Ischemic Stroke in Hemodialysis Patients: Case Report

Stroke Iskemik pada Pasien Hemodialisis : Laporan Kasus

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ABSTRACT

Stroke and chronic kidney disease are major health problems worldwide. Acute ischemic stroke is a significant complication in patients with end-stage renal disease undergoing hemodialysis. The incidence of stroke is about 8-10 times higher in chronic renal failure patients on hemodialysis compared to the general population. The annual incidence rate of acute ischemic stroke is reported to be about 4% in chronic renal failure patients on hemodialysis. Initiation of dialysis in chronic renal failure patients is associated with an increased risk of stroke. Chronic renal failure disease is an independent risk factor for stroke. A 57-year-old woman complained of left-side weakness during hemodialysis. Paresis of cranial nerve VII and XII and grade 3 flaccid hemiparesis sinistra were found. Electrocardiogram showed normal atrial fibrillation response. Non-contrast head CT scan showed subacute ischemic cerebral infarction in the right internal capsule. Factors that cause stroke in chronic renal failure are endothelial dysfunction, accelerated arteriosclerosis, and impaired cerebral autoregulation.

Keywords: Ischemic Stroke; Chronic Renal Failure; Hemodialysis

ABSTRAK


Keywords: Stroke Iskemik; Gagal Ginjal Kronik; Hemodialisis
INTRODUCTION

Stroke and chronic kidney disease are major health problems worldwide. Stroke is the second leading cause of death and the leading cause of chronic neurological disability worldwide. Women with chronic kidney failure have five times the risk of stroke. In contrast, men have a double risk of stroke. The United States Renal Data System (USRDS) reports that ischemic stroke is 5.3 times higher than hemorrhagic stroke in chronic kidney failure. European studies observing the risk of stroke in hemodialysis patients showed a first stroke rate of 14.9/1000 patients per year, with the predominance of the ischemic subtype compared to the hemorrhagic subtype (3.7/1000 patients per year). Hemorrhagic stroke occurs more frequently in patients of South Asian ethnicity compared to ischemic stroke, which occurs mainly in Caucasian patients.

Acute ischemic stroke is a significant complication in patients with chronic renal failure undergoing hemodialysis. The incidence of stroke is substantially higher in hemodialysis patients than in patients with early stages of renal failure. However, the extent to which initiation of dialysis accelerates stroke risk is poorly understood. Patients with stage 3–5 renal failure (defined as an estimated GFR <60 ml/min per 1.73 m$^2$) have a higher risk of stroke than patients without renal failure. This risk increases further during the first year after initiation of hemodialysis. The transition period beginning one year before and one year after initiation of hemodialysis is characterized by adverse cardiovascular complications and death, including higher rates of acute stroke.

Older patients undergoing hemodialysis have several risk factors for arteriosclerosis, so unsurprisingly, the risk for ischemic stroke increases in hemodialysis patients. Diabetes mellitus (DM), hyperlipidemia, and smoking are risk factors for atherosclerosis and increase the risk of ischemic stroke. Atrial Fibrillation (AF) is associated with an increased risk of thromboembolic stroke. Chronic kidney failure is associated with a number of arrhythmogenic substrates that can lead to AF. The relationship between chronic kidney failure and stroke risk involves cardiovascular risk factors with comorbidities such as hypertension, diabetes mellitus, and atrial fibrillation (AF). The causal mechanism suspected in ischemic stroke in chronic kidney failure includes chronic inflammation, oxidative stress, and thrombogenic factors caused by high urea, which contribute to vascular injury and endotheliopathy.

CASE ILLUSTRATIONS

A 57-year-old woman undergoing hemodialysis at the Wangaya Hospital in Denpasar City complained of weakness on the left side when the hemodialysis had only been running for 1 hour. The patient feels heavy when trying to lift the left arm and leg. The patient's speech becomes slurred, and their lips pucker. They denied a history of headaches, nausea, vomiting, spinning sensations, seizures, visual disturbances, and decreased consciousness. The patient has a history of chronic kidney failure with hemodialysis since one year ago. The patient underwent hemodialysis two times a week using standard heparin. The patient also has a history of irregular heart rhythms. History of other diseases was denied. Family history with the same complaint, hypertension, diabetes, kidney failure, and heart was denied.

At the initial examination, GCS was found in patient E4V5M6 with vital signs of blood pressure 100/73 mmHg, pulse 85x/minute, respiration 20x/minute, temperature 36 degrees Celsius, oxygen saturation 99% without oxygen. General physical examination within normal limits. Paresis of the right VII and XII cranial nerves was found on neurological examination. The patient found
grade 3 left flaccid hemiparesis. Normal physiological reflexes in the form of Biceps Pees Reflex (BPR) +2/+2, Triceps Pees Reflex (TPR) +2/+2, Knee Pees Reflex (KPR) +2/+2, Achilles Pees Reflex (APR) +2/+2. Hoffman/Trommer, Babinski, Chaddock, Oppenheim, Gonda, Gordon, and Schaeffer's pathological reflexes are negative. Examination of the strength of the superior and inferior extremities of the left side of the body grade 3. Sensory examination showed sensibility within normal limits.

On supporting examinations, significant laboratory results were obtained as follows: incomplete blood (DL) Hemoglobin 10.8 g/Dl, Hematocrit 36.6%, Platelets 129,000/ul, Potassium electrolyte 3.2 mmol/L, Urea kidney function level 71 mg/Dl, creatinine 8.3 mg/dL, uric acid 6.8 mg/dL. Laboratory tests show anemia and high levels of urea and creatinine, which are found in patients with chronic kidney failure.

The electrocardiogram showed a normal response to atrial fibrillation. PA chest x-ray showed core and pulmo within normal limits. A non-contrast head CT scan showed a subacute ischemic cerebral infarction in the right internal capsule. Treatment is given by infusion of 0.9% NaCl 20 drops per minute, Citicoline 2x500 mg intravenously, Clopidogrel 1x75 mg orally, and Omeprazole 1x40 mg intravenously. Citicoline, clopidogrel, and omeprazole were given for 7 days. Then he was consulted by the internal medicine department to treat the patient's kidney failure.

At the beginning of treatment, there were complaints from patients who complained of weakness in the extremities on the left side of the body and slurred speech. Paresis of the right VII and XII cranial nerves was found on neurological examination. In the patient's muscle strength, grade 3 left flaccid hemiparesis was found. On the second to the fifth day of treatment, the patient still felt heavy when moving the left extremity of the body, but the slurred speech had improved. There was paresis of the right VII and XII cranial nerves, and the patient's muscle strength was found with grade 3 left flaccid hemiparesis. The patient was then consulted by the medical rehabilitation department on the fifth day of treatment. The patient underwent physiotherapy with exercises such as proper positioning and ROM exercises. On the sixth day of treatment, the patient began to be able to lift his left arm and left leg with light resistance. There was paresis of the right VII and XII cranial nerves, and the patient's muscle strength was found with grade 4 left flaccid hemiparesis.

On the seventh day of treatment, the patient was allowed to go home from the hospital. The patient feels that the left extremity has improved by being able to lift the arms and legs and is given light resistance. At the initial examination, GCS was found in patient E4V5M6 with vital signs of blood pressure 112/86 mmHg, pulse 85x/minute, respiration 20 x/minute, temperature 36 degrees Celsius, oxygen saturation 99% without oxygen. General physical examination within normal limits. Paresis of the right VII and XII cranial nerves was found on neurological examination. The patient found grade 4 left flaccid hemiparesis. Normal physiological reflexes include Biceps Pees Reflex (BPR), Triceps Pees Reflex (TPR), Knee Pees Reflex (KPR), and Achilles Pees Reflex (APR). The pathological reflexes of Hoffman/ Trommer, Babinski, Chaddock, Oppenheim, Gonda, Gordon, and Schaeffer are negative. Examination of the strength of the superior and inferior extremities of the left side of the body grade 4. Sensory examination showed sensibility within normal limits. The patient was given medication to go home to the hospital in the form of Citicoline 2x500 mg orally, Clopidogrel 1x75 mg orally, and Omeprazole 1x20 mg orally and was scheduled for control at the neurology polyclinic and medical rehabilitation one week later.
Figure 1. Non-contrast CT scan of the head shows a subacute ischemic cerebral infarction in the right internal capsule.

Figure 2. PA chest X-ray showing cor and pulmo within normal limits
**DISCUSSION**

Chronic kidney failure (CKD) has increased incidence and prevalence with age. The age factor causes changes in the physiology of the cardiovascular system, which causes a decrease in the elasticity of blood vessels and increases the stiffness of the arteries. CRF patients are a very high-risk population for developing stroke. The incidence of ischemic stroke is greater than hemorrhagic stroke because the risk factors are more commonly found in patients with CKD, such as thromboembolism, atherosclerosis, inflammation, and cardio embolism.¹¹

Proteinuria and low glomerular filtration rate (GFR) are independent risk factors for decreased cerebral perfusion and stroke. The increased risk of stroke in patients with chronic renal failure is a consequence of uremia-associated vascular calcification and atherosclerotic syndrome due to inflammatory malnutrition.¹² Vascular calcification in elderly patients taking anticoagulants may result in greater ischemic stroke or lacunar infarction. In the watershed region.¹³ Patients with chronic renal failure have more severe atherosclerosis than the general population. This study showed higher CRP levels in cerebral ischemic and cerebral small vessel disease (CSVD) patients. Inflammation contributes to the formation of atherosclerosis.⁸

Chronic renal failure is associated with a thrombogenic increase in the left atrium of the heart in patients with AF, severe calcification and large amounts of unstable plaque in large artery disease, and blood-uremic disturbances of the blood-brain barrier, which may have implications for small vessel disease and risk of lacunar stroke.¹⁰ Cerebrovascular disease is a major cause of death in dialysis patients due to progressive atherosclerosis and chronic uremia.¹⁴

Atrial fibrillation (AF) is a frequent comorbidity in hemodialysis patients, with a prevalence of up to 27%, significantly increasing the risk of ischemic stroke.¹⁵ Toyoda et al. reported ischemic stroke involving the vertebrobasilar artery region in hemodialysis patients.² Atrial fibrillation is clearly involved in ischemic cerebrovascular disease. In studies, the presence of AF increases the likelihood of ischemic stroke.⁶ Irregular atrial contraction with reduced atrial blood flow, atrial fibrosis, endothelial and endocardial injury and dysfunction, increased expression of tissue factor and von Willebrand factor, increased platelet activation, and fibrinolysis can all predispose to thrombus formation and systemic embolization in patients with chronic renal failure with AF.⁹

AF is associated with increased thromboembolic events in patients with chronic renal failure. The incidence of stroke is also greater in patients diagnosed with AF than in those with sinus rhythm. The results of this study confirm previous findings, which have shown that arrhythmias in dialysis patients are an important risk factor in the presentation of ischemic stroke.¹⁷ AF increases the risk of thromboembolic stroke in the general population and appears to be the same in the chronic renal failure patient population.¹⁸ Hemodialysis leads to the initiation of AF through rapid shifts of fluid and electrolytes (potassium), and episodes of AF are common during hemodialysis.

Observational studies in the general population show an association between low haemoglobin and a high composite incidence of stroke.²⁰ The increased risk of stroke due to severe anemia in stage V chronic kidney failure undergoing hemodialysis can biologically be due to low oxygen-carrying capacity in brain areas, resulting in poor perfusion. Decreased production of erythropoietin due to decreased kidney function can cause anemia. Anemia can increase the risk of stroke by inducing atherosclerosis through increased oxidative stress and left ventricular hypertrophy in patients with chronic kidney disease.

Uremia conditions cause erythropoietin deficiency which causes anemia resulting in decreased oxygenation to the brain and causes ischemic stroke. Likewise, uremia disrupts the bond...
between IIb-IIa receptors and the von Willebrand factor, leading to impaired platelet aggregation and a hemorrhagic stroke. Raymond et al. reported that an increased risk of stroke in kidney disease is associated with a creatinine level of >1.3 mg/dl.

The study found that patients who underwent HD > 12 months had a 4.05 times risk of experiencing an ischemic stroke. This is because the duration of HD reflects the length of time the patient has been exposed to uremic conditions, which cause accelerated atherosclerosis, resulting in a stroke. Toyoda et al. found that ischemic strokes are more common during or immediately after dialysis procedures than hemorrhagic strokes. The frequency of HD is related to persistently high urea levels, namely the uremic condition causes accelerated vascular calcification, increases carotid atherosclerosis, prothrombotic tendencies, and impaired cerebral autoregulation.11

Blood pressure plays a role in tissue perfusion and cellular oxygen supply.21 Both the kidney and the brain require a continuous and steady high blood flow in a low vascular resistance system. Pressure arterioles supply both of these organs. Due to the branching nature of these arterioles, they are susceptible to changes in blood pressure. The arterial endothelium and tunica media are negatively affected in patients with chronic renal failure, making them susceptible to cerebrovascular injury. Furthermore, baroreceptor reflexes are altered in hemodialysis patients due to impaired autonomic function, which results in poor tolerance to changes in fluid and blood pressure during dialysis.22

Hemodialysis can also result in decreased myocardial function, causing inadequate cerebral perfusion and ischemic brain injury.12 Decreased myocardial function affects at least two-thirds of hemodialysis patients. Due to the loss of contractile function simultaneously, a higher cardiac output is required to compensate for systemic hypotension, resulting in decreased cerebral microperfusion.

Decreased blood pressure values during ultrafiltration can impair perfusion and ischemic stroke.11 Individuals with decreased eGFR have less effective cerebral autoregulation. A prospective study of patients after acute ischemic stroke found poorer autoregulation correlated with lower eGFR and was associated with an increased risk of hemorrhagic transformation of ischemic stroke.23 Stroke risk increased by 7% for every 10 ml/min/1.73 decrease in GFR. m2. An increase in the albumin/creatinine ratio of 25 mg/mmol correlates with a 10% increased risk of stroke.24

The mean cerebral arterial flow velocity has been shown to decrease significantly during dialysis, and this intradialytic hemodynamic instability leads to a transient decrease in cerebral function leading to ischemia and white matter over time.25 Once cerebral ischemia has occurred, local lactic acidosis can further impair post-ischemic recovery because of direct neuronal toxicity.26 Cerebral Blood Flow (CBF) decreases by 10%–15% during conventional hemodialysis sessions in elderly patients.27 Heparin is the most commonly used anticoagulant, and apart from the rare acute anaphylactic reaction, heparin can be associated with Antibody-mediated thrombocytopenia, characterized by thrombosis, especially of the arteries.28

CONCLUSIONS

Renal impairment is an influential risk factor for stroke, a major cause of morbidity and mortality worldwide. Dialysis patients experience a 10-fold higher incidence of stroke, with a mortality rate of up to 90%. It is important to understand the factors that predispose to stroke in patients with chronic kidney disease coupled with prevention strategies. It is very important to
understand the risk, treatment, and prevention of stroke in all stages of chronic kidney disease. Hemodialysis patients need to know the dialysis treatment's elements to mediate stroke risk and control recovery from acute stroke. Clinicians should remain aware of the poorer prognosis of stroke in patients receiving dialysis compared to the general population. Prevention and management schemes that are effective in the general population do not benefit patients receiving dialysis.

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CONFLICT OF INTEREST
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