

A CASE OF SPONTANEOUS HEMORRHAGIC TRANSFORMATION IN A PATIENT WITH CARDIOEMBOLIC STROKE DUE TO ATRIAL FIBRILLATION

Raymond Pranata¹, Veresa Chintya², Emir Yonas³

¹General Practitioner, Tabanan General Hospital, Tabanan, Bali, Indonesia ²General Practitioner, Sanjiwani General Hospital, Gianyar, Bali, Indonesia ³Faculty of Medicine, YARSI University, Jakarta, Indonesia

ABSTRACT

INTRODUCTION: Hemorrhagic transformation (HT) refers to spectrum of ischemia-related brain hemorrhage and is associated with increased morbidity and mortality of acute ischemic stroke.

CASE ILLUSTRATION: An 83 years old female presented with loss of consciousness 30 minutes before admission. Her past medical history of congestive heart failure, hypertension, atrial fibrillation (AF), and stroke. Physical examination showed GCS 7 and BP 190/100 mmHg. Electrocardiography showed Atrial Fibrillation NormoVentricular Response and Left Ventricular Hypertrophy. Laboratory examination showed thrombocytopenia, hypokalemia, and INR of 1.8. National Institutes of Health Stroke Scale Score: 16 CHA₂DS₂-VASc: 7, HAS-BLED: 4. Thorax Xray revealed cardiomegaly and Thorax CT Scan depicted characteristic of hemorrhagic transformation of an ischemic infarct. The patient was treated with hemorrhagic stroke protocol and mannitol.

DISCUSSION: Atrial fibrillation is associated with greater volumes of more severe baseline hypoperfusion, leading to higher infarct growth, more frequent severe HT and worse stroke outcomes. This patient has massive infarction and AF which were independent predictors of HT risk. In patients with AF probability of bleeding was about 95% if the volume of infarction edema >10 cm³. Hemorrhagic transformations may occur in patients with acute ischemic stroke who received thrombolytic, however, it may also occur spontaneously in 12.3 % of patients with ischemic stroke. Warfarin has been associated with increased HT risk irrespective of INR and aPTT values. Hemorrhage risk stratification score might be used to predict HT in acute ischemic stroke. Anticoagulant may be reinitiated after 4-8 weeks. Long-term anticoagulation with NOAC (similar efficacy with lower bleeding risk compared to VKA) or Left atrial appendage occlusion.

CONCLUSION: One-third of ischemic stroke patient may experience hemorrhagic transformation. Physician must strike a balance between stroke recurrence and HT.

Keywords: Atrial Fibrillation, Stroke, Anticoagulant

PENDAHULUAN: Transformasi perdarahan merupakan spektrum dari perdarahan otak yang berhubungan dengan iskemia serta dihubungkan dengan meningkatnya morbiditas dan mortalitas dari stroke iskemik akut.

ILUSTRASI KASUS: Seorang perempuan 83 tahun datang dengan penurunan kesadaran sejak 30 menit sebelum masuk rumah sakit. Memiliki riwayat gagal jantung, hipertensi, fibrilasi atrium dan stroke. Pemeriksaan fisik menunjukkan adanya GCS 7 serta TD 190/100 mmHg. EKG menunjukkan AF NVR dan LVH. Pemeriksaan laboratorium menunjukkan trombositopenia, hypokalemia, dan INR 1.8. Skor NIHSS: 16. CHA₂DS₂-VASc: 7, HAS-BLED: 4. X-ray thoraks: kardiomegali, CT scan: terdapat karakteristik dari transformasi hemoragik dari infark iskemik. Pasien ditatalaksana dengan protokol stroke perdarahan dan mannitol.

DISKUSI

Fibrilasi atrium dihubungkan dengan volume hipoperfusi baseline yang lebih berat dapat menyebabkan pertumbuhan luas infark yang lebih cepat, transformasi perdarahan yang lebih sering dan luaran stroke yang lebih buruk. Pasien ini mengalami infark masif dan fibrilasi atrium yang merupakan faktor prediktor independen dari pada resiko transformasi perdarahan. Transformasi perdarahan dapat terjadi pada pasien dengan stroke iskemik akut yang mendapatkan thrombolitik, namun, dapat terjadi secara spontan pada 12,3% pasien stroke iskemik. Warfarin dihubungkan dengan peningkatan transformasi perdarahan yang tidak terpengaruhi oleh nilai INR dan PTT. Hemorrhage risk stratification score dapat digunakan untuk memprediksi transformasi

perdarahan pada pasien stroke iskemik akut. Antikoagulan dapat diberikan kembali setelah 4-8 minggu. Antikoagulansi jangka panjang dengan NOAC (resiko perdarahan yang sama dengan resiko perdarahan yang lebih rendah dibanding antagonis vitamin K) atau oklusi appendiks atrium kiri.

KONKLUSI

Satupertiga dari pasien iskemik stroke dapat mengalami transformasi perdarahan. Oleh karena itu, klinis haruslah dapat menyeimbangkan antara pencegahan stroke berulang dan transformasi perdarahan.

Kata kunci: Fibrilasi Atrium, Stroke, Antikoagulan

Correspondence :

Raymond Pranata¹, Veresa Chintya², Emir Yonas³

¹General Practitioner, Tabanan General Hospital, Tabanan, Bali, Indonesia ²General Practitioner, Sanjiwani General Hospital, Gianyar, Bali, Indonesia ³Faculty of Medicine, YARSI University, Jakarta, Indonesia

Ph:0811 813 086

How to cite this article :

A CASE OF SPONTANEOUS HEMORRHAGIC TRANSFORMATION IN A PATIENT WITH CARDIOEMBOLIC STROKE DUE TO ATRIAL FIBRILLATION

INTRODUCTION

Hemorrhagic transformation (HT) refers to a spectrum of ischemia-related brain hemorrhage and is associated with increased morbidity and mortality of acute ischemic stroke.^{1,2} Atrial fibrillation (AF) is associated with greater volumes of more severe baseline hypoperfusion, leading to higher infarct growth, more frequent severe HT and worse stroke outcomes. Anticoagulation is a double-edged knife by preventing further embolization and worsening of ischemia in such patients at the cost of increased bleeding risk.

CASE ILLUSTRATION

An 83 years old female presented with loss of consciousness 30 minutes before admission. Past medical history of chronic heart failure, hypertension, AF and stroke 3 years prior. The patient took warfarin but is non-compliant. GCS 7, blood pressure of 190/100 mmHg, heart rate 84x/minute and respiratory rate of 20x/minute. Electrocardiography showed AF normal ventricular response and left ventricular hypertrophy (Fig 1). Laboratory examination showed thrombocytopenia of $114.000 \times 10^3/\mu\text{L}$, hypokalemia of 3,2mmol/L and INR of 1,8. NIHSS Score for this patient was 16 (moderate to severe stroke). CHA₂DS₂-VASc score was 7 and the HAS-BLED score was 4. Chest X-Ray showed cardiomegaly and thorax CT Scan showed the characteristic of hemorrhagic transformation of an ischemic infarct and cerebral edema. The patient was treated with hemorrhagic stroke protocol and mannitol.

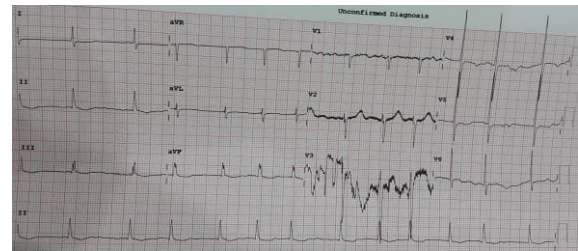


Fig 1. Patient's ECG showing atrial fibrillation

DISCUSSION

Atrial fibrillation is associated with greater volumes of more severe baseline hypoperfusion, leading to higher infarct growth, more frequent severe HT, and worse stroke outcomes.³ This patient has thrombocytopenia and AF with cerebral embolism resulting in massive infarction which were independent predictors of HT risk.^{1,4} Infarction of gray matter, hyperglycemia, poor collateral vessels, high NIHSS score, low total cholesterol and LDL-C levels are related to increased risk of HT. In patient with AF probability of bleeding was about 95% if the volume of infarction edema $>10 \text{ cm}^3$.¹ Hemorrhagic transformations may occur in patients with acute ischemic stroke who received thrombolytic, however, it may also occur spontaneously in 12.3 % of patients with ischemic stroke, and atrial fibrillation and large infarct area were independent predictors.⁴ Warfarin has been associated with larger volumes, higher rates of expansion of intracerebral haemorrhage irrespective of INR and aPTT values and increased HT risk.^{5,6} Hemorrhage risk stratification (HeRS) score might be used to predict HT in acute ischemic stroke in which age, infarct volume, and even mild renal impairment are predictors of HT.² Measures to prevent HT in stroke in patient with AF includes stopping warfarin and restarting it 14 days later, however, come with consequence of 5-8% recurrence. Some start

UFH/LMWH early, dabigatran was postulated to be the drug to start early anticoagulation as it might be safer than warfarin in terms of intracerebral hemorrhage, especially after a stroke.^{7,8} Prothrombin complex concentrates used in animal studies demonstrate rapid reversal of warfarin effect and might be used before rt-PA to achieve better stroke outcome and reducing HT risk. Cilostazol (phosphodiesterase-III inhibitor) has been reported to offer neuro protection and endothelial protection in animals with ischemic brain injury.¹ In acute ischemic stroke with NIHSS 16 ideal approach according to European Society of Cardiology guideline would be to repeat CT scan at day 12 to evaluate and starts anticoagulant if possible if the patient does. However, due to presence of hemorrhagic transformation the anticoagulant may be reinitiated after 4-8 weeks. Long-term anticoagulation with novel anticoagulant (similar efficacy with lower bleeding risk compared to vitamin K antagonist) may be sought. In those with contraindication to novel anticoagulant or other factors such as very poor drug compliance, left atrial appendage occlusion may be an alternative.⁹

CONCLUSION

One-third of ischemic stroke patient may experience hemorrhagic transformation, anticoagulation increases the volume, expansion and leads to a worse prognosis. Physicians must strike a balance between stroke recurrence and HT. A multidisciplinary approach is mandatory for a better patient outcome.

REFERENCES

1. Zhang J, Yang Y, Sun H, Xing Y. Hemorrhagic transformation after cerebral infarction: current concepts and

- challenges. *Ann Transl Med* 2014;2: 2305–5839.
2. Marsh EB, Llinas RH, Schneider ALC, Hillis AE, Lawrence E, Dziedzic P, et al. Predicting Hemorrhagic Transformation of Acute Ischemic Stroke: Prospective Validation of the HeRSScore. *Medicine (Baltimore)*. 2016 Jan;95(2):e2430.
3. Tu HT, Campbell BC, Christensen S, De Silva DA, Butcher KS, Parsons MW, et al. Worse stroke outcome in atrial fibrillation is explained by more severe hypoperfusion, infarct growth, and hemorrhagic transformation. *Int J Stroke* 2015; 10:534–540
4. Tan S, Wang D, Liu M, Zhang S, Wu B, Liu B. Frequency and predictors of spontaneous hemorrhagic transformation in ischemic stroke and its association with prognosis. *J Neurol*. 2014; 261(5):905–12.
5. Pfeilschifter W, Spitzer D, Czech-Zechmeister B, Steinmetz H, Foerch C. Increased risk of hemorrhagic transformation in ischemic stroke occurring during warfarin anticoagulation: an experimental study in mice. *Stroke*. 2011;42:1116–21.
6. Flibotte JJ, Hagan N, O'Donnell J, Greenberg SM, Rosand J. Warfarin, hematoma expansion, and outcome of intracerebral hemorrhage. *Neurology*. 2004;63:1059–1064.
7. Mudd PD, James MA. Anticoagulation for atrial fibrillation: should warfarin be temporarily stopped or continued after acute cardioembolic stroke? *Age Ageing* 2010;39:670–3
8. Pfeilschifter W, Bohmann F, Baumgarten P, Mittelbronn M, Pfeilschifter J, Lindhoff-Last E, et al.. Thrombolysis with recombinant tissue plasminogen activator under dabigatran anticoagulation in experimental stroke. *Ann Neurol*. 2012;71(5):624–33.

9. Lewalter T, Ibrahim R, Albers B, Camm AJ. An update and current expert opinions on percutaneous left atrial appendage occlusion for stroke prevention in atrial fibrillation. *Europace* 2013;15:652–656
10. Pfeilschifter W, Spitzer D, Pfeilschifter J, Steinmetz H, Foerch C, Borlongan CV. Warfarin anticoagulation exacerbates the risk of hemorrhagic transformation after rt-PA treatment in experimental stroke: therapeutic potential of PCC. *PLoS ONE*. 2011;6:e26087