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Case Report

A Rare Case of Vaso-occlusive Retinopathy in Systemic Lupus Erythematosus (SLE)

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Received: November 08, 2018; **Published:** February 26, 2019

Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic, autoimmune inflammatory disease of unknown etiology that may affect multiple organ system. The eye is not a primary target of immune-mediated damage in SLE, but it may be affected in various ways that result in significant ocular morbidity.

Case Illustration: A 26 year-old male complained about painless sudden blurred vision in both eyes two weeks before admission. He had history of low-grade fever, fatigue, photosensitivity, arthalgia, hair loss, erythema over the cheeks, neck, hands, chest and back 2 months prior to presentation. Visual acuity of the right eye was 1/60 and during fundus examination extensive cotton wool spots, optic disc haemorrhage, and flame-shaped hemorrhages were found. Visual acuity of left eye was 1/300 and round optic disc covered by exudates was observed. Macular optical coherence tomography (OCT) test showed severe retinal atrophy on both eyes. Serological test revealed positive ANA and anti-ds DNA result. The patient was consulted to Internal Medicine department and was diagnosed as systemic SLE disease with mucocutaneous and ocular involvement.

Results: Oral corticosteroid 3 x 16 mg was given for one month. Six weeks after treatment, visual acuity of the right eye had improved and cotton wool spots on both eyes had decreased.

Conclusion: Prompt diagnosis and treatment could prevent further irreversible visual loss. Management needs to be holistic, both systemic and ocular wise. The control of the systemic disease often improves the ophthalmologic outcome.

Keywords: *Autoimmune; Management; Systemic Lupus Erythematosus; Vaso-occlusive Retinopathy*

Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune inflammatory disease of unknown etiology characterized by the presence of auto-antibodies circulating in one or more components of cell nuclei and mediate immune complex tissue destruction [1]. This connective tissue disorder may affect multiple organ system with musculoskeletal and cutaneous manifestations being the most common [1,2]. Signs and symptoms of SLE in any organ of the body including the eye may be affected due to inflammatory response to the circulating immune complexes [3]. Ocular manifestations are markers for overall systemic disease activity and may affect the eyes and/or visual system in up to a third of patients ranging from relatively mild manifestations to severe, sight-threatening disease [3,4].

The incidence and prevalence of SLE show great variation worldwide. Differences are seen between age, gender, geographical and racial distributions [5]. Senga and colleagues reported annual incidence ranging from 0.3 to 8.7 per 100,000 per year in 2011, with prevalence ranging from 1.1 to 534.9 per 100,000. USA, Caribbean, Brazil, and Sweden were the areas marked with the highest incidence.

However, there has been no epidemiological data covering all regions of Indonesia [6]. Data from Rheumatology Clinic in Cipto Mangunkusumo General Hospital showed that 1,4% patients were affected from SLE amongst total patient visits in 2002 [6]. The incidence of retinal involvement in SLE is 7 - 26% and the most common vision-threatening complications of SLE are seen in patients with active systemic disease [3,7]. SLE predominantly affects females of childbearing age [5]. A study by Feldman., *et al.* found that SLE prevalence was over 6 times higher in women. The median age of onset is between late teens and early 40s with female-to-male ratio close to 9-14:1 [6,8,9].

Diagnostic criteria for SLE were developed by American College of Rheumatology (ACR), according to the 1997 revised criteria [6,8,9]. It was based on 4 of 11 criteria, either present or at some time in the past, including malar rash, discoid rash, photosensitivity, oral ulcers, non-erosive arthritis, serositis, renal disorder, neurological disorder (i.e. seizures or psychosis), haematological disorder (i.e., anemia, leukopenia, thrombocytopenia), immunological disorder (anti-DNA antibody. Anti-Sm antibody, and false positive VDRL) and presence of antinuclear antibodies. The eye is not a primary target of immune-mediated damage in SLE, but it may be affected in various ways that result in significant ocular morbidity [10]. Anterior segment findings may include abnormalities of the eyelid, keratoconjunctivitis sicca, episcleritis, keratitis, iridocyclitis [4,8-10]. Posterior segment manifestation includes retinopathy, retinal vein occlusion and/or retinal artery occlusion, retinal vasculitis, choroidopathy, and optic neuropathy. There are a number of mechanisms that induce ocular symptoms in SLE. Immune complex deposition, the formation of autoantibodies, vasculitis, and thrombosis may cause inflammatory responses and activates complement system [4]. Originally, SLE patients develop at least two major clinical forms of retinopathy: classic retinopathy and occlusion of the larger retinal vessels involving both the arterial and/or venous vascular [11]. The classic retinal findings are cotton wool spots, retinal hemorrhages and vascular abnormalities (arterial narrowing with capillary dilation, and venous dilation and tortuosity) [7,9,12]. However, severe vaso-occlusive retinopathy are also associated with widespread of nonperfusion retinal capillary, multiple branch retinal artery occlusions, ocular neovascularization, vitreous hemorrhage, traction retinal detachment, neovascular glaucoma, and significant resultant vision loss [9].

The general goals of therapy are to induce and maintain remission of the disease and prevent relapses [9]. Management needs to be holistic, both systemic and ocular wise. For systemic management of SLE, treatment ranges from non-steroidal anti-inflammatory drugs, hydroxy-chloroquine, systemic corticosteroids, immunosuppressive therapy, to biologics [9,11,13]. In SLE, control of the systemic disease often improves the ophthalmologic outcome [7,13]. Additional local and regional treatment may also be indicated depending on the type of ocular complication. Retinal neovascularization usually requires laser panretinal photocoagulation in cases of severe vaso-occlusive disease [7,9,13]. Vitreoretinal surgery may be indicated for patients with vitreous hemorrhage or traction retinal detachment. In general, the visual prognosis of retinopathy SLE depends on the pattern of retinopathy and vaso-occlusion usually leads to poor visual outcome [13]. Herewith a rare case of SLE retinopathy is presented, with ocular clinical features resemble other posterior uveitis. This case demonstrates the typical ocular manifestation of SLE and integrates collaboration with other disciplines. Comprehensive evaluation is required to help making a definitive diagnosis. Thus, early management could prevent further irreversible visual loss and risk of death.

Case Presentations

A 26-year-old male was admitted with complaints of sudden blurred vision in both eyes for two weeks. He felt his left eye vision was worse than his right eye. There were no redness, swelling, or discharge, and both were painless. The patient did not receive any treatment beforehand. There was history of low-grade fever, fatigue, photosensitivity, arthralgia, hair loss, erythema over the cheeks, neck, hands, chest and the back 2 months prior to presentation (Figure 1). The patient was also sexually active with a single partner. No history of chronic productive cough, sweating at night, decreased body weight, mouth and genital ulcer, animal contact, trauma, skin depigmentation, tinnitus, and the use of drugs. History of using spectacles, allergy, hypertension, and diabetes mellitus were denied.

During ophthalmological examination, it was revealed that right eye's visual acuity was 1/60, with normal IOP and good anterior segment (Figure 2). The iris and pupil were round, located at the central, had good light reflex and negative RAPD. The lens was clear. Round

optic disc covered by exudates/infiltrates (cotton wool spots), optic disc haemorrhage and flame-shaped haemorrhages in the fundus were observed. Meanwhile, visual acuity of left eye was 1/300, with normal IOP and good anterior segment. Iris and pupil were round, located at the central, had good light reflex and negative RAPD. The lens was also clear. In fundus we found round optic disc, covered by exudates/infiltrates (cotton wool spots) (Figure 2). The patient was diagnosed with bilateral posterior uveitis. Etiological differential diagnosis was CMV retinitis with suspected HIV. Therefore, uveitis work-up was performed to rule out the differential diagnosis and macular OCT. Macular OCT test showed severe retinal atrophy on both eyes with retinal thickness of 118 and 119 μm for the right and left eye, respectively (Figure 3).

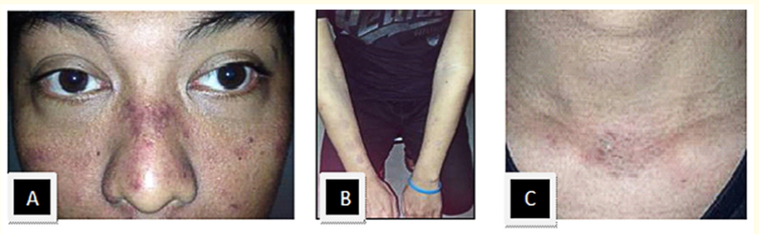

Figure 1: *Systemic clinical appaearance includes face, neck, back and wrist. A. Sign of acute cutaneous lupus erythematous butterfly rash on facial region, B,C. Sign of chronic cutaneous lupus erythematous: raised erythematosus patches include neck, chest, back and wrist region.*

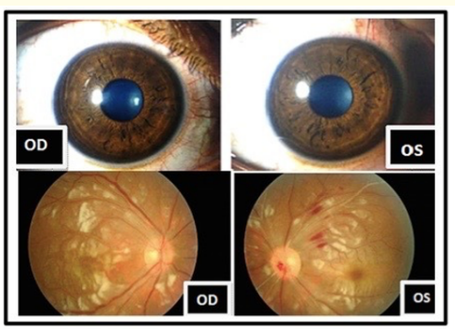

Figure 2: *Anterior segment of both eyes shows normal findings without any signs of inflammation. As in funduscopy at initial visit, right eye (OD) showed extensive exudates/infiltrates (cotton wool spot). On the left eye (OS) showed nasal optic disc haemorrhage, simillary extensive cotton wool spot with flame-shaped hemorrhages. The visual acuity of the right eye was 1/60 and left eye was 1/300.*

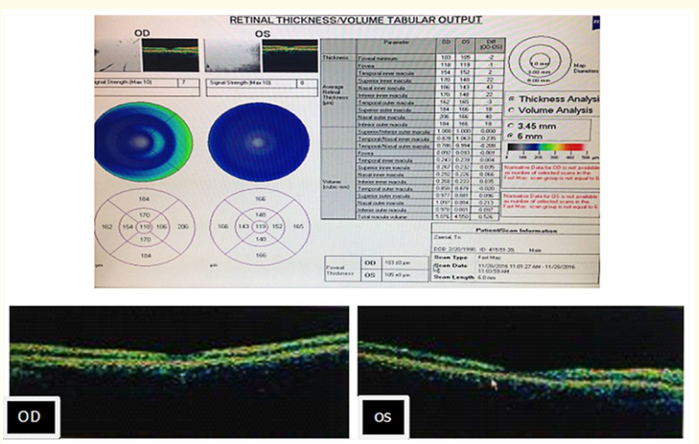

Figure 3: *Macular OCT showed thin retinal and macular thickness due to atrophy on both eyes with retinal thickness of 118 and 119 μm for the right (OD) and left (OS), respectively.*

One week afterwards, the anterior segment remained quiet and there was no sign of improvement on the posterior segment. Laboratory test recorded decreased hemoglobin count to 11,5 g/dL and leukocyte count to 4.220/µL, normal thrombocyte count, increased ESR to 60 mm, and decreased CD4 count to 329 cells. There was a positive result of IgG Rubella, with titer increased to 961.9 IU/mL (n: < 5.I0 IU/mL), alongside with non-reactive IgM. Serology IgG CMV result was also positive with non-reactive IgM. Screening of anti-HIV showed non-reactive result. An antinuclear antibody (ANAs) test was positive at a titer of 1:1000. Chest X-Ray examination showed sign of bilateral paracardial infiltrate with pneumonia as differential diagnosis. Based on clinical and laboratory result, patient was diagnosed with bilateral posterior uveitis caused by CMV infection. Thereafter, the case was consulted further to Allergy-Immunology Division from Department of Internal Medicine in order to find the underlying etiology.

The Allergy-Immunology Division Team diagnosed systemic SLE disease with mucocutaneous and ocular involvement. The patient was then prescribed oral methylprednisolone 3 x 16 mg, cavit D3 3 x 500 mg, folavit 1 x 400 mg, and lansoprazole 1 x 30 mg. He was also consulted to Dermatology Department, diagnosed as chronic cutaneous lupus erythematosus.

The patient returned for follow up six weeks after his initial visit. His right eye condition was getting better, with visual acuity recorded at 5/60. Meanwhile, the vision of left eye was still hand movement. Examination of posterior segment of the right eye showed round optic disc, CDR 0,3 - 0,4, aa./vv 1/3, cotton wool spots, flame shaped hemorrhages, and ghost vessels. On the other hand, in posterior segment of the left eye, round optic disc, pale and hard to be evaluated CDR, aa./vv 1/3, cotton wool spots, flame shaped hemorrhages, and ghost vessels were found (Figure 4). The patient was then diagnosed with posterior uveitis bilateral e.c. SLE and then Fundus Fluorescence Angiography (FFA) alongside with visual field test was performed (Figure 5). The visual field test showed profound visual field loss in the right eye, but it was not performed on the left eye because visual acuity was hand movement. FFA test of the right eye revealed diffuse arteriolar and branch arterial occlusion, capillary non-perfusion (Figure 4).

Due to the improved condition, medication was still continued while the team from internal medicine department tapered off the oral methyl prednisolone.

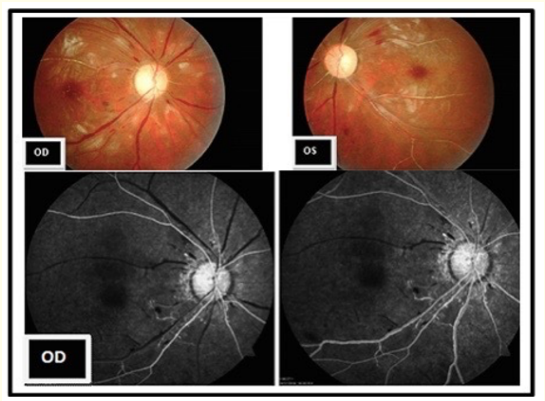

Figure 4: *Funduscopy (OD) showed round optic disc, pale, CDR 0,3 - 0,4, aa./vv 1/3, cotton wool spots, flame shaped hemorrhages, venous beading and ghost vessels; (OS) showed round optic disc, pale, CDR hard to be evaluated, aa./vv 1/3, cotton wool spots, flame shaped hemorrhages, and ghost vessels. Fluorescence angiography of the right eye (OD) revealed diffuse arteriolar and branch arterial occlusion, capillary non-perfusion.*

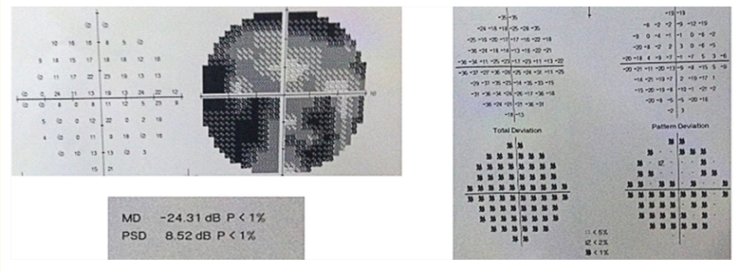

Figure 5: *Humphrey 10-2 visual field at 6 weeks after presentation showed profound visual field loss in the right eye.*

Discussion

This case reported a young male patient with sudden painless vision loss in both eyes since two weeks before admission. Visual acuity of right eye was 1/60 and the left eye was 1/300. The anterior segments of both eyes were normal, and the pathognomonic findings included multiple patches of superficial whitening, intraretinal hemorrhages, and exudates. From this condition, the primary consideration was posterior uveitis with differential diagnosis caused by infection or autoimmune conditions. An infectious cause is more commonly seen in CMV retinitis and tuberculosis ocular, while autoimmune disease may include SLE. Thus work up uveitis was performed to confirm the diagnosis including routine blood test, urinalysis, erythrocyte sedimentation rate (ESR), TORCH, HIV screening, VDRL, TPHA, antinuclear antibody test (ANA); anti- double-stranded DN (dsDNA), Rheumatoid Factor (RF), tuberculin skin test (TST), and chest x-ray.

The result of work up showed the high titer of Rubella IgG, CMV IgG, HSV IgG and non-reactive HIV. An antinuclear antibody test was positive at a titer of 1:1000. From chest x-ray, there was pericardial infiltrate bilateral and negative tuberculin skin test. Diagnosis of SLE retinopathy was considered with the clinical appearance and history of low grade fever, fatigue, arthralgia and facial rash. Laboratory test also showed results of anemia, thrombocytopenia, elevated ESR, and the presence of ANAs. Thorough posterior section examination showed multiple cotton wool spots and intraretinal haemorrhages.

Epidemiologically, SLE most commonly occurs in women, however men may also be affected with a female-to-male ratio close to 9-14:1 [6]. The diagnosis of SLE is clinical and based on presence of 4 of the 11 criteria documented by The American College of Rheumatology criteria. The revised criteria include 1) malar rash, 2) discoid rash, 3) skin photosensitivity, 4) oral ulcer, 5) nonerosive arthritis, 6) serositis, 7) renal involvement, 8) neurological disorder, 9) hematological disorder, 10) immunologic disorder, 11) positive antinuclear antibodies [4-6,8].

However, differential diagnosis of CMV retinitis could not be excluded as well for a number of reasons. Since the patient was still relatively young, the frequency of incidence in Cipto Mangunkusumo Hospital, history of sexual intercourse, and multifocal white exudates with hemorrhage result during retinal examination, may identify the patient's condition to CMV retinitis. The clinical appearance of CMV retinitis is usually divided into 3 variants, including a classic or fulminant form with early stages presents as cotton wool spots. This disease progresses along the retinal blood vessels, causing confluent areas of retinal whitening often associated intraretinal hemorrhages and hard exudates [14]. Cotton wool spots are the most common ocular lesion seen in Acquired Immunodeficiency Syndrome (AIDS), occurring in 25 - 50% of patients and associated with CMV retinitis and retinal hemorrhages [15]. However, it was disputed with the fact that ancillary test of IgG CMV titer and HIV screening test showed negative result.

For further evaluation, the patient was referred to Internal Medicine Department and then he was diagnosed as SLE with mucocutaneous and ocular involvement. This was according to the revised American College of Rheumatology (ACR) classification criteria. In this

case, the diagnosis was based on history of malar rashes, discoid rash, arthralgia, anemia, elevated ANA titer (1:1000) and the elevated anti-double-stranded DNA (anti-ds DNA) antibody titer (134.8 IU/mL compared to the normal titer).

SLE may cause ocular diseases by a number of mechanisms, including immune complex deposition and other antibody related mechanisms, vasculitis and thrombosis to name a few [4]. Antibody dependent cytotoxicity may cause retinal cell death and demyelination of the optic nerve. The mechanism of primary lupus retinopathy is unknown but is thought to be secondary to circulating immune complexes found in this disease [16]. 10% of patients with SLE also have lupus anticoagulant antibodies that are known to increase the incidence of thrombosis. Anti-phospholipid antibodies (APA) is associated with more severe retinopathy and vascular occlusion. In SLE, retinal capillaries are involved and primarily result in cotton-wool spots or microinfarcts of the nerve fiber layer of the retina because of focal ischemia and necrotizing retinal vasculitis [16,17].

Retinopathy is one of the most common forms of intraocular involvement in patients with SLE and is present in 2 - 30% of SLE patients, depending on the activity and severity of the disease [9]. Retinal involvement corresponds to activity of systemic and cerebral SLE. Originally, SLE patients develop major clinical forms of retinopathy. The first type usually occurs in patients with classic retinopathy SLE, characterized by cotton-wool spots with or without intraretinal hemorrhages. The second type of retinopathy is related to the occlusion of the larger retinal vessels involving both the arterial and/or venous vascular, while the third form of retinopathy in SLE is proliferative lupus retinopathy [12,16].

The classic retinal findings are cotton wool spots, which is the expression of localized microinfarction of the retinal nerve fiber layer with or without intraretinal hemorrhages, microaneurysms, and hard exudates [9,12]. Mild lupus retinopathy consists of cotton wool spots, perivascular hard exudates, retinal haemorrhages and may be asymptomatic (Figure 6) [4]. The most common manifestation of lupus retinopathy is microangiopathy presenting with small intraretinal haemorrhages and cotton wool spots account for 80% of cases and are usually associated with a good visual prognosis (Figure 6) [9,18]. In cases with peripheral retinal hemorrhages, retinal nonperfusion may also be observed (Figure 6).

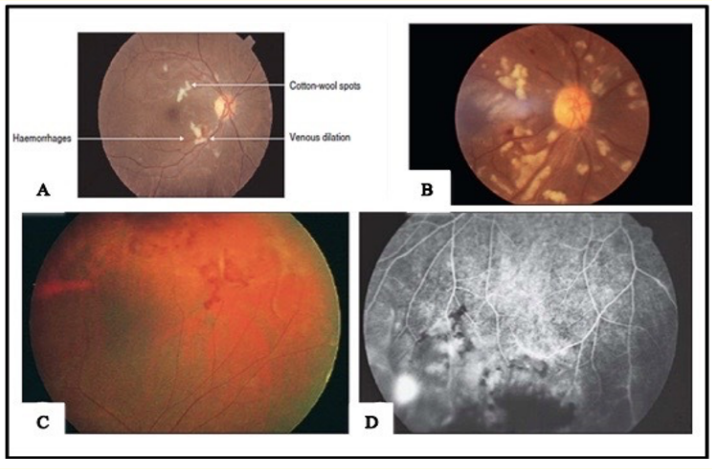

Figure 6: *(A): Acute lupus retinopathy with cotton wool spots, haemorrhages, arterial narrowing, venous dilation and turtosity. (B): Fundus photograph demonstrating diffuse vaso-occlusive disease in a patient with systemic lupus erythematosus. (C,D): Peripheral retinal vasculitis in a patient with systemic lupus erythematosus with areas of intraretinal hemorrhage, retinal nonperfusion, and neovascularization on fluorescein angiography [4,16].*

Conclusion

Prompt diagnosis and treatment could prevent further irreversible visual loss. Management needs to be holistic, both systemic and ocular wise. The control of the systemic disease often improves the ophthalmologic outcome.

Acknowledgments

Address for reprints and sources of support that require acknowledgement is none.

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Volume 10 Issue 3 March 2019