Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine and Pharmacy

Primary Gougerot-Sjogren Syndrome at the Moulay Ismail Military Hospital in Meknes: Epidemiological, Clinical and Immunological Aspects

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DOI: 10.36347/sjams.2022.v10i11.008 | **Received:** 01.10.2022 | **Accepted:** 06.11.2022 | **Published:** 10.11.2022

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Abstract **Original Research Article**

Introduction: Gougerot Sjögren's syndrome (GSS) is a connective tissue disease characterized by lymphocytic infiltration of the exocrine glands, and systemic manifestations of an immuno-inflammatory nature. This infiltration is predominant in the salivary and lacrimal glands, responsible for dry mouth and eyes. Clinically, the dry syndrome characteristic of SS may be mild or even absent, and extra glandular systemic manifestations may be the main circumstance in which this connective tissue is discovered. The diagnosis is based on a bundle of arguments, clinical, histological and immunological. SS is characterized by the fairly frequent presence of autoantibodies whose diagnostic value is indisputable, and some of which testify to the activity of the disease. In addition, these autoantibodies may have a correlation with certain organ damage as well as certain progressive forms. The objective of this work is to determine, through a retrospective and comparative study, the epidemiological, clinical and immunological characteristics of patients with primary Gougerot Sjögren's syndrome (SGSp) followed in the internal medicine department of the Military Hospital. Moulay Ismail from Meknes (HMIM), Morocco. ***Patients and Methods:*** We report a retrospective study of patients with primary Gougerot-Sjörgen syndrome followed in the internal medicine department of the Moulay Ismail military hospital (Meknes), over a period of 08 years (January 2010 - December 2018). All patients meeting AECG diagnostic criteria were included. ***Results:*** 13 cases of S.G.Sp are collected. There was a clear predominance of the female sex, with 12 women (92.3%) and 01 man (7.69%), sex ratio (F/M=12/1). The average age at diagnosis was 48 years with extremes ranging from 20 to 60 years? The clinical picture was dominated by dry syndrome in 100% of cases associated with inflammatory polyarthralgia found in 76.9% of cases. The immunological profile was variable with positive ANA in 61.5% of cases, anti-SSA AC in 61.5% of cases, anti-SSB AC in 46.15% of cases. ***Discussion:*** The results of our study agree with those of the literature concerning the female predominance, age, and the prevalence of clinical and immunological manifestations.

Keywords: Gougerot-Sjörgen syndrome, xerostomia, xerophthalmia, anti-SSA antibodies, anti-SSB antibodies.

INTRODUCTION

Gougerot Sjögren's syndrome (GSS) is a connective tissue disorder characterized by lymphocytic infiltration of the exocrine glands [1], and systemic manifestations of an immuno-inflammatory nature. This infiltration is predominant in the salivary and lacrimal glands, responsible for dry mouth and eyes.

Clinically, the dry syndrome characteristic of SS may be mild or even absent, and extra glandular systemic manifestations may be the main circumstance in which this connective tissue is discovered [2]. The diagnosis is based on a range of clinical, histological and immunological arguments [3].

SS is characterized by the fairly frequent presence of autoantibodies, the diagnostic value of which is indisputable, and some of which testify to the activity of the disease [1]. In addition, these autoantibodies may be correlated with certain organ damage as well as certain progressive forms [3].

SS is said to be primary when xerophthalmia and xerostomia are not associated with a clearly defined

systemic disease but with general manifestations, some of which are particularly frequent and suggestive (polyarthritis, pulmonary fibrosis, neurological involvement). SS is classified as secondary when it is associated with other clearly defined systemic diseases [4].

The objective of this work is to determine, through a retrospective and comparative study, the epidemiological, clinical and immunological characteristics of patients with primary Gougerot Sjögren's syndrome (SGSp) followed in the internal medicine department of the Military Hospital. Moulay Ismail from Meknes (HMIM), Morocco.

MATERIALS AND METHODS

This is a retrospective cross-sectional study with a descriptive aim, concerning 13 patients with primary Gougerot Sjögren's syndrome (SGSp) followed in the internal medicine department of the Moulay Ismail Military Hospital in Meknes (HMIM), Morocco, during an 8-year period from January 2010 to December 2018. All records were explored and only those meeting the diagnostic criteria of the American European Consensus Group (AECG) were included (Table 1) [5].

The collection of clinical data from patients was made from the patient's medical file using a sheet including: age, sex, time to diagnosis, circumstances of discovery, mode of onset, clinical manifestations, the results of the Schirmer test, the anatomopathological study of the biopsy of the accessory salivary glands, biological examinations: blood count, sedimentation rate, creatinine, blood ionogram) and immunological assessment: antinuclear antibodies (AAN), anti-SSA and anti-SSB.

The entry of clinical, paraclinical and immunological data of the patients was made on an Excel database and the statistical analysis concerning the different variables was carried out using the Excel table and the epi info 3.5 software.

Table 1: **European American Consensus Group (AECG) Diagnostic Criteria (2002) [6]**

1) Ocular signs: A positive answer to at least one of the questions: - Have you had an embarrassing, persistent and daily dry eye sensation for three months? - Do you frequently have the feeling of having sand or gravel in your eyes? - Do you use artificial tears more than three times a day? **2) Mouth signs:** A positive answer to at least one of the questions: - Do you have daily and for more than three months the feeling of having the dry mouth? - Have you had recurrent or permanent swelling of the parotids in adulthood? - Do you drink often to help swallow food? **3) Objective eye signs:** At least one of the tests must be positive: - Schirmer's test ≤ 5 mm in 5 minutes. - Rose Bengal test ≥ 4 according to the Van Bijsterveld score.	**4) Histological signs:** - Focus score ≥ 1 on the accessory salivary gland biopsy (focus score = number of foci per examined glandular surface of 4mm2). A focus is defined as a focal accumulation of more than 50 mononuclear cells. **5) Sign of salivary involvement:** Positive of one of the following three tests: - Salivary scintigraphy. - Parotid sialography. - Unstimulated salivary flow (< 1.5 ml in 15min). **6) Autoantibodies:** - Presence in serum of either or both of: anti-SSA and anti-SSB (La) antibodies. Exclusion criteria: pre-existing lymphoma, AIDS, sarcoidosis, graft versus host disease, a history of head and neck radiotherapy, hepatitis C virus infection and use of anticholinergic drugs, (antihypertensives, antidepressants, neuroleptics, ...)

RESULTS

Epidemiological Data

During the period of our study, 13 patients with pSS were collected. The average age of our patients at the time of diagnosis was 48 years with extremes ranging from 20 to 60 years. Represented 61.6% of cases (n=8), the age group between 35 and 44 years old represented 15.4% of cases (n=2) the same for the age group over 55 years old as well that the age group 15 to 24 represented 7.6% of cases (n=1). In our study, 12 cases (92.4%) were female and 1 case male (7.6%), with a sex ratio F/M of 12/1.

Clinical Manifestations

The manifestations revealing the disease were polymorphic, dominated by the association of dry syndrome and inflammatory polyarthralgia, observed in 10 patients (84.6%)' is 6 years old.

Xerophthalmia and xerostomia were observed in all patients. Schirmer's test was positive in 100% of cases. The fluorescein test objectified superficial punctate keratitis (PSK) in 75% of cases. Two patients (15.3%) had bilateral parotid hypertrophy.

Joint involvement was the most frequent systemic manifestation observed in 11 patients (84.6%).

These were inflammatory type arthralgia in 10 patients (76.9%) and destructive arthritis in a single patient. Four patients (30.7%) had presented neuropsychiatric manifestations. Peripheral nervous system involvement was the most frequent, observed in 2 patients (15.35%).

Respiratory involvement was found in 4 patients (30.7%). Chest X-ray was performed in 9 patients. It objectified interstitial syndrome in 2 cases (15.35%). Chest CT was performed in 7 patients, showed diffuse interstitial pneumonitis without fibrosis in 1 case (7.6%) and associated with fibrosis in 1 case (7.6%). The EFR, was performed in 2 patients (15.35%), objectified a mixed syndrome with predominance restrictive in 1 case (7.6%). Renal involvement was detected in 3 patients (23%) including one case with renal failure with distal tubular involvement.

Vascular purpura located in the lower limbs was observed in 3 patients (23%). Raynaud's phenomenon observed in a single patient (7.6%).

Biologically Hematological abnormalities were dominated by anemia in 7 cases (53.8%) followed by leukopenia in three patients (23%) and thrombocytopenia in a single case (7.6%).

The sedimentation rate (ESR) was high in 6 patients (53.8%) with an average value of 69 ± 4 mm at the first hour. CRP (C-reactive protein) was elevated in 8 patients (61.5%). Polyclonal hypergammaglobulinemia was observed in 8 cases (61.5%). Renal failure with distal tubular involvement was noted in a single case (7.6%).

On the immunological level, the search for Anti-Nuclear Antibodies (ANA) by Indirect Immunofluorescence (IFI) was carried out in all our patients, it was positive in 8 patients (61.5%). Soluble Nuclear Antigens (ENA) was positive in 61.5% of cases. Anti-SSA and anti-SSB antibodies were positive respectively in 61.5% and 46.15%.

The BGSA performed in 12 patients showed stage IV sialadenitis in 5 cases, stage III in 5 cases and stage II in 2 cases according to the Chisholm and Mason classification.

DISCUSSION

The prevalence of SS varies between 00.1 and 4% in the general population [1, 7]. Indeed, this prevalence also varies between countries. The annual incidence of pSS according to a retrospective American study was estimated at 3.9 per 100,000 cases [3].

According to the literature, the average age of onset of SS is between 47 and 54 years [7-9], these results are consistent with our series in which we observed an average age of onset of 48 years. A female predominance (92.3%) was observed in our series with a sex ratio of 12/1, our result is consistent with those of the literature [10-13].

Clinically, glandular manifestations are frequent during pSS with a frequency varying from 70 to 100% depending on the studies. They were present in 100% of patients in our study. The frequencies of systemic glandular manifestations during pSS are variously assessed in the literature (Table 2).

Table 2: Frequency of glandular manifestations during pSS according to the series

	Xerophthalmia	Xerostomia	Positive Schimer test
Our series	100%	100%	100%
Zhao *et al.*, [12]	60.5%	77.4%	90.9%
Ramos *et al.*, [14]	96%	96.5%	94%
Botsios *et al.*, [15]	76.1%	71.4%	17%

Extraglandular systemic manifestations during pSS are frequent and widely appreciated in the literature (Table 3). In our study, joint involvement was the most frequent extraglandular involvement with a rate of 84.6%.

Table 3: Frequency of systemic manifestations during pSS according to the series

Symptoms	Arthralgia (%)	Raynaud (%)	Lung involvement (%)	Neurological impairment (%)	Kidney damage (%)
Our series	84.6	7,6	30.7	30.7	23
Vital *et al.*,	23	33	27	21	13
Markusse *et al.*,	94	81	43	12	11
Kelly *et al.*,	94	81	43	12	11
Schearn *et al.*,	62	21	15	-	-

Biological haematological manifestations are frequent during pSS. The main abnormalities are anemia, leukopenia and thrombocytopenia. They were observed respectively in 53.8%, 23% and 7.5% of the cases in our series. They are of variable frequency depending on the series (table 4).

Table 4: Frequency of hematological damage to GSSp according to the series

	Zaho *et al.*, [12]	**S. Lechtman *et al.*, [18]**	**Our series**
Anémia	20,5%	19,65%	23%
Leucopénia	31,7%	12%	7,7%
Thrombocytopénia	6,8%	4%	30,75%

SGS is marked by an increase in the sedimentation rate, sometimes beyond 100 in the first hour; this increase is linked to the presence of polyclonal hypergammaglobulinemia observed in 70% of patients on average [20]. In our series, ESR was high in 53.8% of cases with hypergammaglobulinemia in 61.5% of cases. The CRP was above the normal value in 36% of cases.

On the immunological level, the SGS contains a wealth of antibodies. In our series, the ANA were positive in 61.5% of the cases. Anti-SSA and anti-SSB antibodies are very specific for pSS, the frequency of anti-SSA and anti-SSB antibodies was respectively 61.5% and 46.15% in our series. The prevalence of these different antibodies throughout the literature is illustrated in Table 5.

Table 5: Frequency of Abs according to pGSS series

	AAN	**Ab anti SSA**	**Ab anti SSB**
Our series	61.5%	61.5%	46.15%
Ioannidis *et al.*, [21]	80%	48%	27%
Alamanos *et al.*, [19]	94%	50%	40%
Garciae *et al.*, [22]	74%	40%	26%

CONCLUSION

Gougerot Sjögren's syndrome (GSS) is a connective tissue disease characterized by lymphocytic infiltration of the exocrine glands, and systemic manifestations of an immuno-inflammatory nature. This infiltration is predominant in the salivary and lacrimal glands, responsible for dry mouth and eyes.

Clinically, the dry syndrome characteristic of SS may be mild or even absent, and extra glandular systemic manifestations may be the main circumstance in which this connective tissue is discovered. The diagnosis is based on a bundle of arguments, clinical, histological and immunological. SS is characterized by the fairly frequent presence of autoantibodies, the diagnostic value of which is indisputable, and some of which testify to the activity of the disease [1]. In addition, these autoantibodies may have a correlation with certain organ damage as well as certain progressive forms.

This auto-ACs is detected by various techniques, namely IFI, ELISA, immunodot whose sensitivity and specificity are variable.

The prognosis of this condition can be reserved because of the serious damage it can cause such as neurological damage, kidney damage and respiratory damage.

The results of our study agree with those of the literature concerning the female predominance, age, and the prevalence of clinical and immunological manifestations.

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