

DIFFUSE-WEIGHTED MAGNETIC RESONANCE IMAGING (DW-MRI) FOR CRYPTOGENIC STROKE DIAGNOSIS IN YOUNG ADULT FEMALE: A CASE REPORT

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ABSTRACT

Background: Ischaemic stroke is caused by various aetiology. Cryptogenic stroke diagnosis is established when no aetiologies are discovered although clinical manifestations are consistent with acute stroke. Diffusion-weighted magnetic resonance imaging (DW-MRI) is one neuroimaging modalities which could be useful in exploring aetiology instead of excluding intracranial haemorrhage. There are many conflicting pieces of evidence of the benefit using DW-MRI to confirm the presence or the absence of brain lesions.

Objective: To report a clinical case of ischemic stroke with negative evaluation on advanced neuroimaging studies (DW-MRI).

Case Description: A female, 35 years old, presented to the emergency unit with a 6 hours history of prickling sensation before admission. There were no risk factors of stroke, and no other neurological symptoms. The neurologic examination reveals left hemihypesthesia, with normal results on laboratory examination for stroke risk factors and negative ischemic lesion on brain DW-MRI. Explorative examination on cardiac aetiologies was negative. Patient was given a standard regimen for acute stroke management despite the negative results and established as a cryptogenic stroke case.

Conclusion: Diagnosis of ischemic stroke should rely mainly on clinical findings, with consideration of cryptogenic stroke when there is no aetiology found after thorough examination. Nevertheless, comprehensive examination on cardiac function and coagulation tests should be performed whenever possible to determine the cause of ischaemic stroke.

Keywords: brain ischaemia, stroke, cryptogenic, diffusion magnetic resonance imaging

INTRODUCTION

The diagnosis of ischaemic stroke is generally established with the presence of neurologic deficit from the physical examination and ischaemic lesion from the brain computed tomography (CT) scan. In the past decades, the utilisation of magnetic resonance imaging (MRI), especially diffuse-weighted imaging (DW-MRI), has been increasing in diagnosing ischaemic stroke. DW-MRI is suggested for patients with inconclusive neurologic examination or vague anatomic location of the brain lesion. Therefore, DW-MRI is mostly used for diagnosing ischaemic lesion instead of excluding cerebral haemorrhage.^{1,2}

The optimal management of stroke patients relies on the etiologic diagnosis.³ Based on TOAST criteria, the patient with two or more causes identified, negative evaluation, or incomplete evaluation will be categorised as cryptogenic stroke.⁴ Accordingly, cryptogenic stroke diagnosis must follow a careful approach using the advanced imaging technology, such as DW-MRI.⁵ This article reports a diagnostic approach of cryptogenic stroke case in a young adult Caucasian female treated in Indonesian hospital.

CASE DESCRIPTION

A young adult Caucasian female (35 years old) was presented at the emergency ward with persistent prickling sensation on the left side of the body (face, upper and lower extremity) which suddenly appeared in the last 6 hours before admission. The symptoms persisted even after she received treatment with an unknown intravenous solution and discharged from another hospital previously. She declined any history of head trauma or fever prior to the symptom. She also denied any muscle weaknesses, problems with

micturition and defecation, seizure, loss of consciousness or increased intracranial pressure signs (e.g. severe headache, loss of eyesight, or projectile vomiting). She did not recall any similar symptoms in the past, and also denied the history of cigarette smoking, diabetes mellitus, heart diseases, hypertension, hypercholesterolemia and hormonal contraception consumption.

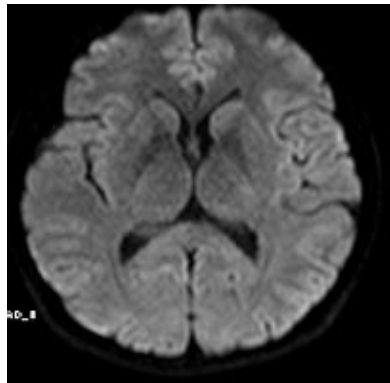
The patient's physical examination was remarkable, with good general condition, no fever, and normal results on cranial nerves examination, muscle strength examination, pathological and physiological reflex examination, and mental and cognitive status examination. There was a significant decreased sensation on the left side of the body (hemihypesthesia). Based on the findings, the patient has NIHSS score 1 which is a mild stroke.

The laboratory examination on complete blood count, liver and renal function, electrolytes, blood glucose and HbA1c, and lipid profile showed normal results. Further brain DW-MRI showed normal imaging of brain parenchyma without visible ischaemic lesion (Figure 1 (a)), and MR angiography showed normal configuration of carotid and intracranial artery without any sign of stenosis (Figure 1 (b)). Further cardiologic examination with electrocardiography showed normal heart rhythm without any sign of conductive anomalies and transthoracic echocardiography showed normal heart ejection function without any sign of thrombus. The final diagnosis is cryptogenic ischaemic stroke.

The patient was admitted and given clopidogrel 75 mg tablet per oral immediately, citicoline 1000 mg intravenous injection every 12 hours, mecobalamin 1000 mcg intravenous injection every 12 hours, and pregabalin 75 mg tablet every 24

hours. On the third day of admission, the prickling sensation declined. The day after, we increased the dose of pregabalin to 150 mg tablet per oral every 24 hours. On the fifth day of admission, the patient did not show

any worsening neurological symptoms, with persisting residual paraesthesia. She was further discharged and continued treatment in the outpatient setting.



(a)



(b)

Figure 1. (a) Axial brain DW-MRI of basal ganglia, focusing on thalamus reveals no restrictive diffusion lesion. (b) Cerebral MR angiography shows normal contour of carotid and intracranial arteries, without visible stenosis.

DISCUSSION

Cryptogenic stroke accounts for 30% to 40% of all ischaemic stroke cases and affects younger patients without known stroke risks.⁶⁻⁹ Compared to other cause of stroke, cryptogenic stroke patients usually have a milder presentation and very low mortality rate.¹⁰ The diagnosis of cryptogenic stroke is mainly based on the exclusion of other distinguishable aetiology (e.g. large-artery atherosclerosis, cardio-embolism, and small-artery occlusion), and concluded after thorough examination shows unknown cause.^{10,11} Table 1 described the criteria for the diagnosis of embolic stroke of undetermined source (ESUS).¹² Further comprehensive examination of cryptogenic stroke patients usually uncovers occult atherosclerosis, non-sclerosing arteriopathy (e.g. dissection or vasculitis), hypercoagulable state, and mild cardio-emboli.¹⁰

Determining Ischaemic Stroke Aetiology

The most common aetiologies to be considered are silent atrial fibrillation (AF), patent foramen ovale (PFO), and coagulopathy.¹³⁻¹⁵ The silent AF usually discovered by cardiac Holter monitoring or implantable cardiac devices for at least 24 hours. The most accurate method to detect PFO is by cardiac catheterisation, while trans-oesophageal echocardiography with bubble study is best to measure the shunt size and determining the anatomical characteristics of PFO.¹⁵⁻¹⁷

There are several coagulopathies that should be thoroughly examined, such as thrombophilia, vasculopathy, hypercoagulable state. Thrombophilia can be confirmed with clotting factors tests, while vasculopathy should be suspected in patients with the history of infection, immunosuppression, autoimmune, and inflammation. Specific tests must be done according to the suspicion (e.g. rheumatoid

factor and anti-phospholipid for autoimmune cause). D-dimer test for hypercoagulability usually corresponds with suspected malignancies.^{5,11,18}

Diagnostic Approach With DW-MRI

Diffuse-weighted MRI has been increasingly used for ischaemic stroke diagnosis, especially in detecting ischaemic lesion with higher sensitivity compared to brain CT-scan.² However, there are contradicting evidence on its accuracy with a high rate (up to a third) of false-negative results.^{2,19,20} Ischaemic lesion on posterior circulation usually results in negative DW-MRI scan.² Moreover, DW-MRI results fail to predict the long-term outcome of stroke patients.²⁰ Therefore, stroke diagnosis and initial treatment should be based more on clinical presentation, despite the negative DW-MRI result. Nevertheless, many countries have incorporated the DW-MRI into their acute stroke management guideline, such as the UK, which should be cautiously adopted to clinical settings in developing countries.¹⁹⁻²¹

The patient in this report was initially suspected having lacunar

stroke syndrome based on OSCP criteria.^{4,22} The patient's demographic characteristics are also consistent with previous cases. However, a thorough examination with DW-MRI did not reveal any brain lesion, inconsistent with suspected anterior circulation lesion. The MR angiography did not show any vessel occlusion, as well. The cryptogenic stroke diagnosis otherwise supported by normal findings on cardiac examination (12-lead ECG and transthoracic echocardiography). Despite the normal findings on neuroimaging and laboratory studies, we gave a standard regimen for acute stroke that present more than 4.5 hours since the first symptoms, which are antiplatelets and neuroprotector agents. The patient's symptoms were alleviated and discharged with residual paraesthesia. Compared to the guideline on the exploration of aetiology, we did not perform Holter monitoring, transoesophageal echocardiography, and laboratory tests on coagulopathies. We also did not perform a further thorough exploration of the other possible explanation of her clinical diagnosis.

Table 1. Criteria for diagnosis of embolic stroke of undetermined source (ESUS)*

Stroke detected by CT or MRI that is not lacunar†
Absence of extracranial or intracranial atherosclerosis causing ≥50% luminal stenosis in arteries supplying the area of ischaemia
No major-risk cardioembolic source of embolism‡
No other specific cause of stroke identified (e.g., arteritis, dissection, migraine/vasospasm, drug misuse)

* Requires minimum diagnostic assessment (Brain CT or MRI, 12-lead ECG, Precordial echocardiography, Cardiac monitoring for ≥24 h with automated rhythm detection, Imaging of both the extracranial and intracranial arteries supplying the area of brain ischaemia (catheter, MR, or CT angiography, or cervical duplex plus transcranial doppler ultrasonography)

† Lacunar defined as a subcortical infarct smaller than or equal to 1.5 cm (≤2.0 cm on MRI diffusion images) in largest dimension, including on MRI diffusion-weighted images, and in the distribution of the small, penetrating cerebral arteries; visualisation by CT usually needs delayed imaging greater than 24–48 h after stroke onset.

‡ Permanent or paroxysmal atrial fibrillation, sustained atrial flutter, intracardiac thrombus, prosthetic cardiac valve, atrial myxoma or other cardiac tumours, mitral stenosis, recent (<4 weeks) myocardial infarction, left ventricular ejection fraction less than 30%, valvular vegetations, or infective endocarditis.

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guideline on the exploration of aetiology, we did not perform Holter monitoring, transoesophageal echocardiography, and laboratory tests on coagulopathies. We also did not perform a further thorough exploration of the other possible explanation of her clinical diagnosis.

CONCLUSION

The absence of positive findings on the neuroimaging and laboratory studies should not exclude the possibility of ischaemic stroke, hence the patient should be given appropriate acute stroke management based on the diagnosis of cryptogenic stroke. Emergency physicians should be aware of the probable cryptogenic stroke, especially in younger adults without any stroke risk factors. Specifically, thorough cardiovascular examination and coagulopathies tests should be performed whenever possible for an appropriate treatment regiment, including secondary prevention.

CONFLICT OF INTEREST AND FUNDING RESOURCES

The author declares no conflict of interest and funding resources.

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