Rheumatology: Current Research

Kan et al., Rheumatology (Sunnyvale) 2014, 4:2
DOI: 10.4172/2161-1149.1000137

Research Article Open Access

Presence of Sjögren's Syndrome in Dry Eye Patients

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Received date: May 10, 2014, **Accepted date:** Jun 27, 2014, **Published date:** Jun 30, 2014

Abstract:

Background: To evaluate the prevalence of Sjögren's syndrome (SS) in patients with dry eye syndrome.

Methods: In this prospective study, patients with dry eye syndrome were evaluated by a single rheumatologist and patients were considered for an underlying rheumatic condition.

Results: Fourty five patients with dry eye syndrome were evaluated. 37 patient was female (82.2%) and 8 was male (17.8%).The mean age was 45,5 ± 10.4. years (18-64). A total of 21 (46.7%) patients had an associated rheumatic disease; the most common being primary SS (14 patients, 66.6%). Other diseases that were associated included scleroderma (5 patients, 23.8%) and undifferentiated connective tissue disease (2 patients, 9.52%).

Conclusions: Our results demonstrate a high frequency of associated SS in a group of patients with dry eye syndrome. We suggest that laboratory evaluation with patient's clinical presentation as well as a detailed review of systems should be performed in all dry eye patients. Primary SS should be considered as a systemic autoimmune disease underlying beyond sicca involvement.

Keywords: Dry eye syndrome; Sjögren's syndrome; Connective tissue disease

Introduction

Dry Eye Syndrome (DES), also known as keratoconjunctivitis sicca (KCS) or keratitis sicca, is a multifactorial disease of the tears and the ocular surface that results in discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. The tear film has 3 layers: lipid, aqueous and mucuous. Any disturbance in the composition of one of the layers may lead to ocular symptoms such as dryness, grittiness, soreness, redness, photophobia, and ocular fatigue. Dry eye was classified as aqueous deficient dry eye and evaporative dry eye by the DEWS report. In aqueous tear deficient (ATD) dry eye, there are insufficient tears secreted by the lacrimal glands, and this is categorizes as SS and non- Sjögren [1]. Sjögren's syndrome is a common autoimmune disorder, characterized by chronic inflammatory infiltration of exocrine glands and systemic immune reactivity, isolated (primary Sjögren's syndrome) or associated with other connective tissue diseases (CTD) (secondary Sjögren's syndrome). Primary SS was diagnosed in patients consisting of the occurrence of aqueous deficient dry eye syndrome in combination with symptoms of dry mouth, in the presence of autoantibodies, evidence of reduced salivary secretion and with a positive minor salivary gland biopsy. These patients are mostly women and do not have a separate, identifiable CTD. Secondary SS is defined as DES that is associated with a diagnosable CTD, which is most commonly rheumatoid arthritis (RA) but could also be systemic lupus erythematosus (SLE) or systemic sclerosis. The diagnosis in adult patients is made using sets of criteria based on a combination of clinical, serological and salivary gland histopathological findings. A salivary gland biopsy is the most reliable objective criterion [2].

Dry eye is diagnosed with biomicroscopic examination and medical history. Schirmer test is the most common used test which measures the amount of the aqueous tear. A value of less than 5 mm wetting in 5 minutes is considered as abnormal. Break up time should also be measured to corralete diagnosis in biomicroscopic examination. A tear film break-up time of less than 10 seconds indicates instability of the of the tear film [3].

In this study we aimed to evaluate the prevalence of SS in dry eye patients.

Materials and Methods

Patients

45 consecutive patients, complaining of foreign body sensation, burning, stinging, itching, dryness, soreness, heaviness of the lids, photophobia, or ocular fatigue were included in this study. Patients with abnormal tear functions in the presence of other primary diagnoses such as Stevens Johnson Syndrome, mucous membrane pemhigoid, lichen planus, superior limbic keratoconjunctivitis, atopic keratoconjunctivitis, etc. were excluded. Patients were informed about the study and informed consent form was obtained from all patients. In order to diagnose dry eye Schirmer and break up time tests were applied to the patients. Aqueous tear deficiency was defined as a Schirmer test value without topical anesthesia of less than 5 mm at 5 minutes. Evaporative dry eye syndrome was defined as a tear film break-up time of less than 10 seconds [3]. Patients with normal

Schirmer's test results as well as tear film break-up time were excluded. Also patients with other ocular surface diseases, systemic diseases and drug use with abnormal Schirmer tests and/or break-up time were excluded. Dry eye patients were referred to the rheumatologist to be researched for an associated rheumatic disease at the initial visit.

Diagnosis of rheumatic diseases

All patients were evaluated by a single rheumatologist for the presence of a rheumatic disease. Evaluation of patients included review of systems with a complete medical history, laboratory evaluation, including anti-SS-A/Ro, anti-SS-B/La, anti-nuclear antibodies (ANA), rheumatoid factor (RF), anti-Sm, anti-Scl-70 and anti-centromere antibodies, was performed in all patients. The Sjögren's syndrome was diagnosed based on the criteria proposed by the American-European Consensus Group [2]. The consensus criteria for the classification of Sjögren's syndrome included both subjective and objective findings, with at least 4 of the 6 criteria required to be present for the diagnosis to be confirmed. The 6 criteria include subjective and objective ocular dryness, subjective and objective oral dryness, the presence of ANA, anti-SS-A/Ro and/or anti-SS-B/La antibodies, and an abnormal minor salivary gland lip biopsy. Medical records were reviewed for the presence of an underlying SS at the diagnosis of the onset of the dry eye syndrome. The study was performed according to the Declaration of Helsinki and was approved by the local ethical committee. Prevelance of the variables were evaluated by using SPSS version 15.0 (SPSS Inc. Chicago, IL, USA).

Results

Forty-five patients (45) were included in this study. 37 patient was female (82.2%) and 8 was male (17.8%). The mean age was 45, 5 ± 10.4 years (18-64). 31 patients (68.9%) had xerostomia, 24 had (53.3%) Raynaud phenomenon and 12 had (26.7%) arthirits (Table 1). 15 patients, with xerostomia had also raynaud phenomenon and ANA test was positive in 11 of these patients (Table 1). Among patients with ANA positive, 14 (66.6%) had positive salivary gland biopsy.

Symptoms	n	%
Xerostomia	31	68.9
Raynaud phenomenon	24	53.3
Arthrits	12	26.7

Table 1: Clinical Characteristics of the Patients Presenting with a Dry Eye Syndrome.(n: number)

Rheumatic disease	n	%
Sjögren syndrome	14	31.1
Scleroderma	5	11.2
Undifferentiated connective tissue disease	2	4.4

Table 2: Diagnosis of dry eye patients without a known rheumatologic disease at presentation (n: number)

Eventually after subjective and objective findings with the presence of antibodies and abnormal minor salivary gland lip biopsy, a total of 21 (46.7%) patients had an associated rheumatic disease; the most common being primary SS (14 patients, 31.1%). Other diseases that were associated included scleroderma (5 patients, 11.2%) and undifferentiated connective tissue disease (2 patients 4.4%) (Table 2).

Discussion

The treatment of dry eye consists of finding the underlying cause and avoiding the conditions that may aggravate the symptoms of dry eye. Aqueous deficient dry eye is common in connective tissue disorders in which, insufficient tears is secreted by the lacrimal glands. Patients with aqueous tear deficiency have SS if they have associated xerostomia or CTD. SS is more prevelant in women and associated with HLA-B8, DR-3 and DRw52a genotipia that affects approximately 1% of the population [4]. In our study the majority of patients were female. Our study demonstrated a significant association of dry eye syndrome with systemic medical conditions, the most common was primary Sjögren's syndrome and xerostomia was found more frequent than the other symptoms. Hydroxychloroquine (HCQ) therapy was intiated to these patients and they were taken to a follow up. In a study, Akpek et al evaluated the medical records of 220 patients with dry eye to find out the rate of SS retrospectively. A total of 57 (25.9%) patients had an underlying rheumatic condition; 25 patients (11.4%) had rheumatoid arthritis and 24 (10.9%) had pSS. They suggested that pSS appears to be underdiagnosed in dry eye patients and should be the focus of diagnostic evaluations [5]. In our study we found a higher rate of underlying rheumatic diseases (46.6 %), nevertheless we studied with a smaller number of patients when compared the previous study. Kabasakal et al determined the prevelance of SS in healty individuals with a baseline questionnaire with collection of blood samples and clinical examination. Positivity for autoantibodies Ro(SS-A), La(SS-B), RF and ANA were determined and in the clinical phase; clinical examination, salivary and ocular tests were performed. Minor salivary gland biopsy was performed for those who had at least three of these five criteria positive. The prevalence of SS was found 0.72% in this study [6]. Similarly, in an another study aiming the prevelance estimates of SS on 1000 adults aged 18-75 years old who were randomly selected from the population. SS was found to affect approximately 3-4% of adults in the general population. The prevalence of the disorder was higher in females and for those subjects aged ≥ 55 years old [7]. In our study, as expected, we found a higher prevelance of SS in dry eye patients when compared to normal population.

The most serious threating ocular surface complication of SS is corneal ulceration. Perforation may occur in the edge of the ulseration [4]. None of our SS patient had any ocular surface complication

Advanced term of SS patients are most likely develop extraglandular manifestations, including cryoglobulinemia, vasculitis, anemia, leukopenia and thrombocytopenia. That's why early diagnosis takes an important place in these patients whom should be monitored more closely [8]. Pathophisology of dry eye is complicated and treatment not only should consist of replacement of insufficient tears, but also should comprimise and resolve the underlying inflammatory prosses. Beside this SS patients with more severe sicca symptoms and those developing systemic disease may need to be treated more aggressively with systemic medications such as HCQ rather than the local measures used in milder sicca symptoms [9]. Thus, early diagnosis of SS is important in dry eye patients to avoid further manifestations of advanced terms of SS.

Hydroxychloroquine is a well-tolerated anti-malarial agent and has been reported to improve laboratory markers of inflammation, but its effect on glandular function has not been investigated in prospective, clinical trials. However, in an earlier retrospective, an improvement of the lacrimal function has been reported with HCQ treatment in SS patients [10]. In another retrospective analysis of patients with pSS, HCQ was found to improve the tear and saliva production due to its antiinflammatory activity in SS patients. As a consequence, HCQ was considered to be beneficial to ameliorate the extra glanduler functions in SS patients [11]. Hydroxy chloroquine treatment was initiated in our patients diagnosed of SS, as well.

In conclusion, our results demonstrate a high frequency of associated SS in a group of patients with dry eye syndrome. We suggest that laboratory evaluation with patient's clinical presentation as well as a detailed review of systems should be performed in all dry eye patients. A larger prospective study is needed to estimate the true rate of SS in dry eye population. Primary SS should be considered as a systemic autoimmune disease underlying beyond sicca involvement

Acknowledgement

Authors have no conflicts of interest to disclose.

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