

Cerebral Infarction Due to Polycythemia Vera: A Case Report

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ABSTRACT

Introduction: Changes in blood viscosity can cause thrombosis in the brain, causing a stroke. Polycythemia vera is one of the causes of blood hyperviscosity. This study aimed to present cases of cerebral infarction related to polycythemia vera. **Case presentation:** A 55-year-old woman came to the emergency room with complaints of sudden weakness in the left limbs. One week before admission, the patient complained of headaches accompanied by spinning dizziness. Her left limbs often tingled and became weaker. There was an asymmetric facial deviation to the right, and the patient had difficulty communicating with unclear articulation. Specific examination of neurology shows dysarthria, left-sided motor type facial paralysis, examination of motor strength of the upper and lower extremities on the left 2 and 5 on the right, and the left upper limb often feels tingling. On the left limb, normal physiological biceps reflex was found, positive Chaddock pathological reflex. Morphological examination of peripheral blood showed normocytic normochromic with erythrosis and thrombocytosis and found giant platelets. This patient was diagnosed with an ischemic stroke caused by cerebral infarction, with polycythemia vera etiology, and accompanied by comorbid diseases of diabetes mellitus and uncontrolled hypertension. **Conclusion:** In patients with high-risk criteria for thrombosis, the management of phlebotomy, administration of low-dose aspirin, and cytoreduction in the form of hydroxyurea aims to achieve a hematocrit <45% so as to prevent worsening and recurrence of stroke.

1. Introduction

Stroke is a cerebrovascular disease in which brain abnormalities occur due to pathological processes of blood vessels, such as blockages, rupture of blood vessel walls, or increased blood viscosity.^{1,2} Stroke is the third leading cause of death in the United States after heart disease and cancer.³ As many as 10.9% of the population in Indonesia have had a stroke, with a prevalence of 74 years of 50.2%.^{4,5}

Polycythemia vera is a myeloproliferative neoplastic disease with an increase in erythrocytes, especially an increase in hemoglobin and hematocrit, and can be followed by an increase in leukocytes and platelets.^{6,7} The main complication of polycythemia vera is an increase in blood viscosity resulting in thrombosis.

Approximately 49% of patients with polycythemia vera have thrombosis.⁵ An increase in hematocrit and blood viscosity causes blood flow to the brain to decrease, accompanied by an increase in platelet activity which can cause local thrombus in the blood vessels of the brain.⁷ This study aimed to present cases of cerebral infarction related to polycythemia vera.

2. Case Presentation

A 55-year-old woman came to the emergency room with complaints of sudden weakness in her left limbs. One week before admission, the patient complained of headaches accompanied by spinning dizziness. Her left limbs often tingled and became weaker. There was an asymmetric facial deviation to the right, and the

patient had difficulty communicating with unclear articulation. No previous history of head trauma, seizures, loss of consciousness, or similar complaints. The patient appeared weak, and previously there were no complaints of shortness of breath, chest pain, fever, skin rash, bleeding, itching, blurred vision, or swelling of both limbs. There is a history of uncontrolled hypertension and diabetes mellitus.

Physical examination shows the patient is in a state of full consciousness (compos mentis, GCS 15), and orientation is good. Vital sign examination showed pulse 112 x / minute, regular sinus tachycardia, blood pressure 172/102 mmHg, respiratory rate 20 x/minute, axilla body temperature 36.7°C, and oxygen saturation 98%. Specific examination of neurology shows dysarthria, left-sided motor type facial paralysis, examination of motor strength of the upper and lower extremities on the left 2 and 5 on the right, and the left upper limb often feels tingling. On the left

limb, normal physiological biceps reflex was found, positive Chaddock pathological reflex. Chest and cardiovascular examinations are within normal limits. There is mild splenomegaly and free fluid in the abdominal cavity.

Routine blood laboratory evaluations are presented in Table 1. Morphological examination of peripheral blood showed normocytic normochromic with erythrosis and thrombocytosis and found giant platelets. There is a cast elongation of the aorta on chest X-ray examination. Evaluation of electromyography describes the sinuses of tachycardia. CT scan of the head showed infarction of hypodense lesions in the parieto-occipital and dextra temporal areas (Figure 1). This patient was diagnosed with an ischemic stroke caused by cerebral infarction, with polycythemia vera etiology, and accompanied by comorbid diseases of diabetes mellitus and uncontrolled hypertension.

Table 1. Results of routine blood tests and clinical chemistry.

Examination	Result
Hemoglobin	18.4 g/dl
Erythrocytes	7.27 x10 ⁶ / μL
Hematocrit	59.3%
Leukocytes	12,500 μL
Neutrophils	78.2%
Platelets	549,000 μL
Random blood sugar	263.8 mg/dL
Sodium	131.6 mmol/L
Potassium	4.1 mmol/L
Chloride	97 mmol/L
Creatinine	1.03 mg/dL

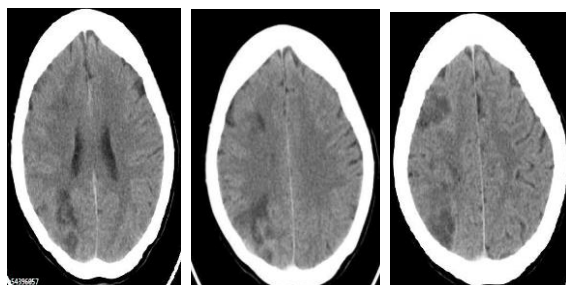


Figure 1. Computed tomography (CT) scan of the head.

Patients were treated with clopidogrel 75 mg/24 hours, hydroxyurea 1000 mg/24 hours, and phlebotomy 2 times. Management of diabetes mellitus in these patients is in the form of rapid-acting insulin 10 units / 8 hours. After 1 week of hospitalization, the

patient's condition improved, and she was later discharged from the hospital. Evaluation of laboratory test results after 1 month showed Hb levels of 15.2 mg/dL; leukocytes 7,900; platelets 273,000; hematocrit 46.7%. Patients showed satisfactory

neurological improvement results after undergoing pharmacological therapy and rehabilitation therapy.

3. Discussion

Polycythemia vera (PV) is one of the risk factors that cause ischemic stroke. Polycythemia vera is a group of chronic myeloproliferative neoplasms that cause excess production of red blood cells and is characterized by increased concentrations of hemoglobin and hematocrit.⁸ Previous studies state that polycythemia vera is caused by mutations in the JAK2V617F gene that cause erythropoietin hypersensitivity resulting in increased red blood cell production.⁹ Clinical symptoms of polycythemia vera can include bleeding of the skin, mucosa, and gastrointestinal system. Microvascular symptoms can be headaches, paresthesias, visual disturbances, and neurological deficits.¹⁰ In 33% of patients with PV, symptoms of thrombosis can occur in the form of stroke, myocardial infarction, deep vein thrombosis, or even pulmonary embolism. Other symptoms can include fatigue, pruritus, tinnitus, hyperemic conjunctivitis, and burning sensation in the face and extremities.⁸

In this case, PV is suspected to be the cause of ischemic stroke. Increased blood viscosity causes a slowdown in blood flow to organs, including the brain. If the brain tissue gets a blood flow of less than 10 ml/100 g of brain tissue per minute, permanent neuronal damage will occur quickly within 6-8 minutes. In addition, an increase in hematocrit is also associated with a decrease in reperfusion due to disrupted oxygen uptake by brain tissue so that brain metabolism switches from aerobic to anaerobic resulting in inadequate brain tissue energy production.¹¹ High viscosity also disrupts collateral blood flow in ischemic areas, resulting in more extensive infarct lesions.^{12,13}

The goals of the management of polycythemia vera are symptomatic improvement and reduced risk of complications such as thrombosis, bleeding, and haematological transformation. Currently, there is no prevention of transformation into myelofibrosis or acute leukemia/myelodysplastic syndrome. Patients at high risk of thrombosis are recommended

cytoreductive therapy along with phlebotomy and aspirin.¹⁴ The first line agent is hydroxyurea with an initial dose of 15 mg/kg BW per day divided twice a day. The goal is to reduce platelets to 100,000 to 400,000/ μ L without excessive neutropenia and anemia.^{14,15}

Patients with intolerance to hydroxyurea can be given pegylated IFN- α , ruxolitinib, and busulfan. The first line is given pegylated IFN- α at a dose of 45 mcg/week and titrated monthly to a maximum of 180 mcg/week.¹⁶ Another drug option is ruxolitinib 10 mg twice a day which is considered capable of reducing hematocrit, resolving splenomegaly, normalizing leukocytes and platelets, and improving symptoms related to polycythemia vera. Alpha interferon can be given at a dose of 500,000-1 million units 3 times a week, progressively increasing up to 2-3 million units 3 times a week, which can reduce spleen size or reduce itching, and this drug does not have a pro-leukemia effect.^{15,16}

4. Conclusion

Polycythemia vera in these patients causes an increase in blood viscosity, reducing blood flow to the brain, and high platelet activation can cause local thrombus, which can cause ischemic stroke. In patients with high-risk criteria for thrombosis, the management of phlebotomy, administration of low-dose aspirin, and cytoreduction in the form of hydroxyurea aim to achieve a hematocrit of less than 45% so as to prevent worsening and recurrence of stroke.

5. References

1. Kang JK, Oh JS, Bae H, Kim BJ, Kim JY. Elevation of blood viscosity in acute ischemic stroke. *Stroke*. 2022; 53: A49.
2. Song SH, Kim JH, Lee JH, Yun YM, Choi DH. Elevated blood viscosity is associated with cerebral small vessel disease in patients with acute ischemic stroke. *BMC Neurol*. 2017; 17: 20.
3. Donkor ES. Stroke in the 21st century: a snapshot of the burden, epidemiology, and

- quality of life. *Stroke Research and Treatment*. 2018.
4. Venketasubramanian N, Yudiarto FL, Tugasworo D. Stroke burden and stroke service in Indonesia. *Cerebrovasc Dis Extra*. 2022; 12(1): 53-7.
5. Setyopranoto I, Bayuangga HF, Panggabean AS, Alifaningdyah S, Lazuardi L. Prevalence of stroke and associated risk factors in Sleman district of Yogyakarta special region, Indonesia. *Stroke Res Treat*. 2019; 2019: 2642458.
6. Iurlo A, Cattaneo D, Bucelli C, Baldini L. New perspectives on polycythemia vera: From diagnosis to therapy. *International Journal of Molecular Sciences*. 2020; 21(16): 1-16.
7. Abdel-Rahman I, Murphy C. Recurrent ischaemic stroke unveils polycythaemia vera. *BMJ Case Reports*. 2015; 2014-6.
8. Tefferi A, Vannucchi AM, Barbui T. Polycythemia vera: historical oversights, diagnostic details, and therapeutic views. *Leukemia*. 2021; 35(12): 3339-51.
9. de Freitas RM, Maranduba CM. Myeloproliferative neoplasms and the JAK/STAT signaling pathway: an overview. *Revista Brasileira de Hematologia e Hemoterapia*. 2015; 37(5): 348-53.
10. Klein-Weigel PF, Volz TS, Richter JG. Erythromelalgia. *Vasa*. 2018; 47(2): 91-7.
11. Cao YY, Cao J, Bi ZJ, Xu SB, Liu CC. Hemorrhagic transformation after acute ischemic stroke caused by polycythemia vera: report of two cases. *World J Clin Cases*. 2021; 9(25): 7551-7.
12. Chen L, Xiao H, Hu Z. Cerebral hemorrhage of a 50-year-old female patient with polycythemia vera. *J Stroke Cerebrovasc Dis*. 2019; 28: e110-e112.
13. Ferro JM, Infante J. Cerebrovascular manifestations in hematological diseases: an update. *J Neurol*. 2021; 268: 3480-92.
14. Squizzato A, Romualdi E, Passamonti F, Middeldorp S. Antiplatelet drugs for polycythaemia vera and essential thrombocythaemia. *Cochrane Database Syst Rev*. 2013; CD006503.
15. Marchioli R, Finazzi G, Specchia G, Cacciola R, Cavazzina R. Cardiovascular events and intensity of treatment in polycythemia vera. *N Engl J Med*. 2013; 368: 22-33.
16. Martin K. Risk factors for and management of MPN-associated bleeding and thrombosis. *Curr Hematol Malig Rep*. 2017; 12: 389-96.