ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Ophthalmic manifestations in systemic lupus

Hamada S Ahmad[1], Ibrahim Shady[2], Sherief E Farrag[1], Ahmad N Al Sheikh[3]

1. Rheumatology & Rehabilitation Department, Mansoura faculty of Medicine, Mansoura University.
2. Community Medicine Department, Mansoura Faculty of Medicine, Mansoura University.
3. Ophthalmology Department, Al Maghrabi Hospital, KSA

Manuscript Info

Manuscript History:

Received: 15 September 2015
Final Accepted: 22 October 2015
Published Online: November 2015

Key words:

Systemic lupus erythematosus, ocular manifestation, lupus activity

Corresponding Author

Hamada S Ahmad

Abstract

Background and aim of work. Ocular manifestations have been reported to occur in up to one third of Systemic Lupus Erythematosus (SLE) patients and are associated with significant morbidity and also a marker for overall systemic disease activity. The aim of this study is to determine the distribution of ocular manifestations among patients with SLE and to determine the association of the ocular manifestations with the disease activity.

Subjects and methods. This is a cross-sectional study included 112 consecutive patients with SLE (98 females and 14 males). Patients underwent clinical assessment and current drug use information was obtained. Lupus disease activity was calculated using the SLE Disease Activity Index (SLEDAI). All patients underwent a complete ophthalmic examination.

Results. Out of the 224 eyes of the 112 SLE patients, 23 (10.3%) eyes in 12 (10.7%) patients had ocular manifestations related to the SLE disease. SLE patients who had ocular manifestations had significantly higher SLEDAI score and are more frequently using systemic corticosteroids and hydroxychloroquine than SLE patients without ocular manifestations.

Conclusions. SLE affected the eyes in a significant sector of patients. Ocular manifestations in SLE should be taken seriously as they may lead to significant morbidity and visual deterioration. Ocular manifestations denoted the disease activity of SLE.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease of unknown etiology. SLE is characterized by a hypersensitive systemic inflammatory reaction in a wide spectrum of tissues, and hence it may cause a wide range of clinical signs and symptoms [1]. It can manifest by inflammation of various organs including skin, heart, joints, blood vessels, liver, kidneys, and nonetheless ocular tissues such as cornea [2,3]. Ocular manifestations has been reported to occur in up to one third of patients and is associated with significant morbidity and also a marker for overall systemic disease activity [4]. Although early recognition and treatment have led to a reduction in severe ocular complications, ocular involvement in SLE is still a potentially blinding condition. Early detection and appropriate treatment of these eye complications may save the patient's sight and also improve their quality of life.

The aim of this study is to determine the distribution of ocular manifestations among patients with SLE and to determine the association of the ocular manifestations with the disease activity.

Patients and Methods

Study population

This is a cross-sectional study included 112 consecutive patients with SLE (98 females and 14 males) collected from the outpatient clinic of Rheumatology and Rehabilitation and the outpatient's clinic of Ophthalmology Departments in different hospitals in Saudi Arabia between August 2013 and May 2015. All patients met the Systemic Lupus International Collaborating Clinics (SLICC) 2012 criteria for diagnosis of SLE [5]. Patients with other systemic diseases that may produce eye pathology e.g. diabetes mellitus and hypertension were excluded from the study. Also, lupus patients with eye diseases that started before the current lupus or patients with eye diseases not related to the current lupus were also excluded from the study. The procedures of the study were explained to the patients and all patients provided a written consent prior to participation in the study.

The clinical assessment of the patients included interview for history taking to report demographic and clinical data regarding age, sex, and duration of the disease. The medical history and current systemic and topical drugs used were obtained during the interview and from the medical files of the patients. Lupus disease activity was calculated using the SLE Disease Activity Index (SLEDAI) [6].

All patients underwent a complete ophthalmic examination. Ophthalmic examination included visual acuity, slit lamp examination, measurement of intraocular pressure, fundus examination. Slit-lamp was used for the examination of the skin of the eye lids and the conjunctiva to detect signs of inflammation e.g. ciliary injection and to detect scleritis and episcleritis. Dry eye syndrome is diagnosed using Schirmer's test and Tear film break up time test (TBUT). Schirmer's test was performed by measuring the amount of wetting of a special filter paper. Wetting of the paper <5 mm indicated impaired lacrimal secretion. TBUT assesses precorneal tear film stability. A TBUT of less there 10 seconds is abnormal.

Statistical Analysis

Continuous data were expressed as mean ± standard deviation (SD) while the categorical data were expressed as number and percent. All continuous data were tested for the skewness and kurtosis prior to any analyses. Comparisons between continuous data were performed using the independent sample Student's t test meanwhile the comparisons between the categorical data were performed using the Chi Square test. Statistical significance was determined at $P<0.05$. All calculations were made using SPSS version 20.0.

Results

The study included 112 consecutive SLE patients (98 females and 14 males). The characteristics of the SLE patients were shown in Table 1. Out of the 224 eyes of the 112 SLE patients, 23 (10.3%) eyes in 12 (10.7%) patients had ocular manifestations related to the SLE disease. The ocular manifestations found in the SLE patients enrolled in the present study are summarized in Table 2.

SLE patients who had ocular manifestations were had significantly higher SLEDAI score and are more frequently using systemic corticosteroids and hydroxychloroquine than SLE patients without ocular manifestations. However, the presence of ocular manifestations was not associated with age, gender, duration of SLE, or with the use of cyclophosphamide, azathioprine or biologics (Table 3).

Table 1. Characteristics of the 112 SLE patients

Age (years)	Range= 16 – 51 years
	Mean ±SD= 35.6 ±10.1
Sex (n, %)	
Female	98 (87.5%)
Male	14 (12.5%)
SLE duration (years)	Range= 3 – 23
	Mean ±SD= 11.8 ±6.2
SLEDAI score	Range= 0 – 52
	Mean ±SD= 21.3 ±10.4
Current drug used (n, %)	
Systemic steroids	81 (72.3%)
Hydroxychloroquine	62 (55,4%)
Azathioprine	27 24.1%)
Cyclophosphamide	17 (15.2%)
Biologics	10 (8.9%)

Table 2. Frequency of the ocular manifestations in 100 eyes of the 50 SLE patients

Ocular findings (n=244 eyes)	n	%
External Eye Involvement		
Discoid lesion on eye lid	6	2.7
Periorbital edema	4	1.8
Lacrimal System Involvement		
Schirmer's test: <4 mm wetting in 5 minutes	7	3.1
Tear break up time <5 seconds	5	2.2
Anterior Eye Segment		
Corneal erosions	1	0.4
Cataract	9	4
Posterior Eye Segment		
Cotton wool spots	13	5.8
Retinal hemorrhage	11	4.9
Vascular tortuosity	5	2.2
Vitreous hemorrhage	6	2.7
Neuro-Ophthalmic Involvement		
Optic neuritis	1	0.4
Visual Disturbance		
Visual field defects	5	2.2
Blurring of vision	6	2.7

Table 3. Comparison of the characteristics between patients with and without eye manifestations

Variables Mean ± SD, n (%)	Patients with eye manifestations	Patients without eye manifestations	p
Age (years)	37.2 ±9.4	33.8 ±8.7	0.207
Females	10 (83.3%)	88 (88%)	0.644
SLE duration (years)	14.1 ±6.9	10.8 ±7.4	0.145
SLEDAI score	32.7 ±8.2	18.1 ±11.4	<0.001
Use Systemic steroids	12 (100%)	69 (69%)	0.023
Use Hydroxychloroquine	12 (100%)	50 (50%)	0.039
Use Azathioprine	4 (33.3%)	23 (23%)	0.429
Use Cyclophosphamide	2 (16.7%)	15 (15%)	0.879
Use Biologics	2 (16.7%)	8 (8%)	0.320

Discussion

Overall, among the SLE patients included in the current study, 10.7% (n=12) patients had ocular manifestations while 89.3% of the patients did not develop ocular manifestations at time of enrolment in the present study. Previous studies showed that eye involvement has been found in 20% [7,8,9], 30% [4,10,11]to 47.3% [12]of patients with SLE.

Also, ***El-Shereef et al.*** [13] enrolled 53 SLE patients SLE in his study. Ophthalmologic examination of the patients revealed that 18 patients (34.6%) had ocular involvement, from which only 13 (25%) patients were symptomatic. ***Silpa-Archa et al.*** [8] reported that ocular manifestations are common in SLE however they did not state the rate of presence of ocular manifestations. Also in agreement with the findings of the current study, several studies found that the majority of SLE patients do not develop ocular symptoms throughout the course of their illness [14,15,16]. ***Klejnberg and Moraes*** examined 70 SLE patients and found that 65.7% of the lupus patients had no ophthalmological complaints [17].

In the present study, each of the discoid lesion and the periorbital edema affected 2.7% and 1.8% eyes in four patients (4%) respectively. In agreement with our findings, periorbital edema was an uncommon manifestation of SLE with an overall incidence ranging from of 0.1% to 4.8% [18,19]. Discoid lesion in the eye lid is exceptionally rare in the course of SLE [20] however, ***Pandhi et al.*** found that discoid lesion had affected only 6% of patients with SLE [21].

In the present study 7 (6.3%) patient had manifestation of dry eye (7 eyes had +ve Schirmer's test and 5 eyes had +ve TBUT test). Dry eye syndrome was frequently reported in patients with SLE [8,9,13].On the other hand, ***Resch et al.*** found that Schirmer's test was significantly lower in the patients with SLE than controls indicating a lower tear production in patients with SLE compared to the controls [22]. Several studies found that dry is the commonest eye manifestation in SLE being affecting 36.7% [23], 39.5% [12] and 50% [2] of the patients**.** ***Klejnberg and Moraes*** found that the dry eye syndrome was diagnosed in 31.4% of the lupus patients [17]. The higher rate of the occurrence of the dry eye reported by these studies compared to the current study can be explained by the fact that the patients recruited in these two studies were all hospitalized due to severe lupus disease.

In the present study, 9 eyes in 5 patients (4.5%) had cataract. ***Alderaan et al.*** [24] found that the prevalence of cataract among the patients after 4 years from onset of lupus was 5.2% which comes in agreement with our findings. In their study, ***Soo et al.*** estimated the frequency of patients with cataract of 14% [25].***Carli et al.*** [26] observed that 29% of the lupus patients had cataract. All patients include in their study were taking steroids for long duration their average age was older than patients in the patients in our study.

In the present study, fundus examination of the patients had shown that 13 eyes in 7 (6.3%) patients had cotton wool spots, 11 eyes in 6 (5.4%) had retinal hemorrhage, 5 eyes in3 (2.7%) and 6 eyes in 3 (2.7%) had vitreous hemorrhage. ***Fouad et al.***[27] stated that the retinopathy frequently seen in patients with SLE generally consists of cotton wool spots with or without retinal hemorrhages. Lupus retinopathy in the form cotton-wool spots, perivascular hard exudates, retinal hemorrhages has been found to affect 2.5% [28] to 3.7% [29]to 10% of the lupus patients[9,15,30,31].Previous studies revealed that the most common retinal findings in SLE are cotton-wool spots, hemorrhage, and vascular abnormalities, these lesions occur in 3% to 29% of cases and generally are found late in the disease [15,32,33,34]. Visual field defects was observed in 5 eyes in 3 (2.7%) and 6 eyes in 3 (2.7%) had blurring of vision. Our results were in agreement with that of ***Lin et al.***[35].

The results of the current study also revealed that the SLEDAI score is significantly higher in SLE patients with ocular manifestations than those without ocular manifestations and are more common among patients taking systemic corticosteroids or hydroxychloroquine. In agreement with our results, ***Silpa-Archa et al.*** [8] reported that ocular manifestations are common in SLE and presence of ocular symptoms is correlated to systemic disease activity. Also in agreement with the results of the current study, ***Donnithorne et al.*** [34] found that the ocular manifestations of SLE are often associated with active systemic disease manifesting in other organ systems and suggested that treating the systemic disease may result in improvement of ocular disease. ***Lin et al.*** [35] reported that ocular manifestations among SLE patients were more frequent among patients taking systemic corticosteroids or hydroxychloroquine.

Conclusion

SLE affected the eyes in a significant sector of patients. Ocular manifestations in SLE patients should be taken seriously as they may lead to significant morbidity and visual deterioration. Ocular manifestations denoted the disease activity of the lupus.

References

1. **Manson JJ, Rahman A.** Systemic lupus erythematosus. *Orphanet Journal of Rare Diseases*. 2006;1(1, article 6)

2. **Davies JB, Rao PK.** Ocular manifestations of systemic lupus erythematosus. *Current Opinion in Ophthalmology*. 2008;19(6):512–518.

3. **Peponis V, Kyttaris VC, Tyradellis C, Vergados I, Sitaras NM.** Ocular manifestations of systemic lupus erythematosus: a clinical review. *Lupus*. 2006;15(1):3–12.

4. **Palejwala NV, Walia HS, Yeh S.** Ocular manifestations of systemic lupus erythematosus: a review of the literature. Autoimmune Dis. 2012;2012:290898.

5. **Petri M, Orbai AM, Alarcón GS, et al.** Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum*. 2012 Aug. 64 (8):2677-86

6. **Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH.** Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum. 1992 Jun;35(6):630-40.

7. **Arevalo JF, Lowder CY, Muci-Mendoza R.** Ocular manifestations of systemic lupus erythematosus. *CurrOpinOphthalmol*. 2002 Dec;13 (6):404-10.

8. **Silpa-Archa S, Lee JJ, Foster CS.** Ocular manifestations in systemic lupus erythematosus. *Br J Ophthalmol*. 2015 Apr 22. [Epub ahead of print]

9. **Ohsie LH, Murchison AP, Wojno TH.** Lupus erythematosus profundus masquerading as idiopathic orbital inflammatory syndrome. Orbit. 2012 Jun;31(3):181-3.

10. **Read RW.** Clinical mini-review: systemic lupus erythematosus and the eye. *OculImmunolInflamm*. 2004 Jun;12(2):87-99.

11. **Rao VA, Pandian DG, Kasturi N, Muthukrishanan V, Thappa DM.** A case to illustrate the role of

ophthalmologist in systemic lupus erythematosus. Indian J Dermatol. 2010 Jul-Sep;55(3):268-70.

12. **Sitaula R, Shah DN, Singh D.** The spectrum of ocular involvement in systemic lupus erythematosus in a tertiary eye care center in Nepal. *OculImmunolInflamm*. 2011 Dec;19(6):422-5.

13. **El-Shereef RR, Mohamed AS, Hamdy L.** Ocular manifestation of systemic lupus erythematosus. Rheumatol Int. 2013 Jun;33(6):1637-42.

14. **Wangkaew S, Kasitanon N, Sivasomboon C, Wichainun R, Sukitawut W, Louthrenoo W.**Sicca symptoms in Thai patients with rheumatoid arthritis, systemic lupus erythematosus and scleroderma: a comparison with age-matched controls and correlation with disease variables. *Asian Pacific Journal of Allergy and Immunology*. 2006;24(4):213–221.

15. **Sivaraj RR, Durrani OM, Denniston AK, Murray PI, Gordon C.** Ocular manifestations of systemic lupus erythematosus. Rheumatology (Oxford). 2007 Dec;46(12):1757-62.

16. **Lin H, Li W, Dong N, et al.** Changes in corneal epithelial layer inflammatory cells in aqueous tear-deficient dry eye. *Investigative Ophthalmology & Visual Science*. 2010;51(1):122–128.

17. **Klejnberg T, Moraes Junior HV.** Ophthalmological alterations in outpatients with systemic lupus erythematosus. *Arq Bras Oftalmol*. 2006 Mar-Apr; 69 (2):233-7.

18. **Erras S, Benjilali L, Essaadouni L.** Periorbital edema as initial manifestation of chronic cutaneous lupus erythematosus. Pan Afr Med J. 2012;12:57.

19. **Ghauri AJ, Valenzuela AA, O'Donnell B, Selva D, Madge SN.**Periorbital discoid lupus erythematosus.Ophthalmology. 2012 Oct;119(10):2193-2194.e11.

20. **Gupta T, Beaconsfield M, Rose GE, Verity DH.** Discoid lupus erythematosus of the periorbita: clinical dilemmas, diagnostic delays. Eye (Lond). 2012 Apr;26(4):609-12.

21. **Pandhi D, Singal A, Rohtagi J.** Eyelid involvement in disseminated chronic cutaneous lupus erythematosus. *Indian J DermatolVenereolLeprol*. 2006;72:370–372.

22. **Resch MD, Marsovszky L, Németh J, Bocskai M, Kovács L, Balog A.** Dry eye and corneal langerhans cells in systemic lupus erythematosus. J Ophthalmol. 2015; 2015: 543835.

23. **Mendes LE, Gonçalves JOR, Costa VP, Belfort Junior R.** Ocular alterations in systemic lupus erythematosus. *Arq Bras Oftalmol*. 1998;61(6):713-6.

24. **Alderaan K, Sekicki V, Magder LS, Petri M.** Risk factors for cataracts in systemic lupus erythematosus (SLE). *Rheumatol Int*. 2015 Apr;35(4):701-8.

25. **Soo MP, Chow SK, Tan CT, Nadior N, Yeap SS, Hoh HB.** The spectrum of ocular involvement in patients with systemic lupus erythematosus without ocular symptoms. *Lupus*. 2000;9(7):511-4.

26. **Carli L, Tani C, Querci F, et al.** Analysis of the prevalence of cataracts and glaucoma in systemic lupus erythematosus and evaluation of the rheumatologists' practice for the monitoring of glucocorticoid eye toxicity. *ClinRheumatol*. 2013 Jul;32(7):1071-3.

27. **Fouad A, Hanane M, Mounir B, Rachid Z, Karim R, AbdelberO.**Severe ischemic retinopathy in a patient with systemic lupus erythematosus without antiphospholipid syndrome: A case report. Saudi J Ophthalmol. 2015 Apr-Jun;29(2):169-71.

28. **Sheraj J, Niţescu D (2012).** Ocular manifestations of connective tissue disease. RevistaRomână De Reumatologie. 21:214-217.

29. **Brydak-Godowska J.** Ocular changes and general condition in lupus erythematosus (SLE)--own observation. KlinOczna. 2007;109(1-3):11-4.

30. **Ushiyama O, Ushiyama K, Koarada S, et al.** Retinal disease in patients with systemic lupus erythematosus. *Ann Rheum Dis*. 2000 Sep; 59 (9):705-8.

31. **Hu CL, Peng KL.** Bilateral macular infarction as an ocular manifestation of systemic lupus

erythematosus (SLE). Clin Ophthalmol. 2014 Sep 12;8:1845-8.

32. **Asherson RA, Merry P, Acheson JF, Harris EN, Hughes GV**. Antiphospholipid antibodies: a risk factor for occlusive ocular vascular disease in systemic lupus erythematosus and the 'primary' antiphospholipid syndrome. *Ann Rheum Dis*. 1989;48:358–361.

33. **Zou X, Zhuang Y, Dong F, Zhang F, Chen Y.** Sequential bilateral central retinal artery occlusion as the primary manifestation of systemic lupus erythematosus. *Chin Med J*. 2012;125:1517–1519.

34. **Donnithorne KJ, Read RW, Lowe R, Weiser P, Cron RQ, BeukelmanT.**Retinal vasculitis in two pediatric patients with systemic lupus erythematosus: a case report. *PediatrRheumatol Online J*. 2013 Jun 4;11(1):25.

35. **Lin YC, Wang AG, Yen MY.** Systemic lupus erythematosus-associated optic neuritis: clinical experience and literature review. *Acta Ophthalmol*. 2009 Mar;87(2):204-10.