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CLINICAL PATTERN OF OCULAR INVOLVEMENT IN INFLAMMATORY RHEUMATIC DISEASE IN A TERTIARY, REFERRAL MULTISPECIALITY HOSPITAL

Medicine

Prof. Radha Annamalai* DO, DNB, FICO, Ph. D. Professor of Ophthalmology, Sri Ramachandra University, Chennai, India. *Corresponding Author

Dr. Harika Velumani MBBS, Post graduate- M.S Ophthalmology, Sri Ramachandra University, Chennai, India

Prof. M. Muthayya M.S., Professor of Ophthalmology, Sri Ramachandra University, Chennai, India

ABSTRACT

Introduction: Ocular inflammation and uveitis is a common feature of rheumatic diseases and can cause visual morbidity. A common immunological mechanism can result in eye involvement and blindness can occur due to ophthalmic involvement if not treated promptly.

Materials and methods: This is a prospective study on 100 patients performed over two years. Patients with rheumatic disease were evaluated for ocular inflammation at the Ophthalmology clinic in Sri Ramachandra University, Chennai. Angiography, complete blood count, X-ray and serological markers of connective tissue disorders were done. Patients were treated with steroids and immunosuppressive agents.

Results: Among 100 patients with rheumatic disease, ocular inflammation occurred in 69% with p=0.02. The types of ocular involvement were Kerato Conjunctivitis Sicca (KCS) in 42%, uveitis in 19%, episcleritis in 23%, scleritis 9% in and retinal vasculitis in 5%. The most common disease with ocular association was rheumatoid arthritis. Visual loss occurred during the acute stage of uveitis or its complications and due to side effects of medications taken to treat systemic rheumatic disease.

Conclusion: The association between rheumatologic disorders and ocular inflammation requires ophthalmic evaluation to prevent complications and blindness.

KEYWORDS

Uveitis, Rheumatologic Diseases, Ocular Inflammation, Scleritis, Kerato Conjunctivitis Sicca.

Introduction

Ophthalmic features and their complications due to inflammatory rheumatic diseases can result in visual morbidity. Uveitis can occur as part of a systemic infection, autoimmune disease or be an isolated ocular inflammation. Other less frequent causes are trauma, intraocular tumours and medications. It has been reported that, in adults, HLA- B27 associated spondyloarthropathies, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are the most common causes of rheumatic diseases causing uveitis[1]. In children, juvenile idioapathic arthritis (JIA) and childhood sarcoidosis also called as Blau syndrome[2] are important differential diagnosis to consider. The clinical signs of uveitis are similar in various etiologies and it is important to distinguish infection from autoimmune disease as treatment is entirely different in the two entities. A thorough diagnostic workup is required to distinguish the cause as precise management with specific antimicrobials or corticosteroids (CS) are required to prevent complications and visual morbidity.

Extensive studies on rheumatic disease have reported that an association with uveitis is seen in 40 – 50% of uveitis [3]. HLA B27 associated seronegative spondyloarthropathy is the most common cause for uveitis[4]. Rheumatoid arthritis, SLE, relapsing polychondritis and granulomatosis with polyangitis (Wegener's) are associated with scleritis more commonly than uveitis [5]. After detection of uveitis in these patients immediate management is required as the inflammation is chronic in nature and recurrent which can cause blinding complications due to inflammation or long term steroids used in treatment. Vision threatening complications can occur during the active and healed stages of uveitis. It has been reported that ocular features and complications occur in 25% of patients with rheumatoid arthritis [6] where the common features of inflammation are keratoconjunctivitis sicca (KCS), uveitis and scleritis. The ocular manifestations with B27 associated disease is predominantly anterior uveitis and is different from rheumatoid arthritis where scleritis and PUK are the main clinical features [7].

Aim

The aim of this study was to define the incidence of uveitis and ocular inflammation in patients with rheumatic disease. The secondary objective was to detect the association between ocular and systemic disease, to identify the most common cause, clinical features, ocular complications in rheumatic diseases and their response to systemic and topical treatment.

Methods

This is a prospective study conducted on 100 patients over a 2 year period and was done in concurrence with the departments of internal medicine rheumatology and paediatrics at Sri Ramachandra University, Chennai, India, a multispeciality tertiary medical centre. Patients were enrolled into the study after obtaining institutional ethics committee approval and informed consent was obtained from all the patients. All patients who attended the rheumatology clinic were evaluated in the department of ophthalmology to look for the evidence of ocular inflammation. Patients with signs suggestive of or proven rheumatic disease with symptoms of ocular involvement such as defective vision, pain, redness and photophobia were included in the study. Exclusion criteria were those who had a proven aetiology of infectious disease process as the cause of uveitis. A detailed and relevant history was obtained from all patients with regard to race, ethnicity, history of past rheumatic disease, previous and present ocular complaints, other co- existing systemic diseases, treatment and immune state. Clinical examinations included visual acuity , intra ocular pressure by applanation tonometry, slit lamp examination, indirect ophthalmoscopy, biomicroscopy using + 78D lens and Shirmer' s test to measure tear film secretion. Systemic investigations were performed based on the underlying autoimmune disease suspected and to rule out infections. Complete blood count, erythrocyte sedimentation rate, (ESR), C-reactive protein (CRP), HLA-B27, rheumatoid factor, angiotensin converting enzyme (ACE) levels, anti-nuclear antibody (ANA) , C- ANCA, P- ANCA, x ray chest and polymerase chain reaction (PCR) were done as directed by clinical guidelines. The Standardization of Uveitis Nomenclature (SUN) of the International Uveitis Study Group[8] was followed during the initial visit to grade the activity of uveitis and during review to look for progress or worsening. The American College of Rheumatology criteria were used by the rheumatologists in our hospital to examine and classify the rheumatic disease. Chi- square test and SPSS software were used for statistical analysis. A $p < 0.05$ was considered as statistically significant.

In addition to the routine laboratory tests, ultrasound and radiological investigations were done after opinion from the treating physician was sought. Fundus photography, fundus fluorescein angiography (FFA), indocyanine green angiography (ICG), B scan ultrasonography and optical coherence tomography (OCT) were the ophthalmic procedures performed. Blood or ocular tissue such as aqueous, vitreous or rarely chorioretinal tissue was used as the sample for analysis when required.

Management comprised of topical or systemic corticosteroids (CS) and immunosuppressive (IS) agents either as a single or combined treatment. Intravenous drug administration was done in some of our patients with macular involvement where vision was threatened or in patients with recalcitrant uveitis. Patients were started on treatment only after investigations had been done to rule out infection and the most common IS drug used was azathioprine or mycophenolate mofetil along with tablet wysolone in the initial stage of treatment. The duration of treatment with IS drugs was based on response seen as a decrease in the activity of uveitis, resolution of clinical signs, improvement of ocular and systemic features. Other drugs that are being used are TNF alpha inhibitors [9], interferons , cyclophosphamide.

Patients with anterior uveitis and scleritis were treated with topical cycloplegic, non- steroidal or corticosteroid eye drops. In some patients who developed posterior segment features such as vasculitis or vascular occlusions secondary to rheumatic disease laser photocoagulation was done. During each follow up visit the patients were monitored for side effects of drugs and consultation was sought from the physician and rheumatologist regarding systemic disease.
The time of review differed for each patient and depended on the extent of inflammation, vision, development of ocular complications such as posterior subcapsular cataract, secondary glaucoma, uveitic cystoid macular oedema, vasculitis and neovascularisation. Side effects of CS such as steroid induce cataract, glaucoma, hypertension, worsening of diabetes, unmasking of systemic infections, osteoporosis and electrolyte disturbances were looked for and if present treated appropriately.

RESULTS

100 patients with rheumatic disease were evaluated for features of ocular inflammation over 2 years. They were evaluated in the department of ophthalmology with a minimum follow up of one year. During each visit opinions were obtained from the rheumatologist and infectious disease specialist.

Ocular involvement was seen in 69% of our patients in varying forms which was statistically significant with p= 0.02. Among those with ophthalmic features, there were 39 males and 61 females. Bilateral involvement was more common and was seen in 67% of patients. Age group affected was predominantly between the 4th and 6th decades of life. A smaller group of 12 patients with paediatric uveitis was seen in our study population. All of them were in their 1st decade and the only eye sign was uveitis. 63% had ocular complaints ,the most common of which was redness and conjunctival congestion. Defective vision was present only in uveitis. 18% had acute loss of vision due to uveitis or macular involvement. Some patients complained of floaters which we thought was because of vitritis.

Table 1 Ocular association of rheumatic disease in our patients

KSC	42%
Episcleritis	23%
Uveitis	19%
Retinal Vasculitis	5%
Scleritis	9%

Among our study patients, KCS was present in 42%, episcleritis in 23%, uveitis in 19%, retinal vasculitis in 5% and scleritis in 9%. Ocular features were most frequently seen in RA (61%). Incidence was 20 % in SLE, 12% in JIA and 7 % in HLA B27 spondyloarthropathy.

Table 2 Incidence of rheumatic disease with visual morbidity

Rheumatoid Arthritis	61%
SLE	20%
JIA	12%
HLA-B27	7%

In our study, the most frequent rheumatic disease which caused uveitis included HLA B27 associated spondyloarthropathy in 33%, systemic lupus erythematosus (SLE) in 18%, juvenile idiopathic arthritis in 12%, and Blau syndrome in 1%. Among those with positive B27, ankylosing spondylitis in 9%, IBD in 3% and psoriasis in 2%. The age of onset of uveitis was found to be earlier in those with rheumatic disease than in those with uveitis due to non- rheumatic etiology. Severe hypopyon with anterior uveitis (Figure 1) with spill over inflammation and vitritis was seen in 12% of HLA B27 positive patients. Recurrence of uveitis was most commonly seen in 12% of SLE and 5% of ankylosing spondylitis and bilateral uveitis in 57% of our patients. Visual loss occurred in 15% and was most frequently due to acute anterior uveitis and retinal vasculitis but was reversible with systemic steroids or IS therapy. .

Episcleritis was seen in 23%. Patients with scleritis were seen in 32% of RA, 12% of SLE. Diffuse anterior scleritis was more common than nodular scleritis. Posterior scleritis was present in 3% of patients and required oral corticosteroids. One patient required intravenous methyl prednisolone in the dose of 1mg per kg body weight. This was administered in the ICU set up after checking for BP, blood sugar and underlying infections which can flare up with large doses of corticosteroids.

Investigations performed showed an elevated ESR and lymphocyte count in 81% and an elevated CRP in 57%. ANA was detected in 45% of patients. In 11 patients with seemingly mild joint involvement where they had not yet met the rheumatologist, ocular evaluation helped suspect rheumatic disease that was not symptomatic as yet. When ophthalmic signs precede joint disease, ocular exam is crucial as it helps detect a more serious underlying disease before joint deformities can set in.

CT was performed in two patients with gout and recalcitrant uveitis before a diagnosis could be made with certainty. Ocular fluid analysis by PCR was done for 7 % of patients due to suspicion of TB uveitis before starting them on oral corticosteroids as they did not respond to topical management.

Treatment was with CS and IS. The most common IS that we used for uveitis was azathioprine in 37% of patients. CS alone produced good clinical response the majority. Combination of CS and IS was required in 27%. Mycophenolate mofetil was the main drug used in scleritis.

Improvement of vision was noted in 78% of our patients. Response to treatment with CS was seen as a decrease in inflammation. In 12% vision loss was irreversible because of complications.

Discussion

Ocular features of rheumatic diseases can be varied and are commonly detected. In our study population conducted over two years in patients with rheumatic diseases we found an association of 69% which was statistically significant. Evaluation to identify the ocular features and manifestations showed that the anterior segment of the eye was affected in many ways, the most common causes being KCS, episcleritis and scleritis. Uveitis and vasculitis were less frequent. Retinal vasculitis was the only form of posterior segment involvement and was seen in very few patients in a mild form. Visual loss in almost all patients was due to uveitis during both the active and healed stages of the disease. The most common rheumatic disorders associated with ocular inflammation was rheumatoid arthritis. Scleritis was mostly of the anterior diffuse type and had waxing and waning episodes with a direct correlation to extent of systemic disease.

Uveitis was mostly due to HLA B 27 associated seronegative spondyloarthropathy. Recurrent and bilateral anterior uveitis seemed to predict active and severe systemic joint disease. Psoraiatic arthritis and inflammatory bowel disease (IBD) which are subsets of seronegative spondyloarthropathies are known to have a more varied form of uveitis. Psoriatic arthropathy associated uveitis was seen in our patients and was more mild and chronic as opposed to acute severe uveitis of other HLA B27 positive entities.

Causes of visual loss due to uveitis was acute inflammation and macular oedema in HLA B27 related disease. Ankylosing spondylitis and scleroderma were rare in our population. Only one patient in our study had scleroderma with chronic uveitis. She had associated eyelid involvement with periorbital pigmentation and KCS.

SLE was a frequent cause of visual loss in our patients. KCS was the most common feature but was very responsive to topical tear substitutes and lubricants. Episcleritis and retinal vasculitis were also common. SLE requires enormous attention during initial screening, active disease, throughout medication course and even after treatment as the eye can get affected in many ways [10]. Hypertension is known to be present in SLE secondary to renal involvement. Many of our SLE patients showed features of hypertensive retinopathy which by itself can cause ocular complications such as retinal vascular occlusions, papilloedema, ischemic optic neuropathy and vitreous haemorrhage all of lead to blindness if not treated early.

The most common symptom was pain or redness. Defective vision was present symptom only in uveitis and retinal vasculitis with macular involvement. Congestion was seen in patients with conjunctivitis, scleritis and uveitis. Conjunctivitis was due to immunological imbalance or underlying rheumatological disorders and was not infective in nature. Scleritis was more common than episcleritis and was mostly due to rheumatoid arthritis (Figure 2).

Another important part of ocular examination in these patients is the detection of ocular complications due to the side effects of medications used to treat rheumatic disease. Hydroxychloroquine maculopathy and steroid induced cataract and glaucoma have to be looked for during each visit and treated with topical, systemic drugs or surgery. The most common immunosuppressive agent we used was tablet azathioprine 150mg tapered to 50 mg. Complete blood count, blood sugar, blood pressure, renal and liver function tests and development of infection were monitored throughout the course of treatment and during each review and managed in collaboration with the infectious disease specialist.

In children, juvenile idiopathic arthritis was the most common cause of paediatric uveitis. Visual loss is severe in these patients due to corneal complications such as leucomatous corneal opacity that occurs after band shaped keratopathy. Patients had severe joint involvement and deformities during initial referral itself. Though the incidence of uveitis is chronic in these patients, they need meticulous follow up for fear of corneal involvement which can result in blindness.

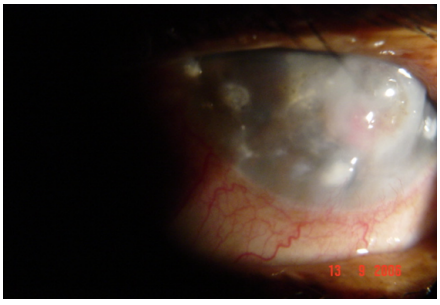
Peripheral ulcerative keratitis has been reported to occur due to IBD[11]. PUK is progressive and can result in central corneal involvement with eventual corneal perforation if not identified and treated. PUK was not noted in our study but marginal corneal thinning was looked for in every patient. Most of the ocular manifestations can be recognised easily but a regular ophthalmic consultation and opinion is required for all these patients to ensure early detection and correct management. We did not see any patient with Wegener's granulamatosis or polyarteritis nodosa although literature reports that they are frequent causes.

Conclusion

We conclude from our study that a definite and significant association exists between uveitis and rheumatic disease. The course of the uveitis and the clinical manifestations can be varied in these patients and is largely dependent on the nature of systemic involvement. A presentation of uveitis, ocular inflammation and sometimes even orbital disease may be the initial feature of rheumatic disease when systemic clinical signs have not yet evolved [12]. The presence of uveitis and its improvement or worsening can indicate the state of the systemic disease. Examination for uveitis and detection in patients with rheumatic diseases can be used to predict prognosis and to assess response to treatment. We recommend a routine screening of all patients with rheumatic disease to identify ophthalmic signs and other forms of ocular morbidity during their early stages.

Figure 1: Anterior uveitis with hypopyon

Figure 2: Leucomatous corneal opacity with scleritis



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