SECOND ATTACK HEMORRHAGE STROKE IN PATIENTS WITH A PREVIOUS HISTORY OF ISCHEMIC STROKE WITH HYDROCEPHALUS EXVACUO

Cantika Vadia Aqli, Feda Anisah Makkiyah*

Neurosurgery Department, Faculty of Medicine, Universitas Pembangunan Nasional "Veteran" Jakarta, South Jakarta, Jakarta, Indonesia 12450

*Correspondence: fedaanisah@upnvj.ac.id

ABSTRACT

A second attack stroke is a nightmare for patients, especially elderly patients. This stroke is the most prevalent consequence of stroke, with a substantially greater fatality rate than a first stroke, supported by a history of uncontrolled hypertension of diabetes mellitus (DM), individual experience with ischemic stroke, family record of ICH, low cholesterol levels, as well as warfarin administration, especially in the event of ICH. A woman, Mis. M, 68 years old, with complaints of sudden weakening on the right side and slurred speech since 1 hour before entering the hospital, the patient has a record of hypertension, DM, and a history of sudden visual impairment with a final diagnosis of ischemic stroke 6 months ago. The results of the CT scan (Computed Tomogrpahy) without contrast showed a hyperdense lesion in the left temporalis; the bleeding volume was ±34.28 cc, surrounded by cerebral edema; the cortical sulci looked wide; the gyri were prominent; the ventricular system also looked wide; there was no midline shift; and there was cerebral atrophy with hydrocephalus communicans type hydrocephalus ex vacuo infarction long in the left occipital lobe. The patient received therapy with medication for hypertension, DM, mannitol, and vitamin K, and intracerebral bleeding was carried out with craniotomy for indications of hematoma, and there is no therapy for ex vacuo hydrocephalus.

Keywords: Exvacuo Hydrocephalus; Intracerebral Hemorrhage; Second Attack; Stroke

Received: Month Year, *Accepted: Month Year,* *Published: Month Year*

INTRODUCTION

Stroke is a clinical manifestation of impaired brain function that occurs focally or globally. Solely caused by disorders of the cerebral blood vessels (Chen et al., 2014). This condition is extremely serious because the brain is a crucial organ that regulates all bodily activities. If you have a stroke, it will result in motor organ dysfunction in the human body (Muhammad, 2017). About 80% of strokes are ischemic, due to occlusion of cerebral blood vessels, while hemorrhagic strokes occur when cerebral blood vessels rupture and cause bleeding (Unnithan et al., 2023). The World Health Organization explains that stroke is a disease that can cause disability and death (WHO, 2019). Stroke causes 87% of deaths and disabilities worldwide. According to the findings of Basic Health Research, the incidence of stroke in Indonesia is increasing year after year. In 2013, the stroke incidence rate in Indonesia was 7% per mile, but now it is 10.9% per mile (Kemenkes, 2018).

The problem is that this burden continues to increase; therefore, there is a need to focus on increasing the reduction in death rates due to intracranial hemorrhage and increasing the number of survivors after hemorrhagic stroke (DeLago et al., 2022). Stroke is not only a threat to life; nevertheless, it is also a significant cause of important, especially in the elderly, and contributes significantly to the loss of productive years both nationally and globally (WHO, 2019). One of the most common complications of stroke

is a second attack stroke, which shows a much higher mortality rate than the first stroke, supported by a history of uncontrolled hypertension or DM, individual experiences with ischemic stroke, family records of ICH, low cholesterol levels, and the consumption of warfarin, especially in cases of ICH. By playing a role in controlling these risk factors, we can optimally prevent a second stroke (Avan et al., 2019).

Optimal first-line acute stroke treatment and subsequent prevention play a vital role in minimizing patient losses, maintaining quality of life, and preventing second-attack strokes. Control of major risk factors, including hypertension, DM, hyperlipidemia, and lifestyle changes, is the foundation for effective prevention strategies (Siswanto, 2005). Secondary prevention for ischemic stroke involves dietary modification, aerobic exercise, aspirin, statins, and antihypertensive drugs (Guzik et al., 2017). Tailoring treatment to the stroke subtype is critical to reducing the risk of recurrence. Then the treatment of ICH varies from medication therapy to open surgery to actively remove the hematoma (Lapchak et al., 2007).

This case report highlights second attack stroke, intracerebral hemorrhage, and hydrocephalus exvacuo.

CASE

A woman, Mis. M, 68 years old, came to the emergency unit at Meri Hospital (type C hospital in Java) with complaints of sudden right side weakness and slurred speech since 1 hour before entering the hospital. According to the relative who brought the patient, for the previous 6 days he often complained of headaches until he suddenly felt weakness in his right arm and leg, accompanied by slurred speech, and vomited once. Other complaints, such as numbness, tingling, decreased consciousness, fever, and convulsions during attacks, are denied, as are normal defecation and urination. Complaints of a slanted mouth, slurred speech, and weakness on the right side have persisted since they first appeared. After receiving treatment in the emergency room, the patient received a CT scan, and the results showed ICH. After observation, the patient suddenly experienced a loss of consciousness, so the patient was advised to undergo a craniotomy to evacuate the existing blood.

There is no history of fever or trauma to the head, but he has a history of hypertension and DM for approximately 10 years at SMRS and regularly comes to the neurology clinic because he has a history of blockages in the brain, and during treatment, these blockages were discovered at first to have symptoms in the patient's view that suddenly decreased until the family decided to go to a neurologist, and this was discovered; this happened approximately 6 months ago. The patient also has a history of heart disease and chronic kidney disease. Relevant family history is that his mother suffered from hypertension and died due to stroke. The patient has taken medications such as amlodipine 10 mg, metformin 500 mg, atorvastatin 20 mg, and thrombospirin 30 mg. The patient's family said the patient did not normally take these medicines.

Physical diagnosis: GCS E3VTM3, BP 200/100, HR 110, the same on both sides, lifting strength, and fully loaded, RR 20, T 37.8. The general survey showed no abnormalities on this physical examination. Neurological examination showed that facial nerve VII examination showed asymmetrical nasolabial folds, flattened to the right, and examination of NXII hypoglossal examination found dysarthria. For the motor examination, it was found that movement was limited and lacking in the right limb, with a strength of 222 and spastic tone. Then for normal physiological reflexes, no pathological reflexes were found.

Imaging findings show a hyperdense lesion in the left temporalis, with a bleeding volume of ± 34.28 cc surrounded by cerebral edema, and the cortical sulci look widened; the gyri are prominent; the ventricular system also looks widened; there is no midline shift; there is cerebral atrophy with hydrocephalus communicans; and there is an infarction long in the left occipital lobe (Figure 1).

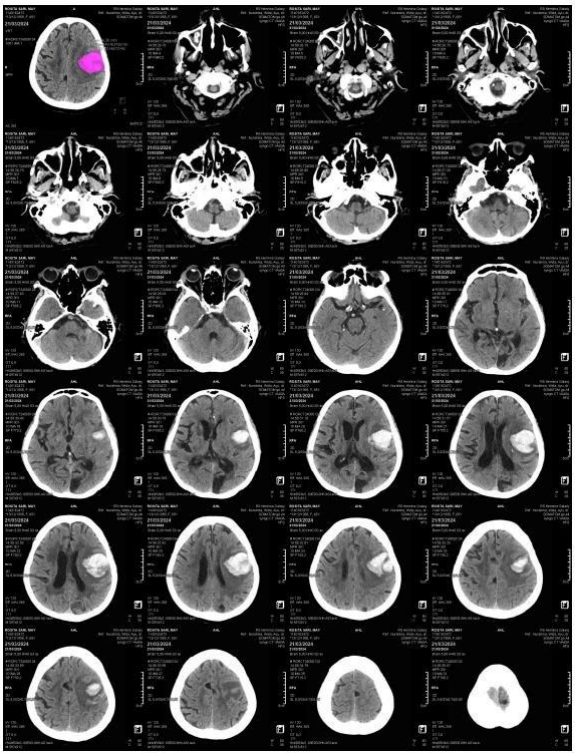

Figure 1. CT scan without contrast show hyperdense lesion in the left temporalis, bleeding volume ± 34.28 cc, surrounded by cerebral edema, and the sacral cortex looks widened; the gyri are prominent; the ventricular system also looks widened; there is no midline shift; cerebral atrophy with hydrocephalus communicans; and infarction long in the left occipital lobe.

The treatment given to the patient was a primary survey starting from airway, breathing, circulation, and head elevation of 30°. 1 day later, the patient underwent a craniotomy procedure to evacuate blood in the patient's brain, and an external ventricular drain (EVD) was installed. Then post-operation day 1, the patient was treated in the ICU with GCS E3M5VT, prescribed IV tranexamic acid 1 amp every 8 hours, and mannitol 100 cc within 6 hours, and consulted a doctor in the field of nerves. There were no results from the drain that was installed, and then after 2 days the drain was removed.

The weaknesses of this case report of lack of early intervention or explanation of the pre-hospital timeline. The report does not provide much detail on the reasons for non-adherence (whether it was due to side effects, misunderstanding of the treatment plan, or other factors). Then, long-term care and rehabilitation strategies. Then, the report provides no mention of long-term care plans, including rehabilitation, for a patient with significant neurological deficits post-stroke.

DISCUSSION

This case report was obtained from a female patient, Mis. M, 68 years old, with complaints of sudden weakness on the right side and slurred speech since 1 hour before entering the hospital. Accompanied by a history of vomiting once accompanied by complaints of headaches for 6 days, the patient is known to have a history of hypertension and DM since 10 years ago and a history of ischemic stroke ± 6 months ago. The patient has taken medications such as amlodipine 10 mg, metformin 500 mg, atorvastatin 20 mg, and thrombospirin 30 mg. The patient's family said that the patient did not regularly take these medicines, and physical examination showed GCS E3VTM3, which indicates decreased consciousness and hypertensive emergency, while neurological examination showed that facial nerve VII examination showed asymmetrical nasolabial folds, flattened to the right, and examination of NXII hypoglossal examination found dysarthria. For motor examination, it was found that movement was limited and lacking in the right limb, with a strength of 2222 and spastic tone.

Hemorrhagic stroke itself occurs when the brain parenchymal blood vessels rupture into the subarachnoid layer (SAH) or into the brain (ICH). This is based on various causes, such as wall damage due to atherosclerosis, trauma, inflammation (vasculitis), or congenital abnormalities (aneurysms, arteriovenous malformations), and this is made easier when there is a sudden increase in blood pressure or in hypertensive patients (Kuriakose et al., 2020). The bleeding that occurs causes an increase in intracranial pressure with symptoms of headache, nausea, vomiting, and decreased consciousness, as can be seen in the patient in this case.

The incidence of primary strokes and second attack strokes is associated with various risk factors, both modifiable and non-modifiable. Modifiable factors include hypertension, coagulopathy (related to drug use), using antiplatelet drugs, smoking, alcohol, and DM, while non-modifiable factors include chronic kidney disease, congenital coagulopathy, tumors, and blood vessel lesions such as aneurysms and AVMs (Fekadu et al., 2019). This patient had both modifiable risk factors, namely a history of hypertension, DM, and history of use of antiplatelet drugs, and also had non-modifiable risk factors, namely old age.

The incidence of recurrent stroke is 1.2% in the first 30 days, 3.4% in 90 days, 7/4% in 1 year, and 19.4% in 5 years (Stahmeyer et al., 2019) and is known to show a much higher mortality rate than the first stroke. In Indonesia, the incidence of strokes is around 750.000 per year, with the number of recurrent strokes being 200.000 people, including (Amila, 2019). The occurrence is closely related to risk factors that still exist and are not managed, namely a history of uncontrolled hypertension or DM, personal experience of ischemic stroke, family history of ICH, along with low cholesterol levels, and consumption of warfarin, especially the number of cases of ICH, and are associated with risk factors of age, gender, race, and genetics, where patients with risk factors >1 have an increased risk factor for recurrent strokes (Avan et al., 2019). It is said to be a second attack if there is a new neurological deficit or an exacerbation of a previous deficit and is not due to a toxic condition or other acute illness. The event includes an anatomical area or blood vessels that are different from the first stroke, and the event has a different subtype of stroke from the first stroke.

This is in line with patients who have factors, namely old age, genetics, a history of uncontrolled hypertension and DM, and a history of previous ischemic stroke. According to the Hankey et al. cohort study, older age >65 years at the first stroke has a higher risk of having a recurrent stroke (Hankey et al., 2014). Next is genetics, namely if both patients have a history of stroke then the possibility of it occurring stroke is greater, namely in mothers who suffer from stroke it presents an important risk in blood pressure, plasma fibrinogen, and obesity which supports this occurrence.

The next factors, namely hypertension, are linked to progressive atherosclerosis in the arch of the aorta and cervicocerebral arteries, arteriosclerosis, and lipohyalinosis in small diameter and cerebral arteries. This is in accordance with the results of a cohort study by Friday et al. in 2002, which reported the incidence of recurrent strokes of 9.7% among 535 patients with blood pressure follow-up. It was found that patients with diastolic blood pressure >80 mmHg had a 2.4 times greater risk of developing second attacks as well as systolic BP > 140 mmHg (Friday et al., 2002). Furthermore, the last risk factor that patients have is DM, which is in accordance with the results of research by Husni in 2001, namely that patients who have DM have a 3.18 times higher risk of recurrent stroke; this is associated with the occurrence of atherosclerosis, both microangiopathy and macroangiopathy throughout the disease. The body, including the brain, and diabetes patients are unable to handle sugar properly, cannot process fat efficiently, and therefore have a high risk of hypertension, which also leads to an increased risk of recurrent strokes (Siswanto, 2005).

CT-scan is a simple and very sensitive tool for diagnosing ICH and intraventricular hemorrhage (IVH), given that blood density is higher than the brain and using the ABC method and assessing the extent of IVH, both of which impact clinical outcomes. The initial appearance on the CT scan (blend, island, swirl, and black hole signs) indicates the possibility of extensive bleeding. Contrast enhanced CT-scan and angiography allow imaging of other features such as spot signs (contrast leakage also indicates ongoing bleeding) and can reveal underlying aneurysms and arteriovenous malformations (secondary ICH) (Kim et al., 2017). In addition, magnetic resonance imaging (MRI)

can also be used, which provides for enhanced visualization of hematoma evolution through time and is more sensitive than CT to identify underlying malignancies, arterial or venous infarction, and angiographically hidden vascular abnormalities (Macellari et al., 2014).

In this patient, the results showed a hyperdense lesion on the left temporalis, the bleeding volume was ± 34.28 cc, surrounded by cerebral edema, and the sacral cortex looked widened; the gyri were prominent; the ventricular system also looked widened; there was no midline shift; cerebral atrophy with hydrocephalus communicans; as well as an old infarction in the left occipital lobe. This shows several things, namely the presence of new hemorrhagic lesions accompanied by ischemic lesions that have occurred before, which supports the result of anamnesis with the patient's family; namely, ± 6 months ago, he complained of sudden decreased vision, then he was taken to a neurologist and diagnosed with a blockage in the brain, supported by results of the CT scan performed. This indicates the presence of recurrent strokes, and from these results, apart from the signs of strokes, hydrocephalus also occurred in this patient.

This patient's CT scan showed a picture of comminating hydrocephalus. Hydrocephalus is caused by anything that disrupts the balance mechanism between CSF absorption, production, and flow (Bramall, 2022). Looking at the results of the CT scan that was carried out on this patient, it was found that the patient had hydrocephalus communicans; this can be associated with cerebral atrophy in the patient. This is seen from the results; there is a prominent image of the sulcus accompanied by lateral ventricles, or what is called ventriculomegaly, which is widened without a hyperdense image in it, which indicates that the hydrocephalus experienced by the patient is not caused by the influence of the stroke hemorrhage that occurred but is suspected to be due to a process of cerebral atrophy. This can occur because the loss of brain tissue is related to the aging process of the brain so that the empty space will be filled passively by CSF, eventually resulting in communicant-type hydrocephalus; the term that can describe this situation is ex vacuo hydrocephalus (Hattingan et al., 2010).

Hydrocephalus ex vacuo is often compared with the diagnosis of normal pressure hydrocephalus (NPH). This patient was directed to hydrocephalus ex vacuo apart from the CT-scan results mentioned previously, as well as the absence of the NPH triad, which was not fulfilled, either urinary incontinence, dementia, or gait disturbance (Hwang et al., 2016). NPH with hydrocephalus ex vacuo can be differentiated by the presence of dilatation of the temporal horns (Tans, 2004). To further strengthen the diagnosis, comparing NPH with hydrocephalus ex vacuo, MRI can be used, namely in NPH a small callosal angel, dilatation of the sylvian fissure, and narrowing of the superior parietal sulcus are found (Kim et al., 2021). Unfortunately, an MRI has not been performed yet in this patient.

In practice, ICH management looks at it from a multifactorial perspective, starting from managing risk factors, medical management to prevent worsening after initial bleeding, and consideration of surgical management, as well as preventing recurrent strokes.

Management of the first risk factors is the administration of antihypertensive drugs; this is associated with poor outcomes, including death, and persistent increases in blood pressure reduce the patient's condition during hospitalization (Unnithan et al., 2023) and several studies have shown that variability. High SBP during acute ICH is associated with poor outcomes (Moullaali et al., 2019). Blood pressure targets are still under debate, but the Association/American Stroke Association in 2015 concluded that an acute reduction in SBP to <140 mmHg is safe and can improve outcomes. Administration of drugs to control blood pressure must be fast and precise without inducing hypotension, so agents can be used, such as fast-acting titration such as nicardipine (Qureshi et al., 2010).

In other sources, it is said that there has not been enough information to inform the selection of blood pressure-lowering medicines during the hyperacute phase after ICH, including bolus or drip treatment. Intravenous nicardipine is one of the recommended drugs (Bath et al., 2019). Other guidelines also recommend administering intravenous nicardipine to control increased blood pressure in acute ICH at a dose of 5–15 mg/hour (Bioderrick et al., 2023). Nicardipine works as a dihyropyridine calcium channel blocker, which functions in the role of a vasodilator, lowering blood pressure without affecting cardiac contractility. Multiple research studies have demonstrated that reductions in SBP are related to both plasma levels of nicardipine and that the time to achieve a therapeutic response is shorter with higher doses of the drug. Additionally, the minimum of 5 mg/hour of intravenous nicardipine must be administered to achieve a substantial decrease in blood pressure in significantly hypertensive patients with pretreatment DBP greater than 115 mmHg. It needs to be mentioned that nicardipine has acidic qualities (pH 4.0) and occasionally causes phlebitis; hence, it is often essential to dilute nicardipine with the same or greater amount of salt (Koga et al., 2014).

Management of the second risk factor is controlling blood glucose levels. This is supported by the fact that hyperglycemia in the easily symptoms indicate a worse prognosis for the patient (Kim et al., 2017), but it is also necessary to pay attention to low sugar levels/hypoglycemia (<40-60 mg/dL) can also worsen the existing prognosis (Van den Beighe et al., 2012). The recommended target blood sugar (BG) level is <180 mg/dL; this target is supported by research results that show lower mortality rates in hospitals for this BG target and management of BG control given subcutaneous insulin (Finfei et al., 2009).

Management of the third risk factor provides management if there are indications of ICH related to previous consumption of anticoagulant drugs (OAK). The risk of hematoma expansion (HE), rapid deterioration, and poor outcome is increased in ICH patients undergoing anticoagulation therapy. Management requires immediate termination and immediate reversal of emergency anticoagulation without waiting for the INR test results to be available or not (Steiner et al., 2016). It is known that life expectancy increases in patients who are given immediate anticoagulation treatment with a significant reduction in HE and lower hospital mortality (Kuramatsu et al., 2015). The drugs recommended for use are adjusted to the OAK used, such as OAK warfarin given vitamin K, UFH and LMWH given piotamine sulfate, dabigatian, apixaban, and rivaroxaban can be given prothrombin complex concentrate (PCC) (Ray et al., 2014)**.**

Management of the fourth risk factor is given to patients who are diagnosed with antiplatelet-related hemorrhage. The true impact of antiplatelet medicines on ICH outcomes is unknown. But according to the journal, it is said that antiplatelets cause recurrent strokes, which are associated with antiplatelet resistance. This, with resistance, can still cause thrombi to occur, one of which is in the intracranial arteries, which can trigger recurrent strokes. Based on the mechanism, antiplatelet resistance is divided into 2, namely presence of antiplatelet resistance when inhibition is inadequate in COX-1 or thromboxane A2 or antiplatelet resistance occurs despite COX-1 or P2Y12 inhibition being adequate (Prisco et al., 2009). A systematic evaluation of 25 observational studies discovered that antiplatelet medication at the exact moment of bleeding was related to a 27% increase in mortality but no functional results (Thompson et al., 2010). In RCTs, a subset of patients on antiplatelet therapy had better functional outcomes and higher mortality rates. Platelet transfusions, desmopressin, and tianexamic acid have been shown to reduce bleeding (Desborough et al., 2017). In addition, TCX also provides broader HE prevention results after ICH, resulting in better outcomes (Salman et al., 2018). The dose of desmopressin that can be given is 0.3–0.4 µg/kg (Feldman et al., 2019), and tracexamic acid is given 1 g in 100 mL of

0.9% NaCl (Roberts et al., 2011). From the results of the history of the patient's treatment history, it was found that the patient consumed thrombospirin, which is a class of antiplatelet drugs, so it could be a risk factor for IC in the patient. Giving tranexamic acid to patients can be a good way to prevent the expansion of HE.

The next step in treating stroke patients is to monitor intracranial pressure (ICP) and manage existing edema. ICP monitoring can be done by measuring by inserting an ICP monitor into the brain parenchyma or an EVD into the ventricle. Ventricular drainage should be performed as a first line of treatment for patients with ICH.IVH who have hydrocephalus that is causing a loss in consciousness. The indications for ICP monitoring are less apparent. For ICH patients with a GCS score ≤ 8, ICP monitoring and treatment may reduce mortality and improve prognosis. Hyperosmolar therapy (hypertonic saline infusion, mannitol) may be considered to reduce ICP (Herrick et al., 2014). The method of administration of this prescription drug indicated the possibility of benefits of hyperosmolar infusion on cerebral blood flow, edema progression, and the incidence of ICP catastrophes (Wagner et al., 2011). Additionally, it can be done by elevating the head of the bed 30° (Ojaghihaghighi et al., 2017).

Furthermore, patients with large bleeding volumes who are difficult to treat with medical therapy may be advised to undergo a surgical procedure; currently, this can be done with a minimally invasive surgery (MIS) procedure, which has the benefit of reducing hematoma volume, reducing perihematomal edema, and minimizing tissue disruption. The key recommendation is that minimally invasive hematoma evacuation via endoscopic or stereotactic aspiration with or without the administration of thrombolytics is safe and helpful for lowering mortality (Sun et al., 2020). It should be noted that MIS intervention requires the skill and experience of the surgeon and medical center as the basis for this recommendation of surgical management if the patient has an indication. The only mandatory indication for neurosurgery is cerebral hemorrhage causing decreased consciousness, hydrocephalus, or compression of the brain stem (Mandelow, 2005). Apart from MIS therapy, craniotomy can also be performed where the best surgical candidates are patients with an initial Glasgow coma scale (GCS) < 14 and a hematoma > 40 mL, while patients with a higher GCS and smaller lesions tend to get good results with conservative and non-invasive management. Surgery: surgical procedures that can also be carried out include the installation of an EVD, especially in this patient who has a picture of hydrocephalus from the CT-scan results (Hattori et al., 2004).

Apart from all medical and surgical therapy, education regarding preventing strokes and complications by changing lifestyle needs to be carried out. Lifestyle modification is one way to prevent second attack strokes (Godbout et al., 2009). Ginsberg (2008) said that a second attack can be prevented by controlling risk factors through treatment and lifestyle modification. Lifestyle modification at risk of stroke is an effective promotion for secondary stroke. The lifestyle in question includes an unhealthy diet, obesity, smoking, alcohol, and a lack of physical activity (Lawrence, 2010). As a result, attempts must be made to limit the number of strokes by eating a well-balanced diet that includes more vegetables, fresh fruit, low-fat protein, and fiber, which is particularly helpful to blood vessels, and don't forget to do regular exercise. By exercising frequently, you can regulate your weight and minimize your risk of stroke. As noted by Pinzon, periodic control, a nutritious diet, frequent physical activity, and stopping smoking can help stroke victims avoid recurring attacks (Center, 2007).

This case provides valuable insights into the challenges of managing a patient with a history of multiple comorbidities and a subsequent acute stroke. The key takeaway is the importance of timely intervention, appropriate surgical management, and strict control of risk factors such as hypertension. It also highlights the need for ongoing

monitoring, multidisciplinary care, and long-term rehabilitation planning to optimize patient outcomes.

The case underscores the critical importance of managing hypertension as a key risk factor for stroke. The patient's uncontrolled blood pressure (200/100 mmHg) at admission highlights the significant contribution of poorly managed hypertension to the development of intracranial hemorrhage (ICH) and ischemic events. This reinforces the need for better hypertension control and adherences to medications regimens, particularly in patients with a history of cardiovascular and cerebrovascular disease.

CONCLUSION

This article shows that a second stroke is strongly influenced by existing risk factors, plus if management is not carried out properly, apart from that, with increasing age, it can have an impact on decreasing brain mass, which can result in exvacuohydrocephalus. It needs to be noted that the incidence of a second attack stroke is known to show a much higher mortality rate than managed, like in this patient who has a history of uncontrolled hypertension or DM, a personal history of ischemic stroke, or a family history of ICH. Using antiplatelet drugs, especially in the incidence of ICH, is associated with the risk factors of age and genetics, where patients with risk factors >1 have an increased risk factor for recurrent strokes. Patients should implement appropriate preventive and therapeutic interventions that can minimize the morbidity and mortality associated with second stroke.

REFERENCES

Amila, A., Sinaga, J., Sembiring, E. (2018). Pencegahan stroke berulang melalui pemberdayaan keluarga dan modifikasi gaya. *Journal Abdimas*, 22(2). https://doi.org/10.15294/abdimas.v22i2.15808.

Avan, A., Digaleh, H., Napoli, M.D., et al. (2019). Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: an ecological analysis form the Global Burden of Diesease Study 2017. *BMC Medicine*, 17(1): 191. https://doi.org/10.1186/s12916-019-1397-3.

Bath, P.M., Woodhous, L.J., Krishan, L.J., et al. (2019). Prehospital transdermal glyceryl trinitrate for ultra-acute intracerebral haemorrhage: data from right 2 trial. *Stroke*, 50: 3064-3071. Https://doi.org/10.1161/STROKEAHA.119.026389.

Bethesda Stroke Centre. (2007). Faktor risiko stroke usia muda. https://www.strokebethesda.com.

Bramall, A.N., Anton, E.S., Tahle, K.T., et al. (2022). Navigating the ventricles: novel insights into the pathogenesis of hydrocephalus. *eBiomediicine*, 78: 103931. https://doi.org/10.1016/j.ebiom.2022.103931.

Broderick, J., Connolly, S., Feldman, E., et al. (2007). Guidelines for the management of spontaneous intracerebral haemorrhage in adults: 2007 update. *Stroke*, 38: 2001-2023.

Chen, S., Zeng, L., Hu, Z. (2014). Progressing haemorrhagic stroke: categories, causes, mechanisms and managements. *Journal of Neurology*, 261(11): 2061-2078.

DeLago Jr, A.J., Singh, H., Jani, C., et al. (2022). An observational epidemiology study to analyze intracerebral hemmorhage across the Univesity States: Incidence and mortality trends from 1990 to 2017. *Journal of Stroke and Cerebrovascular Disease*, 31(4): 106216. https://doi.org/10.1016/j.strokecerebrovasdis.20.

Desborough, M.J.R., Oakland, K.A., Landoni, G., et al. (2017). Desmopressin for treatment of platelet dysfunction and reversal of antiplatelet agents: a systemtic review and meta-analysis of randomized controlled trials. *Journal of Thrombosis and Haemostasis*, 15(2): P262-272. https://doi.org/10.1111/jth.13576.

Fekadu, G., Chelkeba, L., Kebede, A. (2019). Risk factors, clilnical presentations and predictors of stroke among adult patients admitted to stroke unit of Jimma university medical center, south west ethipia: prospective observational study. *BMC Neurology*, 19(187). https://doi.org/10.1186/s12883-019-1409-1.

Feldman, E.A., Meola, G.P., Zyck, S., et al. (2019). Restrospective assessment of desmopressin effectiveness and safety in patients with antiplatelet-associated intracranial hemorrhage. *Neurologi Critical Care*, 47(12): 1750-1765. https://doi.org/10.1097/CCM.0000000000004021.

Finfer, S., Chittock, D.R., Su, S.Y-S., Blair, D., et al. (2009). Intensive versus conventional glucose control in critically ill patients. *The New England Journal of Medicine*, 360(13): 1283-1297. https://doi.org/10.1056/NEJMoa0810625.

Friday, G., Alter, M., Lai, S-M. (2002). Control of hypertension and risk of stroke recurrence. *Stroke*, 33(11). https://doi.org/10.1161/01.STR.0000033929.62136.6F.

Ginsberg, M.D. (2008). Neuroprotection for ischemic stroke: past, present and future. *Neuropharmacology*, 55(3): 3636-89. https://doi.org/10.1016/j.neuropharm.2007.12.007.

Godbout, S., Goldberger, J., Dupont, G., et al. (2009). Secondary stroke prevention. *Stroke Engine*.

Guzik, A., Bushnell, C. (2017). Stroke epidemiology and risk factor management. *Cerebrovascular Disease*, 23(1): 15-39. https://doi.org/10.1212/CON.0000000000000416.

Hankey, G.J., Jamrozik, K., Broadhurst, R.J., et al. Long-term risk of first recurrent stroke in the Perth Community Stroke study. *Stroke*, 29(12): 2491-500. https://doi.org/10.1161/01.str.29.12.2491

Hattori, N., Katayama, Y., Maya, Y., et al. (2004). Impact of stereotactic hematoma evacuation on activities of daily living during the chronic period following spontaneous putaminal hemorrhage: a randomized study. *Journal of Neurosurgery*, 101(3): 417-20. https://doi.org/10.3171/jns/2004.101.3.0417.

Hattingen, E., Jurcoane, A., Melber, J., et al. (2010). Diffusion tensor imaging in patients with adult chronic idiopathic hydrocephalus. *Neurosurgery*, 66(5): 917-24.

Herrick, D.B., Ullman, N., Nekoovaght-Tak, S., Hanley, D.F., et al. (2014). Determinents of external ventricular drain placement and associated outcomes in patients with spontaneous intraventricular hemorrhage. *Neurocritical Care*, 21: 426-434. https://doi.org/10.1007/s12028-014-9959-x.

Husni, A., Laksmawati. (2001). Faktor yang mempengaruhi stroke no hemoragik ulang. *Media Indonesiana*, 36(3): 133-134.

Hwang, I., Ha, S-W., Yang, Y., Kim, S.M. (2016). Hydrocephalus in patient with multiple system atrophy: innocent bystander of guilty party?. *Dementia and Neurocognitive Disorder*, 15(2): 49-51. https://doi.org/10.12779/dnd.2016.15.2.49.

Kim, M., Park, S-W., Lee, J-Y., et al. (2021). Differences in brain morphology between hydrocephalus ex vacuo and idiopathic normal pressure hydrocephalus. *Psychiatry Investigation*m 18(7): 628-635. https://doi.org/10.30773/pi.2020.0352.

Kim, Y., Han, M-H., Kim, C-H., et al. (2017). Increased short-term mortality in patients with spontaneous intracerebral hemorrhage and its association with admission glucose levels and leukocytosis. *World Neurosurgery*, 98: 503-511. https://doi.org/10.1016/j.wneu.2016.11.087.

Koga, M., Arihiro, S., Hasegawa, Y., et al. (2014). Intravenous nicardipine dosing

for blood pressure lowering in acute intracerebral hemorrhage: the stroke acute management with urgent risk-factor assessment and improvement-intracerebral hemorrhage study. *Journal of Stroke & Cerebrovascular Disease*, 23(10): P2780-2787. https://doi.org/10.1016/j.strokecerebrovasdis.2014.06.029.

Kuramatsu, J.B., Gerner, S.T., Schellinger, P.D. (2015). Patient with anticoagulation-related intracerebral hemorrhage. *JAMA Network*, 313(8): 824-836. https://doi.org/10.1001/jama.2015.0846.

Kuriakose, D., Xiao, Z. (2020). Pathophysiology and treatment of stroke: present status and future perspectives. *International Journal of Molecular Sciences*, 21(20): 7609. https://doi.org/10.3390/ijms21207609.

Lapchak, P.A., Arauji, D.M. (2007). Advances in hemorrhagic stroke therapy: conventional and novel approaches. *Expert Opinion on Emerging Drugs*, 12(3): 389-406. https://doi.org/10.1517/14728214.12.3.389.

Lawrence, M., Kerr, S., Watson, H, et al. (2009). A summary of the guidance relating to four lifestyle risk factors for recurrent stroke: tobacco use, alcohol consumption, diet and physical activity. *British Journal of Neuroscience Nursing*, 5(10): 471-476.

Macellari, F., Paciaroni, M., Agnelly, G., et al. (2014). Neuroimaging in intracerebral hemorrhage. *Stroke*, 45(3). https://doi.org/10.1161/STROKEAHA.113.003701.

Mendelow, A.D., Grengson, B.A., Frenandes, H.M., et al. (2005). Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the international surgical trial in intracerebral haemorrhage (STICH): a randomised trial. *Lancet*, 365(9457): 387-397. https://doi.org/10.1016/S01400-6736(05)17826-X.

Kemenkes RI. (2018). Hasil riset kesehatan dasar tahun 2018 (RISKESDAS). Kementrian Kesehatan RI, 53(9).

Moullaali, T.J., Wang, X., Martin, R.H., et al. (2019). Blood pressure control and clinical outcomes in acute intracerebral haemorrhage: a preplanned pooled analysis of individual participant data. *The Lancet Neurology*, 18(9): 857-864. https://doi.org/10.1016/S1474-4422(19)30196-6.

Ojaghihaghighi, S., Vahdati, S.S., Mikaeilpour, A., et al. (2017). Comparison of neurological clinical manifestation in patients with hemorrhage and ischemic stroke. *World Journal of Emergency Medicine*, 8(1): 34-38. https://doi.org/10.5847/wjem.j.1920-8642.2017.01.006.

Prisco, D., Marcucci, R. (2009). Antiplatelet drig's resistance. *The open atherosclerosis & Thrombosis Journal*, 2: 24028.

Qureshi, A.I., Palesch, Y.Y., Martin, R., et al. (2010). Intracerebral hemorrhage results from the antihypertensive treatment of acute cerebral hemorrhage study. *JAMA Neurology*, 67(5): 570-57. https://doi.org/10.1001/archneurol.2010.61.

Ray, B., Keyrous, S.G. (2014). Management of anticoagulant-related intracranial hemorrhage: an evidence-based review. *Critical Cara*, 18(223). https://doi.org/10.1186/cc13889.

Roberts, I., Shakur, H., Afolabi, A., et al. (2011). The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. *Lancet*, 377(9771): 1096-101. https://doi.org/10.1016/S0140-6736(11)60278-X.

Siswanto, Y. (2005). Beberapa faktor risiko yang mempengaruhi kejadian stroke berulang (studi kasus di RS. Dr. Kariadi Semarang). *Jurnal Epidemiologi*, 1-10.

Stahmeyer, J.T., Stubenrauch, S., Geyer, S., et al. (2019). The frequency and timing of

recurrent stroke. *Deutsches Arzteblatt*, 116(42): 711-777. https://doi.org/10.3238/arztebl.2019.0711.

Steiner, T., Poli, S., Griebe, M., et al. (2016). Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial. *The Lancet Neurology*, 15(6): 566-573. https://doi.org/10.1016/S1474-4422(16)00110-1.

Sun, S., Li, Y., Zhang, H., et al. (2020). Neuroendoscopic surgery versus craniotomy for supratentorial hypertensive intracerebral hemmorhage: a systematic review and meta-analysis. *World Neurosurgery*, 134: 477-488. https://doi.org/10.1016/j.wneu.2019.10.115.

Tans, J.T.J. (2004). Differentiation of normal pressure hydrocephalus and cerebral atrophy by computed tomography anspinal infusion test. *Journal of Neurology*, 222: 109-118. https://doi.org/10.1007/BF00313004.

Thompson, B.B., Bejot, Y., Caso, V., et al. (2010). Prior antiplatelet therapy and outcome following intracerebral hemorrhage. *Neurology Journals*, 75(15): 1333-1342. https://doi.org/10.1212/WNL.0b013e3181f735e5.

Unnithan, A.K.A., Das, J.M., Mehta, P. (2023). Hemorrhage stroke. In: StatPearls. StatPearls Publishing.

Wagner, I., Hauer, E-M., Staykov, D., et al. (2011). Effects of continuous hypertonic saline infusion on perihemorrhagic edema evolution. *Stroke*, 42(6). 1540-1545. https://doi.org/10.1161/STROKEAHA.110.609479.

World Health Organization. (2019). Stroke Statistic. Published Online.