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Original Article

Ocular manifestations in Egyptian systemic lupus erythematosus patients and their relation with disease activity and anti-phospholipid antibodies

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ABSTRACT

Aim of the work: To identify the ocular manifestations in Egyptian SLE patients and its relation with disease activity and antiphospholipid (aPL) antibodies.

Patients and methods: The study included 100 patients and 30 matched controls. In patients, SLE disease activity index was scored and anti-phospholipids measured. All participants underwent complete ophthalmological examination including assessment of visual acuity, slit-lamp examination to assess anterior chamber and fundus examination to assess retina, choroid and optic disc.

Results: Patients were 86 females and 14 males (F:M 6.1:1) with a mean age of 31.3 ± 12.2 years and disease duration 4.8 ± 4.7 years. 46% had ocular manifestations in the form of dry eye (24%), retinopathy (24%), reduced visual acuity in 17%, redness, ocular headache and glaucoma in 6% each, blurring of vision in 7% and cataract in 3%. Cotton-wool spots were the most common retinal abnormal finding followed by vasculitis, attenuated blood vessels, papilledema and pale optic disc. SLE patients with ocular affection especially retinopathy had significantly higher levels of anticardiolipin antibodies (ACL) IgM (11.9 ± 5.3 vs 9.9 ± 4.1 MPL), lupus anticoagulant (LAC) (41.9 ± 15.1 vs 36.3 ± 11.9 s), disease duration and SLEDAI compared to those without (p = .039, p = .04, p = .02 and p = .026 respectively). SLE patients with severe activity had more retinal affection (35%) than those with moderate (14.8%) and mild (14%) (p = .04).

Conclusions: Ocular affection is frequent in SLE patients. Dry eyes and retinopathy (especially cotton-wool spots) are the most common findings. Anti-phospholipids (ACLIgM and LAC), active disease and disease duration are significantly related to eye affection especially retinopathy among SLE patients.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune connective tissue disease that can affect multiple organ systems with a relapsing and remitting clinical course. It can affect the skin, joints, kidneys, eye, brain and other organs [1].

Anti-phospholipid (aPL) antibodies are prothrombotic in SLE patients with an increased risk of development of premature atherosclerosis [2], dyslipidemia [3] and renal involvement [4]. Moreover, increased anti-double stranded deoxyribonucleic acid (anti-dsDNA) was related to the presence of secondary anti-phospholipid (APL) syndrome [5].

Ocular involvement is moderately common in SLE and can be vision threatening. Findings may include abnormalities of the eyelid, ocular adnexa, keratoconjunctivitis sicca, iridocyclitis, retinal vasculitis, vaso-occlusive disorder, choroidopathy and optic neuropathy. Keratoconjunctivitis sicca is the most common manifestation while retinal and choroidal involvements are most associated with visual loss [6]. Orbital involvement is a rare manifestation of SLE. Vasculitis, myositis, and panniculitis have all been described. Signs and symptoms include proptosis, enophthalmos, orbital pain, blurred vision, chemosis, and restriction of extraocular movements [7]. Typical lesions of discoid lupus erythematosus are slightly raised, scaly, and atrophic rarely affecting the eyelids. Episcleritis is generally a benign inflammation of the episclera and typically occurring in young females with incidence 2.4% in SLE patients [8]. Corneal epitheliopathy, scarring, ulceration and filamentary keratitis can all occur secondary to keratoconjunctivitis sicca. More rare corneal complications include peripheral ulcerative keratitis [9], which can be a marker of active systemic vasculitis, interstitial keratitis, and keratoendothelitis [10]. Lupus retinopathy is one

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of the most common vision-threatening complications of SLE with an incidence of up to 29% in patients with active systemic disease. A strong correlation exists between presence of retinopathy and central nervous system (CNS) disease [11]. Ocular manifestations were reported in another study on Egyptian SLE patients with symptomatic dry eyes being the most frequent in almost a third of the cases [12].

In this study we aimed to identify the ocular manifestations in Egyptian SLE patients and its relation with disease activity and antiphospholipid (aPL) antibodies.

2. Patients and methods

One hundred SLE patients were randomly recruited from the Rheumatology outpatient clinic and Internal Medicine Department inpatients–Rheumatology division, Ain Shams University Hospitals and enrolled in this cross-sectional case control study. All patients fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE [13]. 30 age and sex matched healthy controls were also included. Patients with diabetes mellitus, hypertension and other rheumatologic disease were excluded from the study. Patients were recruited from April 2016 to March 2017. An informed consent was obtained from each participant after explanation of the study aim and procedures. Study protocol gained approval of local ethical committee of Ain Shams University.

All patients were subjected to detailed medical history taking emphasizing on SLE symptoms including constitutional, mucocutaneous, musculoskeletal, cardiopulmonary, renal, neuro-psychiatric and ocular. Thorough clinical examination was performed with assessment of the SLE disease activity index (SLEDAI) [14]. Patients were further classified according to the SLEDAI score into: mild activity (score 1–5), moderate activity (6–10) and severe activity (> 10). Routine biochemistry tests were collected from patients' records. Complete blood count (CBC) and the erythrocyte sedimentation rate (ESR) (1st h) were assessed. Complete urine analysis, Protein/creatinine ratio (P/C) and 24-h urinary proteins were investigated. Imunological tests performed included the assessment of the antinuclear antibody (ANA), anti-dsDNA titre (indirect immunofluorescence) and complement C3 and C4 (turbitimer). Antiphospholipids including anticardiolipin (ACL) IgG/IgM using indirect phase enzyme linked immunosorbent assay and lupus anticoagulant (LAC) were investigated.

All participants underwent complete ophthalmological examination including assessment of visual acuity, slit-lamp examination to assess anterior chamber and fundus examination to assess retina, choroid and optic disc. The ophthalmological examination was done in the ophthalmology outpatient clinic, Ain Shams University Hospitals.

Statistical Analysis: Data were entered to the Statistical Package for Social Science (SPSS) version 20. Qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges. The comparison between 2 groups with qualitative data were done using Chi-square test and Fisher exact test was used when the expected count in any cell was < 5. The comparison between 2 quantitative data with parametric distribution was done using Independent *t*-test. P-value < .05 was considered significant.

3. Results

This study was performed on 100 SLE patients and 30 controls. Patients were 86 females and 14 males (F:M 6.1:1) with a mean age of 31.3 ± 12.2 years (18–61 years) and disease duration 4.8 ± 4.7 years (1–20 years). The control were gender (24 females and 6 males; F:M 6:1) and age (30.5 ± 11.9 years; 17–55 years) matched.

Among SLE patients, 90% had constitutional symptoms (fever, weight loss, fatigue), 78% with mucocutaneous manifestations (malar rash, photosensitivity, oral ulcers, alopecia and discoid lupus), 75% with musculoskeletal affection (arthralgia, arthritis, fibromyalgia and myositis), 41% with renal involvement (haematuria, proteinuria, puffiness of the eye lids, lower limb edema, hypertension), 21% with cardiopulmonary manifestations (dyspnea, chest pain, palpitation, cough and expectoration) while neuropsychiatric symptoms (headache, seizures, mononeuritis, psychosis) were the least common being 11%. Laboratory investigations are presented in Table 1. The mean SLEDAI was 9.7 ± 5.2 (2–21): 45% had severe activity, 27% moderate and 28% mild.

Table 1
Laboratory investigations in systemic lupus erythematosus patients.

Parameter mean ± SD (range)/n(%)	SLE patients (n = 100)	
WBCs (10^3/uL)	5.86 ± 3.14	(1.9–19.4)
Lymphocytes (10^3/uL)	1.25 ± 0.56	(0.4–2.1)
Neutrophils (10^3/uL)	4.39 ± 2.79	(0.9–17.4)
Haemoglobin (g/dl)	9.47 ± 1.65	(6.5–13.1)
Platelet (10^3/uL)	234.04 ± 97.68	(20–552)
ESR (mm/1st h)	67.61 ± 30.63	(10–150)
Serum creatinine (mg/dl)	1.05 ± 0.83	(0.3–6.6)
C3 (mg/dl)	73.67 ± 31.75	(8–135)
C4 (mg/dl)	13.53 ± 5.81	(2.7–33)
ACL IgG (GPL)	24.17 ± 8.74	(13–46)
ACL IgM(MPL)	10.83 ± 4.76	(5 −23)
LAC (seconds)	38.89 ± 13.73	(19–101)
Urine analysis		
Albuminuria	71 (71)	
Granular casts	14 (14)	
Hyaline casts	12 (12)	
RBCs	6.1 ± 14.8 (1–100)	
Pus cells	10.6 ± 12.9 (1 −57)	
Protein/creatinine ratio	1.2 ± 1.8 (0.03–8.9)	
Proteinuria (mg/24hrs)	1195.7 ± 1414.9 (90–7080)	

WBC: white blood cells, ESR: Erythrocyte sedimentation rate. C: Complement, ACL: anticardiolipin, LAC: lupus anticoagulant.

Ocular manifestations were present in 46% of the patients. The ocular symptoms and signs in the SLE patients are presented in Table 2. Cotton-wool spots was the most common retinal finding (10/24; 41.7%) among SLE patients while other findings as vasculitis, attenuated blood vessels, papilledema and pale optic disc were rare with each found in only 3 patients, 2 had dot-shaped haemorrhages and 1 flame-shaped haemorrhages. 17% of the patients had reduced visual acuity; 3 due to cataract (2 males and 1 female) and 14 due to retinopathy. 6 (6%) SLE patients (4 females and 2 males) had elevated intra-ocular pressure. Comparing the clinical manifestations and laboratory investigations between SLE patients with and without ocular affection are presented in Table 3. Granular casts in urine were significantly increased in those

Table 2
Ocular symptoms and findings in systemic lupus erythematosus patients.

Parameter n(%)	SLE patients (n = 100)	
Ocular symptoms		
Dry eye	24	(24)
Redness	8	(8)
Blurred vision	8	(8)
Ocular headache	6	(6)
Eye examination		
Anterior chamber		
Elevated IOP	6	(6)
Cornea	0	(0)
Sclera	0	(0)
Cataract	3	(3)
Posterior chamber		
Choroid	0	(0)
Optic Nerve	0	(0)
Retina	24	(24)
Reduced VA	17	(17)

VA: visual acuity.