

Title Page

Ocular Involvement in Patients with Rheumatoid Arthritis

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ABSTRACT

Aim: The aim of this study was to find out the prevalence of various ocular involvement in patients with rheumatoid arthritis and to assess the relation to immunological alterations.

Methods: This is a cross-sectional study involving 70 patients with rheumatoid arthritis. All patients fulfill the criteria of American College of Rheumatology and the European League against Rheumatism for the diagnosis of rheumatoid arthritis. Serum samples for rheumatoid factor and anti-cyclic citrullinated peptide antibody were obtained. The lacrimal secretion was measured in all patients by Schirmer's test. The patients were referred to the Ophthalmologist for examination of the eyes and interpretation of the related findings.

Results: Ocular manifestations were identified in 13 (19%) of patients with rheumatoid arthritis. Keratoconjunctivitis sicca was identified in 9 (13%) patients, episcleritis in 2 (3%) patients and scleritis in 2 (3%) patients. Patients with positive rheumatoid factor and anti-cyclic citrullinated peptide antibody, were 42 (100.0 %) of whom 10 (23.8 %) represent ocular lesions, while in the other group of 28 (100.0 %) patients seronegative only 3 (10.7 %) patients have ocular lesions.

Conclusion: Ocular involvement are common in rheumatoid arthritis. Keratoconjunctivitis sicca, episcleritis and scleritis are ocular manifestations that occur in rheumatoid arthritis. The most common ocular manifestation was keratoconjunctivitis sicca. Immunological alterations are important factors in ocular manifestations.

Keywords : ocular, keratoconjunctivitis sicca, episcleritis, scleritis

INTRODUCTION

Rheumatoid arthritis is a systemic autoimmune and inflammatory disease that affects not only the articulations but may involve a multiplicity of organs and are of diverse severity (1). Ocular involvement is one of the extra-articular manifestation of rheumatoid arthritis and can cause morbidity in these patients. Ocular manifestations in rheumatoid arthritis are diverse and include dry eye, episcleritis, scleritis and peripheral ulcerative keratitis (2). Ocular involvement, severe dry eye or keratoconjunctivitis sicca in particular, may exist independently from severe rheumatoid arthritis presentations and the eyes should be evaluated in all patients with rheumatoid arthritis, regardless of whether ocular manifestations are present (3). Dry eye diagnosis is based on the clinical features and some diagnostic tests. Schirmer test is one of the diagnostic tools in evaluating ocular surface status. Episcleritis and scleritis are describe as inflammation of the eye and frequently occur as ocular complications of rheumatoid arthritis. Extra-articular manifestations of rheumatoid arthritis are generally more often seen in patients with rheumatoid factor positive and anti-cyclic citrullinated peptide antibody positive (4,5). In clinical practice the most common diagnostic test for rheumatoid arthritis is rheumatoid factor and anti-cyclic citrullinated peptide and is generally accepted by the majority of rheumatologists and recommended by the European League of Arthritis and Rheumatism (6). The aim of this study was to find out the prevalence of various ocular manifestations in patients with rheumatoid arthritis and to assess the relation to immunological alterations

MATERIAL AND METHODS

This is a cross-sectional study involving 70 patients with rheumatoid arthritis. All patients fulfill the criteria of American College of Rheumatology and the European League against Rheumatism for the diagnosis of rheumatoid arthritis (7). These patients were hospitalized in the clinic of Rheumatology or followed as outpatients. All patients were treated with Methotrexate 10-15 mg weekly for at least 3 months and received weekly folic acid 10 mg, low doses of glucocorticoid ≤ 7.5 mg per day and non steroidal anti inflammatory drugs in function of disease activity as is usual in clinical practice. Patients with rheumatoid arthritis who suffering from other diseases such as infectious (e.g. viral infection, bacterial, fungal or parasitic infection) or miscellaneous disease (e.g. atopic syndrome, rosacea, secondary to foreign bodies, chemical lesions or drugs such as alendronate, risedronate, zoledronic acid, ibandronate) which may influence the ocular lesions were excluded from the study (8). We excluded also patients with prior eye surgery, contact lenses users, those taking medications such as anticholinergics, antihistamine, antidepressants, diuretics, etc.

Patients were examined by laboratory tests such as rheumatoid factor and anti-cyclic citrullinated peptide antibody.

A number of diagnostic tests have been performed to establish the diagnosis of keratoconjunctivitis sicca such as Schirmer's test, tear film break up time test and rose Bengal staining. We chose the Schirmer test even though the Schirmer test is used as one of the six major criteria for Sjögren's syndrome diagnosis based on the American-European Consensus Criteria for Sjögren's syndrome (9). The patients were referred to the Ophthalmologist for examination of the eyes and interpretation of the related findings

The lacrimal secretion was measured in all patients by Schirmer's test. It is performed by first drying the tear film, then inserting a Schirmer strip which was 5mm x 35mm into the lower conjunctival cul-de-sac toward the temporal aspect of the lower lid. Both eyes were tested simultaneously. The patient were asked to keep eyes closed. After 5 minutes we removed the strip and wrote down the millimeters moistened in the part of the strip that wasn't inside the eye. The wet portion of the strip was measured in millimeters with the scale. If the strip measures less than 10 mm of wetting the lacrimal glands are not functioning correctly. Episcleritis and scleritis are distinguished on the basis of appearance, symptoms and slit lamp microscopic

examination. The diagnosis of episcleritis and scleritis is mainly clinical. Symptoms of episcleritis and scleritis can include redness, pain, tearing or photophobia, tenderness.

To determine if alterations of immunological examinations are associated with ocular manifestations, patients were classified into two groups. The first group included patients with rheumatoid factor and anti-cyclic citrullinated peptide antibody positive, the second group included patients seronegative.

Statistical analysis

Continuous variables were expressed as mean values and their respective standard deviations. Categorical variables were presented in absolute values and their respective percentages.

Differences between the categorical variables were assessed with Chi square test.

The P value $\leq 0,05$ was considered a statistically significant. Data were analyzed using the Statistical Package for the Social Sciences software, version 19.0

RESULTS

The mean age of the patients was 46.17 (± 8.75) years. The mean duration of disease was 9.21 (± 3.54) years. Female patients are 52 (74.3%) and male patients are 18 (25.7 %). Ocular manifestations were identified in 13 (19%) patients with rheumatoid arthritis. Keratoconjunctivitis sicca, was identified in 9 (13%) patients, episcleritis in 2 (3%) patients and scleritis in 2 (3%) patients (Table 1). Patients with positive rheumatoid factor and anti-cyclic citrullinated peptide, were 42 (100.0 %) of whom 10 (23.8 %) represent ocular manifestations (group 1), while in the other group (group 2) of 28 (100.0 %) patients seronegative only 3 (10.7%) patients have ocular manifestations (Table 2). Ocular involvement were more frequent in patients with positive immunological tests. In patients with positive immunological tests, keratoconjunctivitis sicca is found in 8 patients, episcleritis in 1 patients and scleritis in 1 patient. Ocular manifestations in patients with positive immunological tests are significant versus patients with negative immunological tests $P = 0.02$

DISCUSSION

In our study ocular manifestations were found in 19 % of patients and in our opinion these ocular lesions are frequent in this group of patients with rheumatoid arthritis. This indicates that ocular lesions are important extra-articular manifestations in rheumatoid arthritis. The extra-articular complications of rheumatoid arthritis include ophthalmological manifestations, which can in some cases be the first signs of the disease (10). Approximately 25% of patients with rheumatoid arthritis have ocular symptoms (11). The most common manifestation of ocular involvement in our study was keratoconjunctivitis sicca in 13 % of patients. The incidence of keratoconjunctivitis sicca is between 15 % to 25 % , in literature and in patients with positive immunological tests at least 10% of their (12;13;14). Keratoconjunctivitis sicca is the most frequent complication in rheumatic diseases and is particularly common in rheumatoid arthritis and Sjögren syndrome (12). Episcleritis and scleritis are described in patients with rheumatoid arthritis. Studies have shown that patients with rheumatoid arthritis associated scleritis have more widespread systemic disease and a higher mortality rate than those without scleritis (15,16). In the present study 3 % of patients had episcleritis and 3 % of patients had scleritis. In others study scleritis and episcleritis in patients with rheumatoid arthritis is found at a prevalence rate of 4% to 10 % (17). The prevalence of scleritis on rheumatoid arthritis is reported to be 0.67% to 6.3% (18). Another finding of this study is that ocular involvement in rheumatoid arthritis occur more frequently in patients with alterations of the immune system. According to this study in patients with rheumatoid factor and anti-cyclic citrullinated peptide antibody positive ocular manifestations occurred frequently in 23,8 % patients versus group of patients seronegative and we found correlation. Rheumatoid factor and ant-cyclic citrullinated peptide antibody has been

shown to be predictor of extra-articular manifestations in rheumatoid arthritis, our results seem to suggest that the presence of rheumatoid factor and anti-cyclic citrullinated peptide antibody is associated with ocular manifestations, however there was one patient seronegative who was diagnosed with keratoconjunctivitis sicca, which demonstrates that even rheumatoid factor may be absent in Sjögren syndrome related to keratoconjunctivitis sicca and two patients with episcleritis and scleritis. In other study is found that the combined presence of anti-cyclic citrullinated peptide antibody and rheumatoid factor had more severe ocular involvement compared to those who were negative for these antibodies (2). This indicates that the immune system is implicated in the development of ocular lesions.

Study limitations

The patients in our study were selected from a university hospital center, which could potentially be prone to selection bias by including patients with more severe stages of the disease compared to patients at the community level. However, we tried to minimize this bias by recruiting also all the patients from the hospital's outpatient consultation clinics. Another limitation may be the small sample size.

Table 1. Ocular involvement in Rheumatoid Arthritis

Condition	Number of patients	Percentage (%)
Keratoconjunctivitis sicca	9	13
Episcleritis	2	3
Scleritis	2	3

Table 2. Ocular involvement by immunological alterations

Patients group	Total	Normal	Ocular involvement	P-value
Group 1	42 (100.0)*	32 (76.2)	10 (23.8)	0.02
Group 2	28 (100.0)	25 (89.3)	3 (10.7)	

*Absolute numbers and row percentage (in parentheses).

CONCLUSIONS

Ocular involvement are common in rheumatoid arthritis. Keratoconjunctivitis sicca, episcleritis and scleritis are ocular manifestations that occur in rheumatoid arthritis. The most common ocular manifestation was keratoconjunctivitis sicca. Immunological alterations are important factors in ocular manifestations.

Competing interests

Authors have declared that no competing interests exist.

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