreased expression of ACE-2 during SARS-CoV-2 infection also causes an increase in serum angiotensin-2 which can impair endothelial function and cause dysregulation of blood pressure. This allows the occurrence of hemorrhagic stroke in COVID-19 patients.[9,10]

CT scans have an important role in determining the type of stroke and its location, both in COVID-19 and non-COVID-19 patients. CT scan is sensitive enough to detect lesions such as masses, abscesses, and acute bleeding, although it is not sensitive enough to detect ischemic stroke, especially if it is small, acute, or located in the posterior fossa. The purpose of a CT scan in stroke cases is to detect bleeding and rule out other diseases with symptoms resembling a stroke.[10,11] CT scans are widely chosen as the main modality in examining stroke patients because they are good at detecting bleeding, more readily available, faster and cheaper to operate compared to MRI.

CONCLUSION

Types of stroke in COVID-19 patients can appear as different types of stroke. In general, what happens is an ischemic stroke, but hemorrhagic strokes can also occur, with a less frequent incidence. Of the three cases we reported, two of them were ischemic strokes, while one case was hemorrhagic stroke.

CT scan is an important imaging modality in stroke cases, both COVID-19 and non-COVID-19 cases. CT scan is good at detecting the presence of bleeding, more widely available, faster and cheaper to operate than MRI.

Until now the exact correlation between stroke and COVID-19 is still unclear, but there are several theories that might cause the manifestation of stroke in COVID-19 patients. Among them are Viral Neurotropism, Endothelial Dysfunction, Coagulopathy, and Inflammation. Further research is needed to explain the exact cause of the manifestation of stroke in COVID-19 cases.

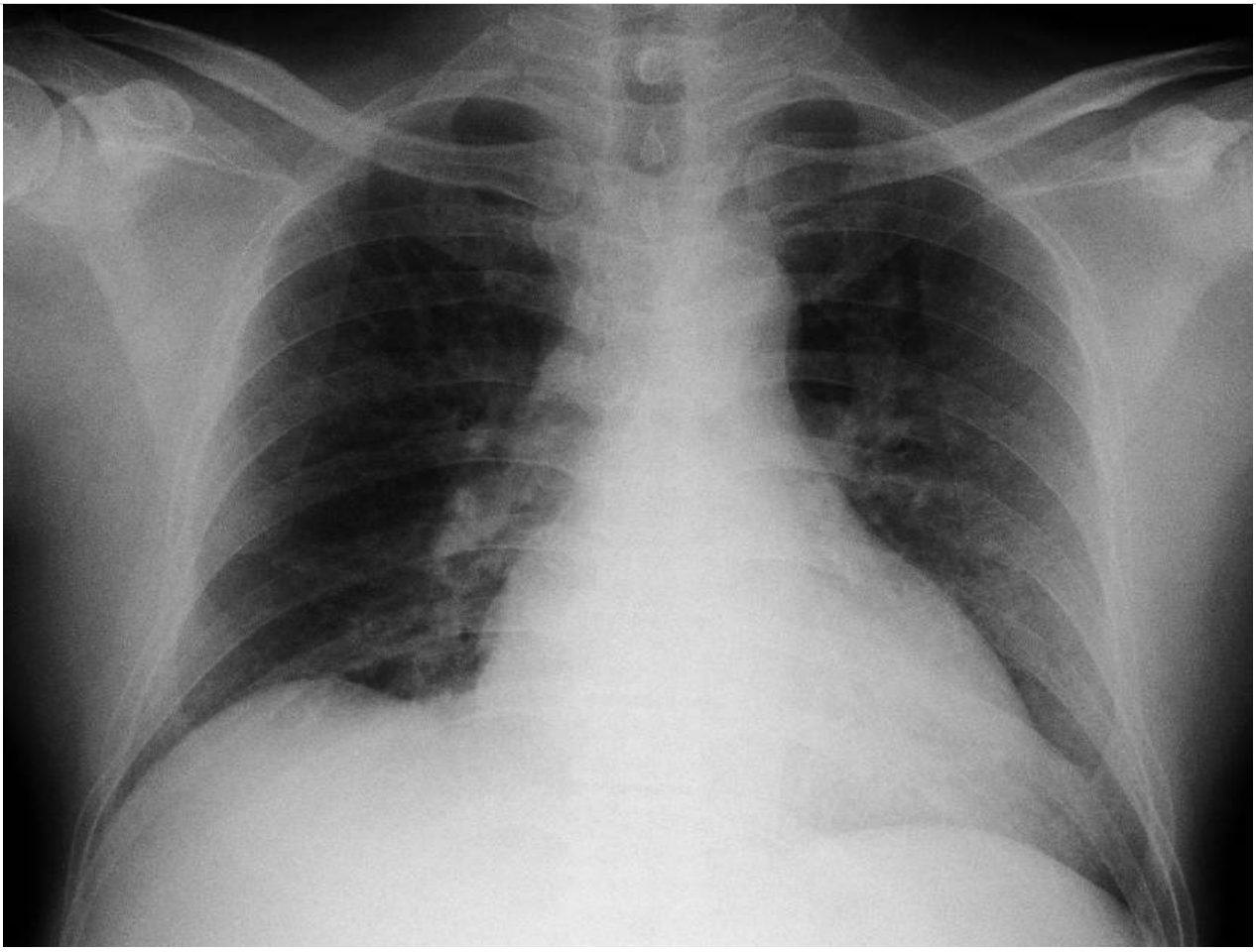


Figure 1. Chest X-Ray result of patient in Case 1. Chest X-Ray was within normal limit, no sign of pneumonia was found.

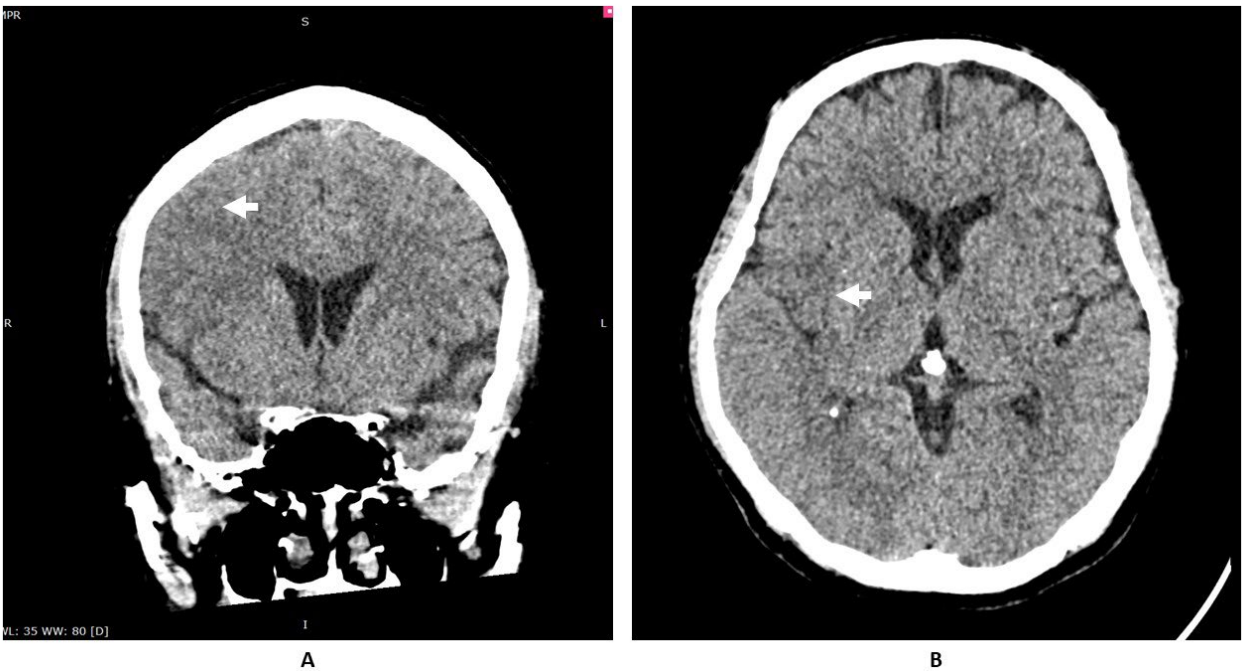


Figure 2. Head CT scan without contrast of patient in Case 1. (A) Sulcal effacement of the right parietal lobe (white arrow); (B) Sulcal effacement of the right insular lobe (white arrow).

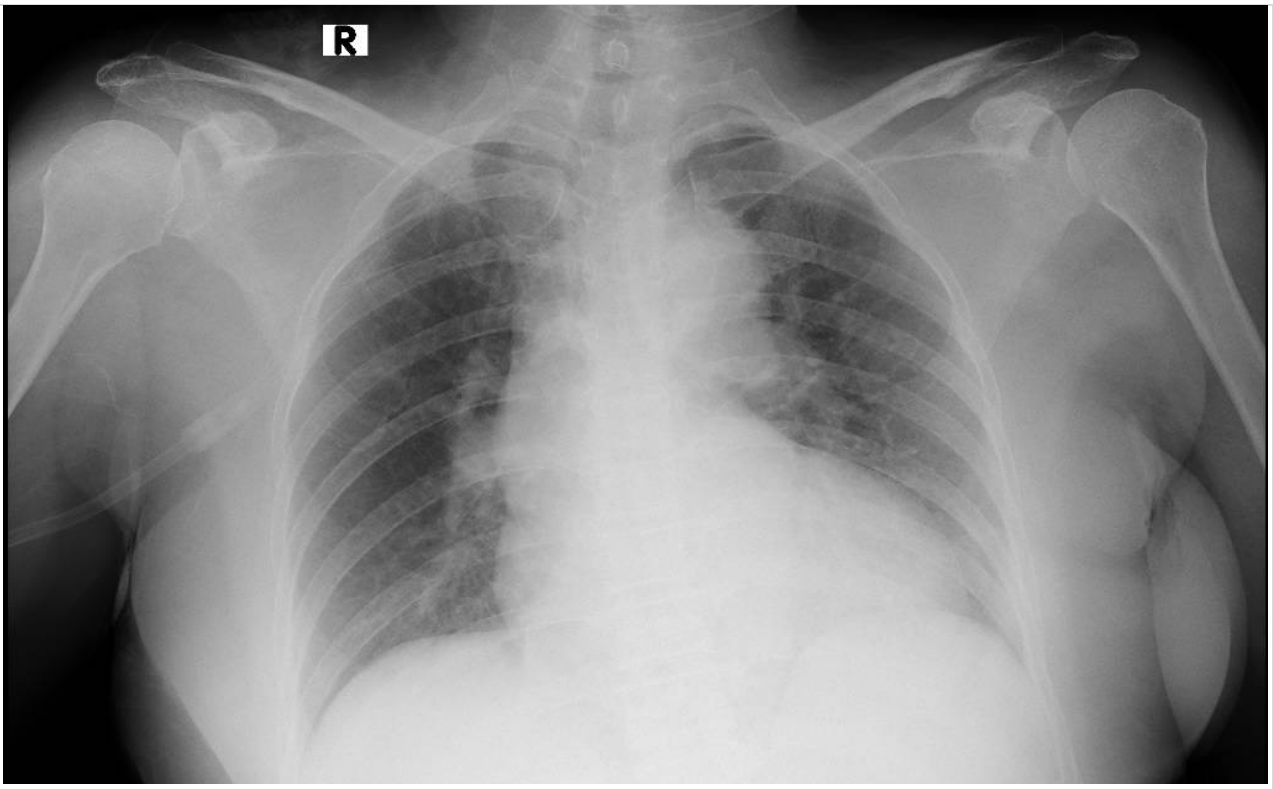
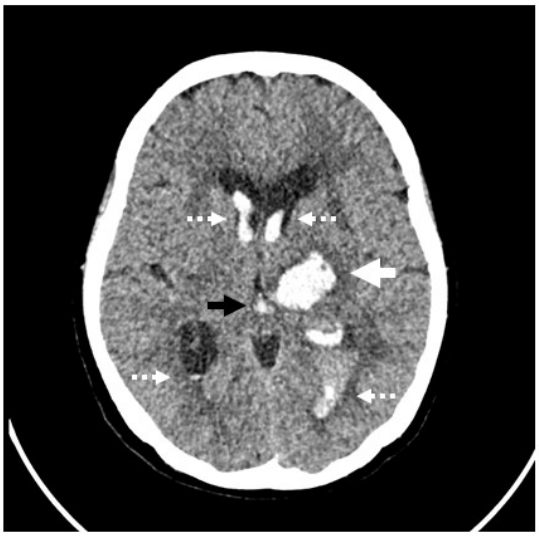
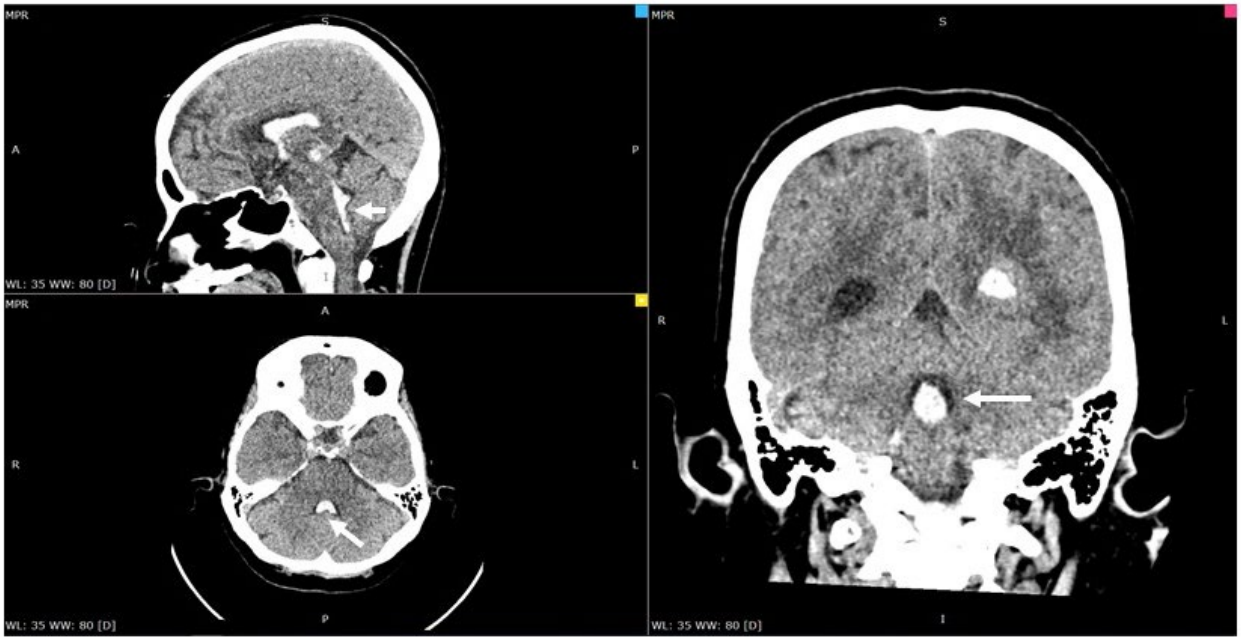


Figure 3. Chest X-Ray result of patient in Case 2 Chest X-Ray showed cardiomegaly, aortic elongation, and pulmonary congestive.



A



B

Figure 4. Head CT scan without contrast of patient in Case 2.
(A) Appearance of hyperdense lesion with perifocal edema of the left thalamus (white arrow), a hyperdense lesion filling the left right lateral ventricle (white dotted arrow) and 3rd ventricle (black arrow), and a midline shift to the right.
(B) Appearance hyperdense lesion filling the 4th ventricle (white arrow).

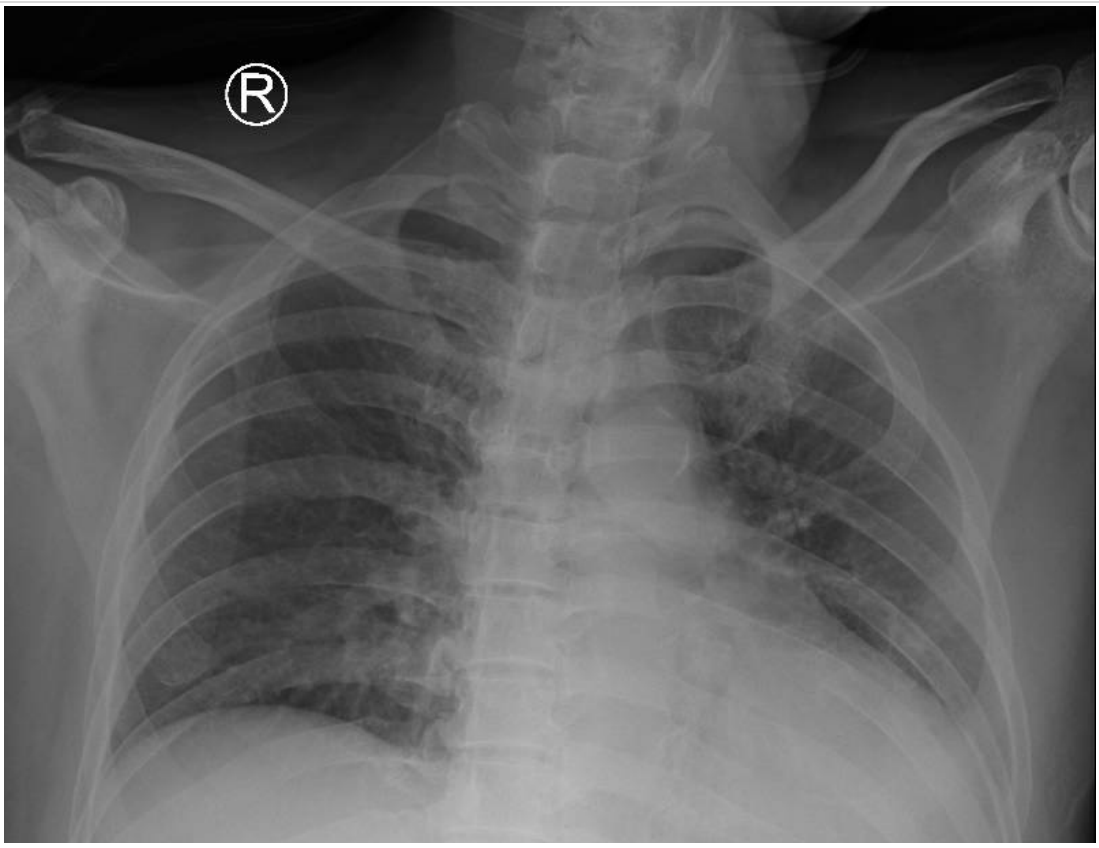


Figure 5. Chest X-Ray result of patient in Case 2. Chest X-Ray showed congestive pulmonary and aortic sclerosis.

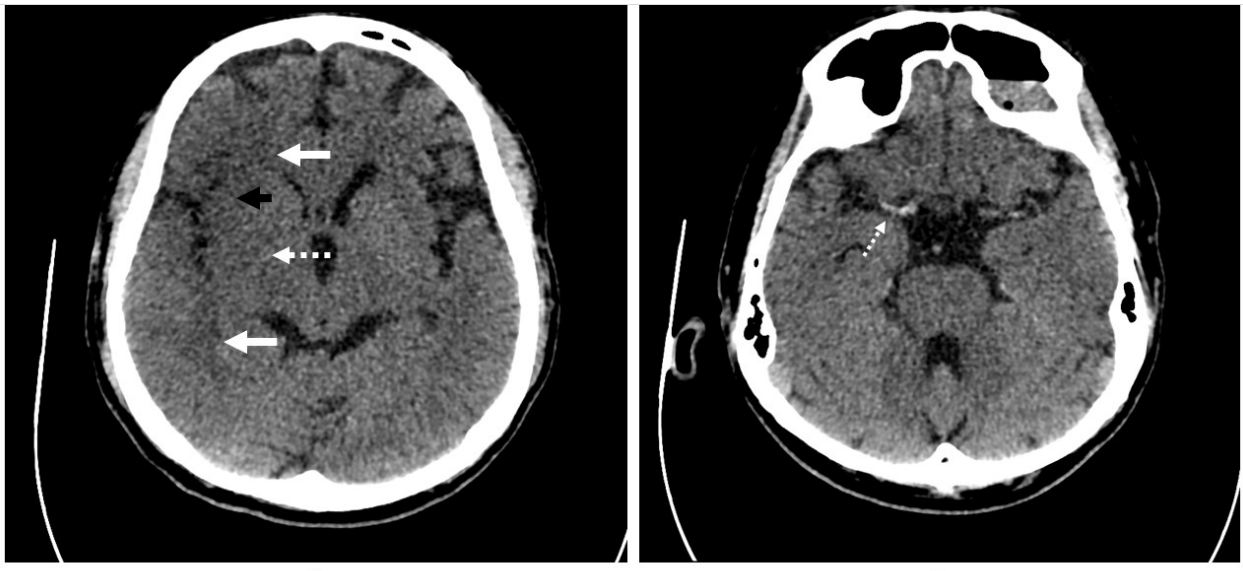


Figure 6. Head CT scan without contrast of patient in Case 3
(A) There were indistinct hypodense lesions on the right frontotemporal lobe (white arrow), right lentiform nucleus (white dotted arrow), and right insular cortex with insular ribbon sign (black arrow);
(B) Appearance of dense arterial sign on the right MCA (white dotted arrow).

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