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Case Report

Rapid aneurysm growth and rupture in systemic lupus erythematosus

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Abstract

Background: Subarachnoid hemorrhage (SAH) due to intracranial aneurysm rupture is a major neurosurgical emergency associated with significant morbidity and mortality. Rapid aneurysm growth is associated with rupture. Systemic lupus erythematosus (SLE) is a multi-system autoimmune disorder whose complications can include cerebral vasculitis and vasculopathy. Intracranial aneurysms are not known to occur more frequently in SLE patients than the general population; however, aneurysm growth rates have not been studied in SLE.

Case Description: We present a 43-year-old female with SLE on prednisone, hydroxychloroquine, and azathioprine with moderate disease activity who presented with severe, acute-onset headache and was found to have Hunt and Hess grade II SAH due to rupture of an 8 mm saccular anterior communicating artery (ACoA) aneurysm. The patient developed severe vasospasm, re-ruptured, and was taken for angiography and embolization, which was challenging due to a high degree of vasospasm and arterial stenosis. Review of imaging from less than 2 years prior demonstrated a normal ACoA complex without evidence of an aneurysm.

Conclusion: We review the literature and discuss the risk factors and pathophysiology of rapid aneurysm growth and rupture, as well as the pathologic vascular changes associated with SLE. Although SLE patients do not develop intracranial aneurysm at an increased rate, these changes may predispose them to higher incidence of growth and rupture. This possibility-coupled with increased morbidity and mortality of SAH in SLE-suggests that SAH should be considered in SLE patients presenting with headache, and advocates for more aggressive treatment of SLE patients with unruptured aneurysms.

Key Words: Aneurysm growth, intracranial aneurysms, subarachnoid hemorrhage, systemic lupus erythematosus

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INTRODUCTION

Rapid aneurysm growth is reported rarely, and risk factors for aneurysm growth are an area of active debate, with considerable disagreement in the neurosurgical literature.[22,32,38,41,44] As rapid aneurysm growth is itself a risk factor for rupture, identification of susceptible patients would inform clinical decision-making.[6,41]

Systemic lupus erythematosus (SLE) is an autoimmune disorder with protean effects on almost every organ system.[52] Central nervous system (CNS) SLE occurs in 24–51% of patients, and although psychosis and seizure are among the diagnostic criteria, cerebrovascular disease is more common.[15,25,52] The majority of CNS SLE pathology is atherothromboembolic disease, or secondary extension of parenchymal hemorrhage; however, aneurysmal subarachnoid hemorrhage (SAH) occurs in up to 3.9%.[11,33,40,43]

In this report, we present a patient with SLE who demonstrated rapid growth of an anterior communicating artery (ACoA) aneurysm with rupture, vasospasm, and rebleed.

CASE REPORT

A 43-year-old right-handed African American female with a history of migraines was followed clinically for SLE for 3 years prior to presentation. Her initial diagnosis was based on American College of Rheumatology criteria of: Antinuclear antibodies, dsDNA antibodies, arthritis, and serositis with pericarditis. Recent disease activity was moderate, with arthralgias, occasional fevers, oral ulcers, fatigue, a truncal maculopapular rash, and abnormal C4, dsDNA, and c-reactive protein. Medications included prednisone, hydroxychloroquine, and azathioprine.

The patient presented to the emergency room after a syncopal event with headache, dizziness, and nausea. She had no focal neurologic deficits, improved on migraine medications, and was discharged. Throughout the following week, headaches and fatigue persisted; however, her family reported that these symptoms were comparable to prior SLE flares.

Six days later, the patient was found unresponsive and with one episode of bowel incontinence. She was taken to the emergency department, where she was arousable and oriented. Neurologic examination was significant for moderate expressive aphasia, left-sided hemineglect, flattening of the left nasolabial fold, 4/5 strength in the right upper and lower extremities, and 0/5 strength in the left upper and lower extremities. Hoffman's and Babinski's signs were negative, no clonus was observed, and her remaining cranial nerves were intact. Musculoskeletal examination was significant for trace bilateral dorsal hand edema, mild proximal interpharyngeal joint tenderness without synovitis, and a papular, erythematous, scaling rash over her thighs bilaterally.

Computed tomography (CT) and CT angiography demonstrated multiple areas of acute infarct, most prominently in the anterior cerebral artery (ACA) distribution, with minimal interhemispheric SAH and a 8 × 5 mm bilobed saccular aneurysm located at the junction of the left ACA and ACoA [Figure 1a and b]. The patient was diagnosed with Hunt and Hess grade II SAH and admitted to the neurosurgical intensive care unit. Initial medical management included oral levetiracetam 500 mg, oral nimodipine 60 mg, and three doses of intravenous methylprednisolone 16 mg/kg.[14] Azathioprine was held, as consideration of alternative immunosuppression with cyclophosphamide or mycophenolate mofetil was deliberated. Since the patient was postbleed day six from initial rupture on admission hospital, the decision was made to withhold endovascular intervention as long as she remained clinically stable and within the vasospasm window.

Five days after admission, the patient became acutely unresponsive, and repeat head CT demonstrated new subarachnoid blood. She was taken emergently for angiography and embolization of the aneurysm [Figure 2a and b]. Vasospasm involving the right internal carotid artery (ICA), bilateral ACA, ACoA, supraclinoid left ICA, and right posterior cerebral artery was observed. Of note, catheterization of the A1 segment was difficult, due to severe vasospasm and arterial stenosis.

Postembolization, the patient awoke with dense left hemiparesis, left hemineglect, and severe expressive aphasia. Over several days, the patient's neglect and aphasia resolved, and she was discharged to acute rehabilitation in stable condition. At follow-up one month after discharge, she demonstrated no signs of aphasia, and was able to converse and interact at her prerupture baseline. She had recovered antigravity strength in her left extremities, and her facial nerve deficit had resolved.

Review of imaging conducted as part of a headache workup 20 months prior to the current admission demonstrated a normal ACoA complex, as per multiple neuroradiologists at our institution [Figure 3]. A renal ultrasound was negative for polycystic kidney disease. Additional history did not reveal any other medical conditions or significant risk factors for aneurysm rupture, such as hypertension or smoking. Family history was negative for polycystic kidney disease, connective tissue disorders, SAH, intracranial aneurysms, or sudden deaths suspicious for undiagnosed aneurysm rupture.

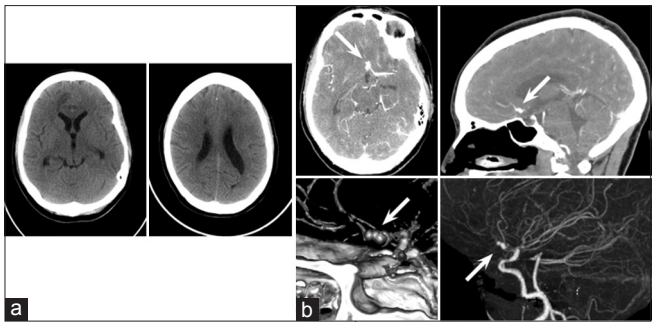

Figure 1: Computed tomography: (a) Axial noncontrast head CT demonstrating minimal interhemispheric SAH and multiple areas of acute infarct, most prominently in the anterior cerebral artery distribution. (b) Axial CTA with sagittal and 3D reconstructions demonstrating an 8 × 5 mm bilobed saccular aneurysm located at the junction of the left anterior cerebral anterior and anterior communicating artery (arrows)

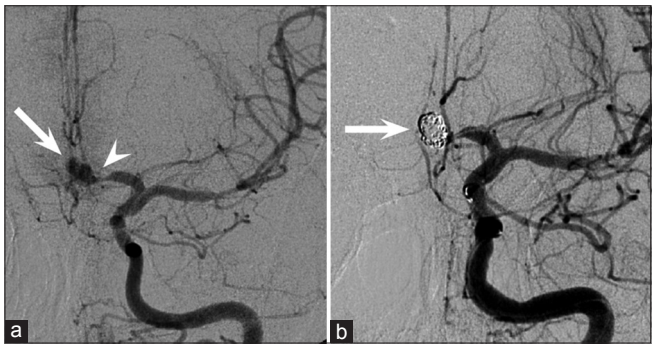

Figure 2: Angiography and embolization: (a) Anterior–posterior projection of a contrast injection of the left internal carotid artery aneurysm that reveals a bilobed aneurysm (arrow) and proximal vasospasm (arrowhead). (b) Postembolization view showing complete occlusion of the aneurysm with a coil mass (arrow)

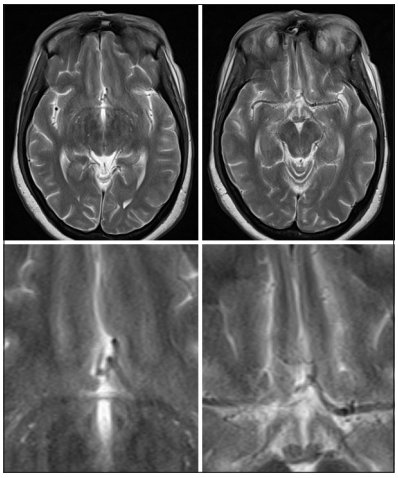

Figure 3: Prior MRI: Adjacent slices from axial T2-weighted MRI of the brain demonstrating normal anterior communicating artery complex, without evidence of intracranial aneurysm. Study performed 20 months prior to patient presentation (see Figures 1 and 2)

DISCUSSION

SAH is a neurosurgical emergency, and 85% of nontraumatic SAH is due to aneurysm rupture.[27] The prognosis among these patients is poor: The overall case fatality rate after rupture is approximately 35%, and although two-thirds of all survivors are able to regain functional independence, half have permanent cognitive impairments, and only a third are able to return to prerupture employment.[2,7,45]

Although prior reports suggested that intracranial aneurysms are more prevalent in SLE patients than the general population, larger and more recent studies have found that the overall incidence is comparable.[18,30,34,40] However, SLE patients bear a worse prognosis, with higher incidence of SAH, increased mortality, and worse Hunt and Hess grades on presentation.[5,18,31,53,54] Data on complications including vasospasm or rebleeding are limited, but anecdotal reports suggest that SLE may predispose to adverse outcomes.[17,30,34]

Risk factors for rupture have been widely studied, and although some disagreement exists, aneurysm growth is a consistently significant finding.[1,3,20,23,32,35]

Correspondingly, other studies have investigated independent risk factors for aneurysm growth, which may include location on the ICA, middle cerebral artery, or basilar artery, large aneurysm size, multiple lobes, family history of SAH, active smoking, and female sex.[6,21,24,41,44]

Aneurysm formation and growth is influenced by hemodynamic and endothelial changes. Abnormal flow produces local changes in blood pressure and wall sheer stress, which lead to endothelial remodeling and consequent changes in aneurysm geometry.[8-10,37,40,42,47-50,55] Progressive geometric alteration begets further hemodynamic stress, and the cycle of positive feedback propagates aneurysm growth and rupture. In parallel, inflammation and ischemia induce endothelial remodeling and seed aneurysm growth, via collagen and fibrin deposition within the walls, thinning of the domes, vascular smooth muscle deficiency, fibroblasts and leukocytes infiltration, degradation of matrix proteins, and elevated elastase and collagenase activity.[8,12,19,28,39,51] The greatest risk for rupture occurs during rapid growth, and simulated patient cohorts with variable growth rates better approximate the incidence of SAH than those based on linear models, suggesting that the natural history of aneurysm rupture is characterized by periods of intermittent, unpredictable vulnerability.[10,26,32,53]

Presently, a definitive, causal relationship has not been established between SLE and aneurysmal SAH. Although SLE is frequently associated with cerebrovascular pathology, small vessels are affected, rather than the Circle of Willis.[40] Notwithstanding, histopathologic studies have identified inflammation, vasculitis, and fibrinoid necrosis within ruptured aneurysm walls from SLE patients.[4,29,30,36,43,46] Other investigations have found large-vessel damage from immune complex deposition, accelerated atherosclerosis, and predisposition to coagulopathy.[11,16,40] Taken together, these findings suggest

a role for autoimmune damage underlying rupture pathophysiology in SLE patients.

Approaching the link between SLE and SAH clinically, a study incorporating the Systemic Lupus International Collaborating Clinics (SLICC) damage score-a metric for quantifying damage from SLE or its treatment-observed scores ≥2 in 80% of ruptures, suggesting that chronic damage contributes to vascular weakness.[5,13] Other studies observed that 60–70% of SAH occurred >5 years after SLE diagnosis, suggesting a dose–response relationship.[5,43] However, other reports observed that SLE disease activity is equally distributed at high and low levels following rupture, suggesting that aneurysm formation, growth, and rupture may be independent of SLE disease activity.[5,40,43] Notwithstanding, if a causative relationship exists between the entities, the crucial pathophysiology is more to occur *prior to rupture* rather than *immediately following*, a mechanism that has not yet been evaluated.

The present case highlights the challenges of balancing immunosuppression against control of autoimmunity. CNS SLE indicates aggressive immunosuppression, yet the relationship between disease activity and symptoms is clear in those patients, for whom the benefits clearly outweigh the risks.[11,25,52] In contrast, given the lack of evidence linking SLE disease activity to SAH, and the likelihood that patients with aneurysm rupture will require neurosurgical intervention, maintaining SLE immunosuppressive following rupture pose a substantial risk of infection, and no defined benefit in terms of neurovascular outcome.[5,40,43] This conflict stresses the need for an understanding of the relationship between SLE vascular pathologies and SAH complications.

Careful consideration should be given to the role of endovascular intervention in these patients. Given the possibility that SLE may predispose to growth and rupture, early intervention may be more beneficial than in the general population. Among SLE patients who rupture, it may be possible to reduce the risk of rebleed by treating emergently, although no current evidence supports or refutes this theory.[53] However, SLE may also predispose to vessel stenosis, potentially limiting the role for angioplasty and superselective drug infusions. In the present case, we elected to attempt slow passage of the microcatheter through the stenotic segment first, with a plan to pursue vasospasm treatment with verapamil or balloon angioplasty if that proved technically unfeasible. Based on our experience, we anticipate that endovascular therapy for ruptured aneurysms in SLE patients will demand highly individual tailoring.

CONCLUSION

This is the first reported case of rapid aneurysm growth and rupture in a patient with SLE to the authors' knowledge, and this review highlights major deficiencies in the current understanding of the relationship between SLE and aneurysm biology. Although aneurysmal SAH is rare in SLE, it should be considered in patients presenting with headache. Further, when aneurysms are identified in patients with SLE, they should be followed closely, and considered for more aggressive treatment with endovascular embolization or open surgical clipping-especially if growth is observed.

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