An Unusual Case of Retinal Vasculitis and Neuroretinitis with Chronic Glomerulonephritis in Systemic Lupus Erythematosus with Hughes Syndrome


Abstract
Retinal vasculitis is an intra-ocular inflammatory condition with diverse etiology and a rare manifestation of systemic lupus erythematosus, often associated with antiphospholipid antibodies. The detection and characterization of Retinal Vasculitis and Neuroretinitis may help in diagnosis and management of certain disorders associated with ocular inflammation. These include systemic autoimmune disorders, few infectious diseases and certain ocular disorders. We report a very unusual case of SLE associated with Hughes Syndrome in a 20 year old normotensive female who presented with retinal vasculitis, neuroretinitis and systemic involvement in the form chronic glomerulonephritis.

INTRODUCTION
Systemic Lupus Erythematosus is an autoimmune disease that affects multiple organ systems including the eye and is associated with polyclonal B-cell activation and production of autoantibodies. Retinal vascular lesions are the most common ophthalmological manifestation of systemic lupus erythematosus (SLE), accounting for 3% to 29% of the cases, generally late in the disease. More rare is the severe vaso-occlusive disease, often termed retinal vasculitis. Retinal Vasculitis is characterized by inflammation of the vessels of the retina. SLE accounts only 4% as the cause of Retinal Vasculitis. Retinal Vasculitis as a primary manifestation of SLE is uncommon. Optic Neuropathy is also rare in SLE, with a prevalence of 1%. Patients with SLE and raised serum concentration of anticyclic cardiolipin antibodies have a higher risk of developing occlusive ocular vascular disease. Ocular involvement in SLE is an indicator of active systemic disease, most importantly nephropathy and cerebral lupus. The causes of ocular manifestations in SLE generally include active lupus, antiphospholipid antibody syndrome (APS, Hughes Syndrome), and drugs used to treat SLE.

CASE REPORT
A 20 year old normotensive female presented with fever and headache since 20 days, blurring of vision in both eyes since 14 days, swelling over lower limbs and face since 10 days and oliguria since 7 days. There was no history of haematuria, pain in abdomen, distention of abdomen, chest pain, dyspnea, haemoptysis, arthralgia, and sore throat. There was no history of seizures. Her menstrual history and past history was insignificant.

On clinical examination her blood pressure was 130/90 mm Hg, tachycardia was present 116 beats/min, pallor was present, there was no glossitis or koilonychia. JVP was normal. Bilateral edema of feet (pitting type), puffiness of face, malar rash sparing nasolabial folds, oral ulcers and arthritis was present.

On investigations, haemoglobin was 9.1gm%. TLC was 8400/mm³. Platelet count was low -1,28,000/microliter of blood. Urine analysis revealed. Urine examination revealed
proteinuria (+++), albuminuria(+), few RBCs (2-3) per high power field, 24 hour urinary protein was 2.7gm/dl, serum urea was 56mg% and serum creatinine was 1.9mg%. HIVI and HIVII by ELISA was negative. Serum ASO titre was negative. Serum ANA was 4.08(>1 is positive) and dsDNA 58.42(>20 is positive). USG abdomen and pelvis revealed shrunken kidney. IgG ACA was 45GPL u (>40 GPL u) done on 1st week and 9th week.

She was referred to Ophthalmology department for complaints of blurring of vision, headache and slight diminution of vision OU. On examination her visual acuity was 6/18 OU. Anterior segments were unremarkable. Fundus examination revealed hyperemic disc, multiple retinal haemorrhages OU and macular star OS representing retinal vasculitis and neuroretinitis OU. There were no signs of hypertensive retinopathy changes in fundus picture OU. Our case was fulfilling the criteria for diagnosis of SLE by the American Rheumatologic Association. She was started on intravenous methyl-prednisolone 1gm daily for 3 days followed by oral prednisolone 1mg/kg/day in tapering dose with diuretics and ACE inhibitor therapy. After 15 days, her edema subsided, proteinuria reduced(24 hour urinary protein was 1.7gms), urine output increased and vision improved to 6/9 OU. Serum creatinine after 2 weeks decreased to 0.67mg%. The patient was discharged with 40mg prednisolone and was advised for follow-up after 2 weeks.

Figure 1
Fig. 1: Fundus pic showing Retinal Vasculitis

Figure 2
Fig 2: Fundus Pic Showing Neuroretinitis

Figure 3
Fig 3: CT Brain showing Lacunar Infarct in Basal Ganglia suggestive of SVD.
Figure 4

Fig 4: USG abdomen showing shrunken kidney secondary to Chronic Glomerulonephritis

DISCUSSION

Retinopathy is one of the important, if not major, manifestation of SLE, which develops with an incidence of 7-26%, reflecting a reduction in frequency associated with improved control of systemic disease. Mild retinopathy may be asymptomatic but more severe disease may cause loss of vision, field defects distortion and floaters. Such visual symptoms are therefore an indication for urgent ophthalmic review. The retinal signs often parallel the severity of systemic inflammation, and may indicate inadequate control of systemic disease. The presence of APA is associated with more severe retinopathy and vascular occlusions. Mild lupus retinopathy consists of cotton-wool spots, perivascular hard exudates, retinal haemorrhages and vascular toxicity. Moderately severe cases may also have focal or generalized arteriolar constriction and venous tortuosity. At the severe end of spectrum there is occlusion of retinal arterioles and consequent retinal infarction, termed vaso-occlusive retinopathy or ‘retinal vasculitis’. Proliferative retinopathy may occur in up to 72% of such cases, often ensuing vitreous haemorrhage, retinal traction and retinal detachment. Other retinal presentations include large vessel occlusions (central and branch retinal vein occlusions, central and branch retinal arteriole occlusions) that are common in the presence of antiphospholipid syndrome (APS), pigmentation changes (pseudo retinitis pigmentosa) and exudative retinal detachment secondary to choroidal disease. In the immunosuppressed state, rare retinal infections may occur: retinal necrosis due to herpes simplex, varicella zoster and cytomegalovirus are all reported. Optic neuritis, ischemic optic neuropathy are also commonly seen.

It is unfortunate that ophthalmological manifestations are not included in the diagnostic criteria of SLE. It is not uncommon to see patients who have not been diagnosed as SLE, who have developed an ocular manifestation in advance of diagnosis of SLE. Though severe visual loss is not seen in the group whose retinopathy improves with corticosteroid/immunosuppressive therapy. In this patient, nephropathy was also present. SLE represents the most frequent cause of renal involvement. The choriocapillaris-Bruch membrane retinal pigment epithelium complex is morphologically similar to glomerular basement membrane (GBM); they are structurally homologus, selectively permeable with positive charge. Both have high content of heparan sulphate, the only difference being the collagenous zone of Bruch membrane which is thicker than the GBM.

The renal presentation is highly variable. The serum dsDNA levels consistently correlate with disease severity, histopathology, clinical course and response to therapy.

The findings of retinopathy as vasculitis and thromboembolism reflect vascular damage. Ocular fundus is the only part of human body where we can directly observe small vessels without injuring the tissue. This suggests that lupus retinopathy reflects systemic vascular damage and that ocular fundus examination should be carried out more often. Although it is unclear whether lupus retinopathy is directly associated with renal disease, retinopathy may develop in severe SLE which involves the kidney or CNS, or both.

aPL are known to be associated with arterial and venous thrombosis. aPL represent a heterogenous group of antibodies against phospholipid binding proteins or their complexes with anionic phospholipids. As the presence of aPL often provokes arterial and venous thrombosis, intrauterine fetal loss, and thrombocytopenia, many organs may be affected by these antibodies.
association of aPL with lupus retinopathy has been found. This indicates that aPL should be added to the list of candidates causing retinopathy. [17]

The mainstay of treatment for significant retinal disease is systemic immunosuppression, but laser therapy and anticoagulant also have a role. Initial treatment is usually with oral corticosteroids (e.g. prednisolone 1mg/kg/day), but may be preceded by methyl prednisolone (e.g. 500mg-1gm daily for 3 days). This is then supplemented with, or replace by, other immunosuppressive agents as a part of steroid sparing strategy or for resistant disease. In unilateral or asymptomatic disease, regional corticosteroid injections are sometimes used in addition. In the presence of significant vaso-occlusive disease (particularly when APA are present), anti-coagulation and addition of low dose acetylsalicylic acid may be beneficial.

**CONCLUSION**

SLE is a multisystem immune disorder. Eye manifestations in SLE may be sight-threatening and can be an indicator of active systemic disease. Significant ocular pain or diminution of vision are serious symptoms requiring urgent assessment by an ophthalmologist. The serious ocular manifestations of SLE (such as scleritis and lupus retinopathy) generally require systemic immunosuppression. Renal involvement can occur at any time during the course of disease. It can be silent. Though renal biopsy is not necessary in SLE patients whose renal function is rapidly deteriorating when they have active urinary sediment, it becomes necessary in atypical presentations not defining a pure nephritic or nephrotic syndrome and/or rising serum creatinine levels, so that early diagnosis will lead to prompt initiation of management.

Future research will hopefully provide more evidence on which to base treatment choice. Early recognition by the rheumatologist, prompt assessment by the ophthalmologist and coordinated treatment strategies are key to reducing the ocular morbidity associated with the disease.

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**References**

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