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Reversible cerebral vasoconstriction syndrome associated with paroxysmal nocturnal hemoglobinuria: A case study

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Abstract

Reversible cerebral vasoconstriction syndrome (RCVS), characterized by thunderclap headaches (TCH) and other clinical and radiological manifestations, typically occurs under some triggering conditions. This is the report of a 43 years old woman with known paroxysmal nocturnal hemoglobinuria (PNH) who received regular blood transfusion and glucocorticoid treatment, and developed RCVS. The association between PNH and RCVS has not been previously reported.

Keywords: Paroxysmal nocturnal hemoglobinuria, reversible cerebral vasoconstriction syndrome, reversible vasospasm; seizures, thunderclap headaches

INTRODUCTION

Reversible cerebral vasoconstriction syndrome (RCVS) has been proposed as an umbrella term encompassing various related syndromes, including Call or Call-Fleming syndrome, benign angiopathy of the central nervous system, postpartum cerebral angiopathy, migrainous vasospasm, migraine angiitis, thunderclap headaches with reversible vasospasm, and drug-induced angiopathy.[1] RCVS is both a clinical and radiologic syndrome, characterized by recurrent acute headaches, particularly thunderclap headaches (TCH), which may occur with or without focal neurological deficits or seizures. Imaging studies, such as magnetic resonance imaging (MRI) and computed tomography (CT) of the brain, or direct cerebral angiography, typically reveal reversible segmental or multifocal vasoconstriction of cerebral arteries, often described as having a "string of beads" or "sausage string" appearance.[2] RCVS can present spontaneously (idiopathic RCVS) or in association with specific conditions or settings (secondary RCVS).[3,4] We present here a patient with known paroxysmal nocturnal hemoglobinuria (PNH) who developed RCVS.

CASE REPORT

In September 2015, a 43-year-old female presented with thunderclap headaches accompanied by generalized tonic-clonic seizures. She had a 10-year history of PNH and had been receiving regular blood transfusions with oral glucocorticoid therapy. Her most recent blood transfusion had occurred 40 days prior to presentation. Upon examination, her vital signs included a pulse rate of 120 beats per minute and a blood pressure of 98 / 50 mmHg. Neurological examination revealed neck stiffness. A head CT scan indicated a left occipito-parietal infarction (Figure 1A, 1B, and 1C), though electroencephalography (EEG) was normal. Urinalysis was positive for protein and occult blood.

On the fifth day following admission, the patient experienced a recurrence of headache after a coughing episode. This was followed by a brief episode of vision loss from cortical blindness, which spontaneously resolved within five hours.

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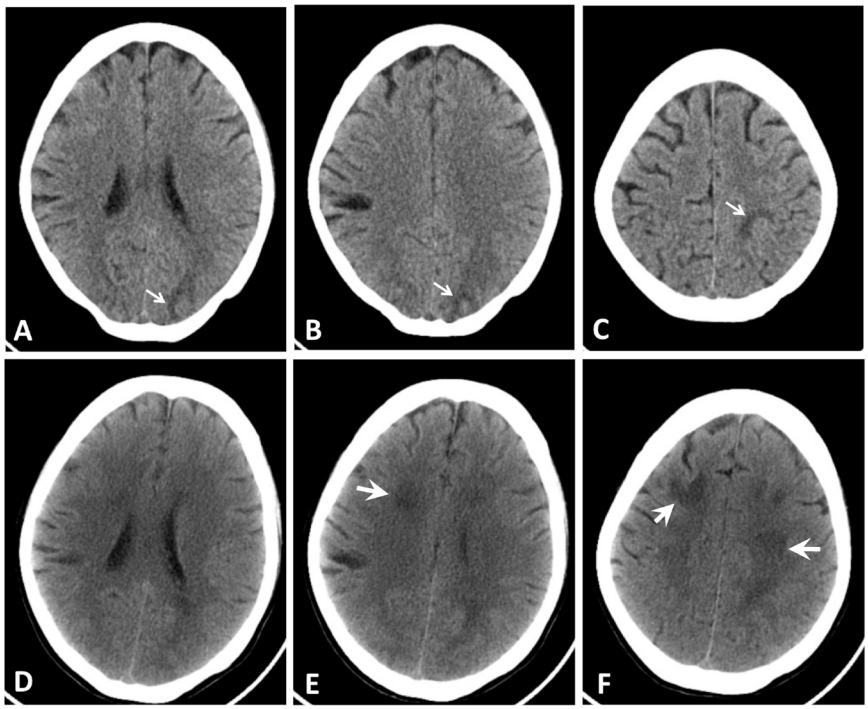

Figure 1. On the fifth day after admission, cranial CT imaging revealed a left occipito-parietal infarction following the initial thunderclap headache. By the sixth day, the infarct size had expanded, as observed in the follow-up images (E, D, and F).

However, 24 hours after the resolution of her vision loss, the patient became disoriented, had nonsensical speech, visual disturbances, and left-sided hemiparesis. A subsequent brain CT scan revealed an expansion of cerebral infarctions, now affecting bilateral frontal, parietal, and left occipital lobes (Figure 1D, 1E, and 1F). Brain MRI showed increased signals in multiple subcortical lesions (Figure 2A, 2B). Cerebral magnetic resonance angiography (MRA) images showed segmental narrowing and dilatation in multiple regions of the middle cerebral artery and the left posterior cerebral artery (Figure 2C, 2D, and 2E), while MR venography was normal. Cerebrospinal fluid (CSF) analysis was also normal.

Upon the diagnosis of suspected RCVS, the patient was administered an oral calcium-channel antagonist, specifically 30 mg of nimodipine every 8 hours. Gradually, her headache began to subside. Forty-five days later, follow-up MRI and MRA confirmed the diagnosis of RCVS, as imaging revealed the complete resolution of the previously observed arterial stenosis (Figure 2F-2I).

DISCUSSION

To our knowledge, this is the first reported case of RCVS in a patient with PNH. RCVS can present as either a primary condition or secondary to various associated triggering factors.[5] Reported associations include non-aneurysmal subarachnoid hemorrhage, neurosurgical procedures, postpartum period, vasoactive drugs, catecholamine-secreting tumors, immunosuppressants, blood products, and other triggers.[6]

Our patient had a history of regular blood transfusion, with the most recent transfusion occurring 40 days prior to admission. Upon presentation, the patient exhibited several neurological symptoms, including seizures, cortical blindness, left hemiplegia, altered consciousness, and photophobia. Neurological symptoms in RCVS can sometimes appear an average of 6.3 days following the last blood transfusion, and the risk for RCVS may extend for several months.[7-9] Braun *et al*. reported cases of symptomatic RCVS occurring up to three months after transfusion.[9] The latency from autoregulatory breakthrough to symptom onset, as well as the development of vasoconstriction in major cerebral arteries, may vary depending on the condition of the patient, underlying diseases, the volume and duration of blood transfusions, and other factors. Additionally, the delayed onset of vasoconstriction could be related to the gradual progression of vasoconstriction over time.[8]

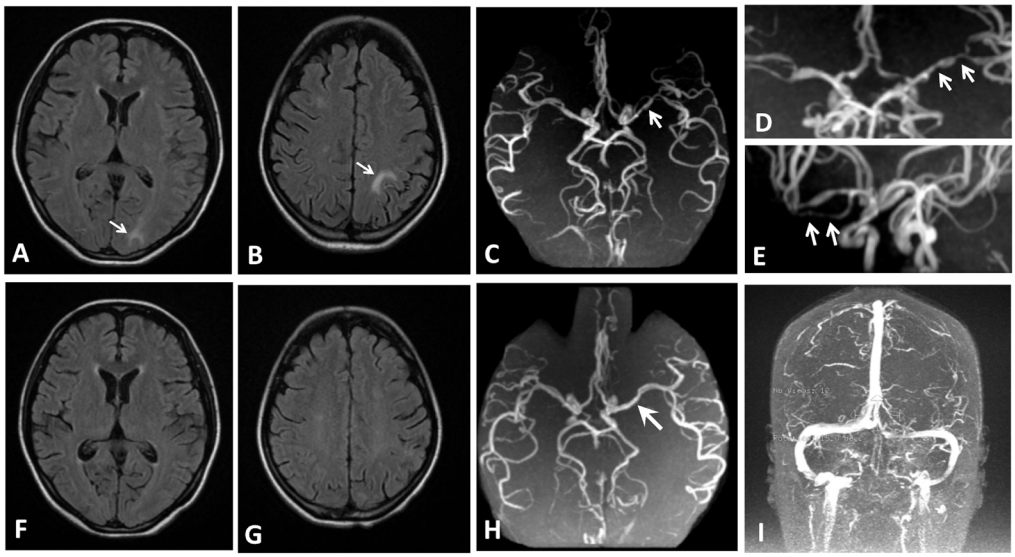

Figure 2. On the ninth day after admission, following a second episode of headache triggered by coughing, cerebral MRI revealed recent infarcts with symmetric hyperintense lesions in the left occipital lobe on T1-weighted images (A and B). MRA showed multiple alternating segments of constriction and dilation of cerebral arteries (C, D, and E). Follow-up MRI, MRA and MRV performed on the 45th day after discharge demonstrated resolution of the previous abnormalities and normalization of segmental vasoconstriction (F, G, H and I).

Several mechanisms have been proposed to explain how blood transfusions might precipitate RCVS. These include an increase in blood volume leading to hypertension, elevated blood viscosity causing endothelial damage and disrupted cerebral vascular autoregulation, and a disruption of cerebral vascular adaptation leading to chronic anemic hypoxia, similar to post-endarterectomy hyperperfusion syndrome.[9] Additionally, a rapid increase in hemoglobin levels and blood viscosity during transfusion may provoke acute vascular endothelial dysfunction, which can induce vasospasm, particularly in the posterior cerebral artery.[10]

The precise pathophysiology of RCVS remains incompletely understood. The prevailing hypothesis suggests that RCVS may involve a transient disturbance in the regulation of cerebral vascular tone, which can occur either spontaneously or as a result of various external factors.[5,8] Contributing factors may include sympathetic overactivity, oxidative stress, endothelial dysfunction, and an imbalance between proangiogenic and antiangiogenic factors.

PNH is characterized by intravascular hemolysis, leading to nitric oxide (NO) depletion, endothelial and smooth muscle dysregulation, and vasculopathy, which often results in progressive hypertension. NO plays a crucial role in vascular homeostasis and is a critical regulator of both basal and stress-mediated smooth muscle relaxation and vasomotor tone. This dysregulation may have contributed to the patient's condition.

Glucocorticoid therapy may be detrimental in RCVS and should be avoided when possible. Evidence suggests that glucocorticoids are ineffective in preventing clinical deterioration in RCVS and may even exacerbate cerebral vasoconstriction by further increasing sympathetic activity.[6] The association between glucocorticoid use and poor outcomes may be partly explained by the fact that these agents are often administered to patients with more severe vasoconstriction or established brain lesions, making it difficult to discern whether treatment directly worsens the condition or is merely a marker of disease severity.[6] In the present case, despite the onset of thunderclap headaches and hospitalization, glucocorticoid treatment was continued due to the patient's underlying PNH. This may have contributed to clinical deterioration by potentiating vasoconstrictive mechanisms.

In conclusion, this report presents a novel association of RCVS with PNH. The exact pathophysiology of RCVS of this case remains unclear, but it may represent a serious complication of PNH. Clinicians should consider the diagnosis

of RCVS in patients who develop severe headaches or neurological deficits following PNH or blood transfusion.

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DISCLOSURE

Ethics: The study was approved by Ethics Committee of the First Affiliated Hospital of Hainan Medical University. The written, informed consent was obtained from the participant for the publication of this case report.

Data availability: All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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Conflict of interests: None

REFERENCES

1. Ducros A. Reversible cerebral vasoconstriction syndrome. *Lancet Neurol* 2012;11(10):906-17. doi: 10.1016/S1474-4422(12)70135-7.
2. Pilato F, Distefano M, Calandrelli R. Posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome: Clinical and radiological considerations. *Front Neurol* 2020;11:34. doi: 10.3389/fneur.2020.00034.
3. Singhal AB. Posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome as syndromes of cerebrovascular dysregulation. *Continuum (Minneapolis, Minn)* 2021;27(5):1301-20. doi: 10.1212/CON.0000000000001037.
4. Levitt A, Zampolin R, Burns J, Bello JA, Slasky SE. Posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome. *Radiol Clin North Am* 2019;57(6):1133-46. doi: 10.1016/j.rcl.2019.07.001.
5. Calic Z, Cappelen-Smith C, Zagami AS. Reversible cerebral vasoconstriction syndrome. *Int Med J* 2015;45(6):599-608. doi: 10.1111/imj.12669.
6. Singhal AB, Hajj-Ali RA, Topcuoglu MA, *et al*. Reversible cerebral vasoconstriction syndromes: analysis of 139 cases. *Arch Neurol* 2011;68(8):1005-12. doi: 10.1001/archneurol.2011.68.
7. Dou YH, Fuh JL, Chen SP, Wang SJ. Reversible cerebral vasoconstriction syndrome after blood transfusion. *Headache* 2014;54(4):736-44. doi: 10.1111/head.12319.
8. Liang H, Xu Z, Zheng Z, Lou H, Yue W. Reversible cerebral vasoconstriction syndrome following red blood cells transfusion: a case series of 7 patients. *Orphanet J Rare Dis* 2015;10:47. doi: 10.1186/s13023-015-0268-z.
9. Braun CN, Hughes RL, Bosque PJ. Reversible cerebral vasoconstriction syndrome 3 months after blood transfusion. *J Stroke Cerebrovasc Dis* 2012;21(8):915.e1-5. doi: 10.1016/j.jstrokecerebrovasdis.2012.01.013.
10. Sato Y, Hirose M, Inoue Y, *et al*. Reversible posterior leukoencephalopathy syndrome after blood transfusion in a patient with end-stage renal disease. *Clin Exp Nephrol* 2011;15(6):942-7. doi: 10.1007/s10157-011-0515-0.