Aneurysmal Subarachnoid and Spinal Hemorrhage Associated With Systemic Lupus Erythematosus

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Case Description

A 42-year-old woman with systemic lupus erythematosus (SLE), positive lupus anticoagulant, elevated titers of IgG and IgM anticardiolipin antibody and β2 glycoprotein antibodies, idiopathic thrombocytopenia, and hemolytic anemia presented with menorrhagia and anemia. She received both platelet and red cell transfusions and had an unrevealing endometrial biopsy. She was treated with intravenous immunoglobulin therapy for autoimmune-mediated thrombocytopenia and was taking hydroxychloroquine 200 mg twice daily which was a home medication. She was started on prednisone 60 mg daily. During her hospitalization, she developed a sudden, severe, sharp, and pounding occipital and nuchal headache with sharp shooting pains radiating down the back of the neck. She was alert and oriented with normal cranial nerve function, motor strength, and sensation. Her headache was unsuccessfully treated with fioricet and acetaminophen.

The day after headache onset, a noncontrast head computed tomography revealed a subarachnoid hemorrhage (SAH) extending from the interpeduncular fossa caudally to the cervicomedullary junction (Figure 1). Computed tomographic angiogram of the head and neck revealed a focal left vertebral artery stenosis with poststenotic aneurysmal dilation of the intradural (V4) segment. There were additional multifocal areas of beading and long tapered vessel narrowing involving the M2 division of the left middle cerebral artery and anterior cerebral arteries and M3 division of the right middle cerebral artery (Figure 1). Magnetic resonance brain demonstrated multifocal but posteriorly predominant T2 hypointense lesions that resembled posterior reversible leukoencephalopathy syndrome (Figure 2). Conventional angiogram confirmed the global small and medium vessel vasculopathy with a left V4 vertebral artery fusiform aneurysm measuring 10.6 mm×5.5 mm distal to the origin of the left posterior inferior cerebellar artery (Figure 2).

She was diagnosed with a lupus vasculitis and resultant aneurysmal dilation of the vertebral artery. The rupture of the vertebral artery aneurysm likely lead to the perimedullary and peripontine SAH. She was started on nimodipine 60 mg 4x daily to prevent vasospasm. Methylprednisolone at a dose of 125 mg was administered for 3 days and transitioned to prednisone 60 mg daily. She continued to have progressive symptoms with worsening headache and mild confusion. She was given 2 infusions of rituximab 1 g separated by 14 days to treat the underlying autoimmune condition. She underwent successful coil embolization of the left vertebral artery aneurysm with preservation of the left posterior inferior cerebellar artery ≈3 weeks after discovery of the SAH. Coiling was delayed to allow for some healing of the vessel and to prevent catheter-induced vasospasm that was apparent on initial conventional angiogram and required intra-arterial verapamil infusion. She had persistent mild to moderate back and neck pain that was alleviated by oxycodone and gabapentin.

Eleven days after coil embolization, she developed rapid onset bilateral iliopecto, quadriiceps, hamstring, and anterior tibialis muscle weakness with sensory loss of pinprick sensation up to the mid thoracic level and urinary retention. Urgent cervical and thoracic spine magnetic resonance imaging revealed the cause of her paraplegia. There was a T2 hyperintense lesion with an associated rim of susceptibility consistent with hemorrhage centered within the left anterior spinal canal at the T4 and T5 levels suggestive of a ruptured intraspinal arterial aneurysm with surrounding hematoma and cord compression. There was extensive abnormal T2 cord signal extending from C5 to the conus. Emergent conventional spinal angiogram demonstrated a radiculopial artery supplying the posterior spinal artery at the left T4 level with a small 1-mm aneurysm and active contrast extravasation into the thecal sac (Figure 3). She underwent emergent T3–T6 laminectomy with intradural exploration and debulking of the intradural hematoma. The left posterior spinal artery aneurysm was surgically obliterated using bipolar coagulation and excision. Repeat magnetic resonance imaging was performed ≈1 week and again 1 month after her SAH. Although she had some posterior circulation infarcts involving the cerebellum possibly related to the vertebral artery coil embolization, the fluid-attenuated inversion recovery hyperintense lesions and previously identified multifocal areas of stenosis were significantly improved. One month after her neurological injuries, she had persistent paraparesis. She was able to move her toes and had some trace...
quadriceps movement but remained wheelchair dependent. She also had debilitating neuropathic pain in the abdomen and legs and persistent fecal and urinary retention.

Discussion

The presentation and radiographic findings of this case are most consistent with a lupus vasculitis causing multifocal constriction of the cerebral vessels. There were focal areas of stenosis in the more proximal vessels and a beading of the distal smaller vessels. There were additional long regions of tapered vessel narrowing. The associated vertebral artery aneurysm was fusiform and distal to a longer segment of narrowing. The cause of the aneurysm was a presumed combination of vasculitic weakening of the vessel wall and poststenotic dilation of the vertebral artery. Although vasospasm related to SAH is possible, this is often seen several days after SAH unlike in this case where the vessel changes seemed coincident with the SAH. In addition, the cooccurrence of pronounced changes in the anterior circulation and posterior reversible leukoencephalopathy syndrome–like changes in the brain parenchyma were more suggestive of lupus vasculitis. The most debilitating event was the spinal hemorrhage related to a posterior spinal artery aneurysm found after she became paraplegic.

Central Nervous System Manifestations of SLE

SLE can affect the central nervous system producing heterogeneous disorders of the brain and spinal cord. When combined with psychosis or mood disturbance, these central nervous system manifestations of lupus are often grouped into the broad and nondescript category of neuropsychiatric lupus. However, this grouping does not inform the variable nature of lupus-associated central nervous system pathology. SLE can present with seizures, encephalopathy, headache, psychosis, and focal neurological deficits related to cerebral infarction and transverse myelitis. Brain magnetic resonance imaging abnormalities associated with SLE vary but have been observed in 40% to 50% of patients with SLE. Small or punctate juxtacortical T2 fluid-attenuated inversion recovery hyperintense lesions and periventricular and subcortical white-matter lesions have been observed. SLE can present with more extensive white-matter lesions and posterior reversible leukoencephalopathy syndrome.1

SLE confers an increased risk of ischemic stroke. Embolic strokes may accompany elevated antiphospholipid antibodies or Libman–Sacks endocarditis. In addition, small vessel lacunar and large vessel atheromatous stroke subtypes have also been reported in SLE.3 However, the association between SLE and hemorrhagic stroke, including SAH, remains less defined.
In 1 study, 5.6% of patients with SLE developed either ischemic stroke (8 of 234), cerebral hemorrhage (2 of 234), or SAH (3 of 234).³

Although SLE has been associated with vasculitis, the combination of SAH and vasculitis is a rare but often devastating occurrence. Several case reports describe SLE-associated cerebral arteriopathy and arteritis.¹,⁴ Cerebral arteriopathy occurs in ≈6% to 13% of SLE cases. In a postmortem analysis of 88 patients, the predominant pathology was a small-vessel angiopathy with intimal proliferation, mucoid hyperplasia, and hyaline deposition. This can be accompanied by small-vessel obliteration with fibrin thrombus. Rarely, additional perivascular inflammation was found supporting the existence of an accompanying vasculitis. The existence of antiphospholipid antibodies seemed to confer an increased risk of vasculopathy.⁵

Aneurysmal SAH
Although the incidence of SAH in SLE is lower than that of ischemic stroke,⁶ 1 retrospective analysis found that 3.9% of hospitalized patients with SLE (10 of 258 cases) had SAH.⁷ In a larger 1077-patient retrospective series, 1% of patients with SLE were diagnosed with SAH.⁴ Both aneurysmal SAH and nonaneurysmal SAH have been described in the literature involving the anterior and posterior cerebral circulations.⁹ In a series of 39 previously published SLE-associated SAH cases, 3 patterns of disease were described—distal fusiform aneurysms with either unusual locations or additional vessel abnormalities, multiple saccular aneurysms, or angiographically negative SAH with poor outcome. In the latter category, 5 of the 11 nonaneurysmal SAH SLE patients either died or had significant persistent morbidity.⁹ Focal transmural angiitis at the location of fusiform aneurysm rupture has been described in a patient with SLE and SAH. These changes accompanied additional vessel irregularities.¹⁰

Although steroids and hydroxychloroquine are used as maintenance therapy in patients with lupus, flares associated with vasculitis should be treated promptly and often require a combination of higher dose steroids, intravenous immunoglobulin therapy, or plasmapheresis. SLE-associated cerebral arteritis may necessitate more aggressive management with immunomodulatory therapy like rituximab or belimumab.²

TAKE-HOME POINTS
• Aneurysmal subarachnoid hemorrhage and central nervous system vasculitis are rare but severe manifestation of SLE often presenting with headaches, neck pain, or encephalopathy.
• Magnetic resonance imaging and angiography may reveal parenchymal hyperintense lesions and varying degrees of beaded and tapered vessel constriction.
• Given the potential for significant morbidity and mortality, aggressive and early treatment with steroids and immunomodulatory agents may be needed to halt the progression of disease.
None.

References

Key Words: aneurysm ▪ lupus erythematosus, systemic ▪ stroke ▪ subarachnoid hemorrhage ▪ vasculitis
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