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Lung in Systemic Lupus Erythematosus: A Single-Center Experience

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is the autoimmune disease with the highest prevalence of pulmonary involvement, which ranges from 20% to 90% of the patients, depending on the criteria employed in the cohorts being studied (symptomatology or histopathology). More than 50% of the patients develop pleuropulmonary manifestations at least once during the course of the disease; likewise, pleuropulmonary involvement has been associated with a higher rate of mortality. The purpose of this study is to determine the frequency of respiratory symptoms, and abnormal lung function in a sample of Brazilian patients with systemic lupus erythematosus (SLE). **Methods:** Retrospective study of 55 SLE patients from a single Rheumatology Unit in Brazil; the patients fulfilling the ACR criteria for SLE. Demographics and clinical characteristics were recorded and the patients were evaluated using chest X-rays, pulmonary function tests (PFTs), and HRCT of the chest to find out the pulmonary involvement. **Results:** Thirty-two patients had respiratory symptoms, 45 (82%) patients had abnormal lung function, 25 (45.4%) patients had abnormal computed tomography and 20 (36.4%) patients had abnormal chest X-ray. **Conclusion:** Respiratory symptoms and abnormal lung function are common in SLE. Clinicians should consider pulmonary evaluation among patients with systemic lupus erythematosus with and without respiratory symptoms.

Subject Areas

Respiratory Medicine

Keywords

Systemic Lupus Erythematosus, Pulmonary Systemic Lupus Erythematosus, Autoimune Diseases

1. Introduction

Systemic lupus erythematosus (SLE) is a potentially severe, frequently disabling autoimmune disease with multiorgan involvement and a typically waxing and waning course. It is characterized by the production of a vast array of autoantibodies and a variable clinical presentation that can include lung disease, although the more common early manifestations include arthritis, photosensitive rashes, immune-mediated cytopenias, and the development of glomerulonephritis [1]. The clinical symptoms and immunologic manifestations of SLE are diverse, and early diagnosis can be difficult and often delayed because of the insidious onset of predominantly nonspecific constitutional symptoms (e.g. fatigue and low-grade fever) [2].

SLE is considered primarily a disease of women of childbearing age, although males or females of any age can be affected. The typical age at diagnosis is between 15 and 45 years. The female to male ratio for the development of SLE is 9:1, although it is interesting that lung involvement is proportionally more common in men. African Americans and Hispanic Americans have a threefold increased incidence of SLE, develop SLE at an earlier age, and have increased morbidity and mortality compared with Caucasians [3] [4].

Systemic lupus erythematosus (SLE) is the autoimmune disease with the highest prevalence of pulmonary involvement, which ranges from 20% to 90% of the patients, depending on the criteria employed in the cohorts being studied (symptomatology or histopathology) [5] [6]. More than 50% of the patients develop pleuropulmonary manifestations at least once during the course of the disease; likewise, pleuropulmonary involvement has been associated with a higher rate of mortality [2]. Symptoms such as pleuritic pain, cough and/or dyspnea are usually the first signs of SLE-related pulmonary involvement, or can be the first manifestation of SLE. Up to 60% [7] of the patients have reported dyspnea at least once throughout the disease and abnormal respiratory function tests have been documented in 30% - 40% [8] [9] [10], as well as anomalies on computed tomographic scans in 55% - 70% [9]. Lung anomalies do not correlate with serum markers of lupus activity. It is essential to rule out pulmonary infection in the initial evaluation, as bacterial infection (67%) has been reported to be the most frequent parenchymatous involvement [5] and is one of the major causes of death [4]. The conditions that constitute pleuropulmonary involvement in SLE are considered primary when they are directly attributed to SLE or secondary when they are attributable to other causes. Among the latter, infections have a prevalence of nearly 60% and have been responsible for from 30% to 50% of the deaths of patients with SLE [4].

Drugs like methotrexate (MTX) and rituximab can result in pneumonitis and even progression to interstitial lung disease. Likewise, a slight increase in the risk of neoplasms in general, pulmonary in particular, has been reported in SLE patients [6].

The pulmonary manifestations of SLE include pleuritis, acute pneumonitis,

chronic interstitial lung disease, diffuse alveolar hemorrhage (DAH), pulmonary arterial hypertension (PAH) [2] [11], pulmonary embolism, and shrinking lung syndrome [12]. An autopsy study detected pleuropulmonary involvement in 97.8% of SLE patients, and a case series reported that 25% of SLE patients had clinical or radiographic evidence of pulmonary involvement [5] [6]. Some manifestations of pulmonary involvement contribute to high morbidity and mortality in SLE, especially DAH and PAH [13].

Finding the true prevalence of pulmonary involvement with SLE is complicated by the high rates of pulmonary infections [2], mainly because some SLE therapies predispose to an increased risk of respiratory infections [14].

We set out to determine the frequency of respiratory symptoms, and abnormalities in pulmonary function tests, chest X-rays (CXRs), and chest computed tomography among consecutive adult patients with SLE at a tertiary referral centre in northeastern Brazil.

2. Methods

2.1. Study Population

Consecutive, prevalent, and incident adult (18 years of age) patients with SLE seen between January 2018-June 2019 were enrolled in a study observational aimed at characterizing pulmonary manifestations of SLE. Patients answered questions regarding pulmonary symptoms, and had pulmonary function tests (PFTs), chest X-rays (CXRs) and chest computed tomography scans (CTs). These studies were done with written consent in accordance with the Declaration of Helsinki and approved by the Research Ethics Board at the Federal University of Piaui (Brazil). All PFTs, CXRs, and chest CTs were performed at the same centre. To be included in the study population, patients had to have available PFT, chest imaging, and CT chest results and fulfill the American College of Rheumatology (ACR) classification criteria for SLE [15]. Patients with a previous diagnosis of another connective tissue disorder such as rheumatoid arthritis, primary Sjogren's syndrome, mixed connective tissue disease, systemic sclerosis, or idiopathic inflammatory myositis were excluded from this study.

2.2. Patient Characteristics

Self-reported ethnicity was recorded as Caucasian and no Caucasian. Age of SLE onset was calculated from the date of birth to the date of physician diagnosis of SLE by ACR criteria [15]. Disease duration at enrollment was defined as duration from the date of physician diagnosis until the date at first study visit. Patients were questioned about smoking habits; ever smokers were defined as having smoked at least one cigarette per day for 3 months over their lifetime and non-smokers were those who did not fulfill this criterion [16].

2.3. Pulmonary Variables

Patients were questioned on recurrent pulmonary symptoms, defined as two or

more episodes per week of shortness of breath, pleuritic chest pain or dry cough, in the four weeks preceding their study visit. When patients had both CT and CXR imaging available, the results of the CT scan were used to ascertain the presence or absence of interstitial lung disease (ILD). Patients were considered to have ILD if there were reticular and/or interstitial opacities with or without ground glass opacities and/or honeycombing on the chest CT scan after excluding alternative etiologies for the ILD. Pleural involvement on chest imaging was defined as the presence of pleural effusions, pleural thickening, or pleural fibrosis on CXR or CT scan.

2.4. Pulmonary Function Tests (PFTs)

PFT included spirometry. Absolute and predicted values of forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and ratio VEF1/CVF. An abnormal PFT was defined as ≤80% predicted FVC, FEV1 ≤80% predicted and FEV1/FVC ratio ≤80% predicted [17].

3. Results

3.1. Study Population

A total of 55 SLE patients comprised the study population and their baseline characteristics are described in detail in **Table 1**. The majority of patients in this study were women (53/55, 96.4%) of not Caucasian ethnicity (36/55, 65.5%) and had an age at study entry of 30.3 ± 13.1 years old and disease duration of 4.2 ± 9.6 years. In terms of current use of medications at study entry, 45/55 (81.8%) of patients were taking prednisone; 10/55 (18.20%) of patients were on methotrexate; 50/55 (90.9%) of patients were on hydroxychloroquine, 03/55 (0.5%) of patients were on mycophenolate mofetil, 05/55 (9.09%) of patients were taking azathioprine and none of the patients were taking cyclophosphamide. Nine of 55 (16.4%) patients reported a history of ever smoking (**Table 1**).

3.2. Results from Pulmonary Investigations

In terms of pulmonary symptoms, 25/55 (45.4%) patients reported dyspnea, 19/55 (34.5%) patients reported pleuritic chest pain; a total of 16/55 (29.1%) patients reported dry cough and two had productive cough (**Table 1**).

All patients had an available CXR and had chest CT results during the inclusion period.

For the 55 patients who had a CXR, 33 (60.0%) patients had a normal CXR, and 22 (40.0%) patients had an abnormal CXR finding; 5(9.1%) patients had possible or definite interstitial infiltrates; 5 (9.1%) patients had pleural thickening. For those who had a CT chest performed, 14/55 (25.4%) patients displayed evidence of ILD and 8/55 (14.5%) patients had pleural involvement. Atelectasis was seen on radiography in 6 (11.1%) patients, but this finding was not seen on CT scans (**Table 2**).

We proceeded to determine the frequency of PFT abnormalities and the type

of PFT abnormalities in this cohort; 51/55 (92.7%) patients had evidence of obstructive or restrictive physiology. All patients had changes in lung function (Table 3).

Table 1. Demographic and clinical measures among patients with systemic lupus erythematosus (SLE) without know related pulmonar disease.

Variables	Population (n = 55)
Demographics	
Age (mean ± SD, years)	30.3 ± 13.1
Gender (women:men)	53:2
Caucasian vs no causasian	34.5:65.5
Smokers vs no smokers	9:46
Disease characteristics	
Disease duration* (mean ± SD, years)	4.2 ± 9.6
Self-reported symptoms	
Alopecia, n(%)	41 (74.5)
Raynaud phenomenon, n(%)	11 (20)
Skin lesions, n(%)	34 (61.8)
Dyspnea**, n(%)	25 (45.4)
Pleuritic chest pain**, n(%)	19 (34.5)
Dry cough**, n(%)	16 (29.1)
Productive cough**, n(%)	2 (3.6)
Medications at study entry	
Prednisone (yes/no)	45
Methotrexate (yes/no)	10
Hydroxychloroquine (yes/no)	50
Mycophenolate mofetil (yes/no)	03
Azathioprine (yes/no)	05

*Defined as years from date of diagnosis; **Defined as 2 episodes per week in the preceding four weeks.

Table 2. CRX findings and HRCT in all studied patients.

Variables	Population (n = 55)	
Normal, n(%)	CRX	HRCT
Abnormalities	33 (60)	23 (41.8)
Pleural involvement, n(%)	05 (9.1)	08 (14.5)
Pulmonary fibrosis, n(%)	05 (9.1)	14 (25.4)
Atelectasis, n(%)	06 (11.1)	-
Pneumonitis, n(%)	03 (5.4)	08 (14.5)
Bronchiectasis, n(%)	03 (5.4)	02 (3.6)

Table 3. PFT-Incidence of patters of abnormality.

Patterns	n (%)
Obstrutive*	15 (27.3)
Restrictive	36 (65.4)
Total	51 (100.0%)

*Obtrutive: Low FEV/VC or low FEF25-75; Restrictive: low VC.

4. Discussion

In the 50 years since Sante and Wyatt [18] described a lack of lung involvement "until the terminal stages of the disease," significant advances in our understanding of SLE-related lung involvement have been made. The earliest reports describe a "waxing and waning, migrating bronchopneumonia" [19] and a diffuse, noninfectious, inflammatory lung disease termed primary atelectizing pneumonitis [20] [21]. In more recent reports, the frequency and characteristics of lung involvement have depended on the clinical phenotype of the population studied along with the methods of investigation and their sensitivities to identifying disease activity.

The exact prevalence of SLE-related lung disease is unknown and previous studies have varied widely in their estimates. Most report that between 20% and 90% of SLE patients will experience some form of lung involvement during the course of their disease [22] [23]. However, more recently it has been suggested that this figure lies in the range of 50% - 70% [24]. Predictors for progression to earlier permanent lung damage, include older age and those positive for anti-RNP antibodies [25]. Pulmonary manifestations of SLE are associated with a higher mortality rate [2] and this varies depending upon the exact type and extent of lung involvement seen. More chronic forms of lung disease relating to SLE can have a significant negative effect on patient wellbeing, physical performance status, and are detrimental to quality of life [26].

Among a cohort of consecutively enrolled patients with SLE, we found that respiratory symptoms and abnormal lung function on PFTs were common, occurring in 45.4% and 92.7% of patients, respectively.

PFT abnormalities in patients with SLE are common [27] [28] [29] and previous investigators have noted a reduction in FVC in up to 60% of patients with SLE [27] [30].

SLE is undoubtedly a disease in which health disparities are clearly present because it affects primarily one sex (women), young persons (reproductive age), and less-privileged individuals (ethnic minorities) around the world [31]. It can explain some disparities observed in our study when compared to other works.

The strengths of this study were its detailed evaluation of a group of SLE patients for pulmonary involvement and all patients had spirometry, chest imaging, and a chest CT scan. This study also has some limitations. We were unable to detect the shrinking lung syndrome, which is very common in patients with

systemic lupus erythematosus.

5. Conclusion

Respiratory symptoms and abnormal lung function were relatively common in patients with SLE. Therefore, we believe that clinicians involved in the care of SLE should maintain a heightened awareness of lung involvement.

Conflicts of Interest

The authors declare no conflicts of interest.

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