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Acute retinal artery occlusion in systemic sclerosis: A rare manifestation of systemic sclerosis fibroproliferative vasculopathy ☆

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ABSTRACT

Objectives: To describe three patients with systemic sclerosis (SSc) who developed acute unilateral blindness in the absence of any common etiologic factor for blindness. In one patient, the affected eye required enucleation and was examined histopathologically.
Methods: Following identification of the first patient with retinal artery occlusion at the Scleroderma Center of Thomas Jefferson University, every patient evaluated at the Center from May 2001 to December 2010 was prospectively assessed for the development of acute unilateral blindness. Two additional cases were identified. Here, we describe the clinical features, laboratory and ancillary examinations of the three patients with SSc who developed acute unilateral blindness and present the histopathological examination of one eye enucleated from one of the patients.
Results: Clinical and angiographic studies were consistent with acute retinal artery occlusion. The histopathological studies showed severe retinal ischemic atrophy and concentric narrowing and fibrosis of small retinal vessels.
Conclusions: These findings suggest that acute retinal artery occlusion in these patients is a manifestation of the fibroproliferative vasculopathy characteristic of SSc.

Introduction

Systemic sclerosis (SSc) is a systemic connective tissue disorder characterized by severe and often progressive cutaneous and visceral fibrosis [1–4]. One of the critical abnormalities in SSc is a diffuse fibroproliferative vasculopathy most commonly involving the microvasculature system [5–11]. Although patients with SSc can present a variety of ophthalmologic abnormalities [12–16], retinal artery occlusion is an unusual complication that has been described in only a few reports [17–20]. Here, we describe the clinical manifestations of three cases of acute blindness caused by retinal artery occlusion in patients with SSc and describe the histopathological features of an enucleated eye from one of these patients.

Methods

Identification of reported cases

Following identification of the first patient with retinal artery occlusion at the Scleroderma Center of Thomas Jefferson University, every patient evaluated at the Center from May 2001 to December 2010 was prospectively assessed by one of the authors (S.A.J.) by questioning of any symptoms indicative of the development of acute unilateral blindness and by evaluation of clinical records from ophthalmologic evaluations. Two additional SSc patients with unilateral blindness were identified. To provide an estimate of the prevalence of this rare complication the number of new patients evaluated for SSc at the Center and the number of follow-up visits during the 10-year period-span (2001–2010) in which the three patients identified were tabulated from the IDX system appointment records.

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Literature search

A systematic review of the literature was performed on PubMed using "systemic sclerosis" and each of the following terms: "blindness", "retinal artery occlusion", "retinal vein occlusion", "ocular manifestations" and "ocular". The search revealed 0, 0, 1, 2, and 32 results, respectively. A second and more focused search was performed using "scleroderma" and "central retinal artery occlusion," which resulted in six publications; however, only two of these were related to SSc. The relevant publications have been discussed and have been cited in the Reference list.

Results

Case reports

Case report 1: A 46-year-old Caucasian woman with rapidly progressive diffuse SSc first developed symptoms in June 2006 with Raynaud phenomenon, bilateral carpal tunnel syndrome, and gastroesophageal reflux, followed shortly by progressive cutaneous induration and tightening. Serologic studies were negative, including antinuclear antibodies (ANA), anti-double stranded DNA (anti-dsDNA), anti-Smith (anti-SM), anti-Scleroderma 70 (anti-Scl-70), anti-centromere, anti-ribonucleoprotein C (anti-RNP), and anti-Sjögren syndrome antigen A and B (anti-SSA/SSB). Pulmonary function tests, echocardiogram and chest computerized tomography scan were normal. A skin biopsy from the forearm confirmed the diagnosis of systemic sclerosis. She began treatment with D-penicillamine in September 2007. About 15 months later, D-penicillamine was discontinued owing to the development of nephrotic range proteinuria, and treatment with mycophenolate mofetil was initiated in April 2008. Over the ensuing 2 years, there was marked skin softening and regrowth of hair follicles in most of her previously involved skin with only residual skin tightening and induration in her hands, fingers, and a small patch on her right thigh. In December 2009, the patient complained of a sudden, painless loss of vision in the lower half of her left visual field. She denied any prior visual symptoms, headaches, temporal artery or scalp tenderness, dysarthria, paresthesias, weakness in her extremities, or problems with her gait. There was no familial history of premature atherosclerosis and clinical examination did not show any abnormalities in the cardiac exam or findings suggestive of atherosclerotic vascular lesions. On examination of her visual fields, the patient exhibited an inferior altitudinal defect in her left eye. Her visual acuity was 20/20 in the right eye and 20/20 in the left eye. Intraocular pressures were within normal limits bilaterally. Dilated fundus exam showed normal findings in the right eye. However, exam of the left eye revealed superior segmental optic disc swelling and absence of spontaneous venous pulsations. These findings were consistent with severe ischemic optic neuropathy of the left eye. Extensive evaluation was performed to investigate the cause of the acute visual loss. Repeated serologic studies showed borderline ANA at a 1:40 titer with speckled pattern. Rheumatoid factor, anti-SM, anti-histidyl-tRNA synthetase (anti-Jo-1), anticardiolipin antibodies, cytoplasmic antineutrophil cytoplasmic antibodies (C-ANCA), perinuclear antineutrophil cytoplasmic antibodies (P-ANCA), and lupus-type anticoagulant were all negative. Serum complement levels, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were normal. Additional testing showed an absence of a mutation in factor V Leiden. Magnetic resonance imaging of the brain and orbits were unremarkable with no evidence of a brain infarction or a demyelinating process. Three weeks later, follow-up examination confirmed persistence of the visual defect in the left eye.

Case report 2: A 76-year-old Hispanic woman with rapidly progressive diffuse systemic sclerosis presented with a typical scleroderma renal crisis in July 2000, resulting in renal insufficiency requiring hemodialysis. The onset of disease was in 1999 when the patient developed Raynaud phenomenon associated with solid food dysphagia and severe heartburn. She was treated with D-penicillamine and showed marked improvement in skin sclerotic changes. The patient underwent hemodialysis three times weekly for 4 years before undergoing bilateral renal transplantation in January 2004. In September 2006, the renal transplants were rejected despite treatment with mycophenolate mofetil (500 mg twice a day) and sirolimus (2 mg/day). The patient resumed hemodialysis and was maintained only on low-dose prednisone (5 mg/day).

Serologic studies for autoantibodies showed a positive fluorescent ANA at 1:1280 titer with a diffuse pattern. Rheumatoid factor, anti-centromere, anti-histone, anti-SM, anti-RNP, anti-ssDNA and anti-dsDNA antibodies were negative. Complement C4 and anticardiolipin IgG antibodies were within the normal range.

In January 2008, the patient suffered a precipitous episode of painless loss of vision in her right eye. Computerized axial tomography of the brain was normal. The ESR (Westergren) was unchanged from previous exams, at 59 mm/h. Her visual acuity was finger counting in the right eye and 20/40 in the left eye. Ophthalmoscopic examination of the posterior segment of the right eye showed marked narrowing of the arterioles with retinal whitening and a cherry-red spot (Fig. 1A). No disc edema or hyperemia was observed, and the peripheral retina was flat in both eyes. Optical coherence tomography disclosed no macular thickening in either eye. Intravenous fluorescein angiography revealed a marked delay in the arteriole-venous transit time in the right eye with a large delay in the venous filling time. The retinal circulation in the left eye was normal. The veins did not appear dilated in either eye (Fig. 1B–D). This constellation of findings was consistent with the diagnosis of central retinal artery occlusion.

Owing to the mild elevation of the erythrocyte sedimentation rate in the setting of retinal artery occlusion, it was deemed

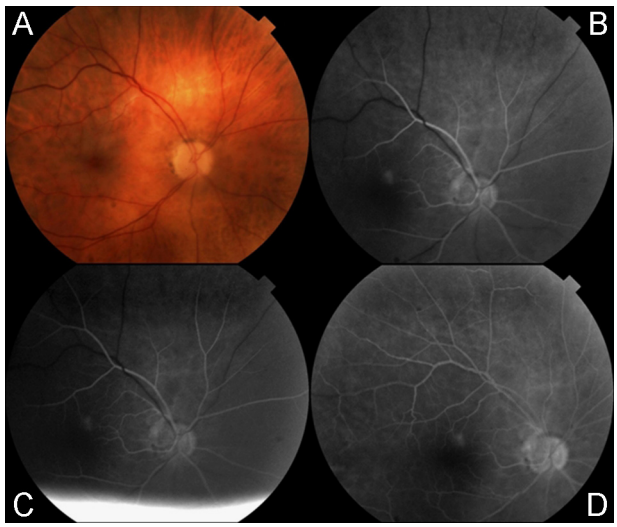

Fig. 1. Funduscopic findings in patient 2. (A) Color fundus image of the right eye demonstrating retinal whitening and a cherry-red spot. (B–D) Fluorescein angiography of the right fundus demonstrating a significant delay in the arteriovenous transit time. (For interpretation of the references to colour in this figure legend, the reader referred to the web version of this article.)