

A Case Report of Reversible Cerebral Vasoconstriction Syndrome in a Patient With Systemic Scleroderma

Review began 04/14/2022
Review ended 04/21/2022
Published 04/21/2022

© Copyright 2022

Liu et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Jieying Liu ¹, Mengni Guo ¹, Richard D. Beegle ², Ruoyu Miao ³, Manoucher Manoucheri ¹

1. Internal Medicine, AdventHealth Orlando, Orlando, USA 2. Radiology, AdventHealth Orlando, Orlando, USA 3. Hematology and Oncology, Moffitt Cancer Center, Tampa, USA

Corresponding author: Jieying Liu, jieying.liu.md@adventhealth.com

Abstract

Reversible cerebral vasoconstriction syndrome (RCVS) is represented by recurrent severe thunderclap headache, with or without neurological symptoms. RCVS can be primary or secondary to several factors. Here, we present a case of RCVS in a patient with systemic scleroderma. A 44-year-old female patient presented to the hospital due to Raynaud's phenomenon, fingertip pain ulceration, skin tightness, and skin depigmentation. She was diagnosed with systemic scleroderma. After four days of steroids, immunosuppressants (mycophenolate mofetil), and hydroxychloroquine, the patient developed severe thunderclap headaches and left lower extremity weakness. The computed tomography angiography (CTA) showed multifocal segmental vasoconstriction of the cerebral arteries. The patient's headache and body weakness resolved after starting an oral calcium channel blocker (nimodipine).

Categories: Internal Medicine, Neurology, Rheumatology

Keywords: calcium channel blocker, steroid, immunosuppressants, systemic scleroderma, reversible cerebral vasoconstriction syndrome

Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a rare but increasingly recognized disease [1]. This syndrome typically presents with a recurrent severe thunderclap headache, with or without neurological symptoms [2]. Interventional catheter angiography is the gold standard test and will show reversible multifocal segmental vasoconstriction of the cerebral arteries [3]. Why RCVS occurs remains unclear. There are some case reports in patients with systemic lupus erythematosus (SLE) with RCVS [4,5], but reports of RCVS are very limited in patients with systemic scleroderma. Here, we report a case of RCVS in a patient with systemic scleroderma with typical radiological change and a good response to treatment.

This article was previously presented as a meeting abstract at the 2021 Southern Medical Association (SMA) Annual Scientific Assembly on October 29, 2021.

Case Presentation

A 44-year-old African female with no past medical history presented with Raynaud's phenomenon, fingertip pain and ulcerations, nail fold capillary changes, facial and back rash, skin tightness and depigmentation (Figure 1), joint pain, morning stiffness, and fatigue. Physical examination showed hypopigmented scarring skin lesions on the face and neck and tenderness and swelling of small joints in the hands and wrists.

How to cite this article

Liu J, Guo M, Beegle R D, et al. (April 21, 2022) A Case Report of Reversible Cerebral Vasoconstriction Syndrome in a Patient With Systemic Scleroderma. Cureus 14(4): e24364. DOI 10.7759/cureus.24364

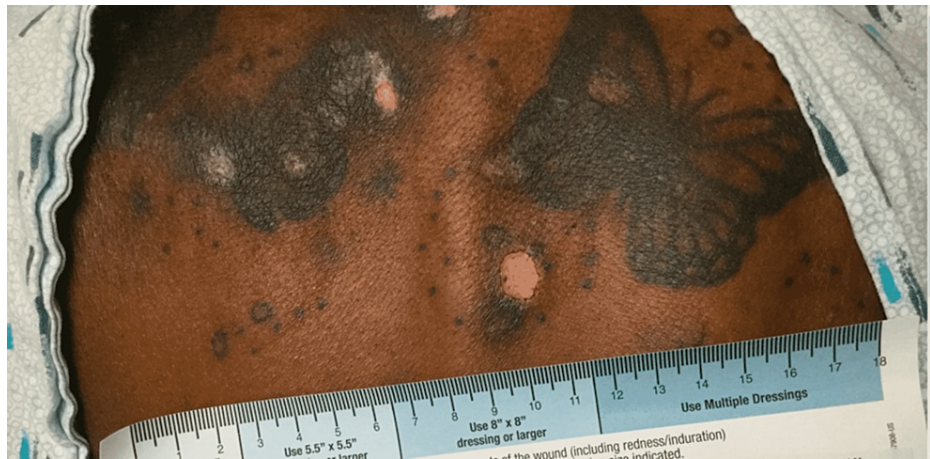


FIGURE 1: Rash on the patient's back

The laboratory results were as follows: antinuclear antibody (ANA) + (1:80, speckled), anti-topoisomerase I (anti-Scl-70) antibody + (4.8 U/mL), cardiolipin IgM + (16 MPL U/mL), and smooth muscle antibody (SMA) + (1:20), and anti-Sjögren's syndrome-related antigen A (anti-Ro/SSA) antibody -, anti-Sjögren's syndrome type B (anti-La/SSB) antibody -, antinuclear ribonucleoprotein (anti-RNP) antibody -, anti-double-stranded DNA (anti-ds DNA) antibody -, and anti-Smith antibody - (Table 1). Flow cytometry and bone marrow biopsy were negative. The patient was diagnosed with systemic scleroderma. Steroids, mycophenolate mofetil, and hydroxychloroquine were started.

Tests	Results	Reference values
ANA	Positive (titer 1:80, speckled)	Negative
Anti-Scl-70 antibody	4.8 U/mL	<1 U/mL
Anti-Ro/SSA antibody	0.2 U/mL	<1 U/mL
Anti-La/SSB antibody	<0.2 U/mL	<1 U/mL
Anti-RNP antibody	0.5 U/mL	<1 U/mL
Anti-ds DNA antibody	2 IU/mL	<5 IU/mL
Cardiolipin IgM	16 MPL U/mL	<11 MPL U/mL
Anti-Smith antibody	0.2 U/mL	<1 U/mL
SMA	Positive (titer 1:20)	Negative

TABLE 1: Laboratory results

ANA: antinuclear antibody; anti-Scl-70 antibody: anti-topoisomerase I antibody; anti-Ro/SSA antibody: anti-Sjögren's syndrome-related antigen A autoantibodies; anti-La/SSB antibody: anti-Sjögren's syndrome type B antibody; anti-RNP antibody: antinuclear ribonucleoprotein antibody; anti-ds DNA antibody: anti-double-stranded DNA antibody; SMA: smooth muscle antibody

After four days of steroids and immunosuppressants, the patient's fatigue, joint pain, and fingertip pain improved during the treatment, but she developed a severe thunderclap headache with left lower extremity weakness. A head computed tomography angiography (CTA) was ordered due to concern of vasculitis. The head CTA showed multifocal long segment stenosis ranging from mild to moderate in severity involving the M2 segments of the right MCA (Figure 2A), sharp transition with reconstitution of the normal caliber of the vessel distally (Figure 2B), focal narrowing of the A1 segment of the right ACA (Figure 3A), focal narrowing of the P1 segment of the right PCA (Figure 3B), and focal narrowing of the proximal left superior cerebellar artery (Figure 3B). Neurology was consulted. The clinical presentation and the image findings were consistent with findings of reversible cerebral vasoconstriction syndrome (RCVS).

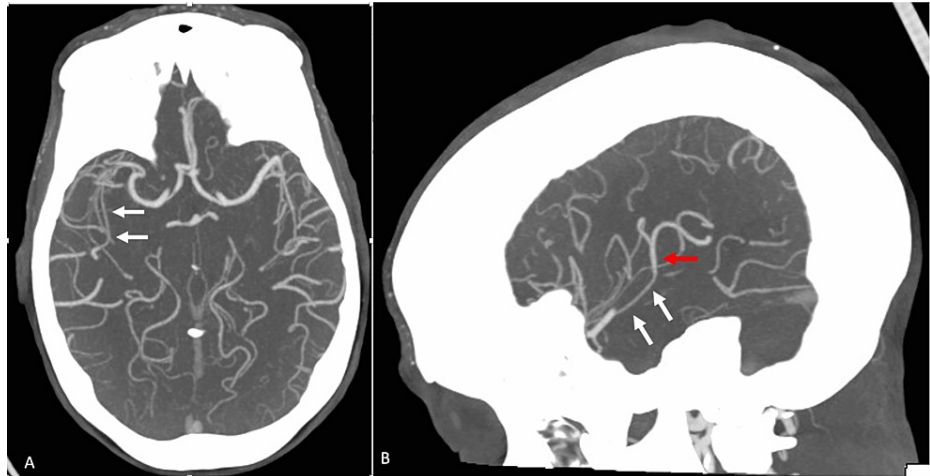


FIGURE 2: Axial and sagittal maximum intensity projection (MIP) post-contrast CTA images of the head

Axial (A) and sagittal (B) maximum intensity projection (MIP) post-contrast CTA images of the head demonstrate a narrowed posterior division M2 branch of the right MCA (white arrows). There is a sharp transition with reconstitution of the normal caliber of the vessel distally (red arrows).

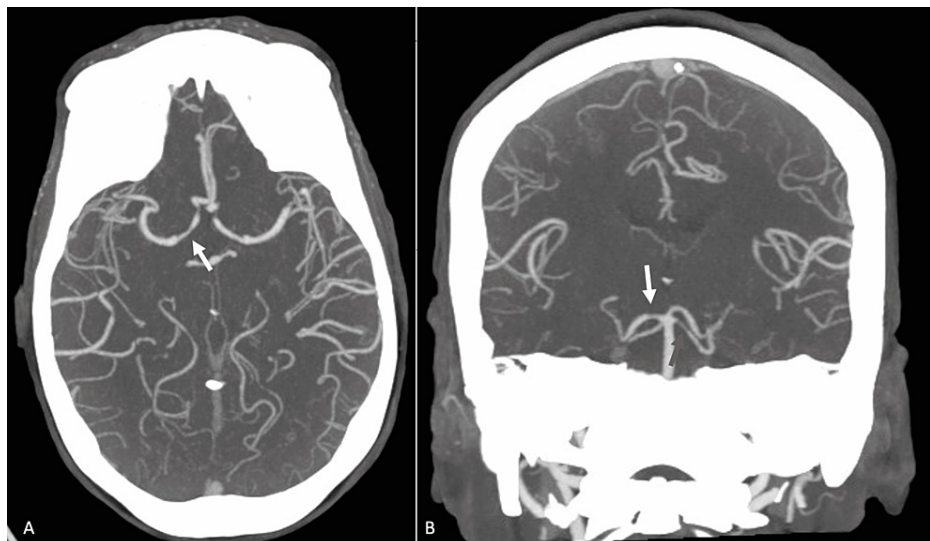


FIGURE 3: Axial and coronal MIP post-contrast CTA image of the head

A: Axial MIP post-contrast CTA image of the head demonstrates a focal narrowing of the A1 segment of the right ACA (white arrow). B: Coronal MIP post-contrast CTA image of the head demonstrates focal narrowing of the P1 segment of the right PCA (white arrow) and focal narrowing of the proximal left superior cerebellar artery (red arrow).

Based on the RCVS diagnosis as the cause of her headache and lower extremity weakness, nimodipine 60 mg QD PO was started. The patient's headache resolved; her left lower extremity weakness improved. The patient's inpatient hospitalization lasted 13 days. After the resolution of the headache and weakness, she was discharged with nimodipine 60 mg QD PO. She has been followed up by her PCP and the rheumatologist for 10 months. She has no more complaints of headaches and extremity weakness.

Discussion

Approximately 24% of patients with systemic scleroderma with central nervous system involvement present with headaches [6]. Patients with systemic scleroderma have a high incidence of headaches. The estimated prevalence of some of them is believed to be due to migraines [7], but other causes remain unclear. The differential diagnosis and treatment for headaches in patients with systemic scleroderma can be challenging.

RCVS is a unifying term to describe a group of disorders characterized by reversible narrowing and dilatation of the cerebral arteries [3]. There are a lot of risk factors and associated conditions related to RCVS, including vasoactive medications, illicit drugs, and postpartum state [1]. There are also several case reports of RCVS related to SLE and immunosuppressant therapy [3-5,8]. The clinical presentation of RCVS is recurrent sudden, severe thunderclap headaches over several days or weeks. Patients can be with or without focal neurological deficits [3]. The diagnosis of RCVS is based on the recurrent thunderclap headache and typical brain imaging findings, which are reversible multifocal segmental narrowing of the cerebral arteries [9]. The diagnosis of RCVS is difficult to distinguish from cerebral vasculitis for the rheumatology patient, but the symptoms can provide some clues. With cerebral vasculitis, the patient has an insidious onset dull headache and stepwise clinical progression, while the headache of a patient with RCVS is acute, self-limited, and thunderclap in nature. Cerebral vasculitis usually involves the distal cerebral arteries, and the RCVS involves the circle of Willis arteries or their proximal branches [8,10]. Some reports show that calcium channel inhibitors may be a treatment for RCVS [11].

During the systemic scleroderma treatment, our patient developed a severe thunderclap headache and left lower extremity weakness. Our patient may have developed RCVS due to the use of steroids and immunosuppressants or systemic scleroderma. There are reports of RCVS secondary to steroid and immunosuppressant use, such as cyclophosphamide, tacrolimus (FK-506), cyclophosphamide, and interferon- α [8,12,13]. Our patient developed a headache after the use of steroids, mycophenolate mofetil, and hydroxychloroquine; the primary cause of RCVS that we considered should be the use of steroids and immunosuppressants, especially the large dose of steroids [14]. Another pathophysiology we should consider is RCVS due to systemic scleroderma. Lee et al. found that brain-blood barrier (BBB) breakdown was present in 69% of patients with definite RCVS [15]. Patients with RCVS also had impaired cerebral endothelial function [16]. Vascular endothelial injury is also reported in patients with systemic scleroderma. This mechanism may be due to the activation of cellular and humoral immunity [17]. These common mechanisms may explain the development of RCVS in patients with systemic scleroderma.

The antimigraine medication, the steroid, and the immunosuppressant all can cause or worsen RCVS [13,18]. It is important to differentiate RCVS from migraine and vasculitis in patients with systemic scleroderma for the right choice of treatment plan.

Conclusions

For the patient with systemic scleroderma who developed thunderclap headache, it is necessary to consider RCVS as a differential diagnosis from systemic scleroderma-related migraine and vasculitis. Steroids and immunosuppressants can cause or worsen RCVS. The clinical presentation of RCVS is recurrent sudden, severe thunderclap headaches. The patient can be with or without focal neurological deficits. The diagnosis of RCVS is based on the recurrent thunderclap headache and typical brain imaging findings, which is reversible multifocal segmental narrowing of the cerebral arteries.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Cappelen-Smith C, Calic Z, Cordato D: Reversible cerebral vasoconstriction syndrome: recognition and treatment. *Curr Treat Options Neurol*. 2017, 19:21. [10.1007/s11940-017-0460-7](https://doi.org/10.1007/s11940-017-0460-7)
2. Calic Z, Cappelen-Smith C, Zagami AS: Reversible cerebral vasoconstriction syndrome. *Intern Med J*. 2015, 45:599-608. [10.1111/imj.12669](https://doi.org/10.1111/imj.12669)
3. Pilato F, Distefano M, Calandrelli R: Posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome: clinical and radiological considerations. *Front Neurol*. 2020, 11:34. [10.3389/fneur.2020.00034](https://doi.org/10.3389/fneur.2020.00034)
4. Ashraf VV, Bhasi R, Ramakrishnan KG, Praveenkumar R, Girija AS: Reversible cerebral vasoconstriction syndrome in a patient with systemic lupus erythematosus. *Neurol India*. 2012, 60:635-7. [10.4103/0028-3886.105200](https://doi.org/10.4103/0028-3886.105200)
5. Chung SW, Lee KM, Heo SH, et al.: A systemic lupus erythematosus patient with thunderclap headache: reversible cerebral vasoconstriction syndrome. *Lupus*. 2019, 28:898-902. [10.1177/0961203319845485](https://doi.org/10.1177/0961203319845485)
6. Amaral TN, Peres FA, Lapa AT, Marques-Neto JF, Appenzeller S: Neurologic involvement in scleroderma: a systematic review. *Semin Arthritis Rheum*. 2013, 43:535-47. [10.1016/j.semarthrit.2013.05.002](https://doi.org/10.1016/j.semarthrit.2013.05.002)
7. Goldberg NC, Duncan SC, Winkelmann RK: Migraine and systemic scleroderma. *Arch Dermatol*. 1978, 114:550-1.
8. Sayegh J, Marc G, Augusto JF, Caroff J, Subra JF, Besson V: Reversible cerebral vasoconstriction syndrome in

- a female patient with systemic lupus erythematosus. *Rheumatology (Oxford)*. 2010, 49:1993-4. [10.1093/rheumatology/keq161](https://doi.org/10.1093/rheumatology/keq161)
9. Singhal AB, Topcuoglu MA, Fok JW, Kursun O, Nogueira RG, Frosch MP, Caviness VS Jr: Reversible cerebral vasoconstriction syndromes and primary angiitis of the central nervous system: clinical, imaging, and angiographic comparison. *Ann Neurol*. 2016, 79:882-94. [10.1002/ana.24652](https://doi.org/10.1002/ana.24652)
 10. Singhal AB, Bernstein RA: Postpartum angiopathy and other cerebral vasoconstriction syndromes. *Neurocrit Care*. 2005, 3:91-7. [10.1385/NCC:3:1:091](https://doi.org/10.1385/NCC:3:1:091)
 11. Nowak DA, Rodiek SO, Henneken S, Zinner J, Schreiner R, Fuchs HH, Topka H: Reversible segmental cerebral vasoconstriction (Call-Fleming syndrome): are calcium channel inhibitors a potential treatment option? *Cephalalgia*. 2003, 23:218-22. [10.1046/j.1468-2982.2003.00507.x](https://doi.org/10.1046/j.1468-2982.2003.00507.x)
 12. Ueki H, Sanayama Y, Miyajima A, Tsuchimochi T, Igarashi S, Sunami S: Reversible cerebral vasoconstriction syndrome promptly diagnosed with magnetic resonance imaging including magnetic resonance angiography during immunosuppressive therapy in a 16-year-old girl with refractory cytopenia of childhood. *Hematol Rep*. 2016, 8:6673. [10.4081/hr.2016.6673](https://doi.org/10.4081/hr.2016.6673)
 13. Chen SP, Fuh JL, Wang SJ: Reversible cerebral vasoconstriction syndrome: an under-recognized clinical emergency. *Ther Adv Neurol Disord*. 2010, 3:161-71. [10.1177/1756285610361795](https://doi.org/10.1177/1756285610361795)
 14. French KF, Hoesch RE, Allred J, Wilder M, Smith AG, Digre KB, La Barge DV 3rd: Repetitive use of intra-arterial verapamil in the treatment of reversible cerebral vasoconstriction syndrome. *J Clin Neurosci*. 2012, 19:174-6. [10.1016/j.jocn.2011.06.016](https://doi.org/10.1016/j.jocn.2011.06.016)
 15. Lee MJ, Cha J, Choi HA, Woo SY, Kim S, Wang SJ, Chung CS: Blood-brain barrier breakdown in reversible cerebral vasoconstriction syndrome: implications for pathophysiology and diagnosis. *Ann Neurol*. 2017, 81:454-66. [10.1002/ana.24891](https://doi.org/10.1002/ana.24891)
 16. Choi HA, Lee MJ, Chung CS: Cerebral endothelial dysfunction in reversible cerebral vasoconstriction syndrome: a case-control study. *J Headache Pain*. 2017, 18:29. [10.1186/s10194-017-0738-x](https://doi.org/10.1186/s10194-017-0738-x)
 17. Kahaleh B: Vascular disease in scleroderma: mechanisms of vascular injury. *Rheum Dis Clin North Am*. 2008, 34:57-71. [10.1016/j.rdc.2007.12.004](https://doi.org/10.1016/j.rdc.2007.12.004)
 18. Ducros A, Boukobza M, Porcher R, Sarov M, Valade D, Bousser MG: The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain*. 2007, 130:3091-101. [10.1093/brain/awm256](https://doi.org/10.1093/brain/awm256)