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Clinical profile of ocular morbidities associated with systemic lupus erythematosus

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is an autoimmune disorder involving multiple organs. Ocular involvement occurs in both the active and chronic phases. We have conducted a study to illustrate the ocular inflammations associated with SLE leading to visual morbidity.

Materials and Methods: This prospective, descriptive, hospital-based study was conducted on 75 patients with SLE over 1 year diagnosed by the physician based on the Systemic Lupus Collaborating Clinics (SLICC) criteria. These patients underwent complete ocular examination. Ancillary investigations were done for patients with clinically suspected ocular pathology.

Results: 69% patients had ocular involvement and keratoconjunctivitis sicca (76%) was the most common.42% patients had multiple ocular tissue pathologies. Corneal involvement was noted in 7 patients (14%), comprising of punctate corneal erosions (10%), pannus (2%) and peripheral corneal ulcer (2%), all during the active phase of the disease. 30% patients had episcleritis, diffuse pattern (73%) being the most common and also the presenting sign of SLE in 9% of patients. Retinopathy was seen in 9 patients (18%), vasculitis in 12% being the most common posterior segment association with SLE. The most common cause of defective vision in these patients was steroid induced or complicated cataract (24%). 42% of patients had associated SLE nephropathy.

Conclusion: Simultaneous and multiple forms of ocular inflammation can occur at any stage of SLE, which could compromise the quality of life of the individual. The onset of uveitis is indicative of active status of the disease. A complete ophthalmic evaluation is an important part of management during the active stage and remission.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder known to affect multiple organs.[1] It has a typical relapsing and remitting course. It particularly involves the connective tissues of the body including the eye. Ocular inflammation associated with SLE can present with symptoms ranging from mild discomfort to visual loss. Ophthalmic involvement can be seen during the active, chronic stage or as an adverse effect of the drugs prescribed for the treatment of SLE. The main pathology behind the disease is immune dysregulation. The anti-double stranded DNA (anti ds DNA) antibodies are bound to circulating nucleosomes, which in turn form immune complexes, that get deposited in end-organ capillary beds, thereby initiating inflammation and immune response.[2] Another hypothesis states that a deficiency of complement factors is an associated risk.[3] SLE notably has exacerbations which are commonly triggered by medications, sunlight and hormonal fluctuations. Ocular inflammation occurs due to deposition of immune complexes in the retinal vessel capillary bed, which cause vasculitis and thrombus formation. This could be one of the earliest manifestations of an evolving SLE.

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Inflammation has been observed in both the anterior and posterior segment of the eye such as in the conjunctiva, ciliary body, retina, sclera, choroid and optic nerve along the visual pathway.[4] Corticosteroids, immunosuppressants and hydroxychloroquine are used in the SLE. Due to the long duration of treatment required, these drugs can adversely cause cataract or retinopathy, leading to visual loss. Anterior segment pathology commonly associated with SLE are iritis, episcleritis, scleritis and keratitis, whereas the posterior segment included choroidopathy, retinitis and optic neuropathy.[5] Posterior segment involvement is a strong indicator of systemic disease with poor prognosis and requires vigilant treatment after discussing with a team consisting of a physician, rheumatologist and ophthalmologist.

African and Asian races are predisposed to SLE but thrombotic complications are more frequent in the caucasian population.[6] The incidence of ocular involvement in patients with SLE ranges from 3-29%.[7] We conducted a study on patients with SLE to analyze the prevalence of the associated ocular manifestations, the impact the condition had on the patient's vision, both during active stage as well as a complication and sequalae of treatment for SLE. To our knowledge this is the first study that is reporting on simultaneous multiple ocular manifestations and complications in SLE.

2. Materials and Methods

This is a prospective, descriptive, observational, non-randomized and population-based study performed on 75 patients with SLE in a tertiary care Centre in South India, over a period of 2 years. All patients with a confirmed diagnosis of SLE based on clinical evaluation and laboratory tests were referred from the rheumatology and dermatology department. Patients above the age of 18 years who were diagnosed with SLE were included in the study. Patients who had other co-existing auto-immune disorders were excluded from the study.

The Institutional ethics committee approval was obtained (CSP-MED/20/SEP/61/80) which abides by the tenets laid down in the Declaration of Helsinki. The patients were enrolled in the study after getting informed consent from them.

SLE was diagnosed based on the criteria given by the Systemic Lupus Collaborating Clinics (SLICC) revised by American College of Rheumatology. Blood investigations which included complete blood count, Mantoux test, erythrocyte sedimentation rate (ESR), VDRL/ FTA- ABS, serum uric acid, serum creatinine, urine analysis, rheumatoid factor, anti-nuclear antibodies and anti-ds DNA, were performed. These patients were referred to our ophthalmology clinic where they underwent a complete ophthalmic evaluation. The patient's demography, history of illness, ocular symptoms, duration of SLE and medications taken were noted. The ophthalmic evaluation comprised of checking visual acuity, refraction, color vision with Ishihara chart, slit lamp bio microscopy examination of the anterior and posterior segment of the eye, measuring the intraocular pressure with non-contact tonometry or Goldman's applanation tonometer when no corneal pathology was detected, followed by a dilated fundus examination with an indirect ophthalmoscope and 20 D lens. Dry eye test included Schirmer's test and tear break-up time. Ancillary ophthalmic investigations such as fundus fluorescein angiography (FFA), optical coherence tomography (OCT) macula and B scan ultrasonography were done for patients with posterior segment pathologies observed on clinical examination during the initial and follow up visits.

We noted the various ophthalmic lesions, analyzed the possible causes of diminution in vision and the extent of visual morbidity of these patients through the duration of the study. All patients had a mean follow up of one year. During active disease, patients were reviewed weekly. When response to treatment was evident, they were reviewed once every 3 weeks to detect any ocular sequelae due to the disease or medications. The physicians monitored their complete blood counts, renal function tests and blood sugars every 3 months after diagnosis.

2.1. Statistical analysis

The data collected was analyzed using IBM-SPSS Software version 23. Descriptive statistics frequency analysis was done for data distribution. Kappa coefficient was used for correlation of test values. Statistical significance was done using CHI square test with $p< 0.05$ taken to be statistically significant.

3. Results

75 patients diagnosed with SLE were examined for ocular manifestations. Our study comprised of 35 female and 15 male patients (the other 25 patients were lost to followup), with their age ranging from of 30 to 55 years (mean age of 45 +/- 5 years). Ocular features were observed in 69% of patients, of whom 21 patients (42%) had simultaneous multiple ocular manifestations. The mean best corrected visual acuity at the first visit was log MAR 0.5 in either eye. Defective vision at presentation was seen in 40% of patients with visual acuity less than 6/18 on log MAR which was reversible in 10% and irreversible in 2%. The predominant symptom during the initial visit was foreign body sensation and grittiness (63%). The various anterior segment signs observed were punctate corneal erosions (10%), pannus (2%), peripheral keratitis (2%), episcleritis (30%) and anterior uveitis (10%). Retinal vasculitis (12%), optic disc edema (3%) and posterior scleritis (2%) were seen in the posterior segment.

The most common ocular presentation was KCS which was seen in 38 patients (76%) and was statistically significant (p=0.001) (Figure 1). Corneal involvement in all patients occurred in the active phase of SLE (Table 1).

Table 1: Corneal involvement

Corneal Signs	Number of patients (%)
Punctate corneal erosions	5 (10)
Pannus	1 (2)
Peripheral corneal ulcer	1 (2)

Episcleritis was noted in 15 patients (30%) and posterior scleritis in 1 patient (2%) and was the presenting sign of SLE in 5 patients (9%). Diffuse episcleritis in 14 patients (93%) was more common than the nodular type in 1 patient (7%) which was statistically significant (p=0.003). 9 patients (18%) developed steroid induced cataract and 6% had complicated cataract.

Retinal involvement was present in 9 patients (18%). Retinal vasculitis occurred in 6 patients (12%) of them had associated CNS disease. Other signs of retinopathy were macular edema, hemorrhages and cotton wool spots. Optic disc edema occurred in 3 patients (6%).

It was noteworthy in our study that several patients presented to us with simultaneous multiple ocular manifestations (42%). Most patients had a combination of signs which included KCS, diffuse scleritis, atrophic maculopathy, complicated cataract (Figure 2).

Most of these patients were on systemic treatment, 60% on monotherapy with steroids and 18% with additional immunosuppressive therapy with AZT or MM. Many patients developed ocular changes due to the long-term adverse effect of the systemic medications such as steroid induced cataract (18%), RPE atrophy (12%), bulls eye maculopathy (3%) and pigments resembling vortex keratopathy (2%). On FFA, RPE atrophy and bull's eye maculopathy showed hyper fluorescence. Macular oedema was confirmed with an OCT.

Following treatment, resolution of ocular signs occurred in 15 patients (30%) in 2 months and 23 patients (46%) within 1 year. Complete resolution was not noted in patients presenting with corneal erosion, macular oedema, uveitis, episcleritis, optic neuritis and vasculitis. At the end of 6 months, an improvement of vision was noted in 17 patients (34%). (Table 2)

Table 2: Treatment outcomes

Outcomes	Number of patients (%)
Resolution in 2 months	15 (30)
Resolution in 1 year	23(46)
Improvement in vision	17 (34)

The most common cause of drop in vision after initiating systemic treatment for SLE was steroid induced cataract in 24 patients (48%) followed by retinal vasculitis in 12%, atrophic maculopathy in 3 patients (6%) and optic atrophy in 1patient (2%) and optic neuritis 1%, papilledema 3%. Irreversible complications with severe visual morbidity (VA less than 3/60) occurred in scleral necrosis, atrophic maculopathy in 3 patients (6%) and vascular occlusions with macular oedema in 2 patients (4%) (Table 3).

All these patients with SLE associated ocular manifestations had elevated levels of anti-ds DNA and ANA antibodies which correlated with the active phase. A significant finding was that 24 of 50 patients (48%) were also diagnosed with SLE nephropathy.

Table 3: Causes of visual loss

Complicated cataract	24%
Vasculitis	12%
Uveitis	10%
Atrophic maculopathy	6%
Vascular occlusion with macular oedema	4%
Papilloedema	3%
Optic atrophy	2%
Optic neuritis	1%

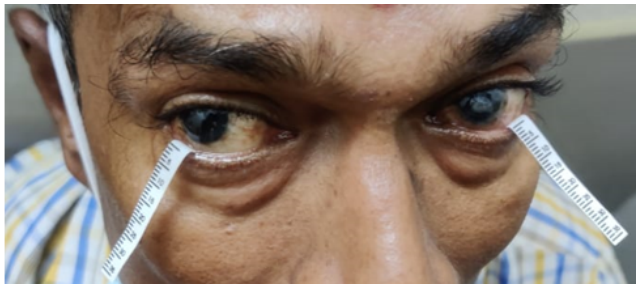

Fig. 1: Schirmer's test showing decreased tear secretion in KCS

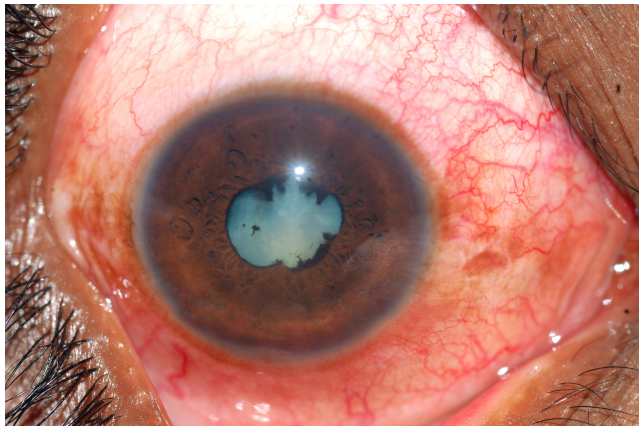

Fig. 2: Complicated cataract with scleritis

4. Discussion

This is a prospective study performed on 75 patients. A diagnosis of SLE was made based on a combination of clinical features and laboratory investigations based on the diagnostic criteria laid down by the SLICC revised by American College of Rheumatology. Patients were regularly examined for associated ocular features. An earlier classification, given by the American College of Rheumatology criteria which was established in 1982, has been used previously to make a diagnosis of SLE but this classification did not include ophthalmic features as a required factor for the diagnosis of SLE.[8] The Systemic Lupus International Collaborating Clinics (SLICC) provided an updated classification which does not include ocular features.[9] The presence and extent of ophthalmic involvement may be reflective of the active form of SYSTEMIC disease and may indicate an evolving systemic flare up.

In our study population, the commonest symptom in the anterior segment disease was foreign body sensation and grittiness (63%). Blurring of vision and field defects were present when the retina or optic nerve was involved. We noted orbital and adnexal involvement such as ectropion and dacryocystitis occurred in some of our patients. Keratoconjunctivitis sicca occurred in the majority and was predominantly due to aqueous tear deficiency. KCS was a feature of active and long term, inactive stage of the disease. Associated punctuate epithelial keratitis was present in a few patients with severe KCS. Peripheral ulcerative keratitis occurred in 3% of patients and responded well to topical medications such as lubricant eye drops, topical antibiotic and corticosteroid eye drops and non-steroidal anti- inflammatory drugs.

Among our study cohort, episcleritis was always a feature of active disease. Vasculitis was the most common cause of visual loss in those with posterior segment involvement and occurred during the active stage of SLE. In our patients, retinal signs that occurred were papilledema, retinal vasculitis, macular star and cotton wool spots suggestive of retinal non- perfusion and ischemia which were also confirmed on FFA. Vasculitis was confirmed on fundus fluorescein angiography (FFA) and required corticosteroids for the management. Treatment with systemic corticosteroids and immunosuppressive drugs decreased retinal infiltration and oedema with eventual resolution. Patients were systemically treated with hydroxychloroquine (300- 400 mg/ daily), azathioprine (150mg daily tapered to 50mg) along with artificial tear substitutes and antibiotics. During acute phases, oral prednisolone in the dose of 1mg/kg body weight was added.

We saw simultaneous, multiple ocular manifestations such as kcs, episcleritis and vasculitis in 42% of our patients. Patients who had hypertension, developed features of hypertensive retinopathy and papilledema. The presence of retinal hemorrhages, cotton wool spots and papilledema may reflect hypertension in SLE. Bilateral optic neuropathy, macular infarction,[10] involvement of the choroid, eye lids, orbit, vaso-occlusive retinal disease[11] has been reported in literature but we did not encounter any such manifestations in our patients.[12]

The appearance and resolution of retinopathy could be correlated with exacerbations and remissions of the systemic disease.[13] Optic neuropathy can cause irreversible visual loss and recurrence causes further deterioration. Ophthalmic management in such cases needs a thorough consultation with the treating physician. Scleritis and retinopathy are absolute indications for immunosuppression.[14] In our study, ocular features associated with SLE were present in 69% of patients. Visual involvement during the active phase occurred in 51% patients and following treatment occurred in 18% patients

Immunosuppression when started in SLE requires regular monitoring to detect infections.[15] A case of cytomegalovirus retinitis in SLE during treatment with immunosuppression has been reported.[16]

Among the various drugs used for the treatment of SLE, 18% of patients had steroid induced cataract. Patients on hydroxy chloroquine were found to have retinal pigmentary disturbances. In our study we found that the incidence of typical Bulls eye maculopathy was uncommon and was seen in only 3% of our patients which is less than reported from other centres.[17] Further assessment on the total duration and dosage of the drug aided by investigations such as perimetry and OCT would provide more insight into incidence of ocular complications due to hydroxychloroquine.

5. Conclusion

A spectrum of ocular manifestations of varying severity with or without visual loss can co-exist in SLE. The presence and extent of ophthalmic features can be a marker of the activity of systemic disease. Patients need ophthalmic evaluation both during the disease and after treatment. The best way to prevent systemic and visual complications in SLE is by adopting a multidisciplinary approach.

New conclusions based on our study

1. Multiple simultaneous ocular manifestations are a common feature in SLE associated eye disease.
2. The presence of severe ocular features is closely related to SLE nephropathy.
3. Retinal vasculitis and papilledemaare linked to CNS involvement.

6. Source of Funding

None.

7. Conflict of Interest

None.

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