RESEARCH ARTICLE

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Ocular Findings in Rheumatoid Arthritis: Different Cases and Their Proportions

ABSTRACT

Objective: The aim of this study is to determine the frequency of the accompanying ocular findings in Rheumatoid Arthritis (RA) patients.

Methods: Patients who were consulted at the eye clinic with the diagnosis of rheumatoid arthritis between 01 March 2017 and 28 February 2022 were included in the study. The patients' files were reviewed retrospectively from the hospital information method system, and the demographic characteristics of the patients and eye examination findings related to rheumatoid arthritis were recorded.

Results: The records of 23840 patients who were consulted to the eye clinic with the diagnosis of rheumatoid arthritis were reviewed retrospectively, and 2691 patients who were seropositive as a result of the examination were included in the study. Anterior segment biomicroscopy, Schirmer test, tear break-up time (BUT) and fundus examination findings of the patients were evaluated in terms of ophthalmological examination. Of all the patients, 2067 were female and 624 were male. The majority of the patients were between the ages of 41 and 65, with 1374 females and 421 males. While the most common finding of ocular involvement due to rheumatoid arthritis was the lack of tears, known as dry eye, with a rate of 25.97%, episcleritis was found in 4.57% of the patients and scleritis in 1.37%.

Conclusions: Rheumatoid Arthritis is a systemic disease that can progress with extra-articular findings and may even appear as its first finding, and may be accompanied by ocular findings at a rate that may impair the quality of life of the patients. A holistic approach in patients with rheumatoid arthritis will positively affect the prognosis of the disease and patients' quality of life in terms of eye health, as is common in chronic diseases in the community.

Keywords: Rheumatoid Arthritis, Eye, Scleritis, Episcleritis.

Romatoid Artritte Göz Bulguları: Retrospektif Çalışma

ÖZET

Amaç: Bu çalışmanın amacı, Romatoid Artrit (RA) hastalarında eşlik eden göz bulguları sıklığını incelemektir.

Gereç ve Yöntem: Çalışmaya 01 Mart 2017 ile 28 Şubat 2022 tarihleri arasında romatoid artrit tanısıyla göz kliniğine konsülte edilmiş olan hastalar dahil edilmiştir. Hastaların dosyaları hastane bilgi yöntemi sisteminden retrospektif olarak incelenerek hastaların sistemde kayıtlı olan demografik özellikleri ve romatoid artrite bağlı olan göz muayenesi bulguları kayıt altına alınmıştır.

Bulgular: Romatoid artrit tanısıyla göz kliniğine konsülte edilen 23840 hastanın kayıtları retrospektif olarak incelenmiş olup, inceleme sonucunda seropozitif olan 2691 hasta çalışmaya dahil edilmiştir. Hastaların oftalmolojik muayene açısından ön segment biyomikroskopisi, Schirmer testi, gözyaşı kırılma süresi (BUT) ve gözdibi muayenesi bulguları değerlendirildi. Hastaların 2067'si kadın 624'ü erkek idi. Hastaların büyük çoğunluğu 41-65 yaş arasında olup, 1374'ü kadın, 421 ise erkek idi. Romatoid artrite bağlı olarak en sık görülen oküler tutulumun bulgusu %25,97 oranıyla kuru göz olarak bilinen gözyaşı eksikliği iken, hastaların %4,57'sinde episklerit, %1,37'sinde ise sklerit bulgsu saptanmıştır.

Sonuç: Romatoid Artrit eklem dışı bulgularla seyredebilen ve hatta ilk bulgusu olarak da ortaya çıkabilen sistemik bir hastalık olup, hastaların yaşam kalitesini bozabilecek oranda göz bulguları eşlik edebilir. Toplumda sık görülen kronik hastalıklarda olduğu gibi romatoid artrit hastalarında bütüncül bir yaklaşım hastalığın prognozu ve hastaların göz sağlığı açısından yaşam kalitesini olumlu etkileyecektir.

Anahtar Kelimeler: Romatoid Artrit, Göz, Sklerit, Episklerit.

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune systemic inflammatory disease, and the etiology is still unknown. There are many different theories on etiopathogenesis. RA does not only cause arthritis, but also many extra-articular findings such as neuropathy, pericarditis, glomerulonephritis, major cutaneous vasculitis, ocular manifestations, and different types of vasculitis (1). Extra-articular manifestations in RA are present, particularly in 10-20% of seropositive patients (2). Ocular manifestations are dry eye, corneal changes, episcleritis, scleritis, and retinal vasculitis in order of frequency. The most common and often the first ocular finding in patients with RA is dry eye. Episcleritis is usually a self-limiting, recurrent inflammatory disease that affects the episcleral tissue located between the conjunctiva and the sclera. Although there may be an underlying systemic disease in one-third of cases, most of them are idiopathic (3). On the contrary, scleritis is a more serious condition. It is a potentially blinding inflammatory disease which is defined by edema and cellular infiltration of scleral and episcleral tissues due to intense inflammation. Scleritis is of two types, anterior and posterior. Anterior scleritis can be nodular, diffuse, necrotizing with inflammation (necrotizing), and necrotizing without inflammation (scleromalacia perforans) (8). The most common clinical conditions are nodular scleritis and diffuse scleritis. Necrotizing scleritis, which may be inflammatory or non-inflammatory, is even less common. Its clinical course is poor and is often associated with autoimmune disorders. Posterior scleritis is defined by retrobulbar edema, thickening of the posterior layers of the eye (choroid and sclera), and flattening of the posterior surface of the globe edema (4).

Peripheral corneal disorders are much more common in patients with RA. Rarely, severe corneal changes such as sclerosing keratitis, peripheral corneal thinning, acute corneal lysis, and acute stromal keratitis may occur. Vasculitis may develop in approximately 1% to 5% of patients with RA (3). Retinal vasculitis usually affects the terminal branches of arteries and veins in the periphery of the retina. The aim of this study is to reveal the different ocular findings and their ratio in RA.

MATERIAL AND METHODS

The study was carried out in Gulhane Training and Research Hospital of the Ministry of Health, following the criteria of the Declaration of Helsinki, after obtaining the necessary permissions from the Health Sciences Gulhane Ethics Committee. In the period of 2017-2022, patient records in ophthalmology outpatient clinic were reviewed and all diagnoses that could be related to RA were evaluated. A total of 23840 patient records with RA and possibly associated diagnoses were detected. Patients aged 18 years and over and diagnosed with seropositive RA were included in the study. The entity of Rheumatoid factor (RFIgM) in the serum was measured with standard test methods based on the agglutination principle in the Immunology Laboratory of our hospital. All patients were found seropositive. Ophthalmological examination (biomicroscopy, tear break-up time (BUT), Schirmer test, and fundus examination) findings obtained from the hospital information management system were recorded.

RESULTS

The records of 23840 Rheumatoid Arthritis and related patients who were consulted with the eye clinic were reviewed. From these patient records, 2691 patients, especially those diagnosed with seropositive Rheumatoid Arthritis, were evaluated in detail within the study. Ophthalmological examination findings obtained from the records, in particular, anterior segment biomicroscopy, BUT, Schirmer test,and fundus examinations of the patients were assessed. 2067 of the patients were female and 624 were male. Regarding the mean age, the majority of those were between the ages of 41-65 with 1795 people (1374 women, 421 men). While the most common sign of ocular involvement was lack of tears (dry eye) (rate 25.9%), episcleritis was found in 4.6% and scleritis in 1.37%. There were no patients with necrotizing scleritis, scleromalacia or retinal vasculitis of the cornea was not detected in our patients.

Age and gender of all seropositive patients evaluated in the eye clinic are presented as follows: Table 1. It is found that the frequency of RA is highest between the ages of 41-65 and it is much more common in women than men.

Table 1. Age and gender of patients with ocular manifestations of RA

Age (year)	Male (n)	Female (n)	Total (n, %)
20-40	68	284	362 (13.4)
41-65	421	1374	1795 (66.7)
>65	149	464	534 (19.8)

Among the 2691 patients examined, ocular symptoms were present in 859 patients (31.9%) (Table 2). Dry eye was found in 25.9% of these patients, episcleritis in 4.6%, and scleritis in 1.37%. Scleritis, one of the eye findings of RA, can have various conditions such as nodular, diffuse, and necrotizing. When the frequency of the forms of scleritis was evaluated in our patients, it is found that they were mostly in nodular form and no necrotizing form was found.

Table 2. Ocular findings in patients with RA

Ocular findings	The number of patients (n, %)
Dry eye	699 (25.9)
Episcleritis	123 (4.6)
Scleritis	37 (1.4)

Dry eye was present in 699 patients which means 25.9% of all patients. Episcleritis was detected in 123 (4.57%) patients, and scleritis was detected in 37 (1.37%) patients. When all patients were examined, no patient with posterior or necrotizing scleritis was observed. Similarly, no retinal vasculitis was diagnosed in our patients.

DISCUSSION

RA, a systemic inflammatory chronic disease of unknown origin, primarily impacts peripheral joints symmetrically. Although there are many theories about its pathogenesis, most scientists support the theory that rheumatoid factor (RF) was discovered based on immunology. RF is an antiimmunoglobulin formed against the Fc fragment of the human IgG molecule. Presumably, B lymphocytes produce autoantibodies (i.e. [RFs]), while CD4 T cells, mononuclear phagocytes, neutrophils, osteoclasts, and fibroblasts, which play important cellular roles in the pathophysiology of RA, contribute to aberrant release of various chemokines, cytokines, and other inflammatory mediators shown in RA patients. RF may be existing in other inflammatory disorders and may be existing in healthy individuals and therefore, is not a pathognomonic manifestation of RA. The other main theory is genetics. HLA-DR 4/DR 1, an important genetic factor of RA, is present in up to 90% of patients with RA. Moreover, genetic features and immune system defects have influence on the development and the spread of the disease. Inflammation and overgrowth of the synovium damage some tissues, including ligaments, tendons, cartilage, blood vessels, and bone. (1). Extra-articular effects of organs such as the lungs, skin, eyes, and heart is significant and is found in 10-20% of patients, more common in seropositive patients (2). In our study, the most frequent finding of ocular involvement was dry eye with a rate of 25.9%. The occurrence of dry eye in the literature ranges from 11.6% to 50% (3). Dry eye in RA is classically described as keratoconjunctivitis sicca. Patients with dry eye need lifelong artificial tear supplementation. Occasionally, disease-modifying antirheumatic drugs (DMARDs) and systemic immunosuppressive agents such as Cyclosporine A or a monoclonal antibody to TNF-alpha such as infliximab may be required to resolve severe symptoms and to improve tear production and (4,11). In our study, episcleritis was diagnosed in 123 patients. In most cases, no treatment was required. Inflammation is localized in the superficial episcleral vascular network and, when examined histopathologically, shows vascular dilatation, perivascular infiltration, and non-granulomatous inflammation. There are two clinical types of episcleritis: simple and nodular. The most frequently observed type is simple episcleritis with recurrent bouts of moderate or severe inflammation, usually at intervals of 1 to 3 months. Attacks usually last 7-10 days and most resolve after 2-3 weeks. Simple episcleritis usually does not require treatment. Artificial tears are helpful for patients with mild to moderate symptoms. Prolonged attacks may be more frequent in patients with systemic conditions. Some patients report that attacks are more common in the spring or autumn. Patients suffering from nodular episcleritis typically have prolonged episodes of inflammation that are more painful than simple episcleritis (5,6,11). The use of artificial tears may be beneficial for patients with mild symptoms. Nodular episcleritis has the potential to accompany a systemic disease. Patients with severe or prolonged attacks may require artificial tears, topical corticosteroids, or anti-inflammatory agents. Topical 0.5% prednisolone, 0.1% dexamethasone or 0.1% betamethasone can be used every day in those patients. Systemic anti-inflammatory agents may also be helpful if nodular episcleritis does not respond to topical therapy. Flurbiprofen (100 mg daily) is usually effective until the inflammation is decreased. It was reduced to 75 mg per day upon response. If there is no response to the first line flurbiprofen, indomethacin should be used. As a rule, a patient who does not respond to any nonsteroidal anti-inflammatory agent (NSAID) may react to another NSAID (7,8).

Scleritis is a much more serious condition. Therefore, accurate and prompt diagnosis is important Immediate initiation of appropriate systemic therapy can halt disruption of both ocular and systemic processes, thereby avoiding globe destroying and prolonging survival. (9). Scleritis is classified into anterior and posterior scleritis. The most frequently observed clinical forms of anterior scleritis are diffuse scleritis and nodular scleritis. It can also occur as inflammatory necrotizing scleritis with inflammation and non-inflammatory necrotizing (scleromalacia perforans) scleritis without inflammation. Although necrotizing scleritis with or without inflammation is rare, the prognosis is much worse, and it is often related with systemic autoimmune disorders. Posterior scleritis, on the other hand, is characterized by flattening of the posterior surface of the eyeball, thickening of the posterior layers of the eye (choroid and sclera), and retrobulbar edema. Ocular complications of scleritis may result in vision loss and eye damage because of prolonged scleral inflammation. Uveitis (approx. 42%), peripheral ulcerative keratitis (13-14%), glaucoma (12-13%), cataract (6-17%), and fundus abnormalities (approx. 6.4%). These conditions are most frequent in necrotizing scleritis, which is the most devastating type of scleritis (11,12). Like the literature studies, 1.7% of all patients had scleritis in this study and anterior scleritis was detected in all of them. The first finding detected was conjunctival hyperemia, which could be localized or involve the entire sclera, most commonly in the interpalpebral region. In the examination, it is an important sign that the redness

does not go away after topical applications of routinely used sympathomimetic dilatation agents. Other symptoms of scleritis are watering, photophobia, pain, and tenderness. In the biomicroscopic examination of the eye, the maximum effect is in the deep episcleral mesh and some in the superficial episcleral mesh. Treatment of scleritis requires regular therapy such as non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs) or corticosteroids (5,13). Posterior scleritis or scleromalacia of the cornea were not detected in the observed patient group. Retinal vasculitis is one of the ocular signs of RA. It affects approximately 1% to 5% of patients with established RA (1,14). Retinal vasculitis is commonly located at the periphery of the retina, involving peripheral branches of veins and arteries. Treatment includes topical corticosteroid, NSAIDs, systemic corticosteroid, and biologic therapy (15,16). Recent studies indicates that new biotechnological treatments such as rituximab provide important efficacy and safety (17-19). Biological therapy in rheumatoid arthritis requires treatment with DMARDs, including ocular signs such as keratoconjunctivitis sicca and retinal vasculitis (20-22).

CONCLUSION

Extra-articular organ involvement is a significant issue in RA as they may cause damage in affected organs. Extra-articular complications include ophthalmologic manifestations, which in some cases may be the first sign of the disease. Ocular manifestations of RA are dry eye and inflammatory ophthalmologic conditions such as scleritis corneal changes, episcleritis, and retinal vasculitis. The main cause of necrotizing scleritis and peripheral ulcerative keratitis is RA. These are the two most severe ocular conditions related with the disease, and these conditions greatly affect the prognosis, especially due to their relation with systemic vasculitis, even mortality. As a result of that, ophthalmologists should cooperate closely with rheumatologists in the diagnosis, treatment, and follow-up of patients with RA.

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