Case Report

Recurrent Intracerebral Hemorrhage as a Result of Cerebral Amyloid Angiopathy

Mohammad Kurniawan¹, Dhara Ayu Lestari², Salim Harris¹, Al Rasyid¹, Taufik Mesiano¹, Rakhmad Hidayat ¹

¹Department of Neurology Cipto Mangunkusumo National Hospital, Faculty of Medicine Universitas Indonesia Jakarta, m.kurniawan@ui.ac.id
²Neurocare Clinic, Jakarta Indonesia

ABSTRACT

Stroke is a major health problem in the world with high mortality dan morbidity rate. Hemorrhagic stroke is a type of stroke with a high mortality rate. One of the most common causes of hemorrhagic stroke in elderly is cerebral amyloid angiopathy. We present a case of recurrent hemorrhagic stroke with clinical manifestations of extremity weakness and seizure. Radiological imaging showed a lobar hemorrhage. Referring to the Boston criteria, based on the results of clinical evaluation and imaging, the patient was diagnosed with intracerebral hemorrhage et causa probable CAA without pathologic feature was established. Patients were treated with antihypertensive medicine for blood pressure control and steroid as anti-inflammatory agents with a good clinical and functional outcome.

Keywords: stroke; intracerebral hemorrhage; cerebral amyloid angiopathy

INTRODUCTION

Stroke is a major health care problem in the world. The main cause of morbidity and the second-largest cause of mortality after heart disease. According to Riset Kesehatan Dasar (Riskesdas) in 2018, the incidence of stroke is rising, from 7 per mil in 2013 to 10.9 per mil in 2018.¹ In general, it can be classified into two types, ischemic stroke due to blood vessel occlusion, and hemorrhagic stroke due to blood vessel rupture. Although it occurs less frequently than ischemic stroke, hemorrhagic stroke has a high morbidity and mortality because of the rapid decrease in neurological function due to focal bleeding in the cerebral parenchyma or the ventricular system, not due to trauma.²

Hypertension, cerebral amyloid angiopathy (CAA), vascular malformation, and blood disorders are some of the causes of hemorrhagic stroke. Hypertension is the most common cause of spontaneous intracerebral hemorrhage, while CAA is the most frequent cause of lobar
hemorrhage, especially in the elderly.²

Although theoretically the cases have relatively considerable number, as one of the most common causes of hemorrhagic strokes after hypertension, the diagnosis, management, and prevention of CAAs to date is still a challenging and still an evolving issue due to variations in symptoms, diagnostic criteria, and treatment. This paper aims to find out how to diagnose CAA accurately from anamnesis, physical examination, and diagnostic test, to find the right therapy for the management and prevention of the disease.

CASE REPORT

Mr. H, a 76-year-old male, came to the emergency room, Dr. Cipto Mangunkusumo General Hospital, Jakarta, with acute right-sided weakness followed by seizure in an hour before. It was a first-time seizure with unknown pre-ictal. During the ictal phase, the patient was conscious, the right arm was stiff and convulsed for two minutes and stopped by itself. There was no history of head trauma, headache, double or blurred vision, hearing loss, one-sided paresthesia, vertigo, and loss of consciousness. There was also no sign of bleeding of the gum and nose, melena, hematochezia, or hematuria.

He had a history of stroke five years ago, with left-sided weakness and dysarthria. The complaints gradually improved, and the patient was able to walk on his own even though there was still a slight weakness. He was diagnosed with hypertension in the last five years but didn’t take antihypertensive drug regularly. According to his family, after the first stroke, he was becoming more forgetful and had difficulty answering immediate questions. He had no history of diabetes mellitus, hematologic and kidney disorder, epilepsy, and cancer. He had been retired for twenty years and could do daily activities independently. He used to have a smoking habit but had stopped thirty years ago, and alcoholic tendency was denied.

During his arrival in the emergency room, he had initial blood pressure of 170/100 mmHg on the right arm and 160/98 mmHg on the left arm, pulse rate of 87x/minute, respiratory rate of
20x/minute, and oxygen saturation of 99%. Physical examinations on lungs, cardiac, abdomen, and extremities were within normal limit. Neurological examination showed the patient to be compos mentis with severe dysarthria and higher cortical function impairment. Cranial nerve examinations showed 7th and 12th nerve palsy and hemiparesis on the right side with manual muscle test (MMT) of 4444/5555 on both upper and lower extremities. He had normal physiological reflexes and negative Babinski’s sign. Sensory and autonomic responses were intact but difficult to evaluate further. The National Institutes of Health Stroke Scale (NIHSS) score on admission was 8.

Initial imaging using non contrast Computed Tomography (CT) showed intracranial hemorrhage with perifocal edema, 5.5 mL estimated volume. There were also bilateral frontoparietal infarction with multiple chronic lacunar infarctions in bilateral centrum semiovale, left corona radiata, bilateral basal ganglia, left external capsule, thalamus, and pons. Cerebral atrophy was also shown in the imaging. Chest x-ray showed no abnormality.

Electroencephalography (EEG) was conducted on the fourth day of hospitalization. It showed a slowing background electroencephalography. Higher cortical function was
examined on the ninth day, and showed impaired cognition and attention, various domains of memory impairment (recent memory, delayed memory, recognition, and remote memory), and Wernicke’s aphasia.

Based on clinical assessment and diagnostic examinations, he was diagnosed with acute symptomatic seizure, right 7th and 12th cranial nerves palsy, right hemiparesis et causa hemorrhagic stroke with suspected cerebral amyloid angiopathy.

During hospitalization, he was given NaCl 0.9% 500 mL/day infusion, and oxygenation using nasal cannula 3 lpm. The patient was also treated with phenytoin 100 mg 3 times a day, methylprednisolone 8 mg once daily with blood sugar monitoring, omeprazole 20 mg twice daily, and sucralfate 15 mL three times daily. Candesartan 8 mg once daily and hydrochlorothiazide 25 mg once daily were given to treat hypertension. Limb physiotherapy and chest physiotherapy were also conducted to prevent pneumonia. The patient was hospitalized for ten days, and discharged with improved neurological deficits, controlled seizure, and walking mobilization.

**DISCUSSION**

We described a case of 76-years-old male came to the hospital with right-sided weakness followed by focal seizure in one hour before. Sudden onset in symptoms with no history of trauma suggested a vascular origin. From anamnesis we could conclude there was no sign of high intracranial pressure. The possibility of ischemic stroke was ruled out by conducting non contrast CT which showed intracranial hemorrhage with perifocal edema, bilateral frontoparietal infarction with multiple chronic lacunar infarctions in bilateral centrum semiovale, left corona radiata, bilateral basal ganglia, left external capsule, thalamus, pons, and cerebral atrophy. He had no history of consuming antiplatelets or anything similar, so the possibility of drug-induced bleeding could be ruled out. The location was less consistent with the location of the predilection of hemorrhagic stroke caused by hypertension. Lobar hemorrhage most often caused by CAA; it was supported with the patient’s age >65.
years where CAA most often occurs in elderly patients. The patient had history of hypertension, but at the time the patient of admission the blood pressure varies within his daily range, so the bleeding was suspected caused by vascular disorders.

The presence of seizure, higher cortical function impairment, memory impairment, and previous hemorrhagic stroke strengthened the suspicion of CAA. Amyloid fibrils deposit distributed in small and medium sized blood vessel, arteries, and arterioles mainly in the leptomeningeal space and cortex, which showed hemorrhage in lobar area, instead of subcortical area as in hypertension-induced intracerebral hemorrhage. Multiple infarctions in both hemispheres in lobar area, lacunar infarct, and white matter lesion showed vascular impairment in CAA patients. Petechiae as one of distinct characteristics in CAA couldn’t be shown in CT. Ideally, Magnetic Resonance Imaging (MRI) sequences are used to see multiple microhemorrhage in cortical and subcortical regions.

Definite diagnosis of CAA is made histologically based on brain tissue samples, this procedure often being carried out postmortem, or during craniotomy to evacuate massive hemorrhage. Double barrel will be found in histopathological test, caused by the separation of internal elastic lamina due to hyalin deposit in blood vessels. In the patient, diagnostic was made using Boston criteria, which assessed clinical features and radiological imaging. CAA can be categorized into four; definite CAA, probable CAA with supporting pathology, probable CAA with supporting MRI/CT, and possible CAA. According to Boston criteria, the patient was diagnosed with probable CAA with supporting MRI/CT imaging.

The presence of seizure that corresponds to the hemorrhage lesion is one of the clinical manifestations often found in CAA, caused by hemorrhage or cortical petechiae which sometimes comes asymptomatic and needs further MRI imaging to confirm. The seizure in our case couldn’t be categorized as epilepsy, it also had unspecific EEG as shown in CAA, and the slowing
background EEG could still be caused by other lesion due to CAA. Cognitive impairment and dementia also have also been associated with CAA. Some studies show in Alzheimer patients, more than 70% are diagnosed with CAA, thus the cognitive impairment can be induced by other means than CAA.

The intracerebral hemorrhage score in the patient was 0, which meant the mortality rate in the next 30 days was 0%, but the repeated hemorrhage due to CAA could affect brain blood vessels and caused functional deterioration in the patient. Observation was being held to examine the patient’s clinical symptoms. Antihypertensive drugs were given to the patient to maintain blood pressure, while in most cases of CAA are normotensive, hypertension in patient needed to be controlled to reduce the risk of repeated bleeding due to CAA. Perindopril Against Recurrent Stroke Study (PROGRESS) reported to reduce the recurrence of hemorrhagic stroke by 0.37, blood pressure of <130/80 mmHg was needed. Hypertension that occurred in the patient can alter the morphology of the blood vessel walls and facilitated amyloid deposits in the blood vessels walls resulting in more severe angiopathy in CAA.

CAA treatment is related to the pathogenesis of CAA due to amyloid deposits and vascular damage due to disruption, occlusion, and permeability changes of blood vessels; the drug that has had positive effect to improve functional capacity in patients CAA is immunosuppressant. The use of corticosteroid in some studies showed improvement in CAA-related inflammation, which is related to an increase in blood-brain-barrier permeability and causing vasogenic edema. In one study, steroid administration could provide improvement with reversible leukoencephalopathy.

Surgical intervention was not performed because of the small bleeding volume on the CT and there was no pressure on the brainstem. Adequate education is needed for the patient and his family about the importance of blood pressure control to prevent recurrences in the future. Education for caregivers is also needed so that the patient's family is
aware of the importance of maintaining the quality of life in elderly patient who are more susceptible.

Ad vitam prognosis in patient was good because of the low ICH score, which meant mortality chance was low. Ad fuctionam prognosis was also good with the rehabilitation and improvement of neurological deficit, the patient was expected to be able to return to daily activities with or without minimal assistance. Ad sanationam prognosis in patient was dubia ad malam (poor), he had a higher risk of repetitive stroke caused by the presence of hypertension, in addition to the underlying CAA.

CONCLUSION

The cause of intracranial hemorrhage can be predicted by looking at the location of the lesion. In elderly patients with lobar hemorrhage, the most common cause is CAA. Vascular disturbance which happens in cerebral blood vessels in CAA has a broad range of clinical spectrum from asymptomatic to lobar hemorrhage.

In addition to bleeding, angiopathy in CAA has an important link with cerebral white matter disease. Vascular functions can be disrupted by various mechanisms in CAA with broad clinical features including transient focal neurological symptoms and signs such as seizure, migraine, and transient ischemic attack (TIA), and cognitive impairment. The disease is often recurrent and hypertensive conditions can increase the rate of recurrence; therefore, it is important to regulate blood pressure and evaluate neurological deficits in patients.
REFERENCE


