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Lupus Aortitis Leading to Aneurysmal Dilatation in the Aortic Root and Ascending Aorta

Derek R. Brinster, MD,[1] John D. Grizzard, MD,[2] Alok Dash, MD[3]

[1]Divisions of Cardiothoracic and Vascular Surgery, [2]Department of Radiology, and [3]Division of Cardiothoracic Surgery, Virginia Commonwealth University Medical Center, Richmond, Virginia, USA

ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs, tissues, and cells undergo damage mediated by tissue-binding autoantibodies and immune complexes. We describe the case of a 23-year-old African American woman with a history of recurrent pneumonias. Computed tomography, magnetic resonance imaging (MRI), and echocardiographic evaluations, as well as clinical and laboratory findings, indicated a diagnosis of SLE with inflammatory aortitis secondary to SLE vasculitis. A repeat MRI revealed a rapidly expanding aortic root and ascending aorta that required prompt operative repair. The ascending aorta and aortic root were replaced with a mechanical valved conduit, and a coronary artery bypass to the posterior descending artery was performed because of related erosion into the intima of the right coronary ostium. The patient has done well postoperatively. Aortitis and aortic aneurysms are an uncommon manifestation of SLE, and a literature search revealed an apparent association between aortic aneurysms and steroid medications for SLE. This case is the first report of aortitis resulting in a nondissecting aortic root aneurysm in an SLE patient without a history of steroid use, indicating that all SLE patients, including those without a history of steroid use, require screening for aortic disease to improve surgical outcomes and to prevent fatal complications.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs, tissues, and cells undergo damage mediated by tissue-binding autoantibodies and immune complexes [Braunwald 2005]. Ninety percent of the patients are women of childbearing age, and people of both sexes and all ethnic groups are susceptible. The prevalence of SLE in the United States is 15 to 50 per 100,000 population, with the highest prevalence being among African Americans. SLE affects almost every organ system, including the cardiopulmonary, neurologic, renal, skin, hematologic, and musculoskeletal systems. Systemic features include fatigue, malaise, fever, anorexia, and weight loss. The cardiopulmonary manifestations include pleurisy, pericarditis, myocarditis, and endocarditis, in addition to coronary artery disease and pulmonary hypertension [Doherty 1985].

Aortitis is a well-known but uncommon complication of SLE that can be a component of several other disease states, including Takayasu arteritis, giant cell arteritis, Behçet syndrome, Cogan syndrome, syphilis, spondylarthropathies, rheumatoid arthritis, sarcoidosis, and others [MacLeod 1992; Hachulla 2001]. Aortitis presents in a variable fashion, with aneurysm, dissection, aortic valve regurgitation, and aortic stenosis being the most common manifestations.

The majority of lupus aortitis cases documented in the literature have either been found on autopsy or been associated with dissection [Silver 2006]. The manner by which aortitis usually leads to aortic dissection has been described by Guard and colleagues [1995]. They proposed that active arteritis in association with fibrinoid necrosis and obliterative endarteritis of the vasa vasorum results in multiple infarcts of differing ages. The multiple infarcts combine with increasing inflammation to lead to a disruption of the aortic wall. This

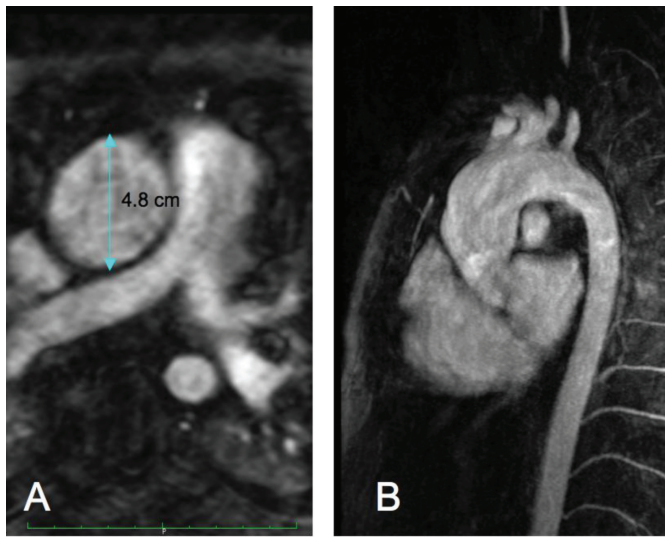

Figure 1. Axial (A) and oblique sagittal (B) magnetic resonance angiographic images demonstrate dilatation and irregularity of the ascending aorta.

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Correspondence: Derek R. Brinster, MD, Assistant Professor of Surgery, Director of the Thoracic Aortic Surgery Program, Divisions of Cardiothoracic and Vascular Surgery, Virginia Commonwealth University Medical Center, Medical College of Virginia Campus, West Hospital Building, 7th Floor, South Wing, 1200 E Broad St, PO Box 980068, Richmond, Virginia 23298-0068, USA; 1-804-828-4663; fax: 1-804-827-0527 (e-mail: dbrinster@mcvh-vcu.edu).

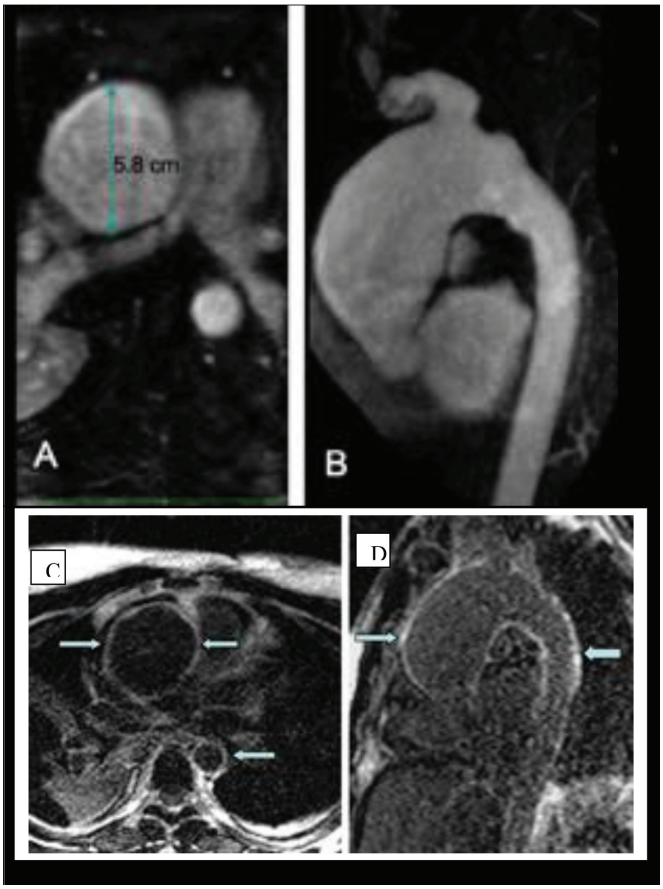

Figure 2. Axial (A) and oblique sagittal (B) magnetic resonance angiographic images obtained 1 week later demonstrate significant progression of the dilatation and irregularity of the ascending aorta. Postcontrast inversion recovery images of the thoracic aorta in the axial (C) and oblique sagittal (D) projections showing intense transmural delayed enhancement of the aortic wall (arrows). Inversion time chosen to null myocardium (TI = 370 ms).

disruption in turn leads to a thinning and weakening of the arterial wall, eventually culminating in dissection.

To date, all reported cases of lupus aortitis requiring operative intervention have been in patients who had a long history of SLE being treated with corticosteroids and whose aortitis progressed over months to several years. Furthermore, in the majority of the patients with diagnosed aortic root aneurysms, aortitis has been found to be an isolated finding without any association with autoimmune diseases [Tavora 2006].

In this report, we describe an unusual case of a 23-year-old African American woman with diagnosed SLE who was incidentally found to have a rapidly expanding aortic root and ascending aorta necessitating operative repair. Our case is yet another example of both the complexity of SLE and the myriad of ways in which it may manifest.

CLINICAL SUMMARY

In July 2007, a 23-year-old African American woman with a medical history significant only for recurrent pneumonias presented to the Virginia Commonwealth University Medical Center (VCUMC) with a 1-week history of fevers, chills, weakness, and pleuritic chest pain. Five days prior to admission at VCUMC, the patient presented to an outside hospital with similar symptoms, received a diagnosis of bronchitis, and was discharged home with oral antibiotics. The patient, however, did not fill her prescription. She was subsequently treated by the Medicine Service for multilobar community-acquired pneumonia and was started on oral antibiotics.

The combination of the patient's nonspecific symptoms of fever, malaise, weakness, nausea, and decreased oral intake with her history of pleurisy and recurrent pneumonias (8 in the previous 2 years) prompted the thought that an immune deficiency or collagen vascular disease might be the underlying pathology. The evidence supporting a noninfectious etiology included the patient's recent negative test result for human immunodeficiency virus, the lack of sick contacts, and no history of sinus infections or earaches. The findings of a physical examination were remarkable for mild splenomegaly and a diffuse rash on her face, chest, abdomen, and back that was associated with hypopigmented macular lesions. In addition, the patient had swelling of her left-hand digits. A laboratory evaluation revealed several complement deficiencies, an immunoglobulin M deficiency, and positivity for rheumatoid factor, antineutrophilic antibody, and anti-Smith antibody.

These clinical and laboratory findings were the basis for a diagnosis of SLE, and the patient was started on a course of intravenous methylprednisolone (Solu-Medrol). Two days into her hospital admission, a noncontrast chest computed tomography (CT) scan was obtained to further evaluate the pneumonia. Contrast was withheld secondary to a diagnosis of acute renal failure. The findings revealed enlarged multifocal axillary lymph nodes in combination with splenomegaly possibly consistent with an immune deficiency syndrome and multilobar consolidations consistent with pneumonia; however, the most ominous finding was a significant change in the appearance of the ascending aorta compared with that on a 2004 chest CT scan, which had been performed after a motor vehicle collision. The 2004 study did not reveal any evidence of aortic injury. The contour abnormality and the presence of an intramural hematoma suggested a diagnosis of dissecting aortic aneurysm.

Prompt cardiac surgery consultation was obtained. After extensive review, the decision was made to obtain a transesophageal echocardiogram, because further CT characterization was limited by the lack of intravenous contrast. The echocardiogram revealed a dilated aortic root and a dilated ascending aorta measuring 4.9 cm in diameter with intimal thickening but no evidence of dissection. Additional findings included moderate aortic insufficiency, severe tricuspid regurgitation, moderate pulmonary hypertension, and an ejection fraction between 50% and 55%.

A cardiac magnetic resonance imaging (MRI) evaluation obtained the next day confirmed a dilated aortic root and proximal ascending aorta (greatest transverse diameters, 4.0 cm and 4.8 cm, respectively; Figure 1). The aortic valve was trileaflet and noted to have central failure of coaptation with significant aortic insufficiency. The mitral valve had trace regurgitation, whereas the tricuspid valve had moderate to severe regurgitation. The pulmonic valve was unremarkable,

and there was no evidence of pericardial effusion, pericarditis, or myocardial scarring.

The overall impression from these findings was an inflammatory aortitis secondary to lupus vasculitis. Serologic tests ruled out syphilitic aortitis. Because the patient remained hemodynamically stable, we continued her treatment with an aggressive steroid regimen with methotrexate added because of the aortitis. A repeat cardiac MRI evaluation was obtained the following week. Compared with the prior study, the repeat MRI revealed significantly increased dilation of the aortic root that extended into the proximal ascending aorta (Figure 2A). The proximal aorta was noted to have expanded to 5.8 × 5.6 cm, compared with the previous measurements of 4.8 × 4.6 cm. In addition, we noted an abnormal transmural delayed enhancement of the aortic wall that involved the entire ascending aorta, the arch, and the proximal descending aorta (Figure 2B). This rapid 1-cm increase in size, the persistent inflammation, and continued thinning of the aortic wall, coupled with the moderate to severe aortic regurgitation, indicated that the risk of rupture and death was substantial. Therefore, after discussion with the patient and her family regarding the risks and benefits of surgery, she was scheduled for operative repair.

Two weeks after admission, the patient underwent replacement of the ascending aorta and aortic root with a 21-mm CarboMedics valved conduit (CarboMedics, Austin, TX, USA) and a hemiarch replacement while under circulatory arrest. A mechanical valved conduit was selected because the patient had no desire for future pregnancies and wished to avoid future cardiac reoperations.

In addition, a coronary artery bypass to the posterior descending artery was performed with a reverse saphenous vein graft because of ulcerations that had eroded into the intima of the right coronary ostium and the fear that the eroded right coronary button may not be hemostatic despite felt-pledgeted reinforcement. The intraoperative findings were quite remarkable (Figure 3). The ascending aorta and myocardium were extremely enlarged, friable, and raw in appearance. A loose gelatinous fibrinous peel was present along the entire surface of the pericardium. Opening of the aorta revealed that the intima had been eroded in multiple ulcerated places, including the right coronary ostium. The intimal ulcerations continued into the descending aorta, but the most significant dilation was limited to the ascending aorta and the proximal arch.

Postoperatively, the patient did well. Her pneumonia and acute renal failure continued to resolve with medical management. She was extubated on postoperative day 4 and was discharged to home at 2 weeks with the standard cardioprotective medications and with prednisone for her SLE. A histopathologic analysis of the aortic wall revealed inflammatory aortitis with adventitial endarteritis and patchy necrosis of the tunica elastica. No giant cells were identified. Close follow-up was scheduled with both the rheumatology and cardiac surgery services.

DISCUSSION

SLE is a systemic autoimmune disorder characterized by the presence of immune complexes and a constellation of clinical features involving almost every organ system. The prognosis is variable and depends largely on the severity and type of organ involvement. The standard therapy is medical management and involves selective use of nonsteroidal anti-inflammatory drugs, antimalarials, glucocorticoids, and immunosuppressive agents [Schur 2007]. The cardiovascular manifestations of SLE are rare but occasionally life-threatening complications that must be recognized in their early stages. As a combined entity, they serve as the third most common cause of death in patients with SLE [Wang 2000]. A pancarditis involving the endocardium, myocardium, and pericardium, as well as cardiomyopathy and coronary artery atherosclerosis, have been well described and increasingly recognized in patients with long-standing SLE [Ohara 2000].

To the contrary, aortitis and aortic aneurysms as a complication of SLE continue to be an uncommon manifestation of the disease, with approximately 25 cases having been reported in the literature. The majority of lupus-associated aortitis cases documented in the literature have been described in conjunction with aortic aneurysms or aortic dissections [Hachulla 2001]. A review of the literature by Ohara et al [2000] found 16 cases of aortic aneurysms in patients with SLE. Of these 16 aortic aneurysms, 4 occurred in the ascending aorta, 3 in the aortic arch, 3 in the descending aorta, 2 in the upper abdominal aorta, and 2 in the infrarenal aorta. In 2 cases, enlargement of the entire aorta was found. Of more significance, however,

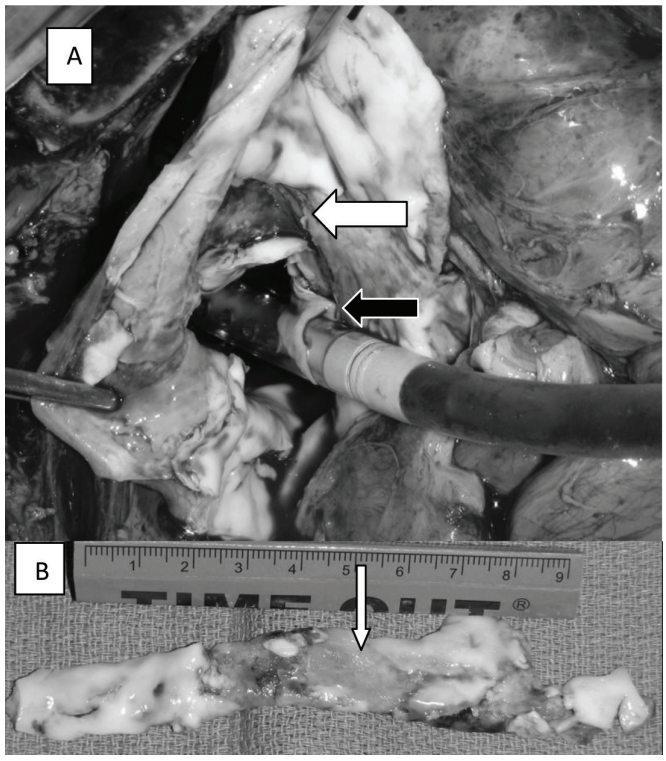

Figure 3. A, Intraoperative picture of the distal ascending aorta opened on circulatory arrest with a drop sucker in the arch. Multiple erosions were encountered with identification of full erosion of the intima and media (white arrow) and loose hanging intima (black arrow). B, Full circumference of the ascending aorta opened at surgery with multiple ulcerations and erosions (white arrow) again identified.

is the type of aneurysm described. Twelve were actual dissections, 3 were fusiform aneurysms, and 1 was a pseudoaneurysm [Ohara 2000]. The only reported nondissecting aneurysm of the aortic arch was described by Chakravarty et al [1992]. These investigators described an SLE patient whose surgical pathology results indicated a mycotic or infectious aneurysm of the aortic arch [Chakravarty 1992]. Ohara et al [2000] described 5 cases of abdominal aortic aneurysms in patients with SLE who underwent surgical repair. All 5 of these patients had received steroid therapy for at least 1 year [Ohara 2000].

Our review of the literature found only 2 cases of aortitis in SLE patients associated with nondissecting aneurysms. Stehbens et al [1993] described a 56-year-old man with a history of SLE who underwent 16 years of steroid therapy and then underwent surgical repair for an abdominal aortic aneurysm. The histopathology results revealed active adventitial and perianeurysmal tissue inflammation supportive of aortitis. Takagi et al [2002] described a nondissecting aneurysm of the distal descending thoracic aorta in a 35-year-old woman who had undergone 24 years of steroid therapy for SLE. The aneurysm was successfully resected and replaced with a tube graft. The pathologic findings included numerous lymphoplasmacytic infiltrates that suggested active aortitis.

To our knowledge, however, there have been no reported cases of lupus aortitis leading to aneurysmal dilatation in the aortic root or ascending aorta. Furthermore, all previously reported cases were of patients on chronic steroid therapy for at least 1 year prior to the development of their aortic aneurysm. This observation is significant in that prolonged steroid administration has been shown to play a leading role in exacerbating hypertension and atherosclerosis in SLE patients [Ohara 2000; Takagi 2002]. Steroids are also known to affect the connective tissues by inhibiting both chondroitin sulfate and the formation of granulation tissue, further accelerating atherosclerosis and contributing to aneurysm formation [Wang 2000; Takagi 2002].

Our patient is the first reported case of aortitis causing a nondissecting aortic root aneurysm in an SLE patient with no prior history of steroid use. This case illustrates that all patients with SLE need close screening for aortic disease, regardless of the time of diagnosis. In addition, all lupus patients, including those without prior steroid administration, are prone to develop aortitis and its sequelae. Finally, lupus-associated aortitis can affect any portion of the aorta, including the aortic root and the proximal ascending aorta. Thus, early recognition of aortitis may prevent fatal complications and lead to improved surgical outcomes.

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