Magna Neurologica Vol. 4, No. 1, January 2026

https://journal.uns.ac.id/magna-neurologica
DOI: 10.20961/magnaneurologica.v4i1.2644
e-ISSN 2985-3729 p-ISSN 2963-6027

CASE REPORT **OPEN ACCESS**

ACUTE MALIGNANT TRANSFORMATION AS A RARE COMPLICATION OF MIDDLE CEREBRAL ARTERY INFARCTION

Annisa Bunga Nafara[1*], Ika Yulieta Margaretha Permatasari[2]

***Correspondence**: annisabunga.gp@gmail.com*
[1]Fatmawati Hospital, Jakarta, Indonesia
[2]Department of Neurology, Fatmawati Hospital, Jakarta, Indonesia

Article History:
Received: August 4, 2025
Accepted: October 6, 2025
Published: January 1, 2026

Cite this as:
Nafara AB, Permatasari IYM. Acute Malignant Transformation as A Rare Complication of Middle Cerebral Artery Infarction. Magna Neurologica. 4(1) January 2026: 58-62. 10.20961/magnaneurologica.v4i1.2644

ABSTRACT

Background: Malignant ischemic stroke is a stroke characterized by extensive acute edema resulting in a space-occupying lesion. This transformation occurs in 10% of ischemic strokes with a mortality rate up to 80%. Hence, it is crucial to early detection and timely treatment.
Case: A 51-year-old male was diagnosed with ischemic stroke, presented with NIHSS 11 and ASPECTS 4. Within 26 hours, the patient's level of consciousness declined progressively from a GCS of 15 to a GCS of 10. Serial brain imaging using CT scan and MRI revealed infarct expansion, a space-occupying lesion, and further midline shift. During decompressive craniectomy, extensive edema was found without hemorrhage, suggesting malignant ischemic stroke. After 6 months, the patient had undergone cranioplasty, with no significant complaints, but left hemiparesis remained.
Discussion: Malignant ischemic stroke occurs within 5 days after onset. Diagnosis of malignant complication should be considered in ischemic stroke patients with younger age, higher NIHSS, not receiving thrombolysis, neurological status decline in 4-6 hours after onset, wide hypoattenuation in MCA territory, and signs of progressive space-occupying lesion in brain imaging. Management of malignant ischemic stroke consists of managing intracranial pressure with pharmacology and decompressive craniectomy.
Conclusion: Malignant transformation is a rare complication of ischemic stroke. Early and accurate diagnosis is crucial to determine the prognosis. Pharmacological therapy and decompressive craniectomy surgery are considered life-saving therapies, but are not able to reduce morbidity in the patient.

Keywords: acute cerebral edema, ischemic stroke, malignant ischemic stroke

Introduction

Malignant ischemic stroke is an acute edema that occurs in ischemic stroke, resulting in a mass effect and intracranial enhancement, as well as tissue shift and herniation. Malignant cerebral edema is a rare complication of ischemic stroke that occurs in around 10% of ischemic strokes.[1,2] In a median time of 4 days, malignant cerebral edema developed in 27.6% of patients.[3] Although these cases are pretty rare, mortality from malignant ischemic stroke is high, 65,1%-80% due to temporal lobe herniation towards the brainstem.[2,4] It is essential to be aware of significant changes in neurologic status so that serial brain imaging evaluation can be performed as soon as possible and timely management can be determined.

Case Report

A 51-year-old man (YA) came to the emergency room of Fatmawati Hospital with complaints of weakness of the left limbs for 3 hours, accompanied by mouth asymmetry, slurred speech, and dizziness. The patient was found to have an active bleeding nosebleed due to a fall before going to the emergency room, and nasogastric tube production was dark, indicating ongoing upper gastrointestinal tract bleeding. The patient had a history of kidney stones and denied any history of hypertension, heart disease, diabetes, or stroke.

On physical examination, the patient was found to have a GCS of 15, vital signs stable, and neurological examination revealed a round pupil isochor 2 mm, positive light reflexes in both pupils, central nervous system VII paralysis, no rigidity was observed, muscle strength was 555/111 555/111, no pathological reflexes appeared, and normal physiological reflexes. Brain CT in the emergency room showed right MCA infarction with slight hypodensity and sulcal narrowing in the right frontotemporoparietal lobe, lentiform nucleus, and insula, suggesting right MCA territory infarction at hyperacute–acute stage (ASPECTS 4) (Figure 1). The blood laboratory results showed a D-dimer level of 4184 ng/ml, an INR of 1.03, and albuminuria at 2+. All other results were expected. The patient received therapy according to ischemic stroke, including omeprazole 2x40 mg, ranitidine 2x25 mg, ceftriaxone 1x1 gr, ketorolac 3x30 mg, Citicholine 2x1 gr, Clopidogrel 1x75 mg. The patient did not receive thrombolysis and thrombectomy due to the low ASPECTS and ongoing gastrointestinal tract bleeding.

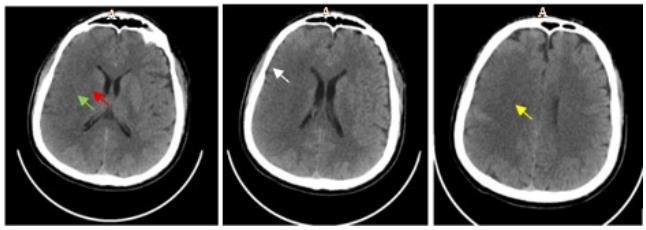

Figure 1. First non-contrast head CT scan, 3 hours after onset, shows sulcal narrowing (white arrow) and slight hypodensity in the right frontotemporoparietal lobe (yellow arrow), lentiform nucleus (red arrow), and insula (green arrow)

One hour after the patient's MRS, the patient experienced a decline in consciousness, with a GCS of E3M6V5. The decline in consciousness continued progressively until 16 hours later, and a CITO head CT scan was performed. Head CT scan results showed widespread MCA infarction, indistinctly circumscribed hypodense accompanied by narrowing of the sulci cerebri in the right fronto-temporoparietal lobe, right lentiform nucleus, and right insula with surrounding perifocal edema and urging bilateral lateral ventricles to the left with a midline shift of 0.7 cm, findings are consistent with an infarction in the right MCA territory, with evidence of an extensive lesion, most likely thrombotic in nature (Figure 2). Mannitol was given 300 ml loading and 4×150 ml maintenance.

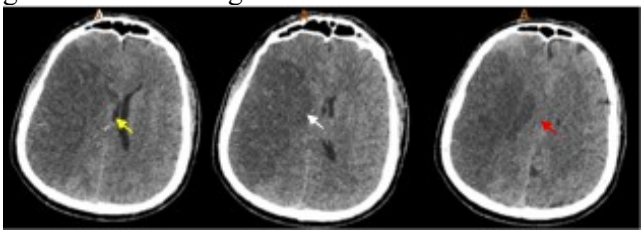

Figure 2. Second non-contrast head CT scan 20 hours after onset shows defined hypodensity with perifocal edema in the right frontotemporoparietal lobe, lentiform nucleus, and insula (white arrow), causing lateral ventricle compression (yellow arrow) and a 0.7 cm leftward midline shift (red arrow)

Intracranial pressure elevation management was given. Twenty-four hours after onset, the patient's GCS was E3M4V3. We performed MRI MRA Brain, and showed a hypointense area on T1WI and hyperintense on T2WI-FLAIR with diffusion restriction, along with a focal slight hyperintensity on T1WI, hypointensity on T2WI-FLAIR, forming a wedge-shaped lesion in the cortical subcortical regions of the right frontotemporoparietal lobe, right basal ganglia, right external capsule, and right insula (corresponding to the right MCA territory). These findings are associated with narrowing of the right lateral ventricle and a midline shift of approximately 1.4 cm to the left. The right middle cerebral artery appears smaller in caliber compared to the left, with its distal branches still visible. Brain MRI MRA concludes acute infarction of the right MCA territory, right M1-6, with suspicion of hemorrhage transformation in the subcortical cortex of the right frontotemporoparietal lobe, right basal ganglia, right external capsule to the right insula, narrowing the right lateral ventricle, and causing a midline shift of 1.4 cm to the left (Figure 3 and Figure 4).

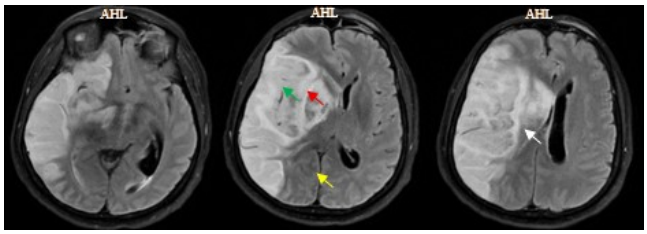

Figure 3. Head MRI 24 hours after onset. Wedge-shaped lesion in the cortical subcortical regions of the right frontotemporoparietal lobe (white arrow), right basal ganglia (yellow arrow), right external capsule (red arrow), and right insula (green arrow), corresponding to the right MCA territory

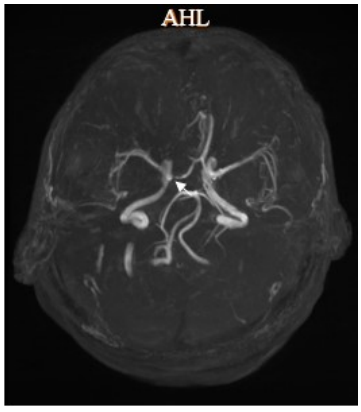

Figure 4. Head MRA 24 hours after onset. The right middle cerebral artery appears smaller in caliber compared to the left, with its distal branches still visible

The patient was referred to Neurosurgery, and a decompressive craniectomy was performed. No bleeding was found during the operation. The postoperative diagnosis was Malignant Stroke Infarction of the right middle cerebral artery. Post-decompressive craniectomy, the patient was admitted to the Intensive Care Unit. Four days post-craniectomy, the

patient's consciousness was alert, complaining of a headache. The patient was transferred to the High Care Unit on the seventh postoperative day, then downgraded to the ward on the 15th postoperative day. The patient was discharged after 30 days postoperatively and routinely controls at the neurosurgery clinic every month. After 4 months, cranioplasty was performed on the patient. At the last post-cranioplasty control, the patient had no complaints, but the sequelae of left hemiparesis persisted.

Discussion

Malignant cerebral infarction usually occurs in ischemia of the middle cerebral artery, where there is acute swelling of the brain within the first 48 hours of stroke onset, resulting in increased intracranial pressure and/or brain herniation.[4] This literature is consistent with this case. The process of edema starts 4 hours after onset and worsens up to 2 days after onset. One of the risk factors for malignant cerebral edema in infarction stroke is atrial fibrillation, younger age (<65 years), high NIHSS score (>17), no thrombolysis, and hypodense MCA territory on initial CT scan >50%.[5,6] It was previously reported that a higher blood glucose level at admission was a risk factor for malignant brain edema.[7] Development. According to a study conducted by Wu, patients with higher NIHSS scores, larger infarcts, and pneumonia were more likely to develop malignant brain edema. Adversely, Wu stated that receiving intravenous thrombolysis or endovascular treatment is a risk factor for developing malignant brain edema.[2] It is caused by a series of pathological cascade reactions triggered by the recovery of oxygenated blood flow into the ischemic brain tissue.[8,9] Currently, the relationship between reperfusion and malignant cerebral edema remains unclear, as opinions on the effect of reperfusion on cerebral edema vary.[2] In this patient, the identified risk factors were a younger age and a large infarct.

Large vessel occlusion can induce space-occupying malignant brain edema that progresses rapidly, causes a high risk of herniation, and contributes to severe neurological deterioration and high mortality.[10] In the acute phase of ischemic stroke, there is an imbalance of energy needed and energy supplied due to cerebral vascular blockage. Additionally, there is a disruption of ion pumps related to energy needs, resulting in an increased intracellular sodium concentration, a decreased extracellular potassium concentration, and an increased calcium influx into cells. With the disruption of ion balance, water is transferred into the cell, resulting in osmotic edema and terminal depolarization of the cell membrane.[11] In the absence of a blood supply, the necrotic area expands, and cell edema continues to result in shrinkage of the extracellular compartment. Necrotic tissue also triggers protein degradation and initiates mediators, such as metalloproteinases, nitric oxide synthase, vascular endothelial growth factors, and thrombin, that trigger vasogenic edema.[12] Cytotoxic edema is the earliest phase in the development of cerebral edema. During the initial period of cerebral ischemia and hypoxia, impairment of Na^+/K^+-ATPase and alterations in the ionic osmotic gradient drive the movement of osmotically active particles, primarily Na^+, Cl^-, and water, into the cell. This influx causes cellular swelling and contributes to the progression of both ionic and vasogenic edema. Ischemic injury in the brain can disrupt the blood–brain barrier (BBB). This disruption allows chemicals, fluids, and circulating cells to penetrate the brain parenchyma, disturbing ionic and water balance, and ultimately leading to cerebral edema.[13]

Non-contrast Computerized Tomography (CT) scan is the standard diagnosis to evaluate the progress of ischemic stroke, including screening for the possibility of bleeding transformation and post-thrombolysis evaluation. It can detect overall changes in brain water content, but it is less capable of identifying fluid redistribution between tissue compartments. Consequently, CT is effective in demonstrating ionic and vasogenic edema, but not cytotoxic edema, as the latter involves fluid movement from the vasculature into interstitial spaces.[14] A recent study focusing on the CTA ASPECTS showed that a score ≤5 was a relatively specific threshold to predict the development of malignant cerebral edema (sensitivity 46%; specificity 97%; positive predictive value 78%; negative predictive value 65%).[15] Malignant cerebral edema can be diagnosed if the midline shift exceeds 5 mm.[16,17] A CT scan allows for faster diagnosis but has lower sensitivity, whereas an MRI requires a longer process but has higher sensitivity than a CT scan.[18] Moreover, the intensity characteristics of MRI reflect the tissue composition, and some sequences are susceptible to changes in water content.[14] Multiple randomized trials have utilized DWI infarct volume on early MRI for patient selection. The DWI threshold in the major trials has been greater than 145 cc.[19]

Hypoattenuation changes greater than 50% in the territory of the Cerebral Media Artery can predict malignant infarction stroke[14] with a sensitivity of 50% and specificity of 86%.[20] An acute DWI volume of >80 ml on MRI acquired within six hours of stroke onset and that of >145 ml when imaged 14 hours from stroke onset have been shown to predict rapid early neurological deterioration and the high risk of malignant oedema.[14] The DWI high-intensity volume/BV ratio and cerebral blood volume lesion volume/CSV ratio have been demonstrated as reliable predictive markers for malignant MCA infarction, with a cut-off value of 0.078 (sensitivity 86%, specificity 87%) and 0.92 (sensitivity 96.2%, specificity 96.2%).[14]

Management strategies of malignant cerebral oedema in ischemic stroke consist of supportive measures, vigilant neurological observation, and the use of hyperosmolar agents. However, the crucial therapeutic consideration lies in deciding on decompressive craniectomy. Evidence from multiple randomized controlled trials and meta-analyses suggests that hemicraniectomy remains the most critical intervention associated with improved survival.[21] Medication administration includes mannitol, hypertonic saline, corticosteroids, and barbiturates.[4] In most cases, medication is not sufficient to regulate edema; thus, surgical decompressive craniectomy may be required. The decompressive craniectomy allows edematous brain tissue to herniate outside, thus preventing neuronal damage in other regions of the brain.[22] In this case, the patient was 51 years old, and a decompressive craniectomy was performed 3 days after onset, longer than the recommendation. Contraindications to decompressive craniectomy include alteplase administered less than 12 hours before surgery, premorbid uncontrolled bleeding, posterior cerebral artery infarction, and trans-tentorial herniation.[4] This patient had no contraindications for decompressive craniectomy.

Cerebral edema is recognized as the major contributor to early neurological decline and mortality in patients with large supratentorial infarcts. While it typically reaches a life-threatening malignant edema between the second and fifth day after stroke onset, most patients already experience significant neurological worsening within the first 24 hours.[23] Multiple factors contribute to early mortality in acute ischemic stroke. Stroke severity on admission is a well-established predictor of mortality, including motor deficits and level of consciousness. In many studies, the level of consciousness was the leading early cause of mortality in malignant edema after acute ischemic stroke.[23] The mortality rate of malignant MCA infarction is nearly 80 % without surgical intervention despite maximal non-surgical medical care.[24] Several studies have consistently shown that decompressive craniectomy (DC) in malignant middle cerebral artery infarction is associated with reduced mortality and better functional recovery. Cohort analyses indicate that acute-phase case fatality ranges from approximately 18% to 35%, while the proportion of patients achieving a moderate disability level (mRS 3) at three months varies between 20% and 59%.[25] In this case, mortality was prevented, but the manifestation of hemiparesis did not improve.

Conclusion

It is important to be alert for signs of malignant transformation in extensive MCA territory ischemic stroke, characterized by significant changes in the patient's neurological status in a short period of time. Serial brain imaging is required to monitor the progression of ischemic stroke, establish a malignant diagnosis, and determine management. Decompressive craniectomy may prevent mortality but may not necessarily reduce morbidity.

References

1. Liebeskind DS, Jüttler E, Shapovalov Y, Yegin A, Landen J, Jauch EC. Cerebral Edema Associated With Large Hemispheric Infarction. Stroke; 2019. 50(9):2619-2625. DOI: 10.1161/STROKEAHA.118.024766
2. Wu S, Wang Y, Yuan R, Guo F, Yang D, Li Z, et al. Predicting the emergence of malignant brain oedema in acute ischaemic stroke: a prospective multicentre study with development and validation of predictive modelling; 2023. 59:101977. DOI: 10.1016/j.eclinm.2023.101977
3. Muscari, A., Faccioli, L., Lega, M.V. et al. Predicting cerebral edema in ischemic stroke patients. Neurol Sci; 2019. 40:745–752. DOI: 10.1007/s10072-019-3717-y
4. Lin J, Frontera JA. Decompressive Hemicraniectomy for Large Hemispheric Strokes. Stroke; 2021. 52(4):1500-1510. DOI: 10.1161/STROKEAHA.120.032359
5. Wu S, Yuan R, Wang Y, Wei C, Zhang S, Yang X, et al. Early Prediction of Malignant Brain Edema After Ischemic Stroke. Stroke; 2018. 49(12):2918-2927. DOI: 10.1161/STROKEAHA.118.022001
6. Foroushani HM, Hamzehloo A, Kumar A, Chen Y, Heitsch L, Slowik A, et al. Accelerating Prediction of Malignant Cerebral Edema After Ischemic Stroke with Automated Image Analysis and Explainable Neural Networks. Neurocrit Care; 2022. 36(2):471-482. DOI: 10.1007/s12028-021-01325-x
7. Thorén M, Azevedo E, Dawson J, Egido JA, Falcou A, Ford GA, et al. Predictors for Cerebral Edema in Acute Ischemic Stroke Treated With Intravenous Thrombolysis. Stroke; 2017. 48(9):2464–71. DOI: 10.1161/STROKEAHA.117.018223
8. Fisher M, Savitz SI. Pharmacological brain cytoprotection in acute ischaemic stroke renewed hope in the reperfusion era. Nat Rev Neurol; 2022. 18(4):193–202. DOI: 10.1038/s41582-021-00605-6
9. Wang Y, Hong F, Yang S. Roles of Nitric Oxide in Brain Ischemia and Reperfusion. Int J Mol Sci; 2022. 23(8):4243. DOI: 10.3390/ijms23084243
10. Miao J, Song X, Sun W, Qiu X, Lan Y, Zhu Z. Predictors of malignant cerebral edema in cerebral artery infarction: A meta-analysis. J Neurol Sci; 2020. 409:116607. DOI: 10.1016/j.jns.2019.116607

11. Hill A, Amendolara AB, Small C, Guzman SC, Pfister D, McFarland K, et al. Metabolic Pathophysiology of Cortical Spreading Depression: A Review. Brain Sci; 2024. 14(10):1026. DOI: 10.3390/brainsci14101026
12. Heiss WD. Malignant MCA Infarction: Pathophysiology and Imaging for Early Diagnosis and Management Decisions. Cerebrovasc Dis; 2016. 41(1–2):1–7. DOI: 10.1159/000441627
13. Gu Y, Zhou C, Piao Z, Yuan H, Jiang H, Wei H, et al. Cerebral edema after ischemic stroke: Pathophysiology and underlying mechanisms. Front Neurosci; 2022. 18;16:988283. DOI: 10.3389/fnins.2022.988283
14. Zhang X, Huang P, Zhang R. Evaluation and Prediction of Post-stroke Cerebral Edema Based on Neuroimaging. Front Neurol; 2022. 11;12:763018. DOI: 10.3389/fneur.2021.763018
15. Davoli A, Motta C, Koch G, Diomedi M, Napolitano S, Giordano A, et al. Pretreatment predictors of malignant evolution in patients with ischemic stroke undergoing mechanical thrombectomy. J NeuroInterventional Surg; 2018. 10(4):340–4. DOI: 10.1016/j.neurol.2020.01.352
16. Du M, Huang X, Li S, Xu L, Yan B, Zhang Y, et al. A Nomogram Model to Predict Malignant Cerebral Edema in Ischemic Stroke Patients Treated with Endovascular Thrombectomy: An Observational Study. Neuropsychiatr Dis Treat; 2020. Volume 16:2913–20. DOI: 10.2147/NDT.S279303
17. Ong CJ, Gluckstein J, Laurido-Soto O, Yan Y, Dhar R, Lee JM. Enhanced Detection of Edema in Malignant Anterior Circulation Stroke (EDEMA) Score: A Risk Prediction Tool. Stroke; 2017. 48(7):1969–72. DOI: 10.1161/STROKEAHA.117.016733
18. Lee CL, Kandasamy R, Mohammad Raffiq MAB. Computed tomography perfusion in detecting malignant middle cerebral artery infarct. Surg Neurol Int; 2019. 10:159. DOI: 10.25259/SNI_64_2019
19. Reinink H, Jüttler E, Hacke W, Hofmeijer J, Vicaut E, Vahedi K, et al. Surgical Decompression for Space-Occupying Hemispheric Infarction: A Systematic Review and Individual Patient Meta-analysis of Randomized Clinical Trials. JAMA Neurol; 2021. 78(2):208. DOI: 10.1001/jamaneurol.2020.3745
20. Goto Y, Kumura E, Watabe T, Nakamura H, Nishino A, Koyama T, et al. Prediction of Malignant Middle Cerebral Artery Infarction in Elderly Patients. J Stroke Cerebrovasc Dis; 2016. 25(6):1389-95. DOI: 10.1016/j.jstrokecerebrovasdis.2015.12.034
21. Dower A, Mulcahy M, Maharaj M, Chen H, Lim CED, Li Y, et al. Surgical decompression for malignant cerebral oedema after ischaemic stroke. Cochrane Database Syst Rev; 2022. 11(11):CD014989. DOI: 10.1002/14651858.CD014989.pub2
22. Alhumaid L, Almaneea A, Al-Khalaf A, AlRuwaita A, AlOraidi A, Omair A, et al. Decompressive craniectomy is a life-saving procedure in malignant MCA infarction. Neurosciences; 2021. 26(3):248–53. DOI: 10.17712/nsj.2021.3.20200187
23. Dostovic Z, Dostovic E, Smajlovic D, Avdic O. Brain Edema After Ischaemic Stroke. Med Arch; 2016. 70(5):339. DOI: 10.5455/medarh.2016.70.339-341
24. Juttler E, Schwab S, Schmiedek P, Unterberg A, Hennerici M, Woitzik J, et al. Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY): A Randomized, Controlled Trial. Stroke; 2007. 38(9):2518–25. DOI: 10.1161/STROKEAHA.107.485649
25. Von Olnhausen O, Thorén M, Von Vogelsang AC, Svensson M, Schechtmann G. Predictive factors for decompressive hemicraniectomy in malignant middle cerebral artery infarction. Acta Neurochir (Wien); 2016. 158(5):865–73. DOI:10.1007/s00701-016-2749-9