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# HASIL PENILAIAN SEJAWAT SEBIDANG ATAU PEER REVIEW KARYA ILMIAH : JURNAL

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: Recombinant tissue plasminogen activator (rTPA) in young adult patient with acute ischemic stroke: a case report

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(Available online: 1 December 2020)

# Vol 9, No 3 (2020): (Available online: 1 December 2020)

# Table of Contents

A network meta-analysis on comparative efficacy and tolerability of on-demand therapy for premature ejaculation

Niwanda Yogiswara Yusuf Azmi Yufi Aulia Azmi

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The functional and physical state of the anal sphincter complex in the patients with rectal prolapse in the post-surgery period Solmaz Soltan Imanova

# CASE REPORT

Tracheostomy in upper airway obstruction on a COVID-19 patient (https://www.balimedicaljournal.org/index.php/bmj/article/view/1903)

Rohaizam Japar Jaafar, Zakinah Yahaya, Mohd Razif Mohamad Yunus, Marina Mat Baki

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Abstract (.pop-up-a-68)

## CASE REPORT

Recombinant tissue plasminogen activator (rTPA) in young adult patient with acute ischemic stroke: a case report

(https://www.balimedicaljournal.org/index.php/bmj/article/view/2148)

Dodik Tugasworo, Aditya Kurnianto, Retnaningsih Retnaningsih, Yovita Andhitara, Rahmi Ardhini, Runy Dyaksani, Jethro Budiman

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Abstract (.pop-up-a-69)

# **CASE REPORT**

Sinister Snoring in A Child (https://www.balimedicaljournal.org/index.php/bmj/article/view/1932)

Boon Chin Te, Zhi Xiang Yeoh, Rohaizam Japar Jaafar, Bee See Goh

Online First: December 01, 2020

DOI: 10.15562/bmj.v9i3.1932 (https://dx.doi.org/10.15562/bmj.v9i3.1932)

# Recombinant tissue plasminogen activator (rTPA) in young adult patient with acute ischemic stroke: a case report

by Dodik Tugasworo

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# Recombinant tissue plasminogen activator (rTPA) in young adult patient with acute ischemic stroke: a case report



Dodik Tugasworo<sup>1\*</sup>, Aditya Kurnianto<sup>1</sup>, Retnaningsih<sup>1</sup>, Yovita Andhitara<sup>1</sup>, Rahmi Ardhini<sup>1</sup>, Runy Dyaksani<sup>1</sup>, Jethro Budiman<sup>1</sup>

# ABSTRACT

Background: Stroke is one of the highest causes of morbidity and mortality in the world. The incidence rate of ischemic stroke is about 80% of all stroke incidents. The use of recombinant tissue plasminogen activator (rtPA) is recommended under 4.5 hours of stroke onset. Stroke in young adults are reported as being uncommon, compromising 10% -15% of all stroke patients. Many studies were reported the most common risk factor in young adults were obesity and dyslipidemia. This case report will discuss a 33-year-old men with ischemic stroke with obesity and dyslipidemia treated at dr. Kariadi Hospital Semarang.

Case presentation: A 33-year old obese man with left-sided

hemiparesis and central facial nerve palsy with an onset of 1 hour. On laboratory examination, it was obtained total cholesterol 179mg/dL, LDL level 123mg/dL, and HDL level 39mg/dL. The protocol code stroke was performed in emergency room with alteplase (r-TPA) 0.6 mg/kgBW, after his head MSCT shows there was no sign of blood in the brain parenchym.

**Conclusion:** The increased risk of ischemic stroke in young patients is due to dyslipidemia, hypertension, obesity, physical inactivity, and smoking. Treatment of the hyperacute phase of ischemic stroke with thrombolysis can reduce the outcome of stroke due to the disability.

Keywords: ischemic stroke, recombinant tissue plasminogen activator (rTPA), young adult stroke

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#### INTRODUCTION

Stroke is the leading cause of death and disability worldwide, especially in developing countries, with the increased incidence in young adults. There are 10% to 15% incidents of stroke in young adults with the incidence of ischemic strokes is more frequent than bleeding strokes, around 80-85% of all strokes.1-6 The most common risk factors of stroke in young adults were dyslipidemia, hypertension, obesity, physical inactivity, and smoking.1,6-8 The pathophysiology of ischemic stroke involves a complex immunological response starting from a thrombotic or embolic process that causes the death of neuron cells in the brain parenchyma which is called the ischemic cascade. The ischemic cascade consists of glutamate exotoxicity, intracellular calcium overload, free radical toxicity, and inflammation of the brain parenchyma. 9,10 The area of the infarct core is surrounded by potentially salvageable neurones, called the penumbra area.2,10,1

Many risk factors are associated with stroke, modifiable and non-modifiable. Modifiable stroke risk factors are hypertension, diabetes mellitus, dyslipidemia, obesity, and many more. The non-modifiable stroke risk factors are relatively few; including genetic, age, and gender. Dyslipidemia

is a lipid metabolism disorder, including an increase in cholesterol levels, an increase in LDL level, increased triglyceride levels and a decrease in HDL levels. Dyslipidemia is one of the most important risk factors for cerebrovascular disease because it is associated with atherosclerosis. People with obesity are at risk of stroke because obesity can increase the risk of another cardiovascular risk factor (hypertension, diabetes mellitus, and coronary heart disease). 13,14

The use of rTPA (recombinant Tissue Plasminogen Activator) is essential when it is given to acute stroke patients with certain conditions, both intravenously or intra-arterial, less than 3 hours after the onset of stroke and as soon as possible (AHA/ASA class I, level of evidence A). Intravenous administration of rTPA in patients in Asia is given with a low dose 0.6 mg/kgBW (maximum 60 mg), 10% of the total dose is given as an initial bolus, and the other is given in an infusion for 60 minutes. The aim of using rTPA is to destruct the thrombus so the reperfusion of brain tissue can be occurred, especially in penumbra area, and the patient clinical outcome will be better. 15,16

The case report that explains about rTPA in young adult patient with dyslipidemia and obesity are still limited. This case report will discuss about

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Received: 2020-10-12 Accepted: 2020-11-26 Published: 2020-12-01 rTPA in 33-year old man with ischemic stroke, dyslipidemia, and obesity who was admitted to Dr. Kariadi General Hospital.

# **CASE PRESENTATION**

A 33-year old man came to the hospital with weakness in the left limb approximately 1 hour before entering hospital, accompanied by his eyes always glanced to the left, his mouth turned to the

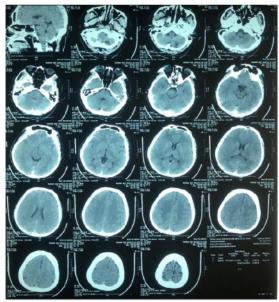


Figure 1. Head MSCT



Figure 2. Chest X-ray

left and, and vomited once. Seizure, fainting, blurred vision was denied by the patient and family. There was no previous history of similar symptoms. The patient had history of smoking and uncontrolled hypertension.

On physical examination, there was found blood pressure: 145/88mmHg, pulse rate: 111 beats/minute, respiratory rate: 20 times/minute, body temperature: 36.5°C, blood oxygen saturation: 98%, and body mass index: 32.11. On neurological examination, there was found glasgow coma scale (GCS): E4M6V5, central right facial nerve paresis, left hemineglect, left spastic hemiparesis with motor strength 555/111 (left limb can only contract and cannot shift) and national institutes of health stroke scare (NIHSS): 13.

Head MSCT examination was performed, there was found a hypodense area accompanied by blurred differentiation of the substance of the alba and grisea on right insula region with a tendency for hyperacute infarction (Figure 1), and the result of chest X-ray was of cardiomegaly and bronchopneumonia (Figure 2). The blood laboratory examination showed leukocytosis (leukocytes: 13300mcL) and dyslipidemia (total cholesterol: 179mg/dL, triglycerides: 111mg/dL, HDL: 39mg/dL, LDL: 123 mg/dL).

Patients were given ringer's lactate infusion 20 drops per minute, a low dose of rTPA (alteplase) 0.6 mg/kgBW (maximum 60 mg), ranitidine injection 50mg every 12 hours intravenously, atorvastatin 40 mg every 24 hours orally, vitamin B1B6B12 1 tablet every 8 hours orally. Oral antiplatelet (aspirin) 80mg every 24 hours was given 24 hours after rTPA treatment. Consciousness, vital signs, and signs of bleeding were monitored routinely every 15 minutes for two hours, then continued every 30 minutes for 6 hours, and continued every hour for a total of 24 hours.

In the fourth day of treatment, the patient's left upper limb could only be shifted, while lower limb was able to against gravity and against mild resistance with NIHSS: 4. Cerebral magnetic resonance imaging (MRI), magnetic resonance angiogram (MRA), and magnetic resonance venogram (MRV) were performed and the results were subacute wide infarction in the right frontotemporoparietal lobe gray matter according to the right middle cerebral artery territory and in the right paramedian frontal lobe according to the right anterior cerebral artery territory, and there was stenosis of the right media cerebral artery segment M1 (Figure 3).

On the tenth day of treatment, the patient was discharged from the hospital with NIHSS:4, and motoric strength of 555/111-555/444.

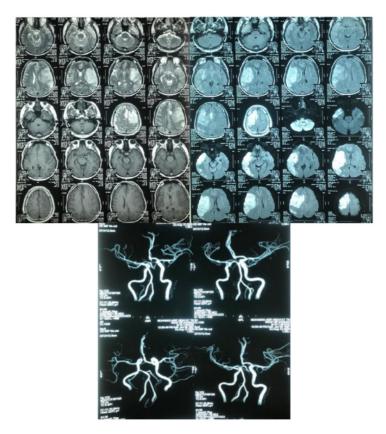


Figure 3. Cerebral MRI, MRA, and MRV

# DISCUSSION

Stroke in young patient is stroke in patient younger than 49 years.<sup>7,17</sup> Classical cardiovascular risk factors, heart disease, vascular disease, monogenic disorder, and genetic variation are associated with the potential causes of stroke in young adults.7 Modifiable risk factors in youngers are same as older age with the differences in prevalence.6 The most common risk factors in older age are hypertension, heart disease, and diabetes mellitus, while in young adults are dyslipidemia, hypertension, obesity, physical inactivity, and smoking. Age-specific risk factor (pregnancy and puerperium and oral contraceptive use) and behavioral risk factors (low physical activity, alcohol consumption, and smoking) had a bigger contribution in young adults.1 Stroke of other determined etiology is the most common etiology in young adults (20-30%) and patients with atherosclerosis, cardio-embolism, and small vessel diseases have the worst prognosis related to survival and recurrent vascular disease events.1,6 The primary prevention of stroke in young adult must be a global concern, because of the effect in major long term socio-economic consequences and the high mortality rate. 6,18

This patient came to the hospital with typical clinical manifestations of stroke (sudden onset, cranial nerve paresis, and spastic hemiparesis). The stroke onset of the patient was under 3 hours, so the used of rTPA can make the better clinical outcome rather than conventional therapy. <sup>15,16,19</sup> Intravenous administration of rTPA can be given at standard dose of 0.9 mg/kgBW (maximum 90 mg). In a study of 855 patients in Asian countries, the dose of rTPA could also be given at 0.6 mg/kgBW (maximum 60 mg) and proved to be no less inferior than the standard dose. <sup>16</sup>

The NIHSS assessment of stroke patients should be assessed, at the time of admission to the hospital, during the first 24 hours of hospitalization, and when discharged from hospital. NIHSS is a validated scale measuring stroke severity that consists of a summary score of the individual elements of the neurological examination. A number of studies have found that initial stroke severity is a strong predictor of clinical outcome, including mortality, length of stay, and functional outcome.20,21 The NIHSS consists of 14 items that are used to assess the degree of severity, including decreased consciousness, ability to answer questions and obey simple commands, presence of hemianopsia, facial palsy, limb weakness, plantar reflexes, limb ataxia, sensory disturbances, visual disturbances, dysarthria and the severity of aphasia. The total score ranges from 0-42 and higher scores reflect a greater degree of stroke severity. The stroke severity based on NIHSS can be classified as: >25: very severe, 15-24: severe, 5-14: mild to moderately severe, and 1-5: mild disorders.20 The advantages of NIHSS are fast and simple and the limitation is assessor dependent. This scale is not very valid in assessing the deficits associated with posterior circulation stroke.21

The relationship between dyslipidemia and stroke is the increase of atherosclerosis event and neuronal loss in the dyslipidemia, which can induce athero-thrombotic and cardio-embolic stroke.22 Atherosclerosis occurs because of damage to the endothelium of blood vessels and results in changes in the endothelial vessels' permeability. Endothelial damage in case of dyslipidemia due to toxic injury, inflammation, and oxidative stress to the endothelium.<sup>22,23</sup> With endothelial damage, growth factors will be released and will stimulate the formation of macrophages, where these macrophages will eat and clean the lipids and their components that have been oxidized through the scavenger receptor. These receptors will cause the formation of fatty streaks. Where these fatty streaks will accumulate in blood vessels and mature plaque will rupture and damage blood vessels. And then

they stimulates adhesion, activation and aggregation of platelets. The platelet aggregation process increases the coagulation of blood and causes the formation of thrombus.<sup>22,24,25</sup> The neuronal loss of dyslipidemia is associated with the transgenic mutation of the metabolism and transport lipids, apolipoprotein E (ApoE). The decrease of ApoE will cause the disruption of lipid transport and induce neuronal death. Abnormal cholesterol level finding is also associated with white matter abnormalities and the use of cholesterol-lowering drugs was reported to have less severe anatomical injury and improve the clinical outcome of stroke. Cholesterollowering drug such as statin has the ability of tissue protection via improvement of microvasculature integrity and the reduction of inflammation and oxidative stress.

There is a linear relationship between body mass index (BMI) with ischemic stroke, where the risk of stroke is increased by 6% for an increase in each unit of BMI.13 The mechanism underlying the risk of ischemic stroke in obesity is the BMI in the category of excess and obesity is associated with the increased of heart disease risk factor (coronary heart disease, congestive heart failure, and atrial fibrillation), blood pressure, cholesterol levels, and blood sugar levels; and all of those are associated with the atherosclerosis event. 13,14,26,27 Obesity is also associated with the activation of sympathetic nervous system activation, inflammation, hypofibrinolysis, and thrombo-embolic event. Wang H-J, et al. (2015) reported about the increased BMI category was related to higher risk of ischemic stroke and thrombo-embolism.14

#### CONCLUSION

The increased risk of ischemic stroke in young patients is due to dyslipidemia, hypertension, obesity, physical inactivity, and smoking. Treatment of the hyperacute phase of ischemic stroke with thrombolysis can reduce the outcome of stroke due to the disability.

#### **AKCNOWLEDGMENTS**

None

## DISCLOSURE (CONFLICT OF INTEREST)

The authors declare that there is no conflict of interest.

# **ETHICAL CONSIDERATION**

Patient had received signed informed consent regarding publication of their respective medical data in medical journals.

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PAGE 2	
PAGE 3	
PAGE 4	
PAGE 5	