Original Article

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Ocular Manifestation in Rheumatoid Arthritis Patients Presenting to Tertiary Care Hospital in South India: A Prospective Study

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Abstract

Introduction: Rheumatoid arthritis (RA) is a systemic inflammatory disease, which is usually associated with a number of extra-articular manifestations, such as pericarditis, pleuritis, major cutaneous vacuities, Felty's syndrome, neuropathy, ocular manifestations, glomerulonephritis, and other types of vacuities.

Aim of the Study: To study the prevalence of ocular manifestations in patients with RA and find out the ocular complications of the routine drug therapy followed to treat RA.

Methods: This is a 1 year prospective clinical study of 50 RA patients, who have attended Ophthalmology Department in Chettinad Hospital and Research Institute. Ocular examination included best corrected visual acuity, color vision, detailed slit lamp and fundus examination, refraction, intraocular pressure measurement, and tests for dry eyes.

Results: About 85% were female patients and 15% male patients. Steroid toxicity in the form of posterior sub capsular cataract was seen in five patients. Chloroquine was used in six patients, out of which one patient developed cornea verticillata and another patient developed bull's eye maculopathy. Ocular manifestations of RA was seen in 32 patients out of which the most common was dry eyes followed by scleritis, episcleritis, iridocyclitis, and secondary glaucoma.

Conclusion: More than half of the patients had ocular manifestations, out of which dry eye was the most common manifestation (90%). The drugs commonly associated with complications are corticosteroids, chloroquine, and hydroxychloroquine. Thus, a regular ophthalmologic evaluation should be done in all RA patients even though they are asymptomatic to ensure early identification of ocular involvement and thus to help alleviate the problems of visual impairment and blindness.

Key words: Chloroquine, Glaucoma, Keratoconjunctivitis, Rheumatoid arthritis, Scleritis

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune systemic disease characterized by a symmetrical, destructive, deforming, inflammatory polyarthropathy, in association with a spectrum of extra articular manifestations and circulating antiglobulin antibodies, termed rheumatoid factors (RF).

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The extra articular manifestation includes epericarditis, pleuritis, major cutaneous vacuities, Felty's syndrome, neuropathy, ocular manifestations, glomerulonephritis, and other types of vasculitis.[1,2] The etiopathogenesis of this autoimmune disorder is still unknown. There are many different theories but not proven yet.[3] Extra-articular manifestation in RA are a more common in seropositive patients.[4]

Ocular manifestations seen in RA patients are keratoconjunctivitis sicca (KCS), episcleritis, scleritis, corneal changes, retinal vacuities, and secondary glaucoma. Sjogren first coined the term KCS to describe the tear deficiency as a result of auto immune damage to the lacrimal gland. Dry eye is the most common ophthalmic

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manifestation of RA, with a reported prevalence of 15-25%. Dry eyes due to RA are classified as secondary Sjogren's syndrome.[5]

Episcleritis is sudden in onset and patient complains of discomfort rather than pain. Attacks last 1-2 weeks and are self-limited but recur at intervals of 1-3 months. The prevalence of episcleritis in RA is reported to be about 0.17% and in patients who present to ophthalmology clinic with episcleritis, about 5.6% have RA. Episcleritis could be simple or nodular. About the one-third are bilateral. Treatment of episcleritis is usually unnecessary but in patients with significant discomfort lubricant and topical nonsteroidal agents may be helpful. For recurrent or severe bouts, oral nonsteroidal agents are the preferred therapeutic modality.[6]

Scleritis in RA is associated with a more ominous prognosis than episcleritis. RA is the most common systemic condition associated with scleritis. Patients complain of insidious onset of a deep, boring pain which may radiate to forehead or jaw. Active scleritis involves inflammation of the deep episcleral layer associated with scleral edema. It tends to be bilateral in patients with RA diffuse anterior scleritis is the most common form of scleritis. Nodular scleritis is characterized by firm foci of inflammation which are tender. On involution of the nodules thinning of underlying sclera may occur. Necrotizing scleritis without inflammation also called scleromalacia perforans is characterized by severe thinning of sclera in an otherwise clinically uninflammed painless eye. Necrotizing scleritis is usually associated with wide spread visceral involvement which is associated with high mortality. Hence, the ophthalmologist and rheumatologist should collaborate in the urgent and long-term care of these patients.[7]

Posterior scleritis is often misdiagnosed. It presents as severe orbital pain, proptosis, limited extraocular movement, and uveitis. Decrease in visual activity is dependent on the degree of retinal and choroidal involvement. Ultrasonography is often required for confirmation of the diagnosis.[8]

Involvement of eye in RA can cause severe disability sometimes even blindness.[9] Beside the disease, disease-modifying antirheumatic drugs (DMARDs) particularly chloroquine can also affect vision by deposition over the macula and cornea.

It is important for early diagnosis of RA and send to ophthalmologist for timely intervention and prevent sight threatening complications. The primary physicians need to be aware of these ocular disorders so as to provide appropriate referrals to the ophthalmologist as soon as ocular morbidity is suspected. Conversely, it is critical that ophthalmologists recognize that ocular problems in patients with RA are often indicative of active or ongoing systemic disease.

The objective of the study is to study the prevalence of ocular manifestations in patients with RA and find out the ocular complications of the routine drug therapy followed to treat RA.

METHODS

This is a 1 year prospective clinical study of 50 RA patients who have attended Ophthalmology Department in Chettinad Hospital and Research Institute. Patients of RA attending ophthalmology outpatient department for evaluation of ocular disease and clearance for treatment protocols were included in the study. Patients with juvenile RA (<16 years of age). Dry eyes due to other diseases such as Steven-Johnson syndrome, ocular cicatricial pemphigoid, and chemical injuries, patients with diabetes mellitus, uveitis, scleritis, glaucoma due to causes other than RA were excluded from the study.

History

The demographic details of the patients were recorded. In all cases, a detailed history pertaining to duration of RA, systemic manifestations of RA, drug use and duration of treatment, family history of RA and symptoms pertaining to ocular manifestations were sought.

Ocular Examination

Ocular examination was done to evaluate for the various ocular manifestation like dry eyes KCS, scleritis, episcleritis, peripheral ulcerative keratitis, anterior uveitis and also for ocular complications of systemic treatment. It included best corrected visual acuity, testing for color vision, Amsler's grid, detailed slit lamp examination of anterior segment, detailed fundus examination, refraction, intraocular pressure measurement, and tests for dry eyes. Visual fields and B-scan if necessary were performed.

Tear function tests/dry eye tests included tear break up time (TBUT) and basal Schirmer's test. TBUT was measured as follows: Fluorescein dye was instilled in to the lower fornix, patient was asked to blink several times, tear film was examined with a broad beam and cobalt blue filter, the time interval for the appearance of black spot in the fluorescein stained film indicating the formation of dry areas was noted. TBUT <10 s was considered abnormal (Figure 1).

Basal Schirmer's test was performed using Schimer strips of 35 mm in length and 5 mm in width. After instilling local anesthetic drops (proparacaine), the eyes were gently

dried of excess tears. The Schirmer strip was folded 5 mm from one end and inserted at the junction of the middle and outer third of the lower lid taking care not to touch the cornea. The patient was asked to keep the eyes gently closed. After 5 min, the strip was removed and the amount of wetting from the fold measured. Value of <10 mm at the end of 5 min was considered abnormal (Figure 2).

RESULTS

Among 50 cases included in the study, the number of females were 40 (80%) and males were 10 (20%) In the study, female were predominant as compared to males (Figure 3).

The majority of patients included in the study were in age group of the fifth decade. 20 patients were between 51 and 60 years and <5 patients were seen in <30 years age group. 14 patients were seen in the fourth decade (Figure 4).

Majority of patients in our study had RA for around 1-5 years and only 4 patients had disease for more than 10 years. Hence, only severe sight threatening complications were less in our study (Table 1).

Among total 50 cases of arthritis patients 32 (64%) cases showed ocular involvement. Out of those 32 cases, only 10 had ocular symptoms while 22 were asymptomatic. Patients with episcleritis, scleritis and iridocyclitis were symptomatic.

Among 32 cases with ocular involvement the most common ocular manifestation was dry eye (mild, moderate, and severe forms) followed by episcleritis, scleritis, iridoccyclitis, corneal ulcers, conjunctivitis, and glaucoma (Table 2).

Table 1: Duration of the disease

Duration of disease (years)	Number of patients
<1	7
1-5	21
5-10	18
More than 10	4

Table 2: Ocular manifestation of RA

Manifestation	Number of patients
Dry eyes	27
Scleritis	1
Episcleritis	2
Iridocyclitis	1
Secondary glaucoma	2
Corneal opacity	1
Total	32

RA: Rheumatoid arthritis

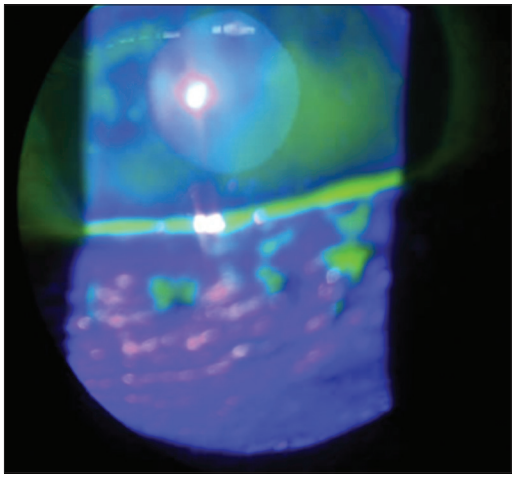

Figure 1: Tear break up time

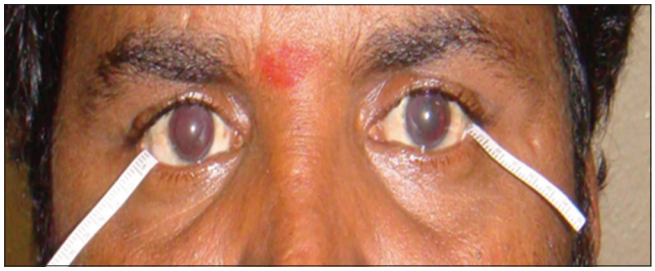

Figure 2: Schirmer's test done in dry eye patient

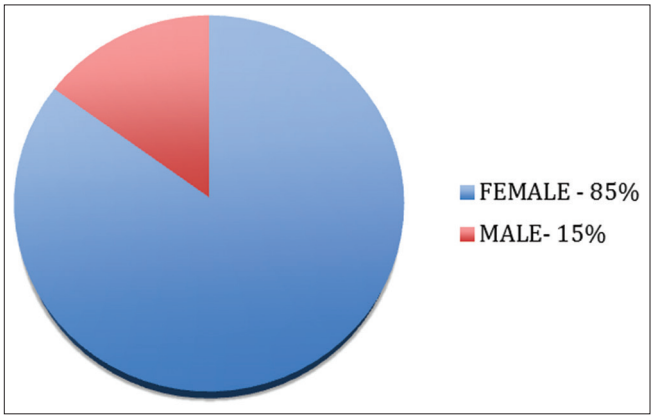

Figure 3: Gender predisposition

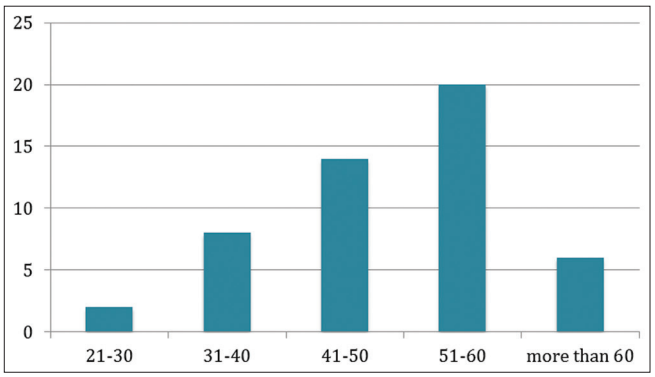

Figure 4: Age group

The complication related to use of drugs for RA also was seen. The patients with RA were commonly using DMARDS, chloroquine, hydroxychloroquine, steroids, nonsteroidal anti-inflammatory drugs, and biological.

Five patients who were on steroids had posterior subcapsular cataract. Steroid induced glaucoma was not seen in our study. Chloroquine was used in six patients, out of which one patient developed cornea verticillata and another patient developed bulls eye maculopathy (Figures 5 and 6). Both the patients were using chloroquine for a more than 8 years without any follow-up or ophthalmological evaluation.

DISCUSSION

RA is usually a more common in women with a ratio of 3:1 and disease onset is in the fourth and fifth decades. In our study, also females were affected more than males.

Reddy *et al.*, study shows that 13 out of 100 patients of RA 39% were found to have eye involvement.[10] The prevalence of different ocular manifestations in this arthritis has been reported differently in different studies. The result of the present study showed 32 (64%) cases out of 50 with ocular involvement. Many of the patients with ocular findings did not have ocular complaint and was detected by routine checkup. Out of 32 cases with ocular involvement 32% cases had symptom while the previous study showed only 37.28% complained of ocular symptom.

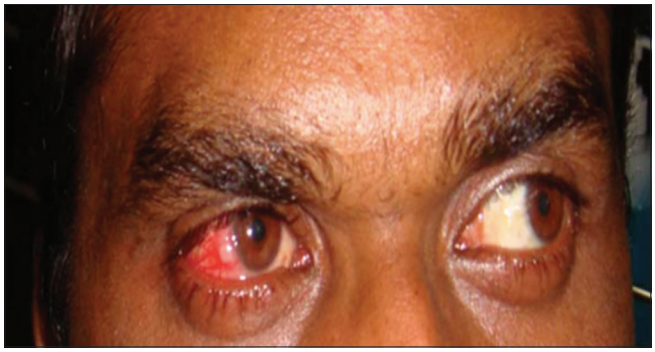

Figure 5: Nodular episleritis in one patient

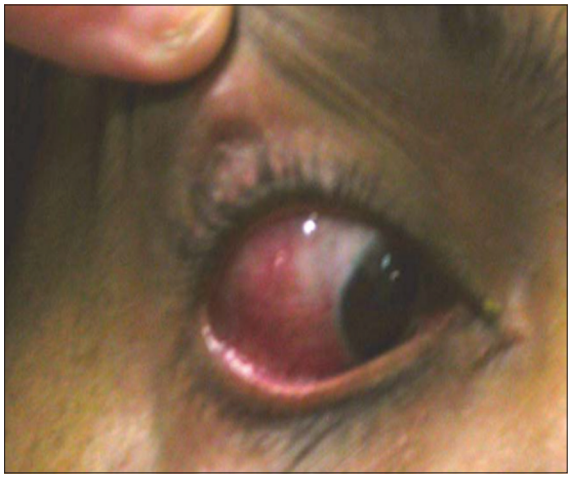

Figure 6: Anterior scleritis in one patient

Moss *et al.*, studied 3,722 individuals and found that 14.4% of patients had dry eyes.[11] Females had more incidence of dry eye (16.7%) compared to males (11.4%). They concluded that the risk factor for developing dry eye was arthritis which was followed by gout. In our study, the most common ocular manifestation was dry eye 44% (22 cases), followed by episcleritis, scleritis and corneal ulcer, viral keratitis, and conjunctivitis.

RA is seen a more common in fourth and fifth decades. Our study showed that majority of the patients with RA was in their fifth decades which comprised 40% (20 cases) with female predominance 4:1. Among 32 cases of RA with ocular involvement, the highest incidence of ocular manifestation was also seen in the fifth decade.

KCS or dry eye is the most common ocular manifestation of RA with reported prevalence of 15-25%.

Watson and Hayreh did a 10 years study of 207 episcleritis and 159 scleritis patients.[12,13] RA was seen in 28 patients in there study group. Seven had out episcleritis, eight with diffuse anterior scleritis, four with nodular anterior scleritis, three with necrotizing scleritis, and six with scleromalacia perforans.

Jabs *et al.*, studied 134 patients with scleral inflammation over a 12-year period.[14] 134 patients were studied and 37 patients had episcleritis and 97 had scleritis. Systemic rheumatic disease was seen in 30% with episleritis and 39.2% with scleritis. The rheumatic disease most common associated with scleral inflammation was RA.

In our study, 32 patients had ocular involvement and in that 4 had episcleritis and 2 had scleritis. Necrotizing scleritis with inflammation and scleromalacia perforans were not seen in our study as these complicated conditions were found in patients with long duration of arthritis with severe forms and in long term untreated cases.

McGavin *et al.*, did a study on 4210 patients with RA and results showed that 7 patients had episcleritis 28 patients had scleritis.[15] Similarly, they found co-existent posterior scleritis was more common in rheumatoid scleritis (22.2%) than in nonrheumatoid scleritis (5.6%). Our study revealed that among 32 RA

patients with ocular manifestation only five (20%) had anterior uveitis but band shaped keratopathy was not noted along with it.

Cases of glaucoma secondary to scleritis and episcleritis have been reported in different studies. In our study secondary glaucoma due to uveitis was noticed in two patients with RA.[16] RF was negative in 22 (44%) of patients with juvenile RA.

Most of the patients of RA patient referred to us were mainly to rule out chloroquine toxicity.

Steroid toxicity in the form of posterior sub capsular cataract was seen in five patients. Chloroquine was used in six patients, out of which one patient developed cornea verticillata and another patient developed bulls eye maculopathy (Figure 7 and 8). Both the patients were using chloroquine for more than 8 years without any follow-up or ophthalmological evaluation. If the cumulative dosage of chloroquine exceeds more than 300 g over period of 5-year, then chances of ocular complications are more.[17] Same thing holds good for hydroxychloroquine use for more than 7 years, dose more than 6.5 mg/kg/dose with cumulative dose more than 1000 g can lead to complications.[18]

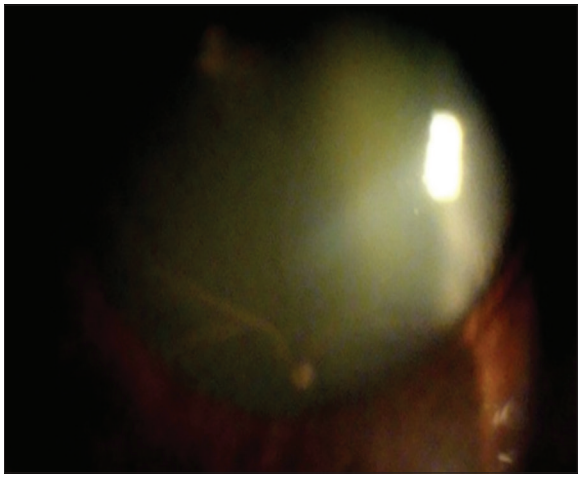

Figure 7: Cornea verticillata in one patient

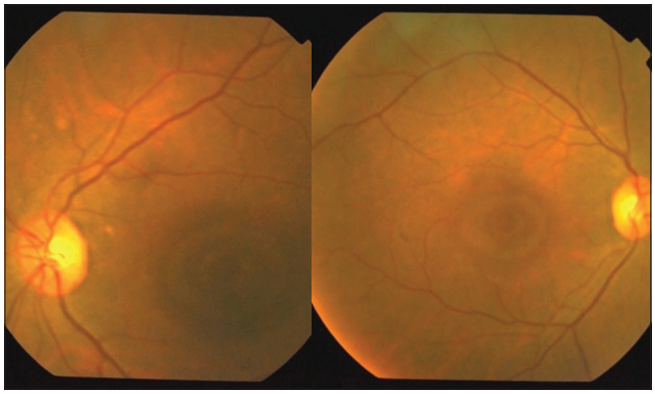

Figure 8: Bulls eye maculopathy

CONCLUSION

Ocular manifestations are common. More than half of the patients (52%) had ocular manifestations, out of which dry eye was the most common manifestation (90%).

Dry eyes are directly related to duration of disease than the severity. Routine Schirmer's test and Rose Bengal staining help to detect the early onset of dry eye syndrome in patients with RA and start treatment. Ocular complications associated with the systemic treatment of RA are well-known. The drugs commonly associated with these complications are corticosteroids, chloroquine, and hydroxychloroquine.

Thus, regular ophthalmologic evaluation should be done in all patients even though they are asymptomatic to ensure early identification of ocular involvement and thus to help alleviate the problems of visual impairment and blindness.

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