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Case Report **Open Access**

Vascular cognitive impairment after ischemic stroke

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Abstract

Background Post-stroke cognitive impairment is the leading cause of post-stroke morbidity and mortality worldwide. This impairment is often associated with ischemic stroke and intracerebral hemorrhage. Cognitive impairment could affect attention, memory, language, orientation, and executive and social functioning domains.

Case We reported a male patient, 45 years old, Javanese, who came with confusion and memory impairment. When asked a question, the patient tends to think and answer slowly with a wrong response. He also felt weakness in the right half of the body, slurred speech, pursed lips, and had been diagnosed with ischemic stroke. One week after he was sent home, patient still had difficulty arranging words to form a sentence and could not work. Cognitive function screening showed impairment in attention and memory domain with a MOCA-INA score of 19/30. Patients received antihypertensive therapy, dual antiplatelet, statin, and cognitive stimulation. His condition improved with this treatment.

Conclusion Early identification of cognitive impairment could reduce morbidity in stroke patients.

Keywords: ischemic stroke; post stroke; vascular cognitive impairment

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Introduction

Stroke defined as brain dysfunction due to disturbance in cerebral blood flow, it was the second leading cause of death and disability in adult worldwide. After an ischemic stroke, mortality is approximately 10% in the first thirty days and 40% by the end of the first year. Survival is dependent upon receiving treatment as soon as possible. Nowadays, more researchers were studying disability caused by stroke. Physical impact caused by stroke was quite debilitating and cause long term disability. This was the reason post -stroke cognitive impairment often gone unnoticed as it was masked by post stroke physical disabilities.[1]

Post-stroke cognitive impairment is the evolution of cerebrovascular disease that leads to spectrum of vascular cognitive impairment (VCI). Vascular Cognitive Impairment spectrum varies from a mild cognitive impairment (VaMCI) to more severe dementia. Its prevalence was difficult to determine and estimated between 30-50% of stroke cases. An extensive cross-sectional study done in 10 countries showed that around 30% ischemic stroke patients had cognitive impairment with MMSE score lower than 27.2 According to demographic data, age and education had significant correlations with risk of VCI. Cohort study with 4010 samples that was led by Elbaz found correlation between excellent cognitive performance with higher education. This means higher education could increase tolerance to cognitive disorders. Beside age and education level, clinical manifestations of post-stroke cognitive impairment vary by volume and location affected by infarction. Recent studies have shown that total infarct volume could explains a small portion of cognitive variation in stroke patients. Infarction such as small vessel disease (SVD), microbleeds and lacunae in strategic areas in brain has major role for post-stroke cognitive impairment mechanism and associated with severity of dementia. Domains of cognitive impairment include attention, memory, language, orientation, executive functioning and social functioning, with attention and executive domain being the most affected one. This is different at the time of stroke

diagnoses, where problems in memory domain was more prominent.[2]

Case presentation

Male 45 years old brought to the hospital on September 14 2022 with confusion and memory impairment. Previously on September 10 2022 he was able to carried out activities as usual, but when returned from work his family said he felt weak and rested in the room all day. The next day when his family wake him up, he was fully alert but when asked about something, he tended to think slowly and gave the incorrect answers. His family also said when asked why he felt weak yesterday, he did not know or remember anything that happened to him. That day, he also felt weakness, drop a spoon while eating, had slurred speech, and was brought to the hospital. Other symptoms like headache, vomiting, blurry or double vision, decrease of consciousness, fever, prolong cough, night sweating was denied by him. Brain CT scan of this patient showed a new onset of ischemic stroke and he was treated for 2 days in a private hospital. After 2 days of treatment, he still confused about where he was, and sometimes forgot the person that take care of him in that hospital. He then referred to Prof Ngoerah Hospital for further treatment.

He had history of hypertension since 1 year ago and diabetes mellitus since 2 months ago but did not take medication (metformin and glibenclamide) regularly. He did not smoke or drink alcohol. He was graduated with bachelor degrees and work as general managers.

Physical examination on September 14 2022 result were blood pressure 170/100 mmHg, pulse rate 82 beats/minute, breathing 16 times/minute, temperature 36^0 C and oxygen saturation at 98% in room air. Neurological examination showed he was fully alert, paresis of nerves VII and XII right supranuclear, right flaccid hemiparesis grade 4+. Magnetic Resonance Angiography examination of the head was performed on September 15, which found an acute cerebral infarct from thalamus to the left posterior horn of internal capsule, small vessel ischemic changes in the lateral periventricular, left and right centrum semiovale, and left corona radiata.

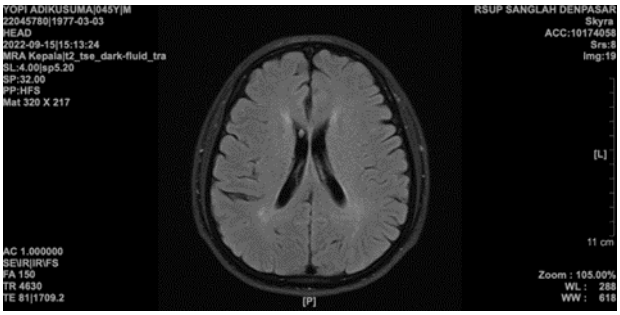

Figure 1. Small vessel ischemic changes in the lateral periventricular, left and right centrum semiovale on the MRA results

After being discharge from the hospital, his family said that he able to carried out daily activities by himself, but he has not been able to go to the office. It was because he keeps forgetting things like his laptop password, and he also confused about paying money when goes to shop. According his family, he felt difficult to make a sentence when talking and his family has to help remind him.

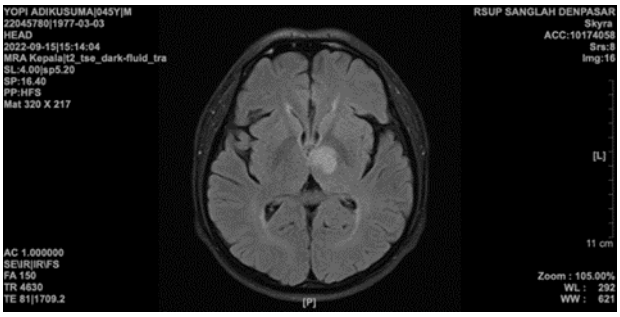

Figure 2. Acute cerebral infarct from thalamus to the left posterior horn of internal capsule (MRA results)

At his first visit as outpatient, his physical examination was abnormal with blood pressure 160/110 mmHg, pulse rate 86 times/minute, breathing 16 times/minute, temperature 36.50 C and oxygen saturation at 99% in room. Neurological examination found that he was fully alert with paresis of nerves VII and XII right supranuclear, right flaccid hemiparesis grade 4+. Cognitive function screening found impairment in attention and memory with MOCA-INA score 19/30 which means he has moderate cognitive impairment and ADL score of 0 with no need for assistance. According to this examination, he was diagnosis with vascular mild cognitive impairment (VaMCI).

At the moment, he is received treatment with aspirin 80 mg once daily, clopidogrel 75 mg once daily, citicoline 500 mg twice daily, simvastatin 20 mg once daily, ramipril 5 mg once daily and amlodipine 5 mg once daily, he also got cognitive stimulation once. His family said that he was getting better, and able to communicate with his friends in the office using chat app.

Result and Discussion

Vascular cognitive impairment (VCI) is a clinical condition which involves vascular brain injury in areas that are important for cognitive function, that span from mild cognitive impairment (VaMCI) to dementia.[3]

Our patient had confusion and impaired memory when asked questions, he also tend to think slowly and gave incorrect answers. He did not remember what happened to him prior to this event. Previously, he felt weakness in the right half of the body that happened suddenly accompanied by slurred speech. His family also notice this condition, where this patient was still able to go to the office and do his usual activities before. Presence of neurologic deficits with sudden changes in behaviour helped diagnose VCI. In this case, VCI appeared in the acute phase of stroke diagnosis because it happened within a few days after he was discharged. Ariswanda reported similar findings, where memory loss, confusion, and headaches happened as VCI manifestation within 29 hours after ischemic stroke was diagnosed.[4] Mellon said that 50% VCI occurred 6 months after stroke diagnosis.[5] Another study also showed that VCI appeared 3 months after stroke diagnosis, and found that infarct with volume of more than 100 ml was correlated with VCI dementia.[2] Vascular Cognitive Impairment was causes by formation of atherosclerosis, small vessel disease, cerebral amyloid angiopathy, and cerebral microbleed as explained by its pathophysiology.[6]

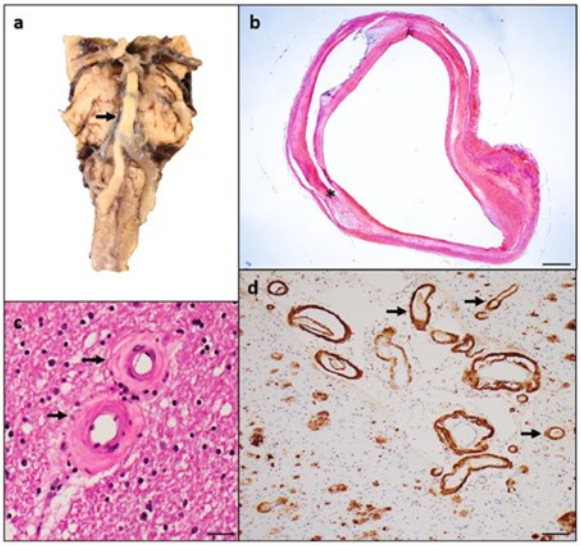

Figure 3. Pathological finding in VCI. (a) Atheroma in basilar artery which narrows the lumen of the blood vessel (b) Cholesterol in intimal hyperplasia (c). Penetrating arteriosclerosis (d). Cerebral amyloid angiopathy in parenchymal blood vessels.

Pathophysiology in atherosclerosis formation involve proliferation and accumulation of macrophages-lipids in the tunica intima in large blood vessel wall like the basilar and carotid arteries. These would cause calcification of atherosclerotic plaques, necrosis and stenosis of vessel wall, which leads to reduced blood flow, thrombus formation, impaired integrity in blood brain barrier (BBB), oxidative stress and inflammation. Risk factors for atherosclerosis formation were aging, LDL cholesterol, HDL cholesterol, triglycerides, hypertension, diabetes mellitus and smoking. Arteriosclerosis was characterized by arteriolar wall thickening, stenosis, and narrowing, of small arteries with diameter of 40-150 µm such as basal ganglia arteriole which extend to peripheral white matter, leptomeningeal, thalamus, cerebellum and brainstem artery. Cerebral amyloid angiopathy was accumulation of amyloid beta (Aβ) deposits in

parenchyma and capillaries of leptomeningeal artery. Cerebral amyloid angiopathy was cause by imbalance in Aβ production and Aβ degradation. This would lead to destructive changes in blood vessel wall such as loss of smooth muscle cells, microaneurysms, and fibrinoid necrosis, which increase vascular fragility. CAA could be found in blood vessels of cingulate cortex, hippocampus, entorhinal and amygdala. Cerebral microbleeds (CMB) was defined as hemorrhages with diameter less than 5 mm, which detected by gradient-echo T2-weighted MRI. Cerebral microbleeds was associated with subcortical small vessel disease and CAA.[6]

In our case, He had history of hypertension since 1 year ago and diabetes mellitus since 2 months ago but did not take medication regularly. People with hypertension have 3-4 times higher risk of having stroke compared to those without hypertension. Continuous high blood pressure will trigger injury in blood vessel endothelial cells. Hypertension also induces remodelling of blood vessel smooth muscle cells in systemic and cerebral vascular systems. Prolonged high intraluminal pressure in cerebral blood vessels will induce smooth muscle hypertrophy, remodelling or thickening, and hyperplasia of blood vessel walls, that cause narrowing of cerebral blood vessels lumen. Moreover, hypertension could cause lipohyalinosis in arteries and arterioles that supply the white matter which will made small infraction and cerebral hemorrhage. It also stimulates the formation of arteriosclerosis plaques in cerebral arteries and arterioles which could cause arterial occlusion.[7,8]

Diabetes mellitus is a very strong predictor of stroke. Hyperglycaemia is a predictor of endothelial dysfunction, arterial stiffness at young age, systemic inflammation, and thickening of vascular basement membrane. Endothelial dysfunction plays major role in inability to maintain structure, function, and integrity of the blood vessel walls, which cause imbalance in the Virchow Triad that leads to atherothrombotic process.[9] Diabetes was one of the risk factors for having thrombophilia, condition where thrombosis more easily develop.[10]

Brain MRA was done in our case, which found an acute cerebral infarct from thalamus to the left posterior horn of internal capsule, small vessel ischemic changes in the lateral periventricular, left and right centrum semiovale, and left corona radiata. Systematic review concluded that while white matter hyperintense (WMHs) explains the degree of cognitive decline, location of specific WMHs is associated with cognitive impairment rather than its volume. Especially impaired executive function and episodic memory. Anatomical sites where WMHs could have cause cognitive decline are thalamus, striatum, connections between frontal to parietal lobes, and the occipital lobes. Several studies showed that correlations between WMHs and cognitive impairment was more prominent in periventricular region which had many long-distance association fibers and inter-hemispheric fibers, than non-periventricular region where deeper transmission of WMHs involves relatively short association fibers. In the anterior-posterior axis, WMHs associated with poor executive function which located mostly in frontal area adjacent to the anterior ventricle. This location was the link between prefrontal cortex and thalamus, which highly relevant for executive function and processing speed. In posterior region, WMHs near the parieto-temporal are associated with worse memory performance, where it interferes the inferior or superior longitudinal fasciculus, and retrosplenial cingulum, which are known to play a role in memory function. Pathology of WMH known as triad of demyelinating, axonal loss, and lacunar infarctions, in periventricular and subcortical white matter. This was caused by microvascular changes due to arteriosclerosis, hyalinosis, and focal fibrinoid necrosis in vessels, with or without occlusion.[11] From our patient brain CT scan, we also found acute cerebral infarct in left thalamus. Impact of this lesion in thalamus depends on which territory of the vessels involved. In this case, there was a lesion in anterior nucleus of the thalamus which is supplied by the tuberothalamic artery causing impairment in short-term memory, visual or verbal learning, autobiographical memory and acalculia.

The Vascular Impairment of Cognition Classification Consensus Study (VICCCS) criteria were designed to reach a more comprehensive consensus on the concept of vascular-induced cognitive impairment, for diagnosis and clinical research.[12] Vascular Mild Cognitive Impairment (VaMCI) is impairment on one cognitive domain that might cause mild interference with activities of daily living (ADL) or instrumental activities of daily living (IADL) regardless of motoric and sensory sequelae. Major VCI (vascular dementia or VAD) is impairment that usually affect multiple cognitive domains, which cause moderate to severe impairment in ADL or instrumental activities daily living (IADL) regardless of motoric and sensory sequelae. Post Stroke Dementia (PSD) were immediate and/or delayed cognitive decline that happen after stroke and persists for 6 months. The PSD was cause by multiple cortico-subcortical infarctions, strategic infarctions, subcortical ischemic vascular dementia. Small vessel disease is the major cause of Subcortical ischemic vascular dementia (SIVaD). Lacunar infarct and white matter lesions are mainly subcortical. Multi-infarct dementia (MID) is associated with multiple cortical infarctions.

Mini-Mental State Examination (MMSE) and MoCA-INA are the test that usually used to evaluate cognitive function. Our patient test found deficit in attention and memory domains with MOCA-INA score 19/30 and ADL score 0. This means that he had moderate cognitive impairment but did not need assistance in daily activity. The

MMSE test result of this patient was 23/30 which means he had probable cognitive disorder. With two affected domains, presence vascular changes as shown by CT scan result, and no dependency in activities of daily living, he was diagnosed with vascular mild cognitive impairment.

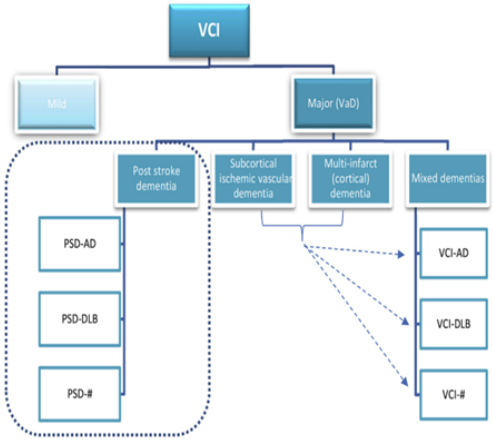

Figure 4. The Vascular Impairment of Cognition Classification Consensus Study (VICCCS)

Cognitive intervention is an effective non-pharmacological approach to address cognitive decline. Cognitive training, rehabilitation, and stimulation are the most well-known types of cognitive interventions. Cognitive training involves guided exercises to improve certain cognitive functions such as memory, attention or executive function. This training used computerized techniques as its media. It is efficient to correct ability to learn name-face associations in patients with amnestic-type MCI, increase visual attention with computerized cognitive exercises for MCI patients, restore functional and cognitive performance in patients with mild to moderate dementia, improved verbal memory, global cognitive function and semantic verbal fluency in patients with mild dementia.[13] Study showed that 12-week program of cognitive stimulation has beneficial effects on cognitive impairment, anxiety, and depression in people with MCI. Improvements were also seen in quality of life, particularly emotions, social functioning, mental and general health.[14]

Conclusion

The conclusion statement should contain a summary and suggestions. The summary should provide examples of answers given to the hypothesis and/or research objectives or findings obtained. The summary should not contain a repetition of the research results and discussion, but rather contain a summation of the research results and findings as expected in the research objectives or hypotheses. The suggestions should present things that will be done next about the concept of further research. Stroke not only cause physical disability, but also cognitive impairment. Vascular cognitive impairment that occurred in acute phase of a stroke may appear within days after patient was discharged. Hypertension and diabetes mellitus are risk factors for stroke. It could cause lipohyalinosis in arteries and arterioles that supply the white matter which will cause small infractions in white matter and thalamus. This condition cause breakdown of association fiber, which result in cognitive impairment with decreased speed of thinking processes, executive functions and memory loss. With early symptoms identification of vascular cognitive impairment, we could give immediate cognitive interventions to improve their quality of life.

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Ethical Consideration

Patient had received signed written informed consent regarding publication of their medical data in journal article.

Acknowledgment

All authors contributed equally in the writing of this report.

Conflict of Interest

The author reports no conflicts of interest in this work.

Author Contribution

All authors had contributed equally on manuscript preparation and agreed to final version of the manuscript for publication.

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