RESPIRATORY COMPROMISE IN PATIENTS WITH PRIMARY SJÖGREN SYNDROME

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Htal. Británico, Htal. Alemán, Sanatorio Allende De Córdoba, Htal Tornú, Ipri, Omi, Htal Rivadavia, Htal Privado de Córdoba. GESSAR database.

ABSTRACT

Sjögren's syndrome (SS) is an autoimmune inflammatory disease that affects exocrine glands and may have extraglandular involvement. Lungs are compromised in 19-65% and the most common type is Nonspecific Interstitial Pneumonia (NSIP) (30-60%).
The objectives of this study were to determine the frequency, time of occurrence and type of Respiratory Compromise (RC) in patients with primary SS and to establish the relationship between RC, laboratory profile, and other extraglandular manifestations.
Observational, transversal and analytical study. Patients who met ACR-EULAR criteria for primary SS, over 18 years old from GESSAR database from Jan/2011 to Jul/2011 inclusive. Variables: demographic data, time of evolution, extraglandular manifestations and laboratory parameters. Categorical variables were compared with chi square test or Fisher test and continuous variables with the Mann-Whitney test. The p was significant when ≤ 0.05. We performed multivariate logistic regression analysis with variables with a p<0.1.
Results: Total N: 285. 95.9% female, age: 55.8 ± 14.8. 72 patients (25.2%) had RC, of which the most frequent were xerotrachea (61.1%), recurrent infections (25%), NSIP (13.8%) and pulmonary fibrosis (12.5). Time of evolution of SS until the RC developed: 4 years (IQR 2-6 a). RC was associated with Raynaud syndrome (22.2% vs 12.3%, p = 0.04), fibromyalgia (26.8% vs 14.3%, p: 0.01) and tinnitus (5.9% vs 1.2%, p: 0.050) with no significant differences in laboratory parameters. In the multivariate logistic regression analysis, RC was independently associated with Raynaud syndrome (OR = 2.32, 95% CI 1.08 to 4.96, P = 0.03) and fibromyalgia (OR = 2.50, 95% CI 1.21 to 5.13, p = 0,01).
CONCLUSION: A quarter of patients with SS had RC of which the most frequent were xerotraquea, recurrent infections, NSIP and pulmonary fibrosis. There was no association with laboratory parameters. RC was independently associated with the presence of raynaud syndrome and fibromyalgia.

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BACKGROUND AND PURPOSES

Sjögren's syndrome (SS) is an autoimmune inflammatory disease that affects exocrine glands and may have extraglandular involvement.[1] Lung compromise occurs in 19% - 65% of the patients [1, 2, 3] and the most common type is nonspecific interstitial pneumonia (NSIP) (30-60%) [2, 3, 4, 5].
The predictors of lung compromise described so far are male sex, older age, elevated ESR, positive Rheumatoid factor (RF), Antinuclear (ANA) and anti Ro and La antibodies, high serum protein concentration and high levels of IgG and B2 microglobulin. All these elements are apparently associated to increased immune activity [2, 3, 6, 7, 8].
The purposes of our study were:

- To determine the frequency, time of occurrence and type of **Respiratory compromise (RC)** in patients with primary SS.
- To establish the relationship between RC and antibody profile, complement levels, leukopenia, and other extraglandular manifestations.

METHODS AND MATERIALS

This is an observational, transversal and analytical study.
We included patients who met ACR-EULAR criteria for primary SS, over 18 years old from the **GESSAR database** (Argentinian Primary SS study group) from Jan/2011 to Jul/2011 inclusive.
We evaluated demographic data (sex and age), time of evolution of SS, the presence of extraglandular manifestations (among which is RC) and laboratory parameters (C3, C4, CH50, ANA, Anti Ro, Anti LA, RNP, RF, cryoglobulins, anticardiolipin antibodies and gammaglobulins among others). Categorical variables were compared with chi square test or Fisher test and continuous variables with the Mann-Whitney test. The p was considered significant when ≤ 0.05. We performed multivariate logistic regression analysis with variables with a p <0.1.

RESULTS

Total number of patients (**N): 285**. 95.9% of them were female. Age: 55.8 ± 14.8 years old.
72 patients (25.2%) had RC with a time of evolution of SS until the RC developed: 4 years (IQR 2-6 y). The most frequent types of RC were xerotrachea (61.11%), recurrent infections (25%), NSIP (13.8%) and pulmonary fibrosis (UIP) (12.5%) (Graphic 1).
In the **univariate analysis,** RC was associated with Raynaud syndrome (22.2% vs 12.3%, p = 0.04), fibromyalgia (26.8% vs 14.3%, p: 0.01) and tinnitus (5.9% vs 1.2%, p: 0.050). There were no significant differences in laboratory parameters. (Tables 1 and 2)
In the **multivariate logistic regression analysis** there was an independent association of RC with Raynaud syndrome and Fibromyalgia (Table 3).

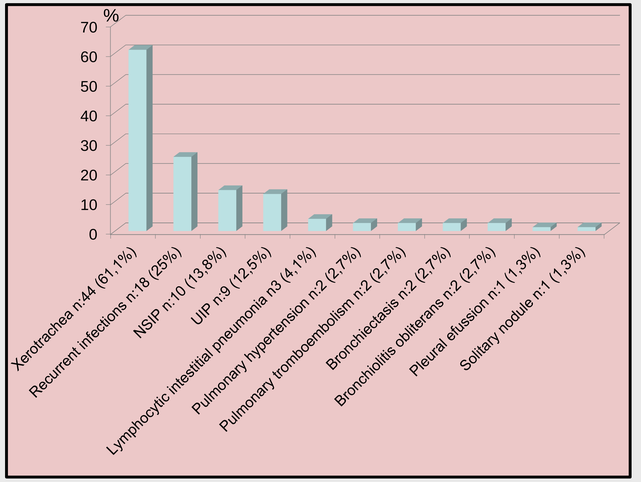
Extraglandular Manifestations	With RC (72 patients) n(%)	Without RC (213) n(%)	P
Arthralgia	48 (66.7)	142 (70.6)	0.52
Arthritis	23 (33.3)	59 (30.1)	0.61
Tenosynovitis	8 (11.3)	10 (5.2)	0.08
Myalgias	14 (19.7)	30 (15.3)	0.39
Fibromyalgia	19 (26.8)	28 (14.3)	0.01
Muscle weakness	4 (5.6)	4 (2.1)	0.21
Purpura	7 (9.7)	17 (8.8)	0.81
Urticaria	1 (1.4)	9 (4.7)	0.29
Petechiae	1 (1.4)	7 (3.6)	0.68
Ulcers	2 (2.8)	7 (3.6)	1.00
Erythema multiforme	0 (0)	1 (0.5)	1.00
Erythema nodosum	0 (0)	2 (1)	1.00
Subcutaneous nodules	0 (0)	4 (2.1)	0.57
Raynaud syndrome	16 (22.2)	24 (12.3)	0.04
Pericarditis	1 (1.4)	0 (0)	0.27
Myocarditis	1 (1.4)	0 (0)	0.27
Reflux esophagitis	9 (12.7)	12 (6.3)	0.07
Chronic atrophic gastritis	6 (8.3)	21 (10.8)	0.55
Ulcerative colitis	1 (1.4)	1 (0.5)	0.47
Primary biliary cirrhosis	4 (5.7)	6 (3.1)	0.27
Autoimmune hepatitis	1 (1.4)	6 (3.1)	0.38
Renal tubular acidosis	3 (4.3)	3 (1.6)	0.20
Glomerulonephritis	0 (0)	3 (1.6)	0.38
Neuropathy	7 (9.9)	17 (8.9)	0.82
Stroke	2 (2.8)	3 (1.6)	0.61
Optic neuritis	1 (1.4)	1 (0.5)	0.46
Migraine	3 (4.2)	9 (4.7)	1.00
CNS vasculitis	0 (0)	2 (1)	1.00
Olfactory loss	2 (2.8)	4 (2.1)	0.52
Dizziness	2 (2.8)	4 (2.1)	0.51
Recurrent epistaxis	2 (2.8)	3 (1.6)	0.41
Recurrent sinusitis	2 (2.8)	6 (3.1)	0.62
Dysphonia	5 (6.9)	9 (4.7)	0.46
Tinnitus	4 (5.9)	2 (1.2)	0.05
Hearing loss	3 (4.2)	5 (2.6)	0.37
Pseudolinfoma	0 (0)	1 (0.5)	0.73
Linfoma	0 (0)	2 (1)	0.54

Laboratory	With RC n(%)	Without RC n(%)	p
Leukopenia	10 (13.9)	28 (13.8)	0.76
Polyclonal hypergammaglobulinemia	24 (47.1)	70 (47)	0.98
Oligoclonal hypergammaglobulinemia	2 (3.9)	5 (3.4)	
C3 hypocomplementemia	5 (11.4)	10 (7.4)	0.41
C4 hypocomplementemia	6 (13.6)	21 (15.7)	0.74
Positive ANA	52 (73.2)	162 (82.3)	0.10
Positive Anti-Ro antibodies	45 (66.2)	145 (73.2)	0.26
Positive Anti-La antibodies	26 (38.2)	98 (50.5)	0.08
Positive Anti-Sm antibodies	2 (3.9)	4 (3.1)	0.54
Positive Anti-RNP antibodies	4 (9.3)	8 (6.1)	0.33
Positive Rheumatoid Factor	30 (44.8)	90 (49.7)	0.48
Positive Cryoglobulins	3 (10.3)	10 (11.5)	0.58
Positive Anti-smooth muscle antibodies	1 (4.5)	4 (7.4)	0.54
Positive Anti-mitochondrial antibodies	2 (8)	7 (13.2)	0.39
Positive Anti-thyroglobulin antibodies	1 (5.3)	7 (14.9)	0.26
Positive Anti-peroxidase antibodies	2 (10)	12 (24.5)	0.15
Positive Lupus anticoagulant test	4 (26.7)	5 (10.6)	0.13
Positive Ig G anticardiolipin	3 (9.7)	7 (9.9)	0.64
Positive Ig M anticardiolipin	3 (9.4)	7 (10.4)	0.58

Tables 1 and 2: Clinical and laboratory variables in patients with and without respiratory compromise. Univariate analysis.

Variables	Standard error	P	OR	CI 95% (lower)	CI 95% (upper)
Raynaud syndrome	0,387	0,03	2,32	1,08	4,96
Fibromyalgia	0,367	0,013	2,50	1,21	5,13

Table 3: Variables independently associated to respiratory compromise. Multivariate logistic regression analysis.
Variables analized: Positive anti-LA antibodies, Raynaud syndrome, Tenosynovitis, Reflux esophagitis, tinnitus and fibromyalgia.



Graphic 1: Distribution of the types of Respiratory compromise (RC)

CONCLUSIONS

A quarter of patients with SS had RC of which the most frequent were xerotraquea, recurrent infections, NSIP and pulmonary fibrosis. There was no association with laboratory parameters.
RC was independently associated with the presence of Raynaud syndrome and Fibromyalgia.

The authors declare no conflicts of interest.

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