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SJÖGREN'S SYNDROME: IS IT JUST DRYNESS?

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Abstract

Objectives: Sjögren's syndrome (SS) is the most common autoimmune, multisystemic rheumatic disease. The wide spectrum of the signs and symptoms of SS often causes difficulties in diagnosis. Patients can apply with different complaints to general practitioners and many different specialists, apart from internists and ophthalmologists, who frequently encounter the disease. Our aim in this study was to evaluate the initial complaints of the patients who have been diagnosed with SS.

Materials and Methods: Sixty-six patients who were diagnosed with primary SS according to 2012 or 2016 classification criteria were included in the study. The clinical and laboratory features were retrospectively evaluated.

Results: The female/male ratio was 60/6. The initial complaint of most patients (n:34) was arthralgia or arthritis (51.51%). ANA was positive in 56 patients (84.84%), RF in 19 (28.78%), but not evaluated in 7 (10.6%), anti-SS-A in 29 (43.93%), and anti-SS-B in 16 (24.24%). Sixty-three patients had a positive Schirmer test. Minor salivary gland biopsy was obtained in 42 patients, and 28 had biopsy findings consistent with SS.

Conclusion: SS is a common disease with a wide variety of clinical presentations. A detailed evaluation of patients is necessary to provide an accurate diagnosis and proper care.

Keywords: Sjögren's syndrome, sicca symptoms, anti-nuclear antibody, Schirmer test.

Introduction

Sjögren's syndrome (SS) is an autoimmune, multisystemic rheumatic disease characterized by sicca symptoms in the eye and mouth caused by the inflammation in salivary and lacrimal glands.[1,2] SS may occur alone. In that case, it is called primary Sjögren's syndrome (pSS) or may be linked to another autoimmune disease and called secondary Sjögren's syndrome (sSS).[3]

PSS is considered to be the most common disorder among all chronic systemic rheumatic diseases.[4] It is more common in females, with a gender ratio of 9:1.[5] Clinical features of SS may be due to exocrine involvement or extra-glandular manifestations.[6] Diagnosing sSS may be easier because of the already diagnosed primary disease. But the wide spectrum of the signs and symptoms of SS often causes difficulties in diagnosis, especially in pSS.[7] Sicca symptoms are common in the general population. Other serious symptoms such as chronic pain, major organ involvement, neuropathies, and lymphomas are so heterogeneous, which makes early diagnosis difficult.[7] Patients can apply with different complaints to general practitioners and many different specialists, apart from internists and ophthalmologists, who frequently encounter the disease, resulting in a delay in diagnosis. Early diagnosis and referral to a rheumatologist are important for preventing serious complications. There are studies ongoing to deeper the characteristics of the disease or find novel biomarkers that may allow an earlier diagnosis.[6] Herein, we aimed to evaluate the initial complaints of the patients who have been diagnosed with SS in a tertiary center internal medicine outpatient clinic.

Materials and Methods

Sixty-six patients who were diagnosed with pSS, according to 2012 or 2016 classification criteria, in our hospital's Internal Medicine Department between 2019-2022 were included in the study.[8,9] The clinical and laboratory features, including the autoantibodies anti-nuclear antibodies (ANA), anti-SS-A, anti-SS-B, and rheumatoid factor (RF), Schirmer test results, and salivary gland biopsy findings, were retrospectively evaluated.

The study was approved by the Eskisehir Osmangazi University Ethics Committee. The study was carried out in accordance with the statement of the Helsinki Declaration. Informed consent was obtained from each participant.

Statistical Analysis

Continuous data are presented as mean ± standard deviation. Categorical data are presented as a percentage (%). IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) is used for analysis.

Results

A total number of 66 patients who were diagnosed with pSS were included in the study. The mean age of the patients was 52.92±12.73 (20-82), and the majority of the patients were female (60/66). The initial complaint of most patients (n:34) was arthralgia or arthritis (51.51%), followed by widespread pain in 9 (13.64%), dry eyes in 6 (9.10%), pulmonary symptoms in 5 (7.58%), hematologic disorders in 3 (4.54%), dry mouth in 3 (4.54%), the positivity of serologic tests in 2 (3.03%) and other non-specific complaints in 4 of them (6.06%). The initial complaints of the patients are shown in Table 1. Of the 66 patients, 44 (66.67%) had fatigue, 46 (69.70%) had complaints of dry eye, and 43 (65.15%) had dry mouth when questioned (Table 2).

Table 1. Initial complaints of the patients

Initial complaint	**Number of patients (n=66)**
Arthralgia/arthritis	34 (51.51%)
Widespread pain	9 (13.64%)
Dry eyes	6 (9.1%)
Pulmonary symptoms	5 (7.58%)
Hematologic disorders	3 (4.54%)
Dry mouth	3 (4.54%)
Serologic test positivity	2 (3.03%)
Other	4 (6.06%)

Table 2. The symptoms of the patients in the questioning in terms of Sjögren's syndrome and physical examination findings

Symptom/ physical examination finding	Number of patients (n=66)
Fatigue	44 (66.67%)
Dry eye	46 (69.69%)
Dry mouth	43 (65.15%)
Arthritis	4 (6.06%)
Fibromyalgia	19 (28.78%)

On the physical examination, four patients (6.06%) had arthritis, and 19 (28.78%) patients' fibromyalgia points were tender. The mean erythrocyte sedimentation rate (ESR) was 30.43±18.21 (5-81), and the mean C-reactive protein (CRP) level was 5.53±6.19 (0-26.2).

ANA was positive in 56 patients (84.84%), RF in 19 (28.78%), but not evaluated in 7 (10.6%), anti-SS-A in 29 (43.93%), and anti-SS-B in 16 (24.24%). The majority of the ANA-positive patients had low titers (66.07% had +1 and +2 positivity), and the most common staining pattern of ANA was granular (65.15%). Details of ANA test results are summarized in Table 3.

Schirmer test was available in our hospital, and 63 patients had positive test results. Minor salivary gland biopsy was obtained in 42 patients, and 28 had biopsy findings consistent with SS.

Table 3. ANA staining patterns of the patients

ANA staining patterns	**Number of patients (50)***
Granular [n (%)]	43 (65.15%)
Nucleolar [n (%)]	20 (30.3%)
Homogenous [n (%)]	7 (10.6%)
Centromere [n (%)]	1 (1.51%)

*Some patients had two different types of staining

Discussion

SS is known as the most common systemic rheumatic disease, and patients mostly apply to clinics other than rheumatology. A careful medical history and physical examination may facilitate diagnosis. This study aimed to define the initial complaints and clinical findings of SS patients.

SS has an unbalanced gender ratio close to a 10/1 female/male ratio was reported in a big data study of >14,000 patients with SS.[10] Exactly similar to the existing data, the female/male ratio in our study was 10/1. SS can occur at all ages but is mainly diagnosed between 30 and 50 years of age.[11] Even though the mean age of the patients in our study group was a little older (52.92±12.73 yrs), there was a wide range (20-82 yrs). Diagnosing SS sometimes may be a challenge; mild symptoms may cause a delay in diagnosis, which may be the explanation for the particular old age of our study population.

Even SS is characterized by dry eyes and mouth, arthralgia-arthritis, and widespread pain were the initial complaints of most patients. Similar to our results, arthralgia and polyarthritis were the most common extra-glandular manifestations of SS in a study from Spain.[12] On the other hand, dry eyes and mouth were less common complaints. Patients are more mindful of pain rather than dryness symptoms or may fail to identify

dryness, especially ocular dryness. Clinicians must always keep in mind SS when evaluating a patient with pain. It may be useful to ask questions such as "Have you had daily, persistent, troublesome dry eyes for more than three months?", "Do you have a recurrent sensation of sand or gravel in the eyes?", or "Do you use tear substitutes more than three times a day?" when questioning dry eye.[13] Increased acute phase reactants may be a clue to autoantibodies.

One of the reasons for diagnostic difficulties, patients may not be aware of ocular dryness. It was the initial symptom of 6 patients (9.10%), but 46 patients (66.70%) complained when questioned, and 95.45% had positive Schirmer test results in our cohort. So, dry eye may not be ruled out without performing objective tests. In our hospital, the Schirmer test was available by the time period of the study, but break-up time and topical application of vital stains (lissamine green or fluorescein) may also be used.[14]

Autoantibodies help diagnose SS, ANA, anti-SS-A, and anti-SS-B are used in the latest classification criteria for SS.[8] RF was used in the former criteria.[9] Among these, ANA has the highest positivity rate, followed by anti-SS-A, anti-SS-B, and RF, in decreasing order.[14] The frequency of ANA, anti-SS-A, anti-SS-B, and RF positivity were in line with the literature in our cohort (84.84%, 43.93%, 24.24 %, and 28.78%, respectively).[14]

Minor salivary gland positivity (showing focal lymphocytic sialadenitis with a focus score ≥1) was shown in 66% and 89% of patients with pSS in different studies.[15,16] Our patient population's positivity rate was 66.67%, similar to the literature.

Our study has some limitations. The most important one is the retrospective evaluation of the patients, which may have caused a loss in data. Also, the small number of the patients included in the study may avoid generalization, but the study was conducted during the Coronavirus disease 2019 (Covid-19) pandemic, and a limited number of patients applied to the hospital. An objective test for salivation was not used. Finally, a minor salivary gland biopsy was not obtained for all participants due to Covid-19 restrictions.

In conclusion, SS is a common disease with a wide variety of clinical presentations. A detailed evaluation of patients is necessary to provide an accurate diagnosis and proper care. Sicca symptoms may not always be dominant, so careful evaluation needs for an exact diagnosis. Also, collaboration between clinics helps to facilitate early and correct diagnosis.

Ethical Considerations: The study was approved by the Eskisehir Osmangazi University Ethics Committee (Approval No: 43, dated Feb 15, 2022). The study was carried out in accordance with the statement of the Helsinki Declaration. Informed consent was obtained from each participant.

Conflict of Interest: The authors declare no conflict of interest. No funding was obtained for this study.

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