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OCULAR MANIFESTATION IN RHEUMATIC DISEASES

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Abstract: *This article comprises studies of this ocular manifestations, the purpose of the study is to identify the role of eyes manifestations in rheumatic diseases from a clinical, epidemiological, path physiology and therapeutic perspective.*

Keywords**:** *ocular manifestation; rheumatic diseases; rheumatic disorder.*

I. INTRODUCTION

The eye is one of the most complex organs of the human body. In the human eye, three layers can be distinguished. The outer region consists of the cornea and the sclera, the cornea refracts and transmits the light to the lens and the retina and protects the eye against infection and structural damage to the deeper parts, the sclera forms a connective tissue coat that protects the eye from internal and external forces and maintains its shape, the cornea and the sclera are connected at the limbos, the visible part of the sclera is covered by a transparent mucous membrane, the conjunctiva.

The middle layer of the eye is composed of the iris, the ciliary body and the choroid. The iris controls the size of the pupil, and thus the amount of light reaching the retina; the ciliary body controls the power and shape of the lens and is the site of aqueous production; and the choroid is a vascular layer that provides oxygen and nutrients to the outer retinal layers. The inner layer of the eye is the retina, a complex, layered structure of neurons that capture and process light. The three transparent structures surrounded by the ocular layers are called the aqueous, the vitreous and the lens. The cornea is the most anterior part of the eye, in front of the iris and pupil. It is the most densely innervated tissue of the body, and most corneal nerves are sensory nerves, derived from the ophthalmic branch of the trigeminal nerve. The cornea of an adult human eye has an average horizontal diameter of about 11.5 mm and a vertical diameter of 10.5 mm, and a curvature that remains rather constant throughout life. The retina is the tissue that lines the inner surface of the eye, surrounding the vitreous cavity. During embryogenesis, the vertebral retina develops from the optic cup [15, 16, and 20].

II. PRIMARY OCULAR DISORDERS

Dry eye (Keratoconjunctivitis sicca) - Also known as dry eye, this produces a burning foreign-body sensation, injection and photophobia. In mild cases the eye appears surprisingly normal, but tears production measured by wetting of a filter paper (schirmer test) is deficient. Variety of systemic drugs, including antihistamine, anti cholinergic, and psychotropic medications, result in dry eye by reduction lachrymal secretion. Patients may develop dry eye after radiation therapy if the treatment field includes orbits. Problems with ocular drying are also common after lesions affecting cranial nerve V or VII. Corneal

anesthesia is particularly dangerous, because the absence of a normal blink reflex exposes the cornea to injury without pain to warn the patient. Dry eye is managed by frequent and liberal application of artificial tears and ocular lubricants. In severe cases the tear punctual can be plugged or cauterized to reduce lachrymal outflow [11].

Keratitis - Is a threat to vision because of the risk of corneal clouding, scarring, and perforation. Worldwide, the two leading causes of blindness from keratitis are trachoma from Chlamydia infection and vitamin A deficiency related to malnutrition. In united stated, contact lenses play a major role in corneal infection and ulceration. They should not be worn by anyone with an active eye infection. In evaluating the cornea, it is important to differentiate between superficial infection (dry eye) and deeper, more serious ulcerative process. The latter is accompanied by greater visual loss, pain, photophobia, redness, and discharge. Slit-lamp examination shows disruption of the corneal epithelium, a cloudy infiltrate or abscess in the Struma, and an inflammatory cellular reaction in the anterior chamber. In severe cases, pus settles at the bottom of the anterior chamber, giving rise to a hypo yon. Immediate empirical antibiotic therapy should be initiated after corneal scrapings are obtained for gram's stain, gems stain, and cultures. Fortified topical antibiotics are most effective, supplemented with sub-conjunctiva antibiotics as required [11]. A fungal etiology should be always considered in a patient with keratitis. Fungal infection is common in warm humid climates, especially after penetration of the cornea by plant or vegetable material [11].

Episcleritis - This is an inflammation of the episclera, a thin layer of connective tissue between the conjunctiva and the sclera. Episcleritis resembles conjunctivitis, but it is a more localized process and discharge is absent. Most cases of episcleritis are idiopathic, but some occur in the setting of an autoimmune disease.

Scleritis - Refers to a deeper; more sever inflammatory process that frequently is associated with a connective tissue disease such as rheumatoid arthritis, lupus erythematous. The inflammation and thickening of the sclera can be diffuse and nodular. In anterior forms of scleritis, the globe assumes a violet hue and the patient complains of severe ocular tenderness and pain. With posterior scleritis the pain and redness may be less marked, but there is often proposes, choroid effusion, reduced motility, and visual loss. Episcleritis and scleritis should be treated with NSAIDs. If these agents fail, topical or even systemic glucocorticoid therapy may be necessary, especially if an underlying autoimmune process is active [11].

Uveitis - Involving the anterior structure of the eye, uveitis also is called iritic or iridocyclitis. The diagnosis requires slit-lamp examination to identify inflammatory cells floating in the aqueous humor or deposited on the corneal endothelium. Anterior Uveitis develops in sarcoidosis, ankylosing spondylitis, juvenile idiopathic arthritis; it also associated with herpes infection, syphilis, Lyme disease, onchocerciasis, tuberculosis and leprosy. Although anterior Uveitis can occur in conjunction with many diseases, no cause is found to explain the majority of cases. For this reason, laboratory evaluation usually is reserved for patients with recurrent or sever anterior uveitis. Treatment is aimed at reducing inflammation and scarring by judicious use of topical glucocorticoids. Dilatation of the pupil reduces pain and prevents the formation of synechiae [11].

III. OVERVIEW OF OPHTHALMOLOGIC FEATURES IN RHEUMATIC DISEASE

RA is a chronic inflammatory multisystem disease with the main target being the synovial. The hallmark of RA is inflammatory synovitis that presents in a symmetric distribution. The intense joint inflammation that occurs has the potential to destroy cartilage and cause bone erosions and eventually deform the joint. The incidence of RA increases between 25-55 years of age, after which it plateaus until age of 75 and then decreases. The cause of RA is unknown. RA may be triggered as a reaction to an infectious agent (mycoplasma, parvovirus) in a susceptible host.

Secondary sjogren's syndrome is defined by the presence of either keratoconjunctivitis sicca (dry eye) or xerostomia(dry mouth) in association with another connective tissue disease, such as RA, approximately 10% of patients with RA have secondary sjogren's syndrome. Diagnostic criteria—need 4 of the following diagnostic criteria.

• Morning stiffness (>1 h) for 6 weeks, Swelling of wrists, MCPs, PIPs for 6 weeks, Swelling of 3 joints for 6 weeks, Symmetric joint swelling for 6 weeks, RF positive or anti-Cyclic citrullinated peptide (ACCP), C-Reactive protein CRP or ESR.

Treatment- Glucocorticoids, may serve in several ways to control disease activity in RA, firstly they may be administrated in low-to-moderate doses to achieve rapid disease control before the onset of fully effective DMARD therapy which often takes several weeks or even months. DMARDs have ability to slow or prevent structural progression of RA, the conventional DMARDs include hydroxychloroquine, sulfasalazine, methotrexate, and leflunomide; they exhibit a delayed onset of action approximately 6-12 weeks, Methotrexate is the DMARD of choice for the treatment of RA and is the anchor drug for most combination therapy.

Biologic Agents, Tumor necrosis factor (TNF) inhibitors, Tumor necrosis factor alpha (TNF-α) is a pro-inflammatory cytokine produced by macrophages and lymphocytes, it is found in large quantities in the rheumatoid joint and is produced locally in the joint by synovial macrophages and lymphocytes infiltrating the joint synovium. TNF inhibitors relieve the signs and symptoms of RA, and slow or halt radiographic damage. These drugs have been shown to be effective in patients who were thought to be resistant to all methotrexate. There are 3 TNF inhibitors approved for the treatment of RA: Infliximab (Remicade) is a monoclonal antibody to TNF-α that binds to TNF-α in the joint and in the circulation. The combination of infliximab and methotrexate is very effective in reducing clinical manifestations of disease. Infliximab is given as an intravenous infusion. Cases of sepsis, disseminated tuberculosis, and other opportunistic infections have been reported for patients treated with infliximab or other anti-TNF therapy. Adalimumab (Humira) is an anti-TNF mAb that differs from infliximab in that its sequences are entirely human. Etanercept (Enbrel) is a human fusion protein that is entirely human, and antietanercept antibodies are relatively uncommon. Complications/Follow-Up, Aggressive disease is likely to occur with the following features: high titers of RF, diffuse rheumatoid nodules, early joint erosions, late age of onset, and certain subtypes of the HLA-DR4 [1].

Sjögren syndrome is a chronic, slowly progressive autoimmune disease characterized by lymphocytic infiltration of exocrine glands resulting in xerostomia and dry eyes. Middle-aged women are primarily affected; although it may occur in all ages, including childhood, the prevalence of primary Sjögren's syndrome is approximately 0.5-1% while 30% of patients with autoimmune rheumatic

diseases suffer from secondary Sjögren's syndrome.

Sjögren's syndrome is characterized by both lymphocytic infiltration of the exocrine glands and B lymphocyte hyperactivity, and an oligomonoclonal B cell process, which is characterized by cryoprecipitable monoclonal immunoglobulin with rheumatoid factor activity, is evident in up to 25% of patients. The majority of Sjögren's syndrome patients have symptoms related to diminish lachrymal and salivary gland functions.

Ocular involvement is a major manifestation of Sjögren's syndrome , patients usually complains of a sandy or gritty feeling under the eyelids , and other symptoms including burning, accumulation of thick strands at the inner anthem , decreased Tearing, redness, itching, eye fatigue and increased photosensitivity.
These symptoms are attributing to the destruction of corneal and bulbar conjunctiva epithelium defined as keratoconjunctivitis sicca.

Diagnostic evaluation of keratoconjunctivitis sicca includes measurement of tears flow by Schirmer's test and tears composition as assessed by the tear breakup time or tear lysosome content, slit-lamp examination of the cornea and conjunctiva after rose Bengal staining reveals punctuate corneal ulcerations and attached filaments of corneal epithelium.

Treatment of Sjögren's syndrome is aimed at symptomatic relief and limiting the damaging local effects of chronic xerostomia and keratoconjunctivitis sicca by substituting or stimulating the missing secretions , to replace deficient tears , there are several readily available ophthalmic preparations (Tear sol ; Liquifilm ; 0.5% methylcellulose ; Hypo tears) , if corneal ulcerations are present eye patching and boric acid ointments are recommended .certain drugs that may decrease lachrymal and salivary secretion such as diuretics, antihypertensive drugs, anticholinergics, antidepressants should be avoided.

For xerostomia the best replacement is water. Prop ionic acid gels may be used to treat vaginal dryness. To stimulate secretions pilocarpine or civimeline administrated to improve sicca manifestation [9, 12].

SLE is autoimmune disease in which organs and cells undergo damage initially mediated by tissue binding auto antibodies and immune complexes, in most patients auto antibodies are present for a few years before the first clinical symptoms appears; clinical manifestations are heterogeneous. 90% of cases at diagnosis are women of childbearing years; people of all genders, ages, and ethnic groups are susceptible; Prevalence of SLE in US is 10-400 per 100,000 depending on race and gender highest prevalence is in black women and lowest in white men.

SLE may involve one or several organ systems; over time, additional manifestations may occur; malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorder, neurologic disorder, hematologic disorder, immunologic disorder, antinuclear antibodies. Severity of SLE varies from mild and intermittent to sever and fulminate, most patient's experience exacerbations interspersed with periods of relative quiescence; permanent complete remissions are rare, systemic symptoms, particularly fatigue and myalgias/arthralgias, are present most of time. Severe systemic illness requiring glucocoticoid therapy can occur with fever, prostration, weight loss, and anemia with or without other organ-targeted manifestation.
Sicca syndrome and nonspecific conjunctivitis are common in SLE and rarely threaten vision. In contrast, retinal

vasculitis and optic neuritis are serious manifestations: blindness can develop over days to weeks.

Aggressive immunosuppressant is recommended, although there are no controlled trials to prove effectiveness, complications of glucocorticoid therapy include cataracts and glaucoma. A positive ANA supports the diagnosis but is not specific for SLE. Complement levels (C3, C4) are in patients with active lupus. Elevated levels of ds-DNA antibodies are seen with active lupus. Treatment, since there is no cure for SLE, treatment is aimed at controlling symptoms.

NSAIDs are used to treat arthritis and pleurisy, corticosteroid creams are used to treat skin rashes. Anti malaria drugs (hydroxychloroquine) and oral corticosteroids may also be used for skin and arthritic symptoms, cytotoxic drugs (azathioprine, cyclophosphamide) are used with severe symptoms (lupus nephritis, heart and lung involvement, hemolytic anemia, central nervous system involvement, etc.), along with corticosteroids, mycophenolate is often used to treat lupus nephritis [4, 12].

SPA are a group of overlapping disorders that share certain clinical features and genetic associations, these disorders include AS , reactive arthritis, psoriatic arthritis and spondylitis, enteropathic arthritis and spondylitis.

The similarities in clinical manifestations and genetic predisposition suggest that these disorders share pathogenic mechanisms. Ankylosing spondylitis (AS) is an inflammatory disorder of unknown etiology that affects primarily the axial skeleton and peripheral joints, AS usually starts by the second to third decade (very rare age >40).

Prevalence in men is 3–4 times that of women—this is one of the few collagen vascular diseases that affect men more than women. 90% of patients are positive for HLA B-27. Presentation, AS will usually present with chronic lower back pain in a young man (in his late twenties to early thirties). The giveaway is the morning stiffness lasting at least 1 h that improves with exercise. The cervical spine is rarely if ever affected and only late in the disease.

The most common extraarticular manifestations are common in AS is acute anterior uveitis, which occurs in 40% of patients and can antedate the spondylitis, attacks are typically unilateral, causing pain, photophobia, and increase lacrimation, these tender to recur, often in the opposite eye. Cataracts and secondary glaucoma are not uncommon sequelae. On examination there will be evidence of decreased spine mobility: positive Schirmer's test (measures spine flexion) and sometimes obliteration of the lumbar lordosis. Because of this, spine fractures are sometimes seen in patients with AS after minimal trauma (know that spine fractures occur with insignificant stress in older people with osteoporosis and young people with long-standing inflammatory disease of the spine, e.g., AS).

X-rays show evidence of sacroiliitis (this is the earliest finding) and eventual fusing of the sacroiliac joint. Chronic spine inflammation will eventually cause the bamboo spine and squaring of the vertebral bodies. The diagnosis of AS is based on clinical and x-ray findings. The HLA-B27 is not commonly used as a diagnostic test.

Treatment - NSAIDs, physical therapy, and exercise. The most promising medications used in the treatment of AS and other SPA are the TNF blockers (infliximab, adalimumab, etanercept). These biologic agents are recommended for axial disease.

Reactive arthritis (ReA) is a seronegative arthropathy that occurs as a complication from an infection somewhere in the body. There are mainly two types of infections causing two different

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syndromes. One (Reiter syndrome) occurs after a nongonococcal urethritis (chlamydia, ureaplasma). These patients have distinct mucocutaneous manifestations: keratoderma blennorrhagica, circinate balanitis, oral or genital ulcers, conjunctivitis, and arthritis, ocular disease is common, ranging from transient, asymptomatic conjunctivitis to an aggressive anterior uveitis that occasionally proves refractory to treatment and may result in blindness.

The other ReA occurs after an infectious diarrhea caused by Campylobacter, Shigella, or Salmonella organisms (think of the organisms that cause enteroinvasive diarrheas; these are the same ones that cause ReA). The most common is Campylobacter. Diagnosis is based on clinical criteria. X-ray findings will be consistent with a seronegative spondyloarthropathy.

Treatment is the same as for AS. There are studies that support an accelerated recovery of Reiter syndrome caused by a Chlamydia infection from prolonged tetracycline use (~3 weeks' duration). There are also studies to support the notion that prompt antibiotic use in urethritis will decrease the chance of Reiter syndrome (this is the only exception to the rule that the SPA are untreatable diseases).

A severe form of Reiter syndrome and reactive arthritis has been described in HIV patients. The skin manifestations are particularly aggressive in these patients and improve with antiretroviral medications.

Psoriatic arthritis refers to an inflammatory arthritis that characteristically occur in individuals with psoriasis. Eye involvement, either conjunctivitis or uveitis, is reported in 7-33% of PSA patients, unlike uveitis is AS, the uveitis is PSA is more bilateral, chronic, posterior. Diagnosis made by CASPAR criteria that have sensitivity and specificity exceeded 90%, and they are useful for early diagnosis. To meet CASPAR criteria, a patient must have inflammatory articular disease (joint, spine) with >3 points from any of the following five categories: evidence of current psoriasis, a personal history, or a family history, typical psoriatic nail dystrophy, negative RF, either current dactylitis or a history of dactylitis, radiographic evidence of juxtaarticular new bone formation in the hand or foot. Using of anti-TNF-alpha agents has revolutionized the treatment of PSA [10].

IV. CONCLUSIONS

Ocular manifestations in rheumatic diseases, Dry eye syndrome, episcleritis and scleritis , uveitis , keratitis, catract and glaucoma as a complication of steroid therapy. Dry eye syndrome is the most common ocular manifestation that associated with rheumatic diseases. Ocular involvement is a significant part of extraarticular manifestations of rheumatic diseases. Early and accurate diagnosis with prompt treatment may prevent serious ocular complications. Treating and managing the rheumatic diseases will help in controlling and relieving the ocular symptoms.

Ocular manifestations of rheumatic disease are rather frequent, dry eye syndrome being the most frequent ocular finding. We confirmed once again that patients with collagen disease may develop ocular damage due to systemic corticosteroid therapy.

The major burden of RA is in the age group of 41-50 years. 64% of the patients had Seropositive and 36% had seronegative rheumatoid arthritis. The prevalence of ocular manifestations was 35%.

The prevalence of ocular manifestation in rheumatic diseases in RA is 30%, in SLE is 20%, and in SPA is 40%, and in s'jogren syndrome is 82%.

Duration of the disease seems to influence the onset of ocular manifestations. Age of the patient has no vital role in the development of ocular manifestations. The disease burden is not related to the clinical symptoms.

Asymptomatic patients are found to have silent underlying ocular manifestations. Hence, routine screening for the above mentioned ocular manifestations is important in RA patients as a part of follow up to prevent ocular morbidity.

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