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CASE REPORT

Acute vision loss in systemic lupus erythematosus: bilateral combined retinal artery and vein occlusion as a catastrophic form of clinical flare

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Presentation of a combination of branch retinal artery occlusion (BRAO)/central retinal artery occlusion (CRAO) and central retinal vein occlusion (CRVO) in systemic lupus erythematosus (SLE) is extremely rare. Herein, we have presented the case of a 29-year-old female with SLE, who simultaneously developed bilateral CRVO and BRAO/CRAO in the absence of antiphospholipid syndrome (APS) as a catastrophic form of clinical flare. A combinatorial diagnosis of CRVO and BRAO/CRAO should be considered during clinical flare-up in a patient with SLE who presents with rapidly progressive visual loss. *Lupus* (2018) **27,** 1023–1026.

Key words: Systemic lupus erythematosus; vision loss; flare; central retinal vein occlusion; branch retinal artery occlusion; central retinal artery occlusion

Introduction

Systemic lupus erythematosus (SLE) is a chronic condition; however, acute manifestations, including acute flares, can be very severe and represent a catastrophic problem.[1,2] In general, changes in patients with SLE over time are unpredictable and abrupt life-threatening presentations in SLE are rarely reported.[1]

SLE can cause severe vision loss as a result of acute damage to the retina or optic nerve. While central retinal artery occlusion (CRAO) is rare, it is considered as an ocular emergency and can cause permanent visual loss due to widespread retinal ischemia. It is often characterized by a rapid, painless visual loss, a Marcus-Gunn afferent pupil defect, arterial attenuation, macular edema, and cherry-red spot of fovea.[2]

To date, in the literature, only seven cases of the combination of the branch and central retinal artery occlusion (BRAO)/CRAO and central retinal vein occlusion (CRVO), as an ophthalmology emergency, have been reported in SLE.[3–9] Among these, only two cases had bilateral involvement,[3,7] whereas none presented with a flare of clinical disease flare.

Our case is unique because it is a case of bilateral CRVO and BRAO/CRAO as a catastrophic form of disease flare with rapid complete blindness in both eyes within three days.

This case highlights the importance of early recognition of an underlying hypercoagulable state and timely management of such diseases in patients with no previous manifestations. We hope that this report will help practitioners, especially ophthalmologists, to become increasingly aware of this condition in SLE patients.

Case presentation

We discuss a case of a 29-year-old female with childhood-onset SLE, who presented to the ophthalmology emergency department with a two-day history of progressive worsening of her vision in both eyes, described as blurry vision.

Her initial systemic symptoms of SLE occurred at age 11, when she was diagnosed with hepatitis

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and right knee arthritis. Over the ensuing seven years since her first symptoms, she revealed other symptoms of SLE. Eventually, she fulfilled 5/11 of the American College of Rheumatology (ACR) criteria for SLE (pleuritis, hematologic disorder (hemolytic anemia), nonerosive arthritis, positive antinuclear antibody (ANA), and immunologic disorder (anti-Smith (anti-Sm))).She reported no history of malar rash, photosensitivity, previous thromboembolic diseases, or miscarriages. The autoimmune workup showed remarkable results for elevated inflammatory markers, positive immunofluorescence (IF)-ANA 1: 640, and positive Sm antibody.

Her family history showed no signs of SLE. She developed pneumonia one week before hospitalization and underwent appropriate treatment. Her recent medications included prednisolone, cyclosporine (recently added to the treatment regimens for leukopenia associated with mycophenolate mofetil), and spironolactone.

Ophthalmic examination revealed no acute pathology. A funduscopic examination of both eyes revealed vitreous hemorrhage and widespread superficial and deep intraretinal hemorrhages, compatible with CRVO. The initial funduscopic examination revealed an area of pale retina in one quadrant compatible with BRAO. Within 24 hours, a more swollen and pale retina compatible with CRAO was observed (Figure 1).

Fluorescein angiogram (FA) disclosed substantial delay in the filling of choroidal and retinal vasculatures, both circulations filling almost simultaneously within 25 seconds after dye injection (normal <11 seconds).

Hereditary coagulopathy workup and infectious workups, including three series of blood cultures, hepatitis panel, human immunodeficiency virus (HIV) screening, and fluorescent treponemal antibody absorption test (FTA-ABS), were negative. Workup for antiphospholipid syndrome (APS) was negative.

The laboratory test results of the patient during the initial presentation is shown in Table 1.

Considering the unremarkable extensive infectious workup, hereditary coagulopathy workup, and clinical presentation, she was diagnosed with lupus hypercoagulable state during SLE flare.

Intravenous heparin and methylprednisolone were immediately administered. Furthermore, azathioprine (100 mg/day) and prednisolone (30 mg/day) were prescribed.

The patient was recommended to take a regular dose of warfarin with an international normalized ratio (INR) goal of 2–3.

Her condition was eventually stable throughout the hospital course except for her vision. She could taper prednisolone up to a dose of 5 mg daily, without any relapse.

Table 1 Time course of laboratory data on initial presentation

Laboratory	*Reference range*	*Initial presentation*
Sodium	135–145 mmol/l	133
Potassium	3.5–5.0 mmol/l	5
Blood urea nitrogen	10–15 mg/dl	15
Serum creatinine	<1.03 mg/dl	1.3
Aspartate transaminase	Up to 31 U/l	40
Alanine transaminase	Up to 31 U/l	44
White blood cell	3.8–10.6 K/μl	2.6
Hemoglobin	12.0–15.0 gm/dl	6.4
Platelet count	150–450 K/μl	80
Sedimentation rate	0–20 mm/hour	130

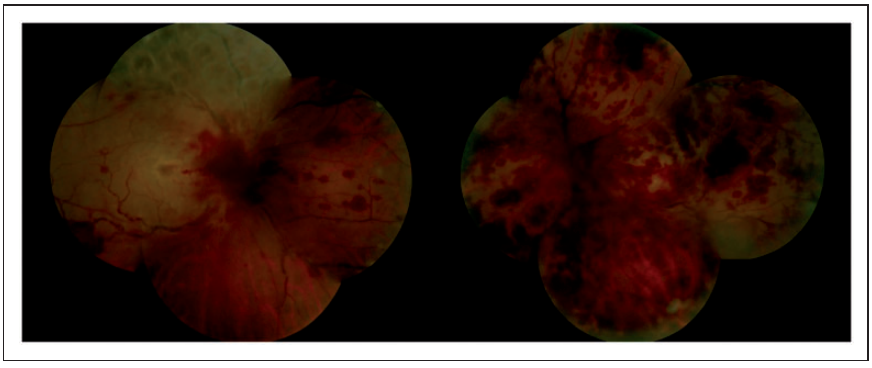

Figure 1 Color fundus photograph of the right (a) and left eye (b) of a patient with systemic lupus erythematosus.
Color fundus photograph shows bilateral combined central retinal artery and vein occlusion. Pale and edematous retina with widespread superficial and deep intraretinal hemorrhages in all four quadrants and engorged and tortuous retinal veins are compatible with the diagnosis of combination of central retinal artery occlusion and central retinal vein occlusion.

No light perception was detected in either eye. The patient had mydriatic pupils, completely unresponsive to light in both eyes. Her vision failed to improve significantly even after repeated intravitreal bevacizumab injections. A periodic ocular examination at two months showed no sign of regained light perception.

Discussion

Only two cases have been reported in SLE, with and without APS-associated bilateral combined CRAO and CRVO; none of these cases presented with clinical flare.[3,4]

In general, multiple, simultaneous thromboembolic disease can develop in less than 1% of patients with APS. About one-half of these patients have SLE.[10] Similarly, these thromboembolic events can also be associated with hypercoagulable state in SLE patients without APS.

In this report, we describe the case of a young female patient who experienced definite SLE with a clinical picture of BRAO/CRAO and CRVO in the absence of circulating antiphospholipid antibodies or lupus anticoagulant.

The exact pathogenesis of simultaneous BRAO/CRAO and CRVO in SLE is still unknown, but hypercoagulable state is considered to be an essential factor.[11]

Factors known to precipitate hypercoagulable state in these patients include acute infection, surgical and obstetric complications, trauma, neoplastic processes, and disease flares.[10]

Immune dysregulation in SLE contributes to disease flares with increased levels of both innate (interleukin (IL)-1α and type I interferon (IFNs)) and adaptive cytokines (Th1-, Th2-, and Th17-type), as well as IFN-associated chemokines and soluble tumor necrosis factor (TNF) superfamily members, weeks before the clinical disease flares.[12]

Therefore, this immune dysregulation can be considered as a trigger for disease flare and associated hypercoagulable state. In our patient, fever and pneumonia were followed by a clinical flare of bilateral combined CRAO and CRVO.

Apart from these factors, some medications such as cyclosporine-A can produce a drug-induced hypercoagulable state in individuals who use this drug.[13]

A previous study reported use of cyclosporine increased the rates of thrombosis.[14]

Cyclosporine-A increases the platelet synthesis of thromboxane A2.[13,15]

Thromboxane A2 triggers vasoconstriction, causes platelet activation, and enhances platelet aggregation; all of these decrease blood flow, increase blood stasis, and promote a coagulation state.[14]

The main pathogenesis in our case was the hypercoagulable state and prompt thrombosis, precipitated by the use of cyclosporine-A and the disease flare. Therefore, the occurrence of acute vision loss can be explained by microvascular occlusions, as a result of thrombosis.

In correlation with a study by Pulido et al.[16] and Levine et al.,[17] in our patient, the treatment with corticosteroid and antithrombotic therapy was effective in controlling the disease activity and reducing the recurrence of thrombosis.

In contrast, the cyclosporine-A antimalarial drug, used as an adjunct to other treatments for SLE, has significantly suppressed the development of hypercoagulable state and disease activity.[18]

Posterior segment hemorrhage-associated SLE is one of the most important causes of blindness in the setting of SLE. It is also postulated that retinal vasculitis associated with SLE during flare of the disease, retinal neovascularization and CRVO may contribute to the posterior segment hemorrhage in SLE patients.[19] In our patient, suspected pathogenesis of vitreous hemorrhage following CRVO may be due to microangiopathy caused by acute endothelial cell apoptosis, increased permeability of vessels and vascular network destabilization following the venous hypertension.[20]

Retinal vascular occlusion as a clinical presentation of SLE dictated a low threshold for thrombosis and should be evaluated for the presence of disease activity.

Conclusion

Our study suggests that simultaneous BRAO/CRAO and CRVO in SLE is a very rare ocular involvement that could be associated with disease flare. For patients revealing this condition in SLE, aggressive treatment could result in an effective control of the disease.

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