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Case Report

Aneurysm of the ascending aorta in systemic lupus erythematosus: Case report and review of the literature

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Abstract

Cardiovascular manifestations in patients with systemic lupus erythematosus (SLE) are common, but aortic aneurysm formation is rare. We present a 63-year-old male SLE patient with a two-year history of skin lesions, leucopenia, pericarditis, mitral valve vegetations consistent with Liebman-Sacks endocarditis, and an aneurysm of the ascending aorta, which was successfully repaired surgically. Histologic examination of the aneurysm showed medial cystic degeneration, smooth muscle necrosis, and mild adventitial perivascular lymphocytic aggregates. This histology is typical of thoracic aneurysms that carry a high risk for aortic dissection and patient death. The case highlights the importance of early detection and treatment of thoracic aortic aneurysms in patients with SLE.

Keywords: Systemic lupus erythematosus, aortic aneurysm, inflammation

Introduction

In patients with systemic lupus erythematosus (SLE), multiple organs suffer an inflammatory response leading to damage. Organ involvement invariably defines the severity and the course of the disease. The prolongation in life expectancy in patients with SLE has revealed the involvement of the cardiovascular system and its increasing contribution to disease fatality (1). Although aortic aneurysms are not a common complication in SLE patients, their incidence is higher in SLE patients compared to age- and sex-matched controls (2, 3). They also occur in all age groups, including children and adolescents, and can have fatal complications (4, 5).

We describe here a patient with SLE who developed a thoracic aortic aneurysm within two years of his SLE diagnosis and without prior treatment with corticosteroids. Histopathologic analysis revealed the presence of medial cystic degeneration and mild perivascular T- and B-cell infiltrates in the adventitia. The clinical presentation and histopathology of the lesion in this SLE patient point to his underlying disease as the contributing factor for the development of the aneurysm.

Case Presentation

A 63-year-old man presented with a two-year history of skin lesions, moderately elevated antinuclear antibodies (1/160), pericarditis, and leukopenia (including lymphocytopenia). There was no history of hypertension, diabetes, obesity, or smoking. The diagnosis of SLE was made, and treatment with hydroxychloroquine was initiated. Echocardiography showed mitral valve changes consistent with a Liebman-Sachs endocarditis. In addition, an ascending aorta aneurysm was noted measuring 4.7 cm. A repeat evaluation showed that the aneurysm diameter had enlarged to 5.0 cm. The aneurysm was successfully repaired surgically, and tissue from the excised aorta was evaluated microscopically. The most consistent histologic finding was the presence of medial cystic degeneration leading to bands of smooth muscle cell loss (Figure 1a) and formation of cystic spaces associated with the accumulation of basophilic material (Figure 1b). There was no intimal thickening, fibrosis, or atheroma formation. Small and predominantly perivascular mononuclear cell infiltrates were observed in the adventitia and to a lesser extent in the media (Figure 1c). No giant cells or granulomas were observed. Occasional thickened arterioles were present in the adventitia (Figure 1d). The results of immunocytochemical staining using commercially available antibodies were as follows: 1) Pan lymphocyte marker showed positive cell clusters dispersed in the adventitia and to a lesser extent in the intima; 2) T-cell markers: a) CD3-positive perivascular cell clusters were present in the adventitia and a few were present in the media and intima (Figure 1 e, f), b) CD4-positive round cells and spindle cells were observed in the adventitia and a few were seen in the intima (Figure 1g); c) several CD8-positive cells were dispersed in the adventitia

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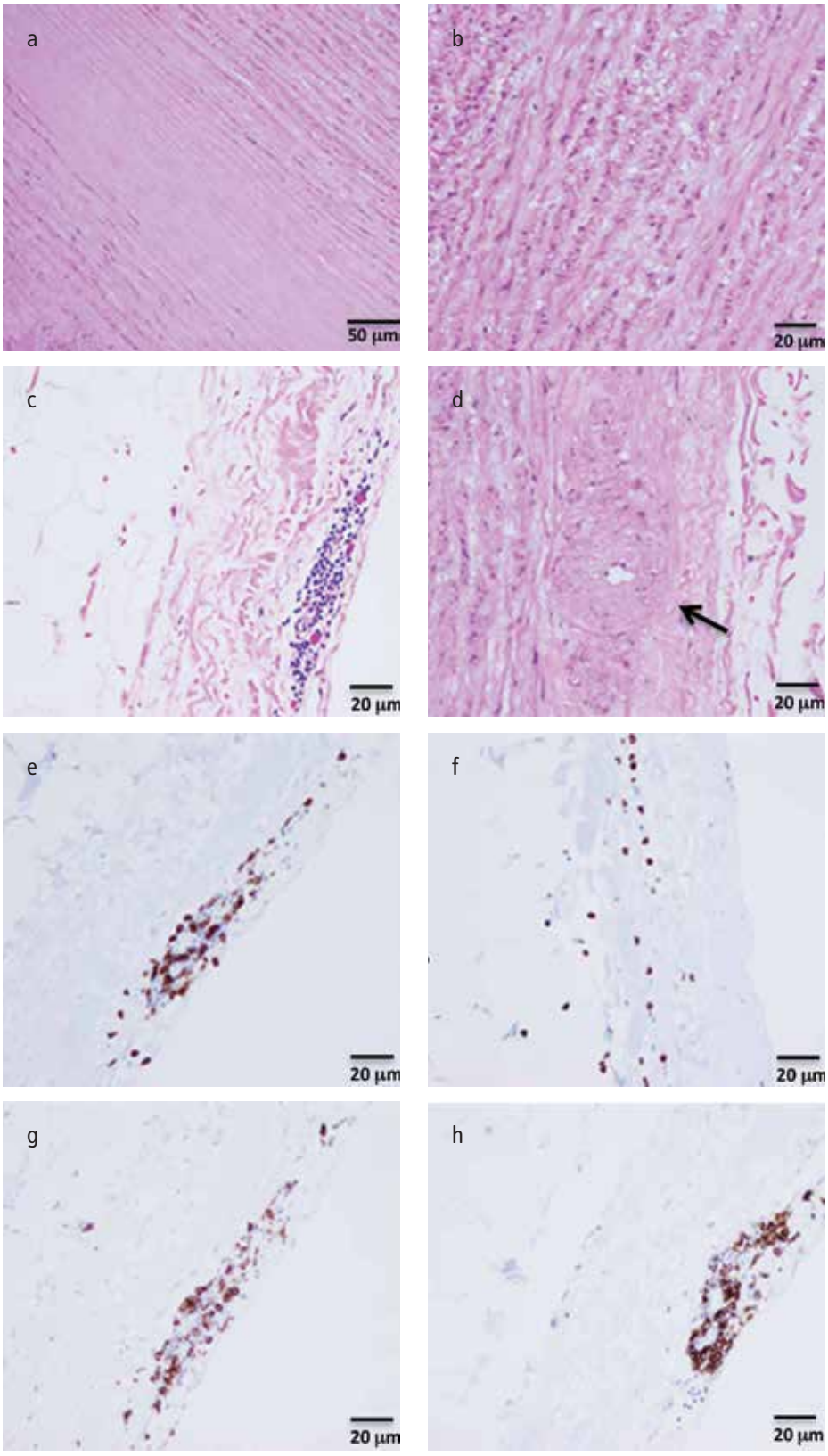

Figure 1. a-h. Histologic and immunohistochemical study of the aortic tissue. Hematoxylin and Eosin staining shows lamellar smooth muscle necrosis characterized by diffuse pink cytoplasm with nuclear loss (original magnification 20×) (a), cystic degeneration of the media with accumulation of basophilic substance in the cell-depleted areas (original magnification 40×) (b), perivascular lymphocytic accumulation in the adventitia (original magnification 40×) (c), and a thickened arteriole in the adventitia (original magnification 40×) (d). Immumohistochemical staining demonstrates CD3+ T lymphocytes around a small vessel (e) and dispersed in the adventitia (f) (original magnification 40×) along with CD4+ T-lymphocytes (g) and L26+ B-lymphocytes (h) (original magnification 40×)

along with CD5-positive cell clusters; 3) B-cell markers: L26-positive and CD19-positive cells were detected in the adventitia (Figure 1h); 4) Immunoglobulins: diffuse staining for IgG was noted in the inner endothelial layers and muscularis, and weak and diffuse IgM staining was seen in the intima; 5) Monocytes/granulocytes: Rare LeuM1-positive cells (monocytes/granulocytes) and myeloperoxidase-positive cells (neutrophil granulocytes) were present in the perivascular aggregates; and 6) HLA-DR (MHC class II cell surface receptor)-positive cells were noted in the adventitia. Rare cells that stained positive for CD21 (mature B-cells and dendritic follicular cells) and KP-1 (CD68) (monocytes/macrophages) were also sometimes seen. We did not observe any positivity with antibodies against CD25 (interleukin-2 receptor a, which is present in activated T-cells and B-cells and in myeloid cells) or complement 4d. FOXP3-positive cells (regulatory T-cells) were sparse.

Discussion

Systemic lupus erythematosus is a heterogeneous chronic inflammatory autoimmune process that can lead to severe organ damage, including the cardiovascular system (2). Aortic aneurysms are an uncommon complication of SLE with only a few cases of aneurysm with or without dissection described to date (4-7). Wang et al. (3) analyzed retrospective data from a large cohort of SLE patients and reported that among 15,209 patients with SLE, only 20 had aortic aneurysms, but 13 developed aortic dissection. When compared with the control non-SLE individuals, SLE patients had a significantly higher overall risk for developing aortic aneurysm or aortic dissection, which was calculated to be 3.34 (95% CI, 1.71-6.91; $p < 0.001$). Similar results were reported in another retrospective study in which the prevalence of aneurysms among 5,018 SLE patients increased with an odds ratio of 4.5 when compared to 25,090 age- and sex-matched controls (95% CI 2.65-7.47, $p<0.001$) (2).

The pathogenesis of aortic aneurysms in SLE patients is not fully understood. A meta-analysis of 35 SLE cases published between the years 1969 and 2008 showed that aneurysms in SLE patients appear at an earlier age (mean age 44.5 years) than in the general population who do not tend to develop aneurysms until they are in their 60s, and in SLE patients they are more commonly observed in the thoracic (71.4%) rather than abdominal (54.3%) aorta, which is in contrast to those in the general population that are more often abdominal (8-10). More importantly, the study showed that thoracic and abdominal aortic aneurysms in SLE patients have distinct

clinical and histopathologic characteristics suggesting different pathogenic mechanisms (10). Specifically, thoracic aneurysms correlated with cystic medial degeneration, dissection, and death, whereas abdominal aneurysms correlated with atherosclerosis and prolonged steroid treatment. Furthermore, cystic medial degeneration in SLE patients occurred at a younger age, was associated with vasculitis rather than atherosclerosis, and affected the thoracic rather than the abdominal aorta, suggesting that thoracic aneurysms in SLE patients are caused by an SLE-related inflammatory process that leads to medial cystic degeneration and dissection.

Several studies have shown that aortic aneurysm formation is an immune-related process. Inflammatory cells accumulate in the adventitia of the abdominal aorta of people who develop aneurysms. T- and B-cells, macrophages, mast cells, dendritic cells, and neutrophils are important for the inflammatory response (11, 12). T-cells have been implicated in aortic aneurysm progression by enhancing macrophage-derived matrix metalloproteinase production and vascular smooth muscle cell apoptosis (12). Atherosclerosis is considered to be an autoimmune/autoinflammatory disease, and studies on immune cells in atherogenesis in mice confirm this claim. CD4+ T-lymphocytes have been shown to accelerate atherosclerosis, and Th1 cells - the CD4+ T-effector cells that produce interferon-γ - are found in atherosclerotic plaques. Th17 cells produce interleukin (IL)-17A and IL-17F cytokines and have also been reported to be present in atherosclerotic lesions (11). B-cells have been reported in the adventitia of abdominal aortic aneurysms and have been implicated in their formation through the production of immunoglobulins and cytokines and by regulation of complement activation and T-cells (12).

Schmidt et al. (13) confirmed the presence of aortitis in 6.1% of the 610 tissue samples that were submitted for pathological examination after resection of the ascending aorta in a 12-year Danish nationwide population-based cross-sectional study and found that the presence of a rheumatic disease, including lupus, was the best predictor for the development of aortic aneurysms. Our exhaustive search for inflammatory evidence in the aortic tissue of this SLE patient showed the clear presence of inflammatory cells that can contribute to the establishment of an aneurysm, similar to a previous report that described the histopathologic features of necrotizing arteritis (14). That study also showed thickened vessels in the adventitia similar to what we observed in our case. Aortitis has been described in case reports of SLE patients with aortic aneurysms, but it is not a common complication in SLE patients (6, 15, 16). A previous study reported increased numbers of lymphocytes and macrophages in ascending aortas with medial cystic degeneration, aneurysms, and dissection and implicated them in the observed increase in the numbers of apoptotic vascular smooth muscle cells (17).

In summary, we report a patient with a short history of SLE who underwent surgical repair of an aneurysm of the ascending aorta. Histologic evaluation revealed medial cystic degeneration, which is usually associated with aortic dissection and poor outcome. Notwithstanding that our patient is 63 years old, the development of a thoracic aneurysm in the absence of additional risk factors for the development of aortic aneurysms places emphasis on the contribution of the underlying SLE and highlights the importance of close monitoring and early intervention to avoid potentially fatal complications.

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