

# Acute necrotizing retinal vasculitis as onset of systemic lupus erythematosus

## A case report

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### Abstract

**Rationale:** Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by autoantibody production, complement activation, and deposition of immune complexes in tissues and organs. SLE can involve any region of the visual system. Although ocular manifestations are not part of the classification criteria for SLE, they can be observed in up to one-third of the patients with SLE. They are rarely reported at the time of disease onset. Retinal vasculitis is usually associated with active generalized disease. Due to its low frequency, we report a case of acute necrotizing retinal vasculitis as onset of SLE.

**Patient concerns and diagnosis:** A 25-year-old white female was referred to the rheumatology clinic with gradually and rapid deterioration of the vision due to abnormal vessel permeability in the right fundus with edema along the vessels, occlusion of arterial branches in the middle periphery with leakage of the dye in these areas and indistinct but less prominent changes with cotton wool spots in the papillomacular area and extensive hemorrhages in the left eye. The onset of malar rash, arthralgias and positive antinuclear, anti-double stranded DNA, anti-ribosomal P and anti-β2 glycoprotein I antibodies with decreased C4 complement levels, as well as the positive lupus-band test confirmed the diagnosis of SLE.

**Interventions:** Aggressive immunomodulating therapy with high-dose methylprednisolone, intravenous immunoglobulin, and cyclophosphamide was used for suppression of the disease activity followed by azathioprine as maintenance therapy.

**Outcomes:** Substantial improvement and partial resorption of the vasculitic changes, including central retinal artery and vein, was achieved prominently in the left eye. The study was conducted in accordance with the Declaration of Helsinki and written informed consent was obtained from the patient. Because of this, there is no need to conduct special ethic review and the ethical approval is not necessary.

**Lessons:** Inclusion of ocular manifestations among the classification criteria for SLE would enable earlier establishment of the diagnosis and therapeutic interventions in some instances of SLE.

**Abbreviations:** ACR = American College of Rheumatology, ANA = antinuclear antibody, anti-β2GPI = anti-β2 glycoprotein I, anti-MPO = antimyeloperoxidase, APA = antiphospholipid antibodies, APS = antiphospholipid syndrome, CMV = cytomegalovirus, CNS = central nervous system, EBV = Epstein–Barr virus, ELISA = enzyme-linked immunosorbent assay, FA = fluorescein angiography, FC = fingers counting, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, HIV = human immunodeficiency virus, IgG = immunoglobulin G, IgM = immunoglobulin M, SLE = Systemic lupus erythematosus, SLICC/ACR = Systemic Lupus International Collaborative Clinics/American College of Rheumatology, SP-OCT = Spectral domain optical coherence tomography, VZV = Varicella–Zoster virus.

**Keywords:** case report, classification criteria, ocular manifestations, retinal vasculitis, systemic lupus erythematosus

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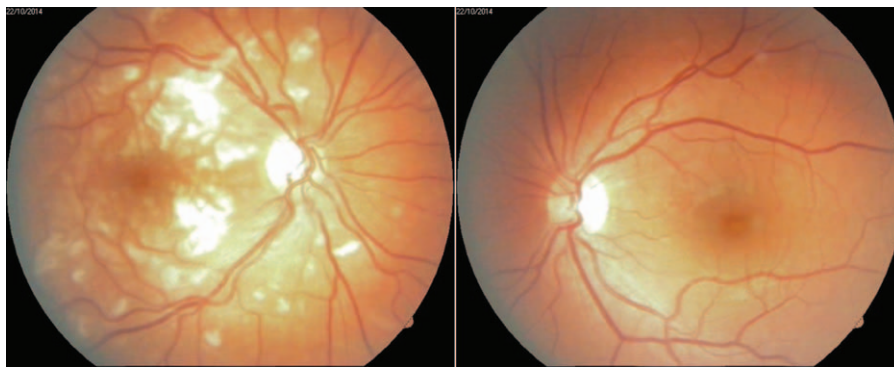
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## 1. Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune, immune complex disease of the connective tissue and may affect almost any part of the visual system.<sup>[1]</sup> Although ocular manifestations are not part of the classification criteria, they can be observed in up to one-third of patients with SLE.<sup>[2–4]</sup> Ocular lesions (cotton wool spots, disc hyperemia, white retinal patches) in SLE were first described in 1929 by R. Bergmeister.<sup>[5]</sup> They are rarely reported at the time of disease onset. Due to its infrequency we report a case of acute necrotizing retinal vasculitis as the first manifestation of SLE.

## 2. Case report

On 20th of October 2014, a 25-year old Lithuanian female was admitted to the Ophthalmology Department at Medical University, Sofia, Bulgaria, with complains of blurred vision of



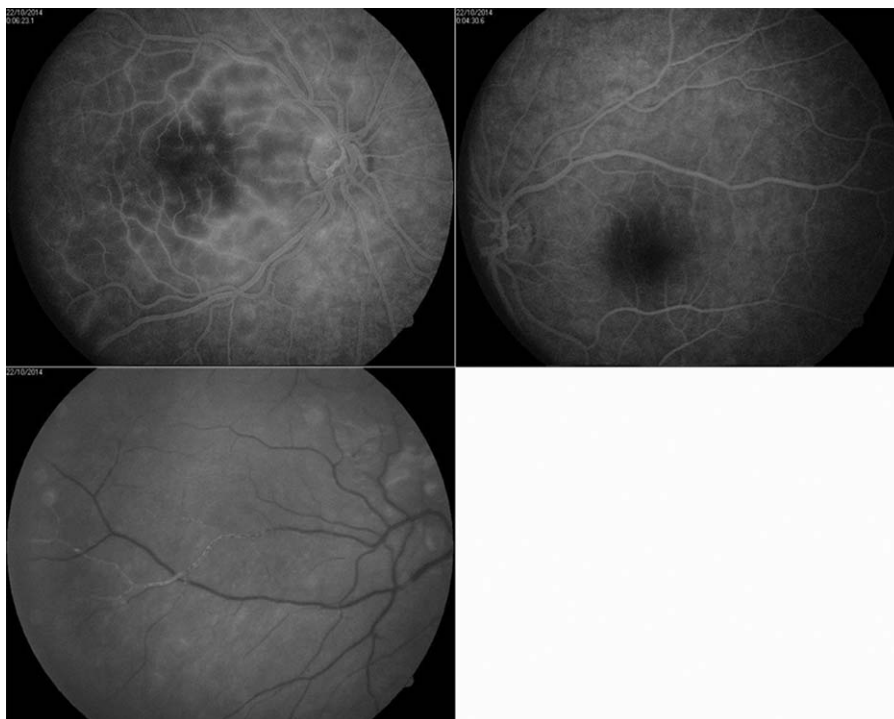
**Figure 1.** Fundus photograph (22/10/2014). Right eye (left picture side) with multiple cotton wool spots in the posterior pole. Left eye (right picture side)—without changes.

the right eye, followed by gradual reduction of visual acuity to 6/20. Visual acuity of the left one was 20/20. The initial ophthalmoscopy of the right eye showed normal optic disc cup, cotton wool spots along the vessels, edema in the posterior pole, and normal view of the left eye. The fluorescein angiography (FA) showed abnormal vessel permeability in the fundus with edema along the vessels, occlusion of arterial branches in the middle periphery with leakage of the dye in these areas in the right eye with no changes in the left eye fundus (Figs. 1 and 2). Spectral domain optical coherence tomography (SP-OCT) revealed neuroretinal detachment in the fovea and retinal edema of the nerve fiber layer (Fig. 3). During the admission period, the left eye was engaged as well, demonstrating similar symptoms and signs in a less prominent pattern. Consequently ischemic macular edema in the right eye developed and as well as peripheral branch retinal arteries occlusion. The examination of

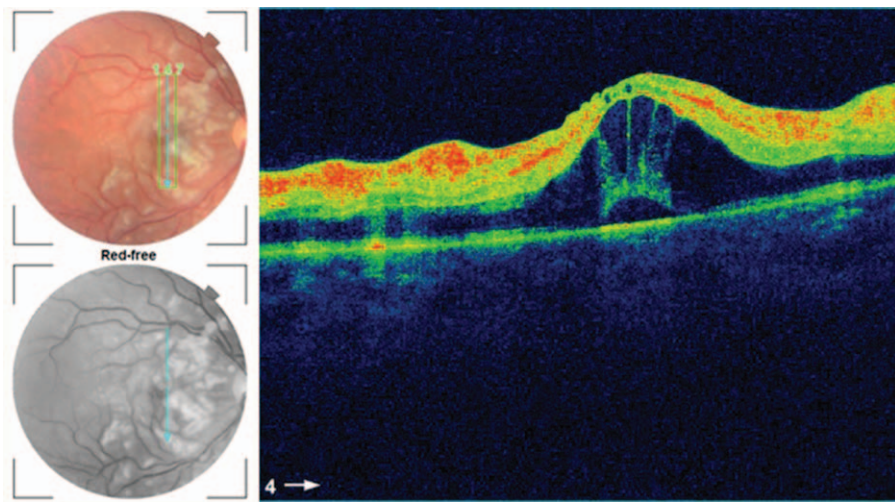
the left eye showed identical but less prominent changes with cotton wool spots in the papillomacular area and extensive hemorrhages. Perimetry showed a central loss of visual field with areas of absolute and relative scotoma

Two days after hospitalization the patient reported for onset of generalized arthralgias, tenderness, and morning stiffness lasting 10 to 15 minutes. The patient had an intermittent fever up to 37.4°C. The ophthalmic status deteriorated rapidly over the next 72 hours and the visual acuity of the right and left eyes dropped to FC (fingers counting) at 50 cm and 8/20, respectively. After consultation with rheumatologist, the patient was admitted in the Clinic of rheumatology for further examination and treatment.

On physical examination in the Clinic of Rheumatology, the patient presented with normal respiratory rate, blood pressure,



**Figure 2.** Fluorescein angiography (22/10/2014). Right eye (left picture side) abnormal vessel permeability and formation of local edema in the posterior pole. Branch retinal artery occlusion can be seen in the middle periphery. Left eye (right picture side)—more discrete changes of the vessel permeability.



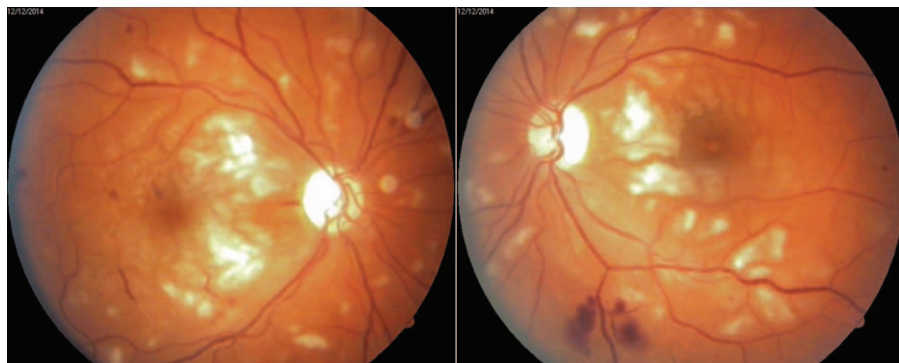
**Figure 3.** SP-OCT of the right eye presenting neuroretinal detachment in the fovea and retinal edema of the nerve fiber layer (taken on 28/10/2014).

and heart rate. The musculoskeletal examination showed no pathological findings. The malar rash occurred in the facial area and on the back accompanied with hair loss. The laboratory investigation revealed normal blood count, liver enzymes, electrolytes and urine tests, and positive antinuclear antibody (ANA) titer (1:640 on immunofluorescence assay), anti-double stranded DNA antibodies (ELISA)—48 U/mL (normal value < 25 U/ml), anti-ribosomal P antibodies—64 (> 50—highly positive value), anti-β2 glycoprotein I antibodies—12.1 U/mL (<10 U/mL—negative) and decreased C4 complement levels to 0.06 g/L (normal ranges 0.165 ± 0.380 g/L). Anti-Smith-, anti-Ro-, anti-La- antibodies, anti-neutrophil cytoplasmic antibodies, anti-myeloperoxidase (anti-MPO)-, anti-proteinase 3 antibodies, anticardiolipin antibodies, lupus anticoagulant and cryoglobulins were negative. Lupus band test showed the presence of a homogeneous band of deposits of IgM along the dermoepidermal junction. No abnormalities in chest x-rays were found. Magnetic resonance imaging of the head documented single gliotic changes in the brain with nonspecific character. Serologic tests for Chlamydia trachomatis, syphilis (*Treponema pallidum* haemagglutination), Varicella-Zoster virus (VZV), human immunodeficiency virus (HIV) 1, 2, hepatitis B surface antigen (HBsAg), anti-HCV (hepatitis C virus) were negative, and testing for

Cytomegalovirus (CMV) IgG and Epstein-Barr virus (EBV) IgG was positive. A diagnosis of SLE was made based on the updated 1982 ACR revised classification criteria for SLE (1997).

In attempt to decrease disease activity and prevent visual loss, an aggressive immunomodulating therapy with high-dose corticosteroids (including methylprednisolone pulse therapy), intravenous immunoglobulin (400 mg/kg/day for 5 days followed by maintenance therapy of 400 mg/kg for 1 day every 3 months), and cyclophosphamide in dose 1 g intravenous every 15 days (6 doses altogether), followed by maintenance therapy with oral azathioprine in dose 2 × 50 mg/daily were administered. Low-molecular-weighted heparin was also given.

On patient follow-up in December 2014, fundus photographs and FA showed ischaemic maculopathy with compromised vessel permeability and with residual hemorrhages in the posterior pole of both eyes (Figs. 4 and 5). The permeability of peripheral retinal arteries shows tendency of improvement. The visual acuity improved to FC at 2 m for the right eye and 20/20 for the left. Second follow-up eye imaging in February 2015 showed substantially reduced subretinal exudates in the posterior pole of the right eye, persistent macroischaemic zone, temporal to the macula, the presence of hemorrhages in the inferior temporal zone. The cotton wool spots and vasculitic changes in both eyes



**Figure 4.** Fundus photograph (taken on 12/12/2014). Right eye (left figure side) and left eye (right figure side) with multiple cotton wool spots, hemorrhages, and branch retinal artery occlusion in the posterior pole.



**Figure 5.** Fluorescein angiography (taken on 12/12/2014). Right eye (left figure side) ischemic maculopathy and tendency of improvement of vessel permeability in the periphery. Left eye (right figure side) ischemic maculopathy begins.

were found to be partially resorbed. There was a substantial improvement in the left eye. Single hemorrhages were present in the zone inferior to the papilla, the ischemic zones were found to be reduced, with the vessel permeability being compromised only in the areas of the hemorrhages (Fig. 6).

Six months after the initial symptoms laboratory and instrumental examination showed improvement—ANA titer decreased to 1:320, C4 was 0.13g/L, and anti-ribosomal P antibodies –16. All the other antibodies were within the normal ranges.

### 3. Discussion

Ocular manifestation of SLE can not only be sight threatening, but the presence of active retinal vasculopathy is an extremely accurate guide to the existence of systemic disease activity. Retinal lesions in SLE are of critical importance, both visually and prognostically.

SLE may cause ocular disease by a number of mechanisms including immune complex deposition and other antibody-related mechanisms, vasculitis, and thrombosis.<sup>[6]</sup> The lesions of lupus retinopathy vary in appearance. Cotton wool spots

represent microinfarcts of the retina are the most common feature of eye involvement in SLE. Despite their characteristic presence in SLE, the cotton wool spots are not pathognomonic for the disease. Other findings can be perivascular exudates, intraretinal hemorrhages, and vasculitis. A less common presentation can be a large vessel occlusion.

We describe a patient with acute necrotizing retinal vasculitis as the first and leading manifestation of SLE. A distinctive sign is the absence of correlation between the picture, found in both eyes and that in CNS (central nervous system), despite the presence of antiribosomal P antibodies. The slightly elevated values of anti-β2GP I antibodies may be a contributing factor in the pathogenesis of the disease, although the antiphospholipid syndrome was excluded. The conducted therapy not only achieved suppression of disease activity, but led to substantial improvement, more prominent in the left eye, and partial resorption of the vasculitic changes, including central retinal artery and vein, which is common in the presence of antiphospholipid antibodies (APA). Hall et al first described the link between severe lupus retinal vasculopathy and the presence of antiphospholipid antibodies in 1984.<sup>[7]</sup> The presence of APA is associated with more severe retinopathy and vascular occlusion.<sup>[8]</sup> SLE shows correlation with antiphospholipid syndrome (APS) and central nervous system (CNS) lupus. Antiribosomal P antibodies are found to correlate with neuropsychiatric SLE.

Vaso-occlusive retinopathy is a rare, potentially vision-threatening manifestation of SLE, which can be an indicator of active disease. Early recognition of this condition and adequate and timely treatment should be administered in order to preserve ocular function. The mainstay of treatment for SLE vaso-occlusive retinopathy is the administration of high doses of corticosteroids and cytotoxic agents, such as cyclophosphamide, followed by low-dose systemic glucocorticoids in combination with other immunosuppressant therapy for preventing disease flares.

Ocular manifestations of lupus are a reflection of systemic disease. The presence of ocular manifestations should alert the clinician to the likelihood of the presence of disease activity elsewhere. Therefore, all patients with ocular lupus should be carefully evaluated for systemic involvement to detect potentially treatable and preventable complications of the disease.

Retinal specialists serve an important role in the overall care of patients with SLE. One large prospective study showed that 88% of SLE patients with retinopathy had active systemic disease.<sup>[9]</sup>



**Figure 6.** Fundus photograph, showing partial resorption of the cotton wool spots in the right eye (taken on 20/02/2015).

The SLE patients who developed retinopathy had a lower overall survival rate as compared to patients without retinopathy over the same time period. Moreover, active CNS involvement in SLE, a significant cause of patient morbidity, is more often found in patients with active retinopathy, retinal vaso-occlusive disease, and optic neuropathy.<sup>[9,10]</sup> Therefore, the presence of posterior segment findings in patients with SLE should prompt the retinal specialist to communicate with the rheumatologist regarding the activity and severity of their mutual patient's disease. In addition, the ophthalmologist should include SLE in the differential diagnosis of many retinal vascular and neuro-ophthalmic disorders. The ophthalmologist may play an important role in the care of patients with SLE, since ocular inflammatory lesions may precede potentially serious extraocular disease. Early recognition by the rheumatologist and prompt assessment by the ophthalmologist coordinated treatment strategies are key to reducing the ocular morbidity associated with the disease.

We believe that inclusion of ocular manifestations among the classification criteria for SLE (not only for assessing the SLICC/ACR Damage Index) would enable earlier establishment of the diagnosis and therapeutic interventions in some instances of SLE and may minimize mortality from this disease.

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