How to Cite:

Pramudya, R. A., Maharani, P., Ardhi, M. S., Sani, A. F., & Yustiarini, I. (2022). Challenging the diagnosis and treatment of central retinal artery occlusion (CRAO) in emergency department: A case report. *International Journal of Health Sciences*, 6(S8), 2779–2787. https://doi.org/10.53730/ijhs.v6nS8.12743

Challenging the diagnosis and treatment of central retinal artery occlusion (CRAO) in emergency department: A case report

Ridza Asrul Pramudya

Department of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia Corresponding author email: asrul.unair@yahoo.com

Putri Maharani

Department of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Mohammad Saiful Ardhi

Department of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Achmad Firdaus Sani

Department of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Ima Yustiarini

Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Abstract---Central retinal artery occlusion (CRAO) is an occlusion of the central retinal artery that causes a disruption of blood flow to the retina and may result in retinal ischemia. According to the American Heart Association/American Stroke Association (AHA/ASA), CRAO is a type of acute ischemic stroke. There is some variation in CRAO management. Determining the most effective therapy remains challenging. We report a male, 58th-years-old, with sudden vision loss in the right eye for 4 hours of onset upon arrival at the Emergency Department. Patient aware, with hypertensive crisis, the right eye visual acuity was 1/300. Brain Magnetic Resonance Imaging (MRI) revealed multiple small vessel ischemic in the cortical-subcortical area. The patient was hospitalized and received ocular massage, antiplatelet, antihypertensive, and lipid-lowering therapy. Visual acuity in the right eye was minimally improved at discharge. CRAO is a form of stroke in the retina and may occur concurrently or progress

Manuscript submitted: 9 May 2022, Manuscript revised: 18 July 2022, Accepted for publication: 27 August 2022

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.

into cerebral ischemia. Treatment with intravenous thrombolysis may be effective within 4.5 hours of onset. Ensuring the patient arrives at the emergency department and confirming the diagnosis of CRAO in this narrow time is still challenging.

Keywords---central retinal artery, CRAO, stroke, thrombolysis.

Introduction

Definition of stroke by American Heart Association/American Stroke Association (AHA/ASA) 2013 includes any objective evidence of brain, spinal cord, or retinal cell death attributed to ischemia based on pathological, imaging or other objective evidence with or without the presence of neurological dysfunction (Sacco et al., 2013). Central retinal artery occlusion (CRAO) is a form of acute ischemic stroke as recognized by the AHA/ASA (Grory et al., 2020a). CRAO is an ophthalmologic and neurologic emergency that causes a disruption in blood flow to the retina, resulting in the acute onset of retinal tissue dysfunction (Grory et al., 2020b). Incidence of CRAO 1 per 100,000 in a single-county US population (Dumitrascu et al., 2020). AHA/ASA guideline for the treatment of acute ischemic stroke do not specifically address CRAO, but according to the current evidence, CRAO should be treated as an emergency as acute cerebral ischemic stroke (Grory et al., 2020b), although controversy still remains regarding the benefit of acute reperfusion therapies in CRAO (Dumitrascu et al., 2020).

Indonesia is facing increasing stroke prevalence in the past 5 years (Mesiano et al., 2021). According to Indonesian basic health research in 2007, the national prevalence of stroke is 8.3 per 100,000 population (Yudiarto et al., 2014). Stroke is a major cause of mortality and disability worldwide (Machfoed et al., 2016), and the cost of treatment is very high (Erawantini et al., 2018). Developing countries like Indonesia should work hard to provide the best hyperacute stroke care with protocol deviation and limitation (Mesiano et al., 2021).

Case Report

We present the case of a 58th years old man, with sudden vision loss on his right eye without ocular pain. Duration of onset was 4 hours before arrival at the Emergency Department. The patient is a heavy smoker, had a history of uncontrolled hypertension and hyperlipidemia, without a previous stroke history or a family history of stroke. The patient had not seen flashes of light, floaters or curtains, and also no red, watery eyes, itchy or drooping of eyelid. Patient aware, with markedly increase in blood pressure. At the time when the patient arrived at the emergency department, blood pressure was 210/120 mm Hg, and the right eye visual acquity was 1/300, with Relative Afferent Pupillary Defect (RAPD). Right eye funduscopic examination revealed to CRAO, with normal color and defined optic disc, retinal image is pale, narrowed blood vessels, cherry red spot sign and decreased macular reflex. There is no neurological deficit in the patient other than decrease of visual acquity. According to laboratory findings, there was an increase in lipid density lipoprotein (LDL) cholesterol 133 mg/dl. Electrocardiogram showed sinus rhythm and no intracardiac thrombus based on echocardiography. Brain MRI was performed and shows multiple small vessel ischemic in cortical and subcortical area. Magnetic Resonance Angiography (MRA) revealed no intracranial arterial stenosis or other vascular malformations. The patient was hospitalized for 5 days. Treatment for the patient include: antiplatelet, acetazolamide, anti hypertensive treatment, lipid-lowering therapy, and ocular massage to dislodging the embolus. There was minimally improvement in visual acquity at discharge. Visual acquity in the right eye improved from light perception upon admission to 50cm counting fingers.



Figure 1. Funduscopic findings. In the right eye there is a sign of "cherry-red spot"



Figure 2. Optical Coherence Tomography (OCT) HD of the patient. The right eye has retinal edema



Figure 3 (A). Optical Coherence Tomography Angiography (OCTA) in the right eye



Figure 3 (B). OCTA in the left eye



Figure 4. Brain MRI of the patient on axial, sagital, coronal view with MRA

Discussion

The Central Retinal Artery (CRA) originates from the ophthalmic artery, a branch of the internal carotid artery (Sharma et al., 2018). Once the central retinal artery is occluded, survival of the retina depends on the completeness of occlusion (Jurado et al., 2022), the degree of collateralization and the duration of retinal ischemia (Grory et al., 2020b). According to this mechanism, CRAO may leads to acute retinal infarction (Dumitrascu et al., 2020). CRAO is a form of acute ischemic stroke as defined by AHA/ASA (Sacco et al., 2013), results in sudden, painless, usually permanent loss of vision in the affected eye (Grory et al., 2020a). An ophthalmological evaluation is necessary to confirm the diagnosis of CRAO and rule out other disorders that can cause acute painless loss of vision (Grory et al., 2021).

There is some reasons why there is no strong evidence-based treatment for CRAO. First there is no significant collateral circulation distal to CRAO predisposes to infarction after occlusion. Second, CRA lumen is tiny and easily occluded. Third, retinal ganglion cells are highly vulnerable to ischemia. Fourth, embolic CRAO is common and resistant to thrombolysis. Finally, CRAO studies are problematic because CRAO is rare disease, and there are only a few controlled studies (Chronopoulos & Schutz, 2019).

Ischemic stroke guidelines do not explicitly mention CRAO at present (Grory et al., 2021), but according to the current evidence, CRAO should be treated as an emergency in the same manner as acute cerebral ischemic stroke (Grory et al., 2020b). According to AHA/ASA guidelines for the early management of acute ischemic stroke 2019, intravenous alteplase is recommended for patients with mild but disabling stroke symptoms within 3 hours of onset (strong recommendation). However, patients within 3 and 4.5 hours onset are given weak recommendations for intravenous alteplase therapy (Powers et al., 2019). In our case presentation, the patient came within 4 hours of onset, classified as mild disabling stroke. Time window for thrombolysis is 4.5 hours of onset. Making an accurate and timely CRAO diagnosis in this limited time with our various limitation in emergency department remains challenging. And the important thing to be considered here is whether the patient still has an indication for intravenous alteplase therapy, or sufficient with dual antiplatelet therapy. There was minimally improvement of visual acquity after administration of antiplatelet, anti hypertensive and lipid lowering therapy. However, thrombolysis is not an approved therapeutical option in CRAO yet (Jurado et al., 2022). Other challenge in evaluating potential therapies for CRAO involves the uncertainty regarding retinal tolerance time or the duration of retinal ischemia, after which irreversible infarction occurs. Ganglion cell layer of nonhuman primates will survive without infarction if central retinal artery perfusion is restored within 90-240 minutes following experimental occlusion (Sharma et al., 2021). Tobalem et al. (2018) reported that retinal infarction is most likely to occur after only 12-15 minutes of complete CRAO (Tobalem et al., 2018).

The first important step in the prehospital cascade of CRAO is to recognize CRAO symptoms and the knowledge of acute CRAO management (Jurado et al., 2022). Code eye stroke team must include an in person or virtual eye care provider to help establish the correct diagnosis and exclude ocular signs that may prohibit thrombolytic therapy (Mehta et al., 2017). The role of the ophthalmologist in the management of acute CRAO is essential (Sharma et al., 2021). Ophthalmological and neurological assessment to exclude possible differential diagnosis, as well as immediate brain and vascular imaging, should be standardized, similar to the

stroke pathways. Losing time in this situation is losing one eye with all its consequences on quality of life (Jurado et al., 2022). Eye care professionals must make a rapid and accurate diagnosis and recognize the need for timely expert intervention by immediately referring patients with acute retinal arterial ischemia to specialized stroke centers (Biousse et al., 2018).

CRAO awareness of the general population and physician about the treatment options as well as the non-standardized prehospital organization, seems to be the main reason for the prehospital delays and impedes treating CRAO patients. Educational efforts should be undertaken to improve awareness about CRAO. A low awareness about the disease as well as right approach lead to treatment delays (Jurado et al., 2022). The recognition of sudden-onset visual changes as stroke-like symptoms prompted the recent upgrade into BE-FAST (adding B for balance and E for Eyes/Vision) and its incorporation into various educational programs (Dumitrascu et al., 2020). Furthermore, the COVID 19 pandemic must be highlighted right now, which associated with a global decline in the volume of overall stroke hospitalizations (Nogueira et al., 2021).

In switzerland, almost 100% of the ophthalmologist and general practitioners recognized CRAO as a medical emergency and 1/3 of them considered IV thrombolysis a potentially beneficial therapy. Concomitant (silent) brain ischemia was detected in 32% of the CRAO patients. This is demonstrates importance of brain imaging before considering thrombolysis, and the the need for speedy etiological stroke work-up of patients with CRAO (Jurado et al., 2022). One major concern related to CRAO relayed by numerous reports in worldwide is the lack of patients presentation in specialized stroke centers or emergency departments in the currently accepted time window for thrombolysis therapy (Dumitrascu et al., 2020). This problem should be a concern in the management of crao in Indonesia. Indonesia is a country with a large geographical area. Transportation problem and referral system is still growing in this large area, and more hospitals have begun to develop a code stroke system. Rasyid et al. (2019) reported that in an Indonesian referral hospital, hemorrhage on CT scan was the most common reason patients did not receive thrombolysis following by low or improved NIHSS score, family refusal, and exceedance of time window (Rasyid et al., 2019).

Conclusion

CRAO can cause visual disturbances, which has a great impact in quality of life of the patient. CRAO causes stroke in the retina and has a risk to develop into cerebral ischemic. Treatment with intravenous thrombolysis may be effective within 4.5 hours of stroke symptoms onset. Ensure the patient to arrive at the emergency room and confirming the diagnosis of CRAO within 4.5 hours of onset, still requires efforts, especially in developing countries with large geographic areas such as Indonesia. Furthermore, the availability of diagnostic support services in hospitals and health care facilities in order to establish a CRAO in a short period of time must be considered. Pre hospital and emergency treatment pathway need to accomplished and requires collaboration of neurologist and ophthalmologist.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the Editor-in Chief of this journal on request.

Highlights

- 1. CRAO is a form of acute ischemic stroke as recognized by the AHA/ASA and should be treated in an emergent fashion in the same manner as acute cerebral ischemic stroke.
- 2. Code eye stroke team must include an ophthalmologist to help establish the correct diagnosis and exclude ocular signs that may prohibit thrombolytic therapy.
- 3. More research is required to determine the efficacy of thrombolytic therapy in CRAO and mild disabling stroke within 3 hours and 4.5 hours of symptom onset.

References

- Ardila Jurado, E., Sturm, V., Brugger, F., Nedeltchev, K., Arnold, M., Bonati, L. H. (2022). Central Retinal Artery Occlusion: Current Practice, Awareness and Prehospital Delays in Switzerland. Frontiers in neurology, 13, 888456. https://doi.org/10.3389/fneur.2022.888456.
- Biousse, V., Nahab, F., Newman, N. J. (2018). Management of acute retinal ischemia: follow the guidelines!. Ophthalmology, 125, 1597-1607. doi: 10.1016/j.ophtha.2018.03.054.
- Chronopoulos, A., & Schutz, J. S. (2019). Central retinal artery occlusion-A new, provisional treatment approach. Survey of ophthalmology, 64(4), 443–451. https://doi.org/10.1016/j.survophthal.2019.01.011.
- Dumitrascu, O. M., Newman, N. J., & Biousse, V. (2020). Thrombolysis for Central Retinal Artery Occlusion in 2020: Time Is Vision!. Journal of neuroophthalmology : the official journal of the North American Neuro-Ophthalmology Society, 40(3), 333–345. https://doi.org/10.1097/WNO.00000000001027.
- Erawantini, F., & Karimah, R. N. (2018). Early Warning Systems (E-Wars) Design for Early Detection of Stroke Incidence. Folia Medica Indonesiana, 54(2), 136– 140. https://doi.org/10.20473/fmi.v54i2.8864.
- Grory, B. M., Lavin, P., Kirshner, H., and Schrag, M. (2020b). Thrombolytic Therapy for Acute Central Retinal Artery Occlusion. Stroke, 51(2), 687–695, 2020b. https://doi.org/10.1161/STROKEAHA.119.027478.
- Grory, B. M., Nackenoff, A., Poli, S., Spitzer, M. S., Nedelmann, M. (2020). Intravenous Fibrinolysis for Central Retinal Artery. Stroke, 51(7), 2018–2025, 2020a. https://doi.org/10.1161/STROKEAHA.119.028743.
- Grory, B. M., Schrag, M., Biousse, V., Furie, K. L., Herman, M. G. (2021). Management of central retinal artery occlusion: A scientific statement from the American heart association. Stroke, 52(6), e282-e294, 2021. https://doi.org/10.1161/STR.00000000000366.
- Intriago, C. Z., & Posligua, T. I. Q. (2020). Telecommunications and virtualization in times of pandemic: impact on the electrical engineering career. *International*

Journal of Physical Sciences and Engineering, 4(3), 38–44. https://doi.org/10.29332/ijpse.v4n3.630

- Machfoed, M. H., Kurniawan, M., & Usman, F. S. (2017). Review article: Does Intra-Arterial Heparin Flushing (Iahf) can Actually Increase Manual Muscle Test (Mmt) Score in Chronic Ischemic Stroke Patients?. Folia Medica Indonesiana, 52(2), 148–153. https://doi.org/10.20473/fmi.v52i2.5232.
- Mehta, N., Marco, R. D., Goldhardt, R., & Modi, Y. (2017). Central Retinal Artery Occlusion: Acute Management and Treatment. Current ophthalmology reports, 5(2), 149–159. https://doi.org/10.1007/s40135-017-0135-2.
- Mesiano, T., Kurniawan, M., Saputri, K. M., Hidayat, R., Permana, A. P., Rasyid, A., Harris, S. (2021). Endovascular Treatment in Acute Ischemic Stroke Adoption and Practice: A Single-Center Indonesian Experience. Cerebrovasc Dis Extra, 11, 72-76. https://doi.org/10.1159/000517183.
- Nogueira, R. G., Abdalkader, M., Qureshi, M. M., Frankel, M. R. (2021). Global impact of COVID-19 on stroke care. International journal of stroke : official journal of the International Stroke Society, 16(5), 573–584. https://doi.org/10.1177/1747493021991652.
- Powers, W. J., Rabinstein, A. A., Ackerson, T., Adeoye, O. M. (2019). Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke," Stroke, 50(12), e344-e418, 2019. https://doi.org/10.1161/STR.00000000000211.
- R. A. Sharma, M. Dattilo, N. J. Newman, and V. Biousse. (2018). Treatment of nonarteritic acute central retinal artery occlusion. Asia-Pacific J. Ophthalmol, 7(4), 235–241. https://doi.org/10.22608/APO.201871.
- Rasyid, A., Harris, S., Kurniawan, M., Mesiano, T., Hidayat, R., Rilianto, B., & Sholeha, R. A. (2019). The Reasons Acute Stroke Patients Not Receiving Thrombolysis in an Indonesian Referral Hospital. International Journal of Pharmacy and Pharmaceutical Sciences, 11(11), 43–46. https://doi.org/10.22159/ijpps.2019v11i11.35373.
- Sacco, R. L., Kasner, S. E., Broderick, J. P., Caplan, L. R., Connors, J. J., Culebras, A., Elkind, M. S., George, M. G., Hamdan, A. D., Higashida, R. T., Hoh, B. L., Janis, L. S., Kase, C. S., Kleindorfer, D. O., Lee, J. M., Moseley, M. E., Peterson, E. D., Turan, T. N., Valderrama, A. L., Vinters, H. V., ... Council on Nutrition, Physical Activity and Metabolism (2013). An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke, 44(7), 2064– 2089. https://doi.org/10.1161/STR.0b013e318296aeca
- Sembiring, T. B., Maruf, I. R., Susilo, C. B., Hidayatulloh, A. N., & Bangkara, B. M. A. S. A. (2022). Health literacy study on approaching forest and boosting immune system strategy. *International Journal of Health Sciences*, 6(1), 40–49. https://doi.org/10.53730/ijhs.v6n1.3145
- Sharma, R. A., Newman, N. J., & Biousse, V. (2020). Conservative treatments for acute nonarteritic central retinal artery occlusion: Do they work?. Taiwan journal of ophthalmology, 11(1), 16–24. https://doi.org/10.4103/tjo.tjo_61_20.
- Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, 6(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949

Tobalem, S., Schutz, J.S. & Chronopoulos, A. (2018). Central retinal artery occlusion – rethinking retinal survival time. BMC Ophthalmol, 18, 101. https://doi.org/10.1186/s12886-018-0768-4.

Yudiarto, F., Machfoed, M., Darwin, A., Ong, A., Karyana, M., and Siswanto. (2014). Indonesia Stroke Registry (S12.003) Apr 2014, 82 (10 Supplement) S12.003. Neurology, 82(10).