

CASE REPORTS

Reversible cerebral vasoconstriction syndrome in patients with polycythemia vera

Hye Weon Kim¹, Kwang Hyun Kim¹, Joong Hyun Park¹, Sang Won Han¹, Sook Young Roh²

1. Department of Neurology, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea. 2. Department of Neurology, Bundang Jesaeng General Hospital, Seongnam, Korea

Correspondence: Sook Young Roh. Address: Department of Neurology, Bundang Jesaeng General Hospital, 20 Seohyeon-ro 180beon-gil, Bundang-gu, Seongnam 13090, Korea. Email: syrohnu@dmc.or.kr

Received: April 6, 2016

Accepted: May 23, 2016

Online Published: May 24, 2016

DOI: 10.5430/ijdi.v3n2p45

URL: <http://dx.doi.org/10.5430/ijdi.v3n2p45>

Abstract

Introduction: Reversible cerebral vasoconstriction syndrome (RCVS) may occur spontaneously, especially in middle-aged women but half the cases are associated with nonaneurysmal subarachnoid hemorrhage, post partum, or vasoactive drugs. RCVS has been also known to occur with diverse clinical diseases but this is the first report to implicate polycythemia vera (PV).

Case report: A 54-year-old woman presented with recurrent thunderclap headaches, aggravated by coughing. She was diagnosed PV 3 years ago and well controlled with aspirin and hydroxyurea. A bone marrow biopsy and a positive JAK-2-V617F mutation provided a diagnosis of PV. She did not take any other medication except aspirin and hydroxyurea in the last 2 months. Her neurologic examination was normal. Brain CT angiography 6 days after symptoms onset showed multiple cerebral arterial irregularities with segmental narrowing and dilatation. Cerebral angiography confirmed multifocal segmental narrowing and dilatation in the same vascular territories. She was treated with oral nimodipine and her symptoms were improved within 3 weeks. Follow-up brain MR angiography 3 months after symptoms onset demonstrated normalization of involved vessels. She had no headache during 12 months follow-up.

Conclusion: Thrombosis does not account for RCVS in patients with PV but endothelial damage from repetitive microvascular thrombosis may be associated with RCVS. In this patient, prothrombotic state affecting to endothelial damage might cause a transient disturbance in the regulation of cerebral vascular tone.

Keywords

Headache, Polycythemia vera, Reversible cerebral vasoconstriction syndrome, Thrombosis

1 Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by rigorous thunderclap headaches with reversible cerebral vasoconstriction that improves spontaneously within several weeks^[1-3]. RCVS may occur spontaneously, especially in middle-aged women but half the cases are associated with nonaneurysmal subarachnoid hemorrhage, post partum, or vasoactive drugs^[3]. RCVS has been also known to occur with diverse clinical diseases but this is the first report to implicate polycythemia vera (PV).

2 Case presentation

A 54-year-old woman presented with recurrent thunderclap headaches for 5 days, aggravated by coughing. The headache was bilateral posterior onset followed by diffuse pain. The onset was acute and peaking in less than 1 min with recurrent episodes of maximum pain. There was no nausea, vomiting, or photophobia. She was diagnosed PV 3 years ago and well controlled with aspirin 100 mg daily and hydroxyurea 1,000 mg twice daily. A bone marrow biopsy and a positive JAK-2-V617F mutation provided a diagnosis of PV. She did not take any other medication except aspirin and hydroxyurea in the last 2 months. On physical examination, the temperature was 36.6°C, the pulse was 72 beats/min and the blood pressure was 132/78 mmHg. She was alert and oriented. Her neurologic examination was normal. The cerebrospinal opening pressure and cerebrospinal fluid analysis were normal. Laboratory testing showed a leukocyte count of $5.7 \times 10^3/\mu\text{l}$ (reference values: 4.0-10.0), a hemoglobin level of 14.2 g/dl (12.0-16.0), a hematocrit 42.5% (36-48), and a platelet count of $239 \times 10^3/\mu\text{l}$ (130-430). Erythrocyte sedimentation rate, serum electrolytes, blood chemistry, antinuclear antibody, anti-cardiolipin antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, and liver and renal function were normal. Blood coagulation tests revealed prothrombin time (PT) international normalized ratio (INR) 1.12 (0.8-1.3) and partial thromboplastin time (PTT) 28.8 sec (20-38). Brain CT angiography 6 days after symptoms onset showed multiple cerebral arterial irregularities with segmental narrowing and dilatation (see Figure 1A). Cerebral angiography 9 days after symptoms onset confirmed multifocal segmental narrowing and dilatation in the same vascular territories (see Figure 1B). She was treated with oral nimodipine and her symptoms were improved within 3 weeks. Follow-up brain MR angiography 3 months after symptoms onset demonstrated normalization of involved vessels (see Figure 1C). She had no headache during 12 months follow-up.

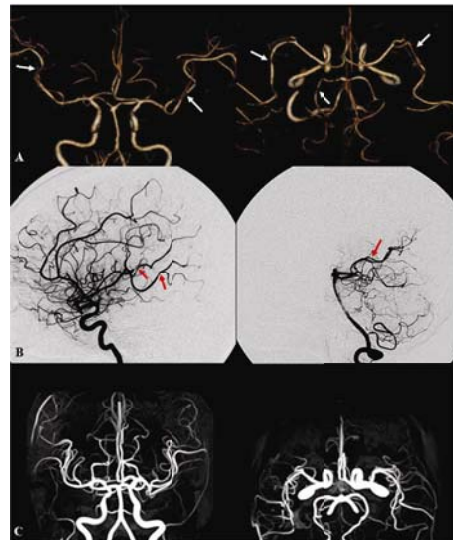


Figure 1. (A). Brain CT angiography 6 days after symptoms onset demonstrating bilateral middle cerebral artery and right posterior cerebral artery cerebral arterial irregularities with segmental narrowing and dilatation (arrows); (B) Cerebral angiography 9 days after symptoms onset confirming multifocal segmental narrowing and dilatation in the same vascular territories (arrows); (C) Follow-up brain MR angiography 3 months after symptoms onset showing regression/normalization of involved vessels

3 Discussion

RCVS is probably caused by transient disturbance in the regulation of cerebral vascular tone, resulting from spontaneous neuronal or vascular driven discharge, leading to diffuse segmental constriction and dilation of cerebral arteries^[2, 3]. The key clinical symptom is severe and repeated headaches peaking in less than 1 min over 1-3 weeks, frequently associated with nausea, vomiting, photophobia, and transient focal deficits^[1, 3]. Severe thunderclap headache is the major manifestation and frequently remains the only symptom of RCVS. The clinical manifestations are usually self limiting but hemorrhagic and ischemic strokes are the most important complications of RCVS. Though the pathomechanisms are not definitely understood, many disorders are associated with RCVS. The essential etiology of RCVS seems to be multifactorial but disturbance in the regulation of cerebral vascular tone may be the final common pathway^[2].

PV is a myeloproliferative disease distinguished by excessive erythrocytosis, leukocytosis, and thrombocytosis [4, 5]. Thrombosis is an important complication and vascular complications such as stroke and coronary artery disease occur among patients with PV. JAK2-V617F mutations are especially associated with increased thrombosis risk in PV. The exact mechanism of thrombogenesis in PV is uncertain but diverse mechanisms have been suggested such as endothelial damage, inhibition of natural anticoagulant pathways, and secretion of procoagulant factors [4-6]. Macrovascular thrombosis does not account for RCVS in patients with PV but endothelial damage from repeated microvascular thrombosis may be associated with RCVS [4, 6, 7]. This endothelial damage promotes leukocyte migration and platelet activation, triggering the dysregulation of cerebral vascular tone and may contribute to the development of RCVS. In this patient, prothrombotic state affecting to endothelial damage might cause a transient disturbance in the regulation of cerebral vascular tone. In addition, though it is not applicable to our patient, the increased hematocrit can produce endothelial dysfunction with involvement of the blood-endothelium interface and thinning of the glycocalyx (protective layer between the endothelium and circulating erythrocytes) [8]. However, these hypotheses should be awaited more concrete evidences and both diseases in our case may be incidental finding.

In conclusion, this case showed that multiple cerebral arterial irregularities with segmental narrowing and dilatation in patient with PV were completely normalized 3 months after symptoms onset with clinical improvement. Physicians may consider RCVS in patients with PV and thunderclap headache (see Table 1). Cerebral angiography in addition to brain imaging is important to evaluate the presence of RCVS.

Table 1. Key issues

Reversible cerebral vasoconstriction syndrome (RCVS) is probably caused by transient disturbance in the regulation of cerebral vascular tone, resulting from spontaneous neuronal or vascular driven discharge, leading to diffuse segmental constriction and dilation of cerebral arteries.
The key clinical symptom of RCVS is severe and repeated headaches peaking in less than 1 min over 1-3 weeks.
Thrombosis is an important complication and vascular complications such as stroke and coronary artery disease occur among patients with polycythemia vera (PV).
Prothrombotic state affecting to endothelial damage might cause a transient disturbance in the regulation of cerebral vascular tone in PV.

References

- [1] Ducros A, Boukobza M, Porcher R, *et al.* The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain*. 2007; 130: 3091-3101. PMID:18025032 <http://dx.doi.org/10.1093/brain/awm256>
- [2] Sattar A, Manousakis G, Jensen MB. Systematic review of reversible cerebral vasoconstriction syndrome. *Expert Rev Cardiovasc Ther*. 2010; 8: 1417-1421. <http://dx.doi.org/10.1586/erc.10.124>
- [3] Ducros A. Reversible cerebral vasoconstriction syndrome. *Lancet Neurol*. 2012; 11: 906-917. [http://dx.doi.org/10.1016/S1474-4422\(12\)70135-7](http://dx.doi.org/10.1016/S1474-4422(12)70135-7)
- [4] Barbui T, Carobbio A, Rambaldi A, *et al.* Perspectives on thrombosis in essential thrombocythemia and polycythemia vera: is leukocytosis a causative factor? *Blood*. 2009; 114: 759-763. <http://dx.doi.org/10.1182/blood-2009-02-206797>
- [5] Kroll MH, Michaelis LC, Verstovsek S. Mechanisms of thrombogenesis in polycythemia vera. *Blood Rev*. 2015; 29: 215-221. <http://dx.doi.org/10.1016/j.blre.2014.12.002>
- [6] Hua le H, Dodd RL, Schwartz NE. Concurrent stenooocclusive disease of intracranial and extracranial arteries in a patient with polycythemia vera. *Case Rep Med*. 2012; 2012: 151767. <http://dx.doi.org/10.1155/2012/151767>
- [7] Lazzaro MA, Cochran EJ, Lopes DK. Moyamoya syndrome in an adult with essential thrombocythemia. *Neurology International*. 2011; 3: e3. <http://dx.doi.org/10.4081/ni.2011.e3>
- [8] Richter V, Savery MD, Gassmann M, *et al.* Excessive erythrocytosis compromises the blood-endothelium interface in erythropoietin-overexpressing mice. *J Physiol*. 2011; 589: 5181-5192. PMID:21859826 <http://dx.doi.org/10.1113/jphysiol.2011.209262>