

Fulminant Vasculitis Associated with Extracranial Dissections and Occlusion, Ischemic Strokes, and Aneurysm Rupture: Case Report and Review of the Literature

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Key words

- Cerebral aneurysm
- Dissections
- Stroke
- Vasculitis

Abbreviations and Acronyms

CNS: Central nervous system

CTA: Computed tomography angiography

ICA: Internal carotid artery

SLE: System lupus erythematosus

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INTRODUCTION

Central nervous system (CNS) vasculitides of either primary or secondary etiology are rare conditions with an incidence of 1–2 per million.^{1,2} Conversely, systemic vasculitis is a more common condition with an estimated incidence of 39 per million.¹ CNS vasculitis generally presents in patients older than 50 years of age.

CNS damage from primary vasculitis may be immune complex–mediated, antibody-mediated, or antineutrophil cytoplasmic antibody–related.¹ Histopathologically, these are recognized by fibrinoid necrosis of the vessel characterized by inflammatory infiltrates within the vessel wall leading to destructive changes. These changes ultimately can lead to vessel occlusion and even infarction with corresponding clinical signs and symptoms. We present an unusual case of a 45-year-old patient with a fulminant presentation of primary idiopathic CNS vasculitis associated with vessel dissections with ischemic strokes and

■ **BACKGROUND:** Central nervous system vasculitis has multiple presentations, including stroke, seizures, cranial nerve palsies, and encephalopathy.

■ **CASE DESCRIPTION:** We present the case of an unresponsive 45-year-old woman with vasculitis associated with fulminant intracranial vessel dissection and occlusion with ischemic strokes and subarachnoid hemorrhage secondary to aneurysm rupture. Imaging studies demonstrated both ischemic and hemorrhagic strokes. She had a ruptured right internal carotid artery dorsal variant aneurysm, right vertebral artery dissection with occlusion and posterior inferior cerebellar artery infarct, left vertebral artery dissection, and severe vasculitis involving intracranial and extracranial vessels. She initially was treated for her vasculitis with high-dose steroids followed by clip wrapping of the dorsal variant aneurysm. Unfortunately, her surgery was complicated by intraprocedural rupture, and the patient died during her hospitalization.

■ **CONCLUSIONS:** Fulminant central nervous system vasculitis can occur with critical vascular anomalies that require emergent intervention and should be part of the differential diagnosis of patients presenting with these multiple vascular pathologies.

simultaneous rupture of a dorsal variant internal carotid artery (ICA) aneurysm.

CASE REPORT

A 45-year-old woman was found unresponsive by her family; she had been seen by her family the previous day in her usual state of good health. She was taken emergently to an outside hospital, intubated for airway protection, and transferred to our facility for further evaluation and treatment. On arrival, the patient had a Glasgow Coma Scale score of 6T (E1, V1T, M4).

Initial computed tomography and computed tomography angiography (CTA) of the head demonstrated several severe vascular abnormalities: intraparenchymal hemorrhage involving the right basal ganglion, subarachnoid hemorrhage involving the basilar cistern, and intraventricular hemorrhage involving the right lateral ventricle (Figure 1). In addition, there were right posterior inferior cerebellar and left posterior cerebral artery territory infarctions, a right vertebral artery

dissection with occlusion of the V3 segment, a 4-mm dorsal variant right ICA aneurysm, and diffuse segmental narrowing in multiple cerebral vascular territories (Figure 1). CTA imaging of the neck also showed segmental narrowing of the right vertebral artery, with occlusion at the C2 transverse foramen, and a left vertebral artery dissection of the V2 segment (not shown).

The patient underwent an emergent placement of an external ventricular drain. A formal diagnostic cerebral angiogram confirmed the findings of the CTA and further documented extensive multisegmental narrowing of both the internal and the external carotid artery branches (Figure 2).

The patient initially underwent emergent suboccipital craniectomy to address the concerns for posterior fossa compression from the large right cerebellar hemispheric stroke. A complete vasculitis work-up was started with the institution of high-dose steroid therapy; however, the hematologic and cerebrospinal vasculitis work-up—including toxicology, human

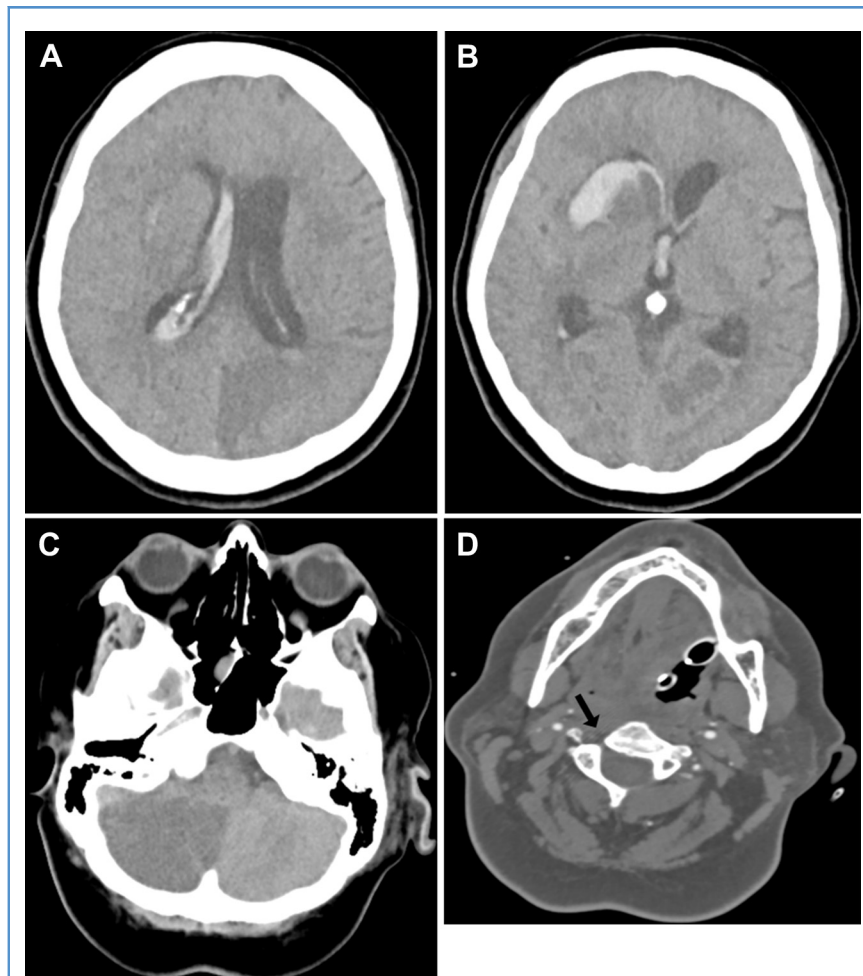


Figure 1. (A and B) Axial computed tomography (CT) of the head demonstrating right basal ganglia intraparenchymal hemorrhage with intraventricular dissection and left posterior cerebral artery infarct. (C) Axial head CT demonstrating right cerebellar hemisphere infarct. (D) Computed tomography angiography of the head demonstrating right V4 occlusion (arrow).

immunodeficiency virus, and hepatitis screening; auto-antibody testing for anti-nuclear antibody, extractable nuclear antigen, anti-neutrophil cytoplasmic antibody, and anti-Ro and anti-La antibodies; cerebrospinal fluid Gram stain and culture, angiotensin-converting enzyme testing, and herpes simplex virus polymerase chain reaction; and fungal culture and listeria antibodies cerebrospinal fluid testing—did not provide any positive results. No biopsy material was obtained during the surgery. Despite the negative laboratory results, the imaging and the clinical picture remained convincing for vasculitis. Because of the severe vasculitis affecting the intracranial circulation, definitive treatment for the cerebral aneurysm initially was deferred.

A repeat cerebral angiogram 3 days later demonstrated marked improvement of the vasculitis after treatment with high-dose steroids (Figure 3). Given the significant improvement in vessel caliber, plans were made to proceed with treatment of the ruptured aneurysm. The patient was deemed to be a poor candidate for endovascular treatment of the aneurysm. The angiomorphology of the aneurysm and the wide neck suggested that the patient would likely require stent-assisted coil embolization or treatment with a flow-diverting stent; however, the patient also presented with an active gastrointestinal hemorrhage that required treatment with a proton pump inhibitor infusion. Thus, the patient was not a good

candidate for dual antiplatelet medications. After discussion of the treatment options with the family, we elected to proceed to surgery for clip-wrapping of the ruptured dorsal variant aneurysm.

At the time of surgery, the aneurysm was found to be extremely friable. The procedure was complicated by rupture of the aneurysm with avulsion of the aneurysm at the neck while we obtained proximal control of the ICA. Ultimately, despite emergent primary microsurgical repair of the parent vessel with clip-wrapping support, the involved supraclinoid ICA thrombosed. On indocyanine green videoangiography, however, there appeared to be sufficient collateral flow across the anterior communicating artery to the middle cerebral artery.

After surgery, the patient's neurologic examination remained poor. The patient developed a new right cerebral hemisphere infarct and despite maximal medical therapy, she progressed to brain herniation. After discussions with the family, care was withdrawn, and the patient died shortly thereafter. A post-mortem study was not performed on this patient.

DISCUSSION

CNS vasculitis is a rare condition with an extensive differential diagnosis that includes Moyamoya syndrome, septic emboli-associated angitis, sympathomimetic drug overdose, Sneddon syndrome, reversible posterior leukoencephalopathy syndrome, Degos disease, MELAS (i.e., mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes), malignant intravascular lymphomatosis, amyloid angiopathy, lipohyalinosis, Fabry disease, and pseudothrombotic elasticum.²⁻⁴ Angiography plays a critical role in the diagnosis of CNS vasculitis,^{4,5} but as a radiographic intervention, it does not provide information to suggest whether the changes seen represent primary or secondary vasculitis or even a nonvasculitic case of segmental arteriopathy. Confirmation generally requires a brain biopsy, which was not performed in our case.⁵

Alhalabi and Moore⁵ retrospectively reviewed the cases of 19 patients with CNS vasculitis and described angiographic changes to the vessel and responses to treatment. The authors

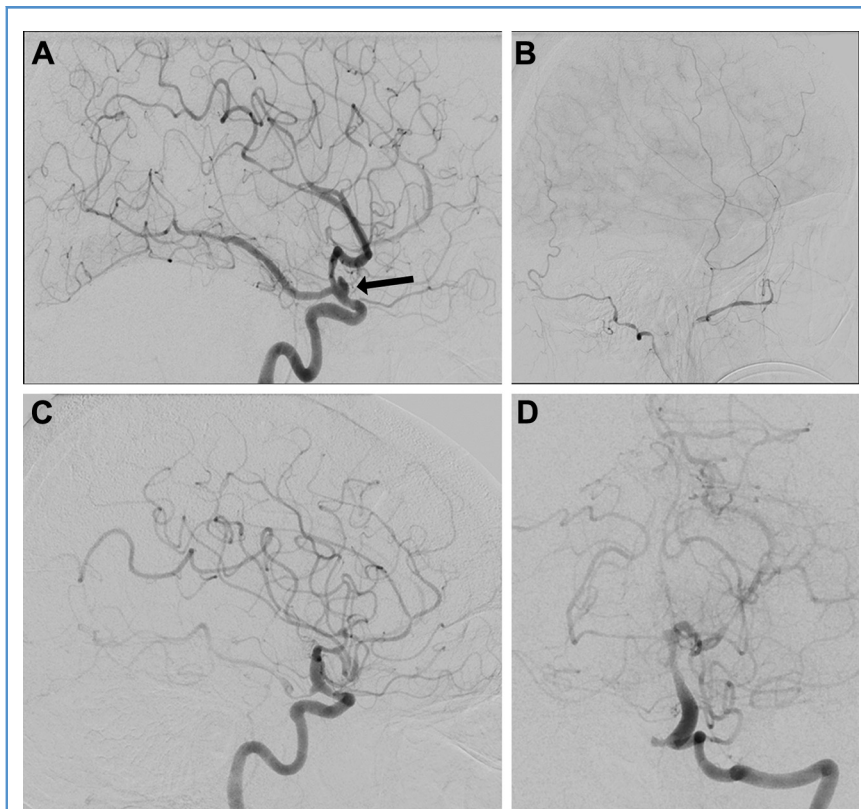


Figure 2. Diagnostic cerebral angiograms demonstrating multifocal segmental narrowing involving the (A) supraclinoid internal carotid artery (ICA), anterior cerebral artery, and middle cerebral artery branches and the right ICA dorsal variant aneurysm (arrow); (B) right external carotid artery branches; (C) left supraclinoid ICA, anterior cerebral artery, and middle cerebral artery branches; and (D) basilar and left posterior cerebral artery.

suggested that angiography is a useful guide for determining the duration of therapy. Angiographic findings of vasculitis included segmental, irregular, or smooth contoured narrowing; occlusion of small-

or medium-sized vessels; beading of the artery; and/or early venous filling. Angiographic changes after initiation of therapy (with cyclophosphamide and prednisone) also were documented. Four patients had

normalization, 8 had improvement, and 5 demonstrated stabilization of angiographic findings. Eleven patients with early initiation of treatment demonstrated a return to a normal angiographic appearance in the previously stenotic areas. In contrast, 3 patients described in another report who were treated after 12 months of symptoms demonstrated either persistent or progressing stenosis.⁵ Early in the course of the disease, stenotic changes can be partially or completely reversible, which we noted in our case after a 3-day course of high-dose steroids. Over time, however, these areas of stenosis become fixed as a result of scarring. In these late stages, continuation of immunosuppressive therapy generally is not recommended unless the patient experiences new or worsening lesions.⁵

Aneurysm formation in patients with CNS vasculitis is generally rare (Table 1)^{3,6-15} but has been described in Behçet disease.⁶ Although 8 cases have been described in the literature, only one was attributed to the vasculitis, and in that case both aneurysm and vasculitis resolved with steroid treatment. Aneurysm formation also has been documented in system lupus erythematosus (SLE)-induced vasculitis. About 1% of the patients with SLE can present with aneurysm-related subarachnoid hemorrhage.^{3,7} These patients have a worse prognosis, higher mortality, and a greater Hunt and Hess grade.^{3,5,7-12,16-19} One reported patient with SLE and aneurysm-related subarachnoid hemorrhage presented with rapidly progressive increase in size of the intracranial aneurysm with subsequent rerupture.³

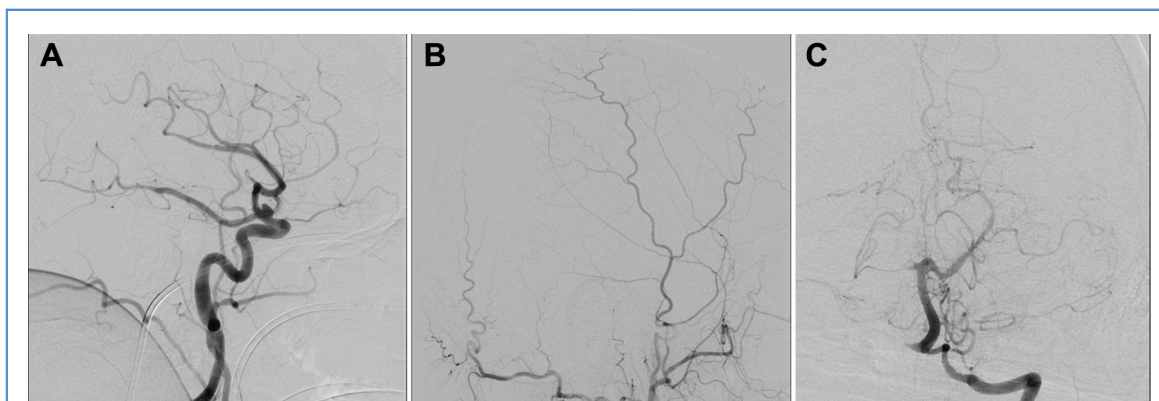


Figure 3. Cerebral angiogram demonstrating significant improvement in the (A) right ICA branches, (B) right external carotid artery branches, and (C) basilar artery and left posterior cerebral artery after high-dose steroid treatment.

Table 1. Overview of Published Literature

Author	Number of Patients	Cause of Vasculitis	Aneurysm Location	Ruptured?	Vasculitis Treatment	Aneurysm Treatment	Mortality
Graffeo et al., 2015 ³	1	SLE	Acomm		Steroids	Embolization	No
Khatibi et al., 2015 ¹⁵	1	PAPA syndrome	PCA	Yes	Steroids	Embolization	No
Saraf et al., 2013 ¹³	1	Tb	MCA	Yes	Tb treatment	Embolization	No
Owada et al., 2009 ¹²	2	SLE	—	—	—	—	—
Baizabal Carvello et al., 2007 ⁷	10	SLE	—	—	—	—	—
Ho et al., 2004 ¹⁴	1	Aspergillosis	SCA	Yes	Amphotericin B	—	Yes
Naksau et al., 2001 ⁶	1	Behçet disease	Bilateral MCA	No	Steroids	Surgical	No
Kitagawa et al., 1990 ⁸	3	SLE	Acomm ×2, MCA	Yes	—	—	—
Asai et al., 1989 ⁹	1	SLE	Bilateral Pcomm, Acomm, MCA, BA	Yes	—	Surgical	Yes
Hashimoto et al., 1986 ¹⁰	2	SLE	BA, Acomm	Yes	—	Surgical	—
Kelley et al., 1980 ¹¹	1	SLE	Pcomm	Yes	Steroids	—	Yes

— indicates data not available.
 SLE, systemic lupus erythematosus; Acomm, anterior communicating artery; PAPA, pyogenic arthritis, pyoderma gangrenosum, and acne; PCA, posterior cerebral artery; Tb, tuberculosis; MCA, middle cerebral artery; SCA, superior cerebellar artery; Pcomm, posterior communicating artery; BA, basilar artery.

Rarely, tuberculosis and CNS aspergillosis have been implicated in vasculitis leading to aneurysm formation with subsequent rupture (Table 1).^{13,14} Khatibi et al.¹⁵ described the case of a young patient with pyogenic arthritis, pyoderma gangrenosum, and acne (i.e., PAPA) syndrome who presented with a thunderclap headache. Imaging demonstrated a dissecting aneurysm of the posterior cerebral artery, which was managed via endovascular coil embolization.

Treatment for CNS vasculitis relies primarily on immunosuppression. An induction regimen of 9–12 weeks of high-dose steroids, such as intravenous methylprednisolone and cyclophosphamide followed by oral prednisolone with weekly tapering of the dose, is recommended. This suppressive regimen is continued for a further 10 months with steroids and azathioprine or methotrexate.¹

Our case is unique because of the fulminant presentation of the vasculitis in conjunction with the development of multiple dissections, the presence of a ruptured dorsal variant ICA aneurysm, and the angiographic response to immunosuppressive treatment, which in combination has not been described previously.

CONCLUSIONS

CNS vasculitis is a rare condition that can have a myriad of clinical presentations. Fulminant presentation in combination with arterial dissections and thrombosis and aneurysm rupture is rare. CNS vasculitis should be a part of the differential diagnosis of individuals presenting with these multiple vascular pathologies.

REFERENCES

- Joseph FG, Scolding NJ. Cerebral vasculitis: a practical approach. *Pract Neurol*. 2002;2:80-93.
- Berlit P. Diagnosis and treatment of cerebral vasculitis. *Ther Adv Neurol Disord*. 2010;3:29-42.
- Graffeo CS, Tanweer O, Nieves CF, Belmont HM, Izmirly PM, Bekske T, et al. Rapid aneurysm growth and rupture in systemic lupus erythematosus. *Surg Neurol Int*. 2015;6:9.
- Hui FK, Bain M, Obuchowski NA, Gordon S, Spiotta AM, Moskowitz S, et al. Mycotic aneurysm detection rates with cerebral angiography in patients with infective endocarditis. *J Neurointerv Surg*. 2015;7:449-452.
- Alhalabi M, Moore PM. Serial angiography in isolated angitis of the central nervous system. *Neurology*. 1994;44:1221-1226.
- Nakasu S, Kaneko M, Matsuda M. Cerebral aneurysms associated with Behçet's disease: a case report. *J Neurol Neurosurg Psychiatr*. 2001;70:682-684.
- Baizabal Carvello JF, Cantu Brito C, Estanol B, Garcia Ramos GS. Subarachnoid hemorrhage as a complication of systemic lupus erythematosus. *Cerebrovasc Dis*. 2007;24:301-304.
- Kitagawa Y, Gotoh F, Koto A, Okayasu H. Stroke in systemic lupus erythematosus. *Stroke*. 1990;21:1533-1539.
- Asai A, Matsutani M, Kohno T, Fujimaki T, Takakura K. Multiple saccular cerebral aneurysms associated with systemic lupus erythematosus—case report. *Neurol Med Chir (Tokyo)*. 1989;29:245-247.
- Hashimoto N, Handa H, Taki W. Ruptured cerebral aneurysms in patients with systemic lupus erythematosus. *Surg Neurol*. 1986;26:512-516.
- Kelley RE, Stokes N, Reyes P, Harik SI. Cerebral transmural angitis and ruptured aneurysm: a complication of systemic lupus erythematosus. *Arch Neurol*. 1980;37:526-527.
- Owada T, Takahashi K, Kita Y. Subarachnoid hemorrhage in systemic lupus erythematosus in Japan: two case reports and a review of the literature. *Mod Rheumatol*. 2009;19:573-580.
- Saraf R, Limaye U. Ruptured intracranial tubercular infectious aneurysm secondary to a tuberculoma and its endovascular management. *Br J Neurosurg*. 2013;27:243-245.
- Ho CL, Deruytter MJ. CNS aspergillosis with mycotic aneurysm, cerebral granuloma and infarction. *Acta Neurochir (Wien)*. 2004;146:851-856.
- Khatibi K, Heit JJ, Telischak NA, Elbers JM, Do HM. Cerebral vascular findings in PAPA syndrome: cerebral arterial vasculopathy or vasculitis and a posterior cerebral artery dissecting aneurysm [e-pub

- ahead of print]. *BMJ Case Rep.* 2015;2015. <http://dx.doi.org/10.1136/bcr-2015-011753>.
16. Hinchey JA, Sila CA. Cerebrovascular complications of rheumatic disease. *Rheum Dis Clin North Am.* 1997;23:293-316.
 17. Krishnan E. Stroke subtypes among young patients with systemic lupus erythematosus. *Am J Med.* 2005;118:1415.
 18. Gladman DD, Goldsmith CH, Urowitz MB, Bacon P, Fortin P, Ginzler E, et al. The Systemic Lupus International Collaborating Clinics/

American College of Rheumatology (SLICC/ACR) Damage Index for Systemic Lupus Erythematosus International Comparison. *J Rheumatol.* 2000;27:373-376.

19. Hanly JG, Walsh NM, Sangalang V. Brain pathology in systemic lupus erythematosus. *J Rheumatol.* 1992;19:732-741.

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