



HEMORRHAGIC TRANSFORMATION IN CARDIOEMBOLIC STROKE WITH ANTICOAGULANT USE: A CASE REPORT

Ari Bandana Tasrif¹ ✉

1) Fakultas Kedokteran, Universitas Syiah Kuala

✉ Corresponding author:
ari_tasrif@usk.ac.id

Abstrak

Stroke emboli merupakan salah satu subtype stroke iskemik yang sering menyebabkan defisit neurologis berat akibat oklusi pembuluh darah secara mendadak. Salah satu komplikasi penting ini adalah transformasi hemoragik, yaitu perdarahan pada jaringan otak yang telah mengalami infark. Laporan kasus ini membahas seorang laki-laki usia 49 tahun dengan riwayat stroke sebelumnya dan penggunaan warfarin yang datang dengan penurunan kesadaran mendadak. Pemeriksaan CT scan menunjukkan infark luas dengan transformasi hemoragik tipe HI-1 berdasarkan klasifikasi ECASS. Transformasi hemoragik terjadi akibat interaksi kompleks antara kerusakan blood-brain barrier, proses reperfusi, serta faktor risiko seperti infark luas dan penggunaan antikoagulan. Penatalaksanaan meliputi stabilisasi hemodinamik, penghentian dan reversal antikoagulan, serta manajemen tekanan intrakranial. Meskipun termasuk kategori lebih ringan dibanding hematoma parenkim, HI-1 tetap memiliki implikasi klinis penting terutama bila disertai edema serebral. Oleh karena itu, deteksi dini dan penatalaksanaan yang tepat sangat berperan dalam memperbaiki luaran pasien.

Kata Kunci: *Stroke emboli, Transformasi perdarahan, Klasifikasi ECASS.*

Abstract

Embolitic stroke is a subtype of ischemic stroke characterized by the sudden onset of severe neurological deficits due to abrupt vascular occlusion. One of its important complications is hemorrhagic transformation (HT), defined as bleeding within infarcted brain tissue. This case report describes a 49-year-old male with a history of prior stroke and warfarin use who presented with decreased consciousness. Brain CT scan revealed extensive cerebral infarction with hemorrhagic transformation classified as HI-1 based on the European Cooperative Acute Stroke Study (ECASS) criteria. HT results from a complex interplay between blood-brain barrier disruption, reperfusion injury, and risk factors such as large infarct size and anticoagulant use. Management includes hemodynamic stabilization, discontinuation and reversal of anticoagulation, and intracranial pressure control. Although HI-1 is considered less severe than parenchymal hematoma, it still carries significant clinical implications, particularly when associated with cerebral edema. Early detection and appropriate management are essential to improve patient outcomes.

Keyword: *Embolitic stroke, Hemorrhagic transformation, ECASS classification*

INTRODUCTION

Stroke continues to be a major cause of death and long-term disability globally, with ischemic stroke accounting for most cases. This condition occurs due to occlusion of cerebral vessels, resulting in reduced blood flow to brain tissue.¹ Among its subtypes, embolic stroke is frequently encountered, particularly those of cardiac origin such as atrial fibrillation, in which a thrombus may detach and suddenly obstruct cerebral circulation.² In comparison with other forms of ischemic stroke, cardioembolic stroke is typically characterized by an abrupt onset and a

tendency to produce larger infarct areas. Consequently, it is often associated with more extensive brain injury, poorer clinical outcomes, and an increased risk of complications.³

One of the key complications of ischemic stroke is hemorrhagic transformation, defined as the occurrence of bleeding within previously infarcted brain tissue.⁴ This complication is relatively common and may develop either spontaneously as part of the natural progression of infarction or following reperfusion therapies such as thrombolysis and mechanical thrombectomy. Hemorrhagic transformation is of considerable clinical importance, as it may worsen the patient's condition, increase the likelihood of neurological deterioration, and ultimately contribute to poorer clinical outcomes in patients with ischemic stroke.⁵

Clinically, hemorrhagic transformation represents a broad spectrum, ranging from petechial hemorrhages without mass effect to the development of substantial parenchymal hematomas. This variability carries important prognostic implications, as the severity of bleeding is closely associated with the risk of neurological deterioration and functional outcomes.⁶ Recent evidence indicates that patients with ischemic stroke who develop hemorrhagic transformation particularly when accompanied by cerebral edema are more likely to experience poorer functional outcomes compared to those without this complication.⁷

Embolic stroke is known to carry a higher risk of hemorrhagic transformation compared to thrombotic stroke. This is largely attributed to the abrupt nature of vascular occlusion, which results in more severe ischemic injury to brain tissue.⁸ In addition, the occurrence of reperfusion either spontaneously or following therapeutic interventions further contributes to the increased risk of hemorrhagic transformation. Reperfusion of previously ischemic tissue may compromise vascular integrity, leading to disruption of the vessel wall and subsequent leakage of blood into the brain parenchyma.⁹

Hemorrhagic transformation carries significant clinical implications, as it is associated with increased mortality, worsening neurological deficits, and challenges in subsequent therapeutic decision-making, particularly regarding the use of anticoagulant and antiplatelet agents.¹⁰ This condition presents a clinical dilemma, requiring clinicians to carefully balance the risk of further bleeding against the need to prevent recurrent thromboembolic events. Therefore, a comprehensive understanding of the underlying mechanisms, risk factors, and clinical impact of hemorrhagic transformation in embolic stroke is essential in modern neurological practice, especially in the era of increasingly widespread use of reperfusion therapies.

CASE REPORT

A 49-year-old male was referred from a regional hospital with a chief complaint of decreased consciousness for one day prior to admission. Initially, the patient was still able to eat, drink, and communicate appropriately; however, he suddenly developed vomiting followed by a decline in consciousness. Prior to this event, the patient reported experiencing a headache. The symptoms had an abrupt onset and progressively worsened. At presentation, the patient did not respond to verbal stimuli and only opened his eyes in response to painful stimulation. Previously, the patient had been fully communicative and able to move all extremities. There was no prior history of headache, seizures, or vomiting. One month earlier, the patient had experienced a thrombotic ischemic stroke accompanied by myocardial infarction, resulting in right-sided weakness and speech difficulties, which had improved following treatment. The patient also had a history of warfarin use.

On physical examination in the emergency department, the patient appeared stuporous with a blood pressure of 147/88 mmHg and a pulse rate of 87 beats per minute, while respiratory rate and body temperature were within normal limits. The Glasgow Coma Scale (GCS) was E2VntMnt, with an impression of global aphasia. Neurological examination revealed isochoric pupils and an intact doll's eye reflex. There was evidence of right-sided upper motor neuron (UMN) paresis involving cranial nerves VII and XII. Corneal reflexes were present bilaterally, with motor findings showing right-sided lateralization.

Non-contrast head CT scan (Figure 1) demonstrated thromboembolic infarction with hemorrhagic transformation (ECASS classification HI-1) involving the left temporoparietal lobe, corresponding to the left middle cerebral artery (MCA) territory (segments M1, M2, M4, and M5; ASPECT score 6), as well as the right parietal lobe within the right MCA territory (segments M3, M5, and M6; ASPECT score 7). The patient was subsequently treated with intravenous vitamin K as a reversal agent for warfarin, along with mannitol infusion to reduce intracranial pressure.

RESULTS AND DISCUSSION

Embolic stroke is a subtype of ischemic stroke characterized by the sudden onset of neurological deficits due to occlusion of cerebral vessels by an embolus. The embolic source most commonly originates from the heart, particularly in conditions such as atrial fibrillation, myocardial infarction, and valvular heart disease.⁸ This abrupt vascular obstruction leads to an immediate cessation of cerebral blood flow, resulting in deprivation of oxygen and nutrients to brain tissue. If not promptly managed with adequate reperfusion therapy, this condition may progress to cerebral infarction.¹

A hallmark feature of embolic stroke is the abrupt onset of symptoms, with neurological deficits reaching maximal severity at presentation. This contrasts with thrombotic stroke, which typically evolves more gradually.¹¹ From a pathophysiological perspective, cardioembolic sources are most commonly composed of thrombi formed as a result of blood stasis or irregular flow, such as in atrial fibrillation. In addition, emboli may also arise from ruptured atherosclerotic plaques in large vessels and subsequently travel through the circulation, a mechanism known as artery-to-artery embolism.⁸

After entering the cerebral circulation, the embolus travels along the bloodstream until it becomes lodged in smaller-caliber vessels, such as at the bifurcations of the middle cerebral artery. This results in an abrupt interruption of blood flow to a specific brain region, triggering ischemia and subsequent tissue injury.¹¹ Unlike thrombotic stroke, embolic stroke is typically not preceded by the development of adequate collateral circulation. Consequently, the affected brain tissue is subjected to more severe and extensive ischemia, increasing the likelihood of irreversible damage. As a result, patients with embolic stroke often present with more pronounced neurological deficits at onset.¹²

One of the major complications of embolic stroke is hemorrhagic transformation, defined as bleeding within previously infarcted brain tissue. This complication reflects a breakdown of vascular integrity as a consequence of severe ischemic injury.¹³ Hemorrhagic transformation may occur spontaneously or as a result of reperfusion therapies. From a pathophysiological standpoint, it is closely associated with disruption of the blood-brain barrier (BBB).⁴ Ischemia induces endothelial dysfunction, activation of inflammatory cells, and the release of mediators such as cytokines and proteolytic enzymes, all of which contribute to structural damage of the vascular wall. This damage increases vascular permeability, allowing blood components to extravasate into the brain parenchyma.⁵

In addition, reperfusion plays a crucial role in the development of hemorrhagic transformation. Reperfusion, whether occurring spontaneously or following therapeutic interventions such as thrombolysis and mechanical thrombectomy, may lead to a phenomenon known as reperfusion injury.¹⁴ This process is characterized by increased oxidative stress, inflammatory responses, and elevated hydrostatic pressure within already compromised blood vessels, further contributing to vascular damage and the risk of hemorrhage.⁵

Embolic stroke has a greater propensity for spontaneous reperfusion compared to thrombotic stroke. This is related to the nature of the embolus, which is more likely to undergo lysis or migrate distally, allowing restoration of blood flow to previously ischemic brain tissue.¹¹ However, the re-establishment of circulation in injured tissue may have detrimental effects, as it increases the risk of hemorrhagic transformation.¹⁴

Clinically, hemorrhagic transformation encompasses a broad spectrum, ranging from small petechial hemorrhages to the development of large parenchymal hematomas.⁴ Its clinical

presentation varies widely, from asymptomatic cases to significant neurological deterioration. The severity of these manifestations is largely determined by the extent of bleeding and the location of the lesion within the brain tissue.¹⁵

To assess the severity of hemorrhagic transformation in stroke, one of the most widely used systems is the European Cooperative Acute Stroke Study (ECASS) classification.¹⁶ This system categorizes hemorrhagic transformation into two main groups: hemorrhagic infarction (HI) and parenchymal hematoma (PH), each of which carries important implications for patient prognosis.⁴

Within the hemorrhagic infarction (HI) category, two subtypes are recognized: HI-1 and HI-2. HI-1 is characterized by small petechial hemorrhages scattered within the infarcted area, whereas HI-2 involves more confluent and extensive petechial bleeding without associated mass effect. In general, hemorrhagic infarction is considered a milder form of hemorrhagic transformation and is less frequently associated with significant clinical deterioration.^{17,18}

In contrast, parenchymal hematoma represents a more severe form of hemorrhagic transformation and is further classified into PH-1 and PH-2. PH-1 is characterized by a hematoma occupying less than 30% of the infarcted area with minimal mass effect. In contrast, PH-2 is a more severe condition, in which the hematoma involves more than 30% of the infarcted area and is accompanied by significant mass effect. This subtype is frequently associated with marked neurological deterioration and a higher risk of mortality.⁴

Overall, the ECASS classification not only facilitates the characterization of radiological findings but also serves as a valuable tool for predicting clinical course and guiding subsequent management in patients with hemorrhagic transformation.⁴ In this case, hemorrhagic transformation was classified as HI-1, indicating the presence of widespread petechial hemorrhage without significant mass effect. Although considered less severe than parenchymal hematoma, this condition still carries important clinical implications, particularly when associated with cerebral edema.¹⁵

Several factors are known to contribute to the development of hemorrhagic transformation in stroke, which can broadly be categorized into patient-related and stroke-related factors. Patient-related factors include advanced age, hypertension, diabetes mellitus, and a history of prior stroke. These conditions lead to chronic vascular changes, such as increased fragility of the vessel wall and impaired autoregulation, thereby increasing susceptibility to hemorrhage.¹⁵ Stroke-related factors include cardioembolic etiology, large infarct size, and the degree of hypoperfusion. Extensive infarction, often reflected by a low ASPECT score, indicates more severe tissue damage, making the affected vasculature more prone to leakage upon reperfusion.¹⁹

In addition, treatment-related factors play a significant role in increasing the risk of hemorrhagic transformation. Reperfusion therapies such as thrombolysis and mechanical thrombectomy, although intended to restore cerebral blood flow, may precipitate reperfusion injury, thereby increasing the risk of bleeding.⁵ Furthermore, the use of anticoagulants such as warfarin may exacerbate bleeding tendencies due to impairment of the hemostatic system.²⁰ Consequently, hemorrhagic transformation represents the result of a complex interplay between patient characteristics, stroke-related factors, and therapeutic interventions, necessitating a comprehensive risk assessment to guide optimal management strategies.⁹ In this case, several major risk factors were identified, including extensive cerebral infarction, a likely embolic etiology, and a history of warfarin use. The combination of these factors significantly increased the risk of hemorrhagic transformation.

The management of hemorrhagic transformation in embolic stroke aims to prevent further bleeding while optimizing the patient's neurological status. The overall approach generally includes initial stabilization, control of risk factors, and supportive therapy.⁵ In the early phase, close monitoring is essential, particularly with regard to neurological status, airway protection, and hemodynamic stability. Maintaining blood pressure within a safe range is crucial, as elevated blood pressure may increase the risk of hemorrhage expansion.²¹

In addition, careful attention should be given to medication management, particularly the use of anticoagulants. In patients previously receiving such therapy, anticoagulants should be

promptly discontinued and their effects reversed.²⁰ For example, in patients on warfarin, vitamin K administration may be initiated, and prothrombin complex concentrate (PCC) can be considered to accelerate the restoration of coagulation function. Management of intracranial pressure is also a critical component of treatment. Measures such as head elevation, administration of osmotic agents like mannitol, and close monitoring are necessary to prevent complications related to increased intracranial pressure and to maintain adequate cerebral perfusion.²² Furthermore, decisions regarding the timing of anticoagulation resumption should be made cautiously. Risk assessment must balance the potential for further bleeding against the risk of recurrent embolic stroke.²³

In cases involving large hematomas or significant mass effect, surgical intervention such as decompression or hematoma evacuation may be considered, particularly in the presence of neurological deterioration or uncontrolled intracranial pressure.¹⁵ However, in cases of hemorrhagic infarction (HI), which are more commonly encountered including in this patient conservative management is generally preferred, as the bleeding typically does not result in substantial mass effect.⁵

Hemorrhagic transformation has significant clinical impact, as it is associated with an increased risk of mortality and poorer functional outcomes. Therefore, early detection through careful clinical and radiological monitoring, along with timely and appropriate management, plays a crucial role in improving patient prognosis.¹⁵

Overall, embolic stroke with hemorrhagic transformation represents a complex condition with multifactorial pathophysiological mechanisms. A thorough understanding of its classification, risk factors, and management principles is essential in clinical practice, enabling more accurate decision-making and ultimately optimizing patient outcomes.

Picture

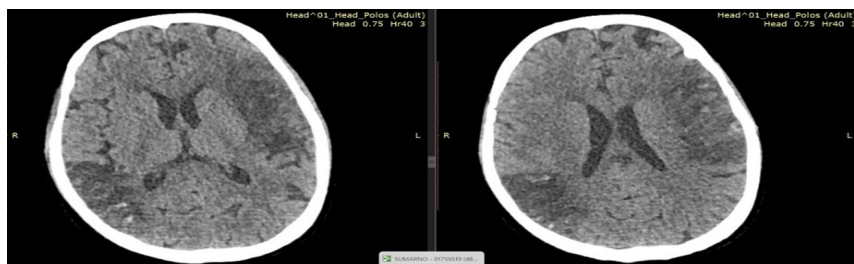


Figure 1. Non-Contrast Head CT Scan

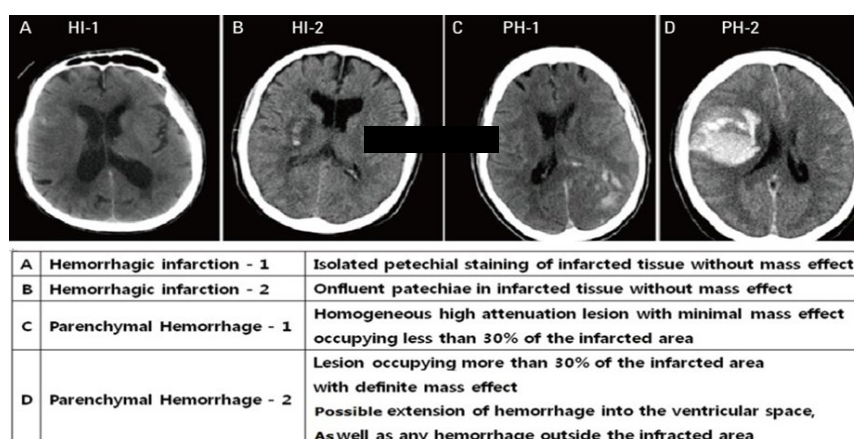


Figure 2. Types of hemorrhagic transformation according to ECASS.¹⁸

CONCLUSION

Hemorrhagic transformation is a critical complication of embolic stroke with substantial clinical impact, as it is associated with increased mortality and poorer functional outcomes. This condition arises from a complex interplay between patient-related factors, stroke characteristics,

and therapeutic interventions, including reperfusion effects and anticoagulant use, which may further increase the risk of bleeding.

Its clinical presentation varies widely, ranging from mild, often asymptomatic petechial hemorrhages to severe parenchymal hematomas. In this context, the ECASS classification plays an essential role in assessing severity and guiding prognostic evaluation.

Management requires a comprehensive approach, including initial stabilization, control of risk factors, and management of intracranial pressure, along with careful consideration of the use and reintroduction of anticoagulant therapy. Therefore, early detection through vigilant clinical and radiological monitoring, combined with timely and appropriate treatment, is crucial to improving patient outcomes.

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