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The Importance of Understanding the Risk Factors for TIA

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ABSTRACT

Transient ischemic attack (TIA) and minor ischemic stroke are associated with brain dysfunction in a circumscribed area caused by a regional reduction in blood flow (i.e., ischemia), resulting in transient or minor observable clinical symptoms. We reported a case study of a female patient with a TIA with symptoms of dizziness, weakness of the left limb, and tingling for about 30 minutes. She was admitted to the emergency room and underwent several tests, including ECG, CT scan, and laboratory test to confirm the diagnosis. The patient probability of stroke infarct was determined by the ABCD2 score. Through ABCD2 score, the patient had 4.1% probability of Ischemic stroke without looking at the imaging features on a CT scan or MRI. By knowing the risk factors of TIA, the patient was suggested to modify lifestyle to prevent the occurrence of TIA due to TIA can be an early sign of ischemic stroke.

Keywords: TIA, risk factors of TIA, TIA's risk stratification

INTRODUCTION

Transient ischemic attack (TIA) and minor ischemic stroke are associated with brain dysfunction in a circumscribed area caused by a regional reduction in blood flow (i.e., ischemia), resulting in either transient or minor observable clinical symptoms (Coutts, 2017). TIA incidence in a population is difficult to estimate due to other mimicking disorders, but available crude annual incidence rates of transient ischemic attack (TIA) range between 29.0 and 61.0 cases per 100000 in Western countries. Additionally, TIA is a known predictor of subsequent ischemic stroke with risk estimates within three months ranging between 7.5% and 17.3%; half of those events were described to occur within 48 hours (Degan et al., 2017).

TIA can be considered as a severe warning to an impending ischemic stroke. The highest risk is found in the first 48 hours following a transient ischemic attack. Differentiating transient ischemic attacks is crucial from other mimicking conditions. Transient ischemic attacks are related to a focal neurologic deficit and speech disturbance in a vascular territory due to underlying cerebrovascular disease. This condition occurs suddenly in onset. TIA evaluation should be done urgently with imaging and laboratory studies to decrease the risk of subsequent strokes. A simple clinical measure can stratify the subsequent risk of TIA or ischemic stroke. TIA subtypes are classified based on the pathophysiological mechanisms that are similar to ischemic stroke subtypes. They include large artery atherothrombosis, cardiac embolism, small vessel (lacunar), cryptogenic, and uncommon subtypes such as vascular dissection and vasculitis. The common risk factors for all TIA include age, alcoholism, diabetes, hypertension, lack of regular physical activity, psychosocial stress, obesity, smoking, and unhealthy diet. Immediate multimodality therapeutic interventions should be initiated. These will include aggressive treatment of blood pressure, high dose statin, antiplatelet therapy, blood sugar control, diet, and exercises. Specific underlying etiology

needs to be managed accordingly. This treatment scheme may substantially reduce the risk of recurrent strokes or future TIA by at least 80% (Abbott et al., 2017).

In this report study, we evaluated a patient who had TIA to understand the risk factors of TIA. We expected that by the understanding of the TIA's etiology, the patient can be treated properly and inhibit an ischemic stroke.

METHODS

Case Description

A 32years-old female presented to the emergency department after feeling temporary weakness and tingling in her left arm. The patient had some complaints suddenly when she woke up from a nap. The weakness was not found when she arrived in ER. The patient's primary complaint at 15.00 p.m. was a weak left hand and tingling, which lasted for 30 minutes. Muscle strength was felt to reappear before the patient received any therapy. Her complaints were dizziness +, nausea -, vomiting -. She had a history of hypertension and diabetes mellitus and regularly took medication such as amlodipine 10mg and glimepiride 2mg. Her blood pressure tends to be high. The patient did not exercise regularly. She only occasionally walked, did not smoke, and had no allergy to food. Her physical examination was normal. Her physical results were GCS 15, BP 201/110 mmHg, HR 79 bpm, respiratory rate 20x/minute, weight 65kg, height 165cm, and BMI 23.9. As the initial treatment in the emergency room, the patient was given oxygenation, iv administration, and paracetamol 1gr as an analgesic.

In our case, the controlling risk factors were needed due to TIA being considered a severe warning to an impending ischemic stroke. The disease initially manifested with neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction, and the typical duration of a TIA is <1 or 2 hours (Easton et al., 2009). Focal or non-focal is the most critical clinical evaluation of neurological symptoms. Regional cerebral ischemia causes focal symptoms. Focal neurologic symptoms usually affect one side of the body (e.g., weakness or sensory abnormality on the right or left side). Non-focal neurologic symptoms include generalized weakness, light-headedness, fainting, blackouts, and bladder or bowel symptoms. Although patients with the non-focal symptoms of syncope or presyncope are sometimes referred for assessment of possible TIA, loss of consciousness is rarely a symptom of stroke or TIA (Coutts, 2017). We did an EKG in patients with acute stroke. A meta-analysis through 2014 found that the proportion of patients diagnosed with post-stroke AF in the emergency department by electrocardiography was 7.7% (95% CI, 5.0–10.8) (Forster et al., 2012).

RESULT

Initially, we observed the EKG results to determine the possibility of TIA causes of cardiac origins, such as atrial fibrillation and cardioembolism. The ECG was normal and expected TIA originate from the heart (Figure 1). Furthermore, ECG could be used to detect pertinent comorbidities that may have therapeutic implications. There were 3% of patients with acute stroke and acute myocardial infarction (MI) (Kleindorfer et al., 2021).

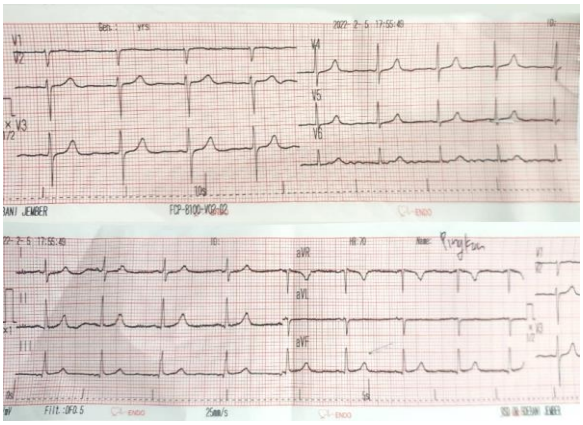

Figure 1. Normal rhythm ECG

As reported in AHA/ASA guideline 2021, control of hypertension, blood glucose, and lipids have been proven

effective for reducing the risk of ischemic stroke. Thus, a therapeutic goal for these metabolic parameters helps optimize therapy (Kleindorfer et al., 2021). The result of laboratory parameters in this study examination is presented in Table 1.

Table 1. Laboratory Parameters

Laboratory Examination	Result	Normal Result
Blood sugar	170	60 – 200 mg/dL
Total cholesterol	224	<200 mg/dL
Ren Function Test **Creatinine serum**	1.4	0.5 – 1.1 mg/dL

Abnormal blood testing helps to stratify risk. Therefore, physicians conduct a prevention effort on those at the highest risk. In patients with lacunar infarction, chronic kidney disease is associated with 50% increase in the risk of recurrent stroke. The patient stated that she had a history of diabetes mellitus since two years ago. As shown in Table 1, the patient has good sugar control by taking daily medication in the form of glimepiride 2 mg. Blood sugar sampling is generally performed by taking patients' blood sugar without previous fasting (Soebagijo et al., 2021). In this case, the patient tends to hypercholesterolemia. Fat and cholesterol are risk factors for ischemic stroke. A recent study showed that higher total cholesterol and systolic blood pressure were eight times higher ischemic stroke risk (Asia Pacific Cohort Studies Collaboration, 2005).

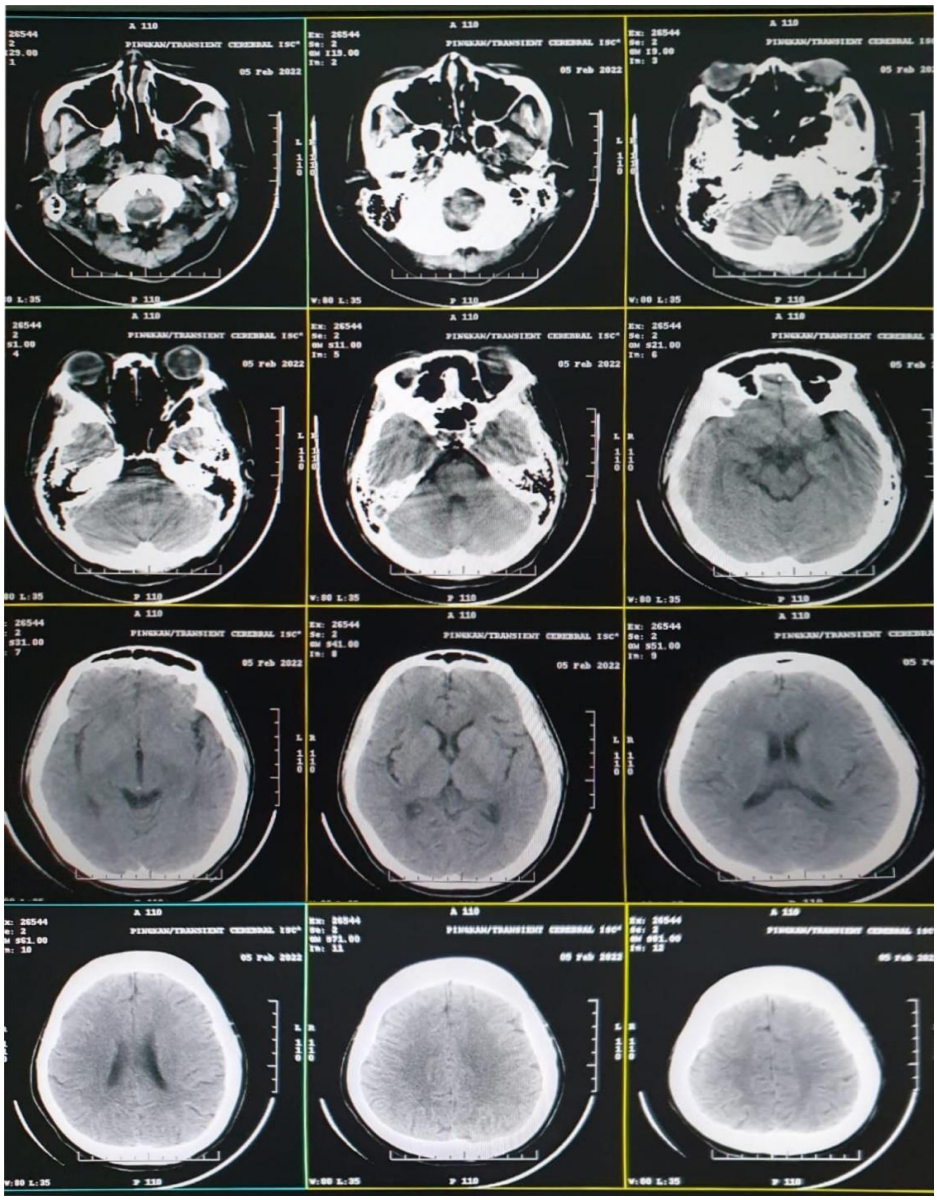

Figure 2. Non contrast Head CT Scan

The TIA goals of the neuroimaging evaluation are (1) to obtain evidence of a vascular origin for the symptoms either directly (evidence of hypoperfusion and acute infarction) or indirectly (identification of a presumptive source such as large-vessel stenosis), (2) to exclude an alternative no ischemic origin, (3) to ascertain the underlying vascular mechanism of the event (e.g., large-vessel atherothrombotic, cardioembolic, small-vessel lacunar), which, in turn, allows selection of the optimal therapy, and (4) to identify prognostic outcome categories.

MRI is not as widely available as CT and is generally more expensive (Easton et al., 2009). We did a non-contrast CT scan on our patient. The result of the CT Scan is normal, as shown in Figure 2. In agreement with previous result, there is a negative result according the result of CT scan. An initial assessment with CT revealed no acute pathology in 154 (95.7%) and possible acute infarction in 7 (4.3%) patients (Forster et al., 2012). About one-quarter of acute stroke cases with an initially negative head CT will have an MRI with acute or subacute infarction evidence. A study reported that 252 patients with atypical stroke symptoms were found in emergency department. There were 29 patients (11.5%) who had a negative CT and an acute ischemic stroke after MRI within 24 hours (Soebagijo et al., 2021). Our results showed the patient had a TIA according to the history, physical examination, and investigations. Therefore, we added therapy such as as pilet 80mg, clopidogrel 75 mg, and candesartan 8mg at night.

DISCUSSION

The first risk factor of our patient was hypertension. Uncontrolled blood pressure is the most common risk factor for stroke. Our result study is in accordance with a previous study, showing 73.9% of stroke subjects had hypertension history. This prevalence risk of hypertension is the highest among other chronic diseases (diabetes and heart disease) with 8.37 (Setyopranoto et al., 2019). Hypertension induces hypertrophy and remodeling of smooth muscle cells in systemic and cerebral arteries. Under a chronic high intraluminal pressure, smooth muscle cells undergo hypertrophy, hyperplasia, or rearrangement and grow inward, encroaching into the lumen of the artery, resulting in narrowing of the vessel lumen. Hypertension also leads to vascular stiffening, increasing pulse pressure, and a good predictor of stroke. Sympathetic perivascular innervation and mechanical effects the elevated intraluminal pressure on the vascular wall, mediated by growth factors, oxidative stress, and NO. Angiotensin II (Ang II) is a critical factor in the mechanisms of cerebrovascular remodeling, with reactive oxygen species (ROS). ROS promotes smooth muscle cell proliferation and initiates remodeling of the extracellular matrix via activation of matrix metalloproteases. Extracellular matrix proteins and integrin αvβ3, emilin-1, and elastin-1 play a critical role in hypertrophy, remodeling, and stiffening. Cerebral arterioles undergoing hypertrophy or remodeling have reduced stiffening. However, changes in cerebrovascular wall composition caused by sustained hypertension may lead to stiffening (Shah and Cole, 2010). Besides, diabetes mellitus is a highly prevalent and growing chronic disease affecting an estimated 415 million people globally in 2015. It is predicted to affect 642 million people by 2040. Additionally, diabetes is a well-recognized risk factor for neurovascular disease (Lau et al., 2019). Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia due to defects in insulin secretion and insulin action (Setyopranoto et al., 2019).

There are several possible mechanisms wherein diabetes leads to stroke. These include vascular endothelial dysfunction, increased early-age arterial stiffness, systemic inflammation, and thickening of the basal capillary membrane. Vascular endothelial function is critical for

maintaining structural and functional integrity of the vessel walls and vasomotor control. Nitric oxide (NO) mediates vasodilation. For example, NO-mediated vasodilation is impaired in individuals with diabetes, possibly due to increased inactivation of NO or decreased reactivity of the smooth muscle to NO. Individuals with type II diabetes have stiffer arteries and decreased elasticity compared to subjects with normal glucose levels. Type I diabetes is more often associated with early structural impairment of the common carotid artery, increased intima-medial thickness, and is considered an early sign of atherosclerosis. An increased inflammatory response is frequently seen in individuals with diabetes. Inflammation plays an essential role in developing atherosclerotic plaque (Chen et al., 2016).

There are non-modifiable risk factors, including age. Age is one of the risk factors for chronic diseases, such as cancer, cardiovascular diseases, and neurodegeneration. For stroke, age is a continuous risk factor with a two-fold increase in the incidence and prevalence rates for every five years after age 65. In this study, the ratio from each age group was 1.73, which is almost twice the risk of stroke for every ten years. Another study also found that the incidence of stroke doubled for each decade after 55 years of age (Setyopranoto et al., 2019). This finding could be explained by increasing other risk factors such as type 2 diabetes, high blood pressure, and atherosclerosis. The 2009 AHA/ASA guidelines include neuroimaging within 24 hours of symptom onset. A head CT preferably with a CT angiogram is recommended if an MRI cannot be performed. Non-contrast CT remains the mainstay of emergency imaging of stroke in order to exclude intracranial haemorrhages. Non-contrast CT may also identify other hemorrhage sites; pathologies that mimic strokes such as tumour or encephalitis. We observed ischemic tissue on non-contrast CT if there is an ischemic stroke. The rate of tissue density decline depends on the severity and duration of ischemia. Our study showed there was no abnormality in the CT scan results.

There is one-third of patients with stroke symptoms for <24 hours with diffusion-weighted imaging–positive lesions. The cost-effectiveness was not cost-effective in TIA patients who used MRI treatment. MRI might be utilized in this population if the imaging is done more than one week after onset of symptoms and with a blood-sensitive sequence. Predictive scores that incorporate MRI findings (e.g., ABCD2-I and ABCD3-I) are better able to discriminate high risk of early stroke from low risk of early stroke than predictive scores that do not incorporate MRI findings (e.g., ABCD2). MRI is done within seven days of onset of symptoms. Based on AHA/ASA in 2009, several studies have identified risk factors for stroke after TIA, which helps initial management decisions (Easton et al., 2009). The ABCD system (ABCD and subsequent ABCD2 score), as presented in Table 2, is a prognostic tool developed to predict stroke risk in the acute phase after TIA. The system was designed to be used in primary and emergency care settings by identifying high-risk individuals to facilitate triage and prevention. The BCD scoring is measured based on clinical features at the initial assessment before specialist evaluation and does not include the results of brain imaging (Giles et al., 2010).

Table 2. ABCD² Scoring

Criterion	Points
Age ≥ 60yrs	1
SBP ≥ 140 mmHg or DBP ≥90 mmHg	1
Clinical features	
Speech impairment	1
Unilateral weakness	2
Duration	
10 – 59 min	1
≥60 min	2
Diabetes	1
DBP= Diastolic Blood Pressure, SBP= Systolic Blood Pressure	

Patients with TIA score points (indicated in parentheses) for each of the following factors: age ≥60 years (1); blood pressure ≥140/90 mm Hg on first evaluation (1); clinical symptoms of focal weakness with the spell (2) or speech impairment

without weakness (1); duration ≥60 minutes (2) or 10 to 59 minutes (1); and diabetes (1). In combined validation cohorts, the 2-day risk of stroke was 0% for scores of 0 or 1, 1.3% for 2 or 3, 4.1% for 4 or 5, and 8.1% for 6 or 7. Our patient had 1 point for hypertension, 2 points for unilateral weakness, 1 point for 10 – 59 minutes, and 1 point for diabetes. Therefore, the total point was 5 points. It was indicated that our patient had 4.1% probability of an ischemic stroke.

CONCLUSION

Hypertension, diabetes, and lack of physical activity were modifiable risk factors for TIA. Patients should be modified their lifestyle to prevent the occurrence of TIA due to TIA itself can be an early sign of ischemic stroke.

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